KET – INDUSTRIAL BIOTECHNOLOGY

Working Group Report

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This document is a working document analysing the status and challenges for industrial biotechnology in Europe, and has been prepared by the Sherpa Group and other stakeholders as input for the KET High Level Group.

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KET – INDUSTRIAL BIOTECHNOLOGY

Industrial biotechnology – also known as white biotechnology – uses enzymes and micro-organisms to make bio-based products in sectors as diverse as chemicals, food and feed, healthcare, detergents, paper and pulp, textiles and bioenergy.

The process works by transforming biomass - e.g. agricultural (by)products, organic waste, algae into biofuels and biobased chemicals, in the same way as crude oil is used as a feedstock in the production of chemicals and fuels. In this way, industrial biotechnology could save energy in production processes and could lead to significant reductions in greenhouse gas emissions, helping to fight global warming. It can also lead to improved performance and sustainability for industry and higher value products.

Bio-based products already on the market include biopolymer fibres used in both construction and household applications, biodegradable plastics, biofuels, lubricants and industrial enzymes such as those used in detergents or in paper and food processing. Biotechnological processes also constitute a key element in the manufacturing of some antibiotics, vitamins, amino acids and other fine chemicals.

Executive summary

Europe holds a very leading position in the development and production of enzymes. It is also strong in biochemicals, intermediates and bio-base polymers, and a weaker position in the biofuels industry. Industrial Biotechnology contributes positively to most of the Societal Challenges such as EU competitiveness, climate change and sustainability.

Industrial Biotechnology is a very promising field because of avoiding limited fossil resources as starting materials, but in some instances competing with edible feedstocks. This important issue, specially raised in the case of biofuels, can be solved by the introduction of 2nd generation biofuels using non-edible biomass as a sole feedstock. Besides biofuels, the wide variety of intermediate products that may enter at different stages in different value chains introduces complexity when analyzing biotechnological products. Because of its wide and diverse applications, industrial biotechnology is much more than a sole industrial or even economical sector. Companies manufacturing biotechnological products, such as biorefineries, have a strong interdisciplinary approach in producing their bio-based products. In fact there is a claim for a bio-based economy. Figure 7 shows the complexity of the production oriented value chain.

It is possible to identify several barriers that hamper the translation of R&D to markets:

- poor understanding between academics and industry,
- the competitiveness of the bio-based products compared to "conventional" products, specifically no monetary added value for the energy and climate-friendly advantages of bio-based products
- the gap between R&D and pre-commercial demonstration and first-of-its-kind production plants,
- the European regulation complexity,
- the need for well-educated and trained scientists and engineers.

When a SWOT analysis is carried out, it is possible to find among the European strengths the existence of a chemical industry, capacity to produce added value products, ecological positions, strong research competences in academia and industry, and a huge capacity to produce cellulosic or sugar based feedstocks. Among the weaknesses, the following ones can be listed: only a few strong technology providers for cellulosic biomass conversion, weak technology transfer, GMOs and transgenic plants not accepted. In terms of options, the chemical industry seeks feedstock of good quality and at competitive price. Finally, in terms of challenges, investment should take place in early technologies for R&D and for demonstration and lighthouse projects, the resistance against GMOs should diminish, and land use for industrial plant cultivation should be addressed.

Among market pull measures the regulatory framework requires further analysis at EU level. Public procurement may play also a relevant role, since Member States have given political support to an increase in Green Public Procurement. On the other hand there is an increasing need to develop standards for bio-based products. A more holistic approach is becoming urgent for the bio-based economy in terms of closer collaboration between different EU policies and programs, as well as Member State Technology Strategies. Existing third countries policies may bring some light into these issues.

For the market push measures, further research priorities will have to be indentified and implemented. Moreover, policies to facilitate access to technology by SMEs will have to be identified and applied, as well as access to manufacturing in Europe. Access to pilot plants and funding for demonstration projects up to full industrial scale are also very important playing the role of required infrastructures. Access to finance, including risk capital, incentives policies such as taxation and finally identification of scope for better cooperation among authorities, industry and researchers are also key measures to be discussed and implemented.

Finally it is worthwhile to mention that ongoing research evolution may play a key role in the development of industrial biotechnology in the short to medium term. The new knowledge being produced in systems biology and synthetic biology may open wide new fields of application in any of the biotechnology areas. It is very important to be aware of the expected progress in nanobiotechnology and bioprocessing in the next few years. Even the latter is needed to bring biobased products into the market and should be part of an overall bio-engineering strategy from invitro synthesis via cells to whole production processes. It should also be kept in mind that convergent technologies, such as the combination of biotechnology, nanotechnology, process engineering and information as well as computing technologies are called to open new technological paradigms.

1. Introduction

When looking at the scope of this KET initiative, it should be noticed that that three main stages have to be considered, as shown in Fig. 1. In the first place the biotechnology techniques, then the technology transfer and deployment, and finally the stimulation of market demand. According to this general layout, this report in the first place will focus on the biotechnology techniques, its technology transfer and deployment as well as the associated challenges.

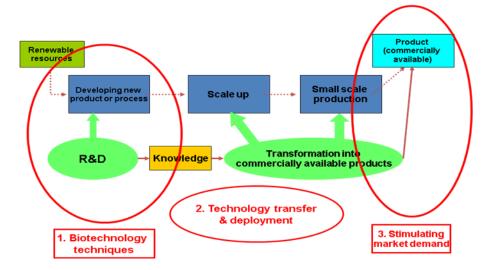


Fig. 1: Stages within the scope of the thematic area.

2. Industrial Biotechnology: the science behind

Biotechnology is defined by the OECD as "the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services." In other words, biotechnology is derived from biological knowledge and finally is associated to the evolution of biological science. In this sense, the main biotechnology techniques can be summarized as¹:

- **DNA/RNA:** Genomics, pharmacogenomics, gene probes, genetic engineering, DNA/RNA sequencing/synthesis/amplification, gene expression profiling, and use of antisense technology.
- **Proteins and other molecules:** Sequencing/synthesis/engineering of proteins and peptides (including large molecule hormones); improved delivery methods for large molecule drugs; proteomics, protein isolation and purification, signaling, identification of cell receptors.
- **Cell and tissue culture and engineering:** Cell/tissue culture, tissue engineering (including tissue scaffolds and biomedical engineering), cellular fusion, vaccine/immune stimulants, embryo manipulation.
- **Process biotechnology techniques:** Fermentation using bioreactors, bioprocessing, bioleaching, biopulping, biobleaching, biodesulphurisation, bioremediation, biofiltration and phytoremediation.
- Gene and RNA vectors: Gene therapy, viral vectors.
- **Bioinformatics:** Construction of databases on genomes, protein sequences; modelling complex biological processes, including systems biology.

¹ OECD (2005) - A framework for biotechnology statistics

• **Nanobiotechnology:** Applies the tools and processes of nano/microfabrication to build devices for studying biosystems and applications in drug delivery, diagnostics etc.

In order to cover the basic activities in the field of biotechnology, it is possible to define a biotechnology product as a good or service, the development of which requires the use of one or more biotechnology techniques listed above. On the other hand, a biotechnology process is defined as a production or other process using one or more biotechnology techniques or products. As a consequence, a biotechnology firm can be defined as a firm which is engaged in biotechnology using at least one biotechnology technique (as defined above) to produce goods or services and/or to perform biotechnology R&D. In that sense, the conceptual model could be summarized as shown in Fig. 2.

Before moving forward into the specific area of interest in this report which is "industrial biotechnology" that will be defined below, it is convenient to highlight that scientific and technological complexity are also inherent to biotechnology and consequently, it should be understood that interfaces and overlaps among techniques (directly associated with biotechnology or not) occur and are not only inevitable, but also extremely convenient, as shown in Fig. 3. In fact, it is well known that many innovative processes stem from cross-fertilization among different technological fields.

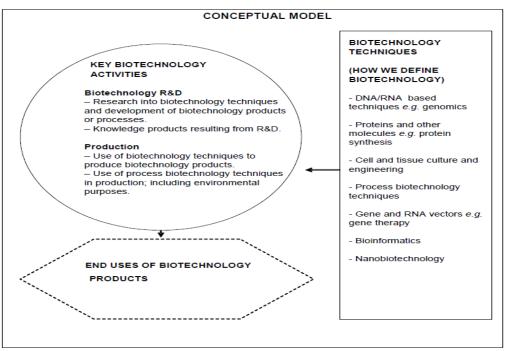


Fig. 2: Conceptual model of the field.²

² OECD (2005) - A framework for biotechnology statistics



Fig. 3: Possible interfaces in the development of a biotechnological product.

Due to different historical reasons biotechnology has been subdivided in three areas:

- **Healthcare/Red Biotechnology** plays a vital role in drug discovery and is improving outcomes for patients today and addressing unmet medical needs for the future.
- Agricultural/Green Biotechnology or Plant Biotechnology provides farmers with the technology to grow food, feed, fuel and fibre with less input and less impact on the environment.
- Industrial/White Biotechnology uses fungi, yeasts, bacteria and/or enzymes as "cell factories" to make sustainable energy, chemicals, detergents, vitamins, paper and a host of other everyday things.

The interest of the present report is focused in Industrial or White Biotechnology that can be defined as follows: "Industrial biotech is the application of biotechnology for the industrial processing and production of chemicals, materials and fuels. It includes the practice of using microorganisms or components of micro-organisms like enzymes to generate industrially useful products, substances and chemical building blocks with specific capabilities that conventional petrochemical processes cannot provide."

Industrial biotechnology is mainly characterized by conversion of renewable biomass to products used in the consumer, chemical or energy industries. It could be distinguished from e.g., discovery research in pharma or agrochemicals, chemical transformation of renewable raw materials, biodiesel production from plant products, chemical degradation of organic waste materials.

Although the applications and objectives of the three biotechnology areas are clearly differentiated, they have the same scientific and technological basis. Therefore they should take advantage of the advances and new knowledge produced in each area. The new knowledge being produced in systems biology and synthetic biology may open new fields of application in any of the biotechnology areas. It is very important to be aware of the expected progress in nanobiotechnology and bioprocessing in

the next few years. Even the latter is needed to bring bio-based products into the market and should be part of an overall bio-engineering strategy from in-vitro synthesis via cells to whole production processes. Cross-over with other KET's such as nano-bio interface may provide new business and growth opportunities on the long term.

3. Industrial biotechnology: applications, products and market³

3.1. Products on the market today

For decades bacterial enzymes have been used widely in food manufacturing and as active ingredients in washing powders. Transgenic Escherichia coli are used to produce human insulin in large-scale fermentation tanks. Europe has become the leading region for the development and production of **enzymes**. Around 64% of all enzyme companies are located in the EU, and the main enzyme producers by volume are in Denmark, where Danish companies account for almost half of worldwide enzyme production. Because enzymes play a crucial role for applications in many other industrial sectors, this sector represents significant potential for the EU in terms of escalating global leadership in the area of biobased products and processes.

The by far highest production volume in industrial biotechnology is **bioethanol**, produced from renewable raw materials. Today, starch from corn, sugar cane and wheat are the main feedstocks used to produce ethanol as a substitute for gasoline. But turning edible feedstocks into fuel leads to competition between food and fuel and is neither the most environmentally nor economically efficient method. The alternative is to derive ethanol from cellulosic material in wood, grasses and, more attractively, agricultural and food processing waste such as straw. Cellulosic ethanol has a 90% reduction in GHG emission and can be used as base chemical and biofuel. The first demonstration plants for cellulosic ethanol are built or in construction in the EU (Spain, Denmark, and Germany) but other markets like the US are ahead of this development. This technology is now ready for industrial deployment.

The **biofuels** industry has expanded rapidly since 2005, largely because of mandatory use regulations and tax incentives. In accordance with the EU's new Renewable Energy Directive the share of renewable energy for transport should rise to a minimum 10% in every Member State by 2020, coming from 1st or 2nd generation biofuels and electricity or hydrogen from renewable energy sources, whereas biofuels from cellulosic feedstocks such as cellulosic ethanol count double for the 10% renewable objective. The Directive also aims to ensure that as we expand the use of biofuels in the EU we use only sustainable biofuels, which generate a clear and net GHG saving and have no negative impact on biodiversity and land use. It is obvious that cellulosic ethanol will become one of the main emerging markets in the industrial biotechnology due to the excess of low cost lignocellulosic feedstocks from agrarian residues, no additional land use and competition to food, high GHG savings and additional supply of transport energy.

³ Based on:

Belgian Presidency Report (2010) – The Knowledge-based Bio-Economy in Europe: Achievements and Challenges

[–] JRC (2007) - Consequences, Opportunities and Challenges of Modern Biotechnology for Europe

⁻ Manfred Kircher (2010) - OECD Workshop on "Outlook on Industrial Biotechnology"

Another established sector is the production of **fine chemicals**, such as amino acids, lipids, organic acids, vitamins, etc., which find applications in the pharmaceutical industry, the food and feed industry, the production of detergents and cosmetics, and many other sectors. Vitamin B2 (riboflavin), for instance, is widely used in animal feed, human food and cosmetics and has traditionally been manufactured in a six-step chemical process.

In the chemical industry, an important step in increasing the share of biobased chemicals is the creation of **biotechnological platform intermediates** based on the use of renewable carbon sources. In this way, renewable feedstock could be transformed into a similar portfolio of end-products (organic chemicals) produced today from fossil fuel. Examples of such bio-based platform chemicals are fumaric, malic, succinic and itaconic acid which are currently used as food acidulants and in the manufacturing of some polyesters, and which can find new application as building blocks for the synthesis of new polymers and biodegradable plastics.

Table 1:Overview of different chemical building blocks that potentially can be produced in biotechnological
processes, with F, E and C indicating the main production process: fermentative, enzymatic or chemical
process, respectively (Leuchtenberger et al., 2005; Patel et al., 2006; Werpy et al., 2004; Xiao et al., 2007;
Zhang et al., 2007)

	Туре						
	Acids and alcohols					Amino acids	
	Building block			Building block	Method of production	Building block	Method of production
C2	Ethanol Acetic acid Glyoxylic acid Oxalic acid	F C C C	C5	Itaconic acid Glutamic acid	FF	L-alanine L-Glutamine L-Histidine L-Hydroxyproline L-Isoleucine L-Leucine L-Proline L-Serine L-Serine L-Arginine L-Arginine L-Arginine L-Aspartate L-Phenylalanine L-Threonine L-Glutamate L-Lysine	F F E F F E
C3	Lactic acid 3-hydroxypropionic acid Glycerol 1,2-propanediol 1,3-propanediol Propionic acid Acetone	F C/F C/E C/F C/F C C	C6	Citric acid Aconic acid <i>Cis-cis</i> muconic acid Gluconic acid Kojic acid Adipic acid	F F C/F F C		F F F F F F
C4	Fumaric acid Succinic acid Malic acid Butyric acid 1-butanol 2,3-butanediol 1,4-butanediol Acetoin Aspartic acid 1,2,4-butanetriol	F C/F C/E C/F C C C C/F F C					

Bio-based polymers are one of the important milestones on the white biotechnology's agenda. Over the past 20 years, these efforts have concentrated on polyesters of 3-hydroxyacids (PHAs), polylactic acid (PLA) and other polymeric building blocks such as 1,3-propandiol (1,3 PDO) or polyethylene from bioethanol which are mainly naturally synthesized by a wide range of microorganisms. These compounds could have properties similar to synthetic plastics and elastomers from propylene to rubber, but are completely and rapidly degraded by bacteria in soil or water. A major limitation of the commercialization of such bio-based plastics has always been their cost and performance in relation to petroleum-based polymers. Much effort has gone into reducing production costs through the development of better bacterial strains and/or the use of cheaper feedstocks, like food processing byproducts and waste, but recently alternatives emerged, e.g. the modification of plants to synthesize PHAs or the utilization of cellulosic feedstocks.

Although bio-based polymers and plastics are still in their infancy, this industry has been characterised by an annual grow rate of almost 50% due to new synergies and collaborations. The global capacity of bio-based polymers was estimated to be 0.36 billion tones in 2007, with an annual growth rate of 48% in Europe and 38% globally, and its market share is expected to be 10-20% by 2020. Fig. 4 gives an overview of the development stage of bio-based polymers. Today we see also the results of the recent developments of new processes combining biotechnology and chemical synthesis, such as the production of polyethylene from bio-ethanol.

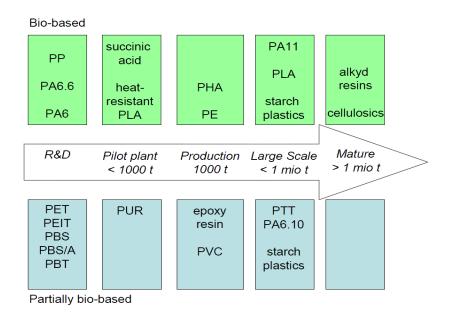


Fig. 4: Development stage of bio-based polymers⁴

3.2. Future trends

The OECD sees following industrial biotechnology applications with a high probability of reaching the market by 2030^{5} :

- Improved enzymes for a growing range of applications in the chemical sector.
- Improved micro-organisms that can produce an increasing number of chemical products in one step, some of which build on genes identified through bioprospecting.
- Biosensors for real-time monitoring of environmental pollutants and biometrics for identifying people.
- High energy-density biofuels produced from sugar cane and cellulosic sources of biomass.
- Greater market share for biomaterials such as bioplastics, especially in niche areas where they provide some advantage.

 ⁴ Source: Shen L., Haue J., Patel M (2009) - Product overview and market projection of emerging bio-based plastics. European Polysaccharide Network of Excellence and European Bioplastics. Utrecht, The Netherlands
 ⁵ OECD (2009) - The Bioeconomy to 2030: Designing a Policy Agenda

The area of biofuels is likely to offer increasing opportunities due to the mounting price of oil and the growing policy support in order to combat climate change. In addition, this will go hand in hand with significant technological progress in order to produce more sustainable advanced biofuels at competitive prices such as cellulosic ethanol.

In the other areas, strong growth is expected for fine chemicals, especially due to the growing importance of chiral active pharmaceutical ingredients and to new simplified synthesis paths (via metabolic engineering) for complex molecules. Significant growth in the bio-based polymers sector will result from the development of new polymers with new properties, greater incentives to reduce costs through the use of renewable materials, and increasing regulatory pressure to reduce carbon footprint (for example for packaging applications). In addition, enzymes will be increasingly used in applications, due to improvements and advantages particularly in the food, cosmetic and textile industries in line with customer requirements and stricter environmental regulations.

Certain building block chemicals derived from sugar sources may potentially substitute petrochemical building blocks; this means the development of biotechnological platform intermediates based on renewable carbon sources as shown in Fig. 5.

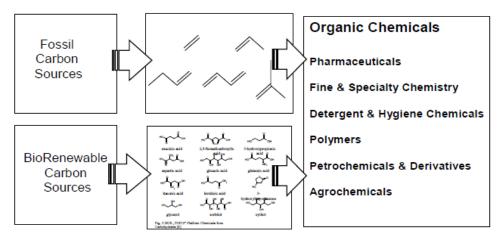


Fig. 5: Biological intermediates substituting petrochemical building blocks.

Future synthesis of polyesters and biobased biodegradable polymers may be achieved by using as building blocks fumaric, succinic or malic acid, among others, used at present in food industry.

Ethanol and succinate are good examples of precursors which are fermented, isolated and purified, that subsequently may enter into synthetic processes to be transformed into ethylene and subsequent polyethylene products, and polyesters, polyurethanes and polyamides respectively. This would mean the combination of biotechnological and chemical technologies that may be decisive in the next future.

In case that these biotech processes and new applications become more and more economically and environmentally sustainable, the industrial relevance of biotechnology will change dramatically. This development opens not only an extremely broad field of new applications, but would also require combination of bio- and chemical processes. One outlet area is the field of biopolymers.

 C_6 -sugar is the dominant carbon source for most biotechnological products. The prospective growing sugar consumption for the production of (bio)-chemicals will compete with the food and increasingly the biofuel industry. As the latter grows, the (bio)-chemical industry should avoid competing with biomass intended for food production. Lignocellulose as carbon source from biomass, plant breeding

for industrial purposes and algae production may represent new ways that contribute to obtain the biotechnological products.

The concept of biorefineries as a combination of integrated plants addressing 1) processing and fractionation of renewable raw materials, 2) transforming feedstocks to various products, and 3) recycling the products after use where possible, is becoming a promising strategy. Finally, synthetic biology represents a very important step forward, since it allows designing chemicals that would not occur by natural pathways. In this sense the tailor-made production of products by modifying bacteria microorganisms (i.e. Escherichia coli) or yeasts opens a wide new field for the production of chemicals suited for very different purposes.

3.3. Economic Relevance

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, and biofuel production could partly shift from starch-based bioethanol to higher energy density fuels manufactured from sugar cane or to cellulosic ethanol from lignocellulosic feedstock such as straw, grasses and wood⁶.

A recent report by the World Economic Forum (WEF)⁷ concluded that converting biomass into fuels, energy, and chemicals has the potential to generate upwards of \$230 billion to the global economy by 2020. The report also identified industrial biorefineries as one possible solution that may help mitigate the threat of climate change and the seemingly boundless demand for energy, fuels, chemicals and materials. However, the report also concludes there are still numerous challenges – including both technical and commercial as well as sustainability challenges – hampering industrial commercialisation on a large scale.

4. Industrial Biotechnology and the grand societal challenges

4.1. Green growth

One of the major questions is how we can boost economic growth while protecting the environment. Together with innovation, going green can be a long-term driver for economic growth, though, for example, investing in renewable energy and improved efficiency in the use of energy and materials⁸. Industrial biotechnology can improve industry's performance and product value and, as the technology develops and matures, industrial biotechnology will yield more and more viable solutions for our environment⁹. These innovative solutions bring added benefits for both our climate and our economy. In addition, the application of industrial biotechnology has been proven to make significant contributions towards mitigating the impacts of climate change¹⁰ in several industrial sectors.

⁶ OECD (2009) - The Bioeconomy to 2030: Designing a Policy Agenda

⁷ World Economic Forum (2010) – The Future of Industrial Biorefineries.

See: http://www3.weforum.org/docs/WEF_FutureIndustrialBiorefineries_Report_2010.pdf ⁸ OECD (2011) - Towards Green Growth

⁹ Belgian Presidency report (2010) – The Knowledge-based Bio-Economy in Europe: Achievements and Challenges

¹⁰ EuropaBio fact sheet (2008) – How industrial biotechnology can tackle climate change. See <u>http://www.bio-economy.net/reports/files/ib_and_climate_change.pdf</u>

One of the major strengths and drivers in Europe is the presence of a strong chemicals industry - which is in itself an important driver for the development of bio-based products - as well as a strong biotechnological and chemistry R&D base in academia and industry. In addition, although availability of renewable raw material is limited, the variety of crops cultivated is diverse (including sugar beet, potato, cereals, etc.) and there are huge opportunities for lignocellulosic feedstocks, e.g. agrarian residues like straw, and the opening up in the Eastern Europe in terms of available farmable land and feedstock. Europe has a tremendous potential of lignocellulosic feedstocks, e.g. straw from cereals is the second highest lignocellulosic feedstock in volume after rice straw in Asia. With around 400 Mio t each year, Europe is above the productivity of the USA with corn stover.

4.2. Climate change

Since the industrial revolution, economic growth has been inextricably linked with accelerating negative environmental impact. The more mankind has produced the more the planet has been exploited. Industrial biotechnology challenges this pattern and breaks the cycle of resource consumption by rethinking traditional industrial processes. By providing a range of options for competitive industrial performance, biotechnology could enhance economic growth, while at the same time saving water, energy, raw materials and reducing waste production.

Industrial biotechnology is based on renewable resources, can save energy in production processes, and can significantly reduce CO₂ emissions¹¹. The impacts of biotechnology on industry are confirmed by scientific studies and reports, such as the OECD's report on the application of biotechnology to industrial sustainability¹² and, most recently, by the World Wide Fund for Nature (WWF) report on the potential of industrial biotechnology to cut CO₂ emissions and help build a greener economy¹³. Even though the industrial biotechnology sector is still in it's infancy, it globally avoids the creation of 33 million tonnes of CO₂ each year through various applications, without taking ethanol use into consideration, whilst globally emitting 2 million tonnes of CO₂. However the WWF report concludes that the full climate change mitigation potential of biotechnology processes and biobased products ranges from between 1 billion and 2.5 billion tons CO₂ equivalent per year by 2030. To put this in context, this represents more than Germany's total reported emissions in 1990.

4.3. Sustainable development

All major facets of European society and economic activity are being challenged to demonstrate their sustainability. Consumers are more and more conscious about the impacts of their consumption and companies want to show the progress they make. In most countries, household consumption, over the life cycle of the products and services, accounts for more than 60% of all impacts of consumption. Industrial biotechnology can contribute to a more sustainable society, not only because it leads to an economy no longer wholly dependent on fossil fuels for energy and industrial raw materials with the potential to reduce greenhouse gas emissions, but also by generating less waste, by a lower energy consumption and by using less water.

As industrial biotechnology makes industry more sustainable, it is expected that the benefits will be seen across a range of critical social dimensions: creation of knowledge driven and attractive jobs, development of new technology platforms as a basis for innovation, and a reduction of society's

¹¹ EuropaBio fact sheet (2008) – How industrial biotechnology can tackle climate change.

 $^{^{\}rm 12}\,$ OECD (2002) - The application of biotechnology to industrial sustainability

¹³ WWF (2009) – Industrial Biotechnology - More than green fuel in a dirty economy?"

dependence on valuable fossil resources, thus conserving them for future generations.

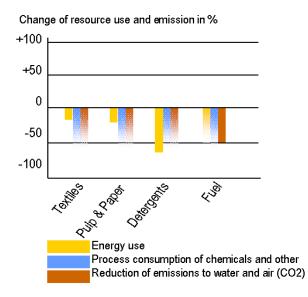


Fig. 6: Process inputs in terms of energy, chemicals and natural resources as well as emissions to water and air were reduced¹⁴

5. Obstacles and Drivers for Industrial Biotechnology: SWOT Analysis¹⁵

The options and challenges of industrial biotechnology in the OECD-regions EU, USA and Japan as well as the BRIC countries are summarised in the following SWOT-analysis. Generally OECD countries are characterized by strong competence in industry as well as science and technology. The US and the EU are well appointed with renewable feedstocks, e.g. corn stover is produced in the same volume as cereal straw in the EU, whereas the resources in Japan are limited. Lacking public acceptance of GMOs might turn out as a special handicap of the EU.

The BRIC states may develop to the world's producer of biorenewable feedstocks. On the long range a renewable-based industry might evolve. It needs developing competence in science and technology in these countries to accelerate this process.

 ¹⁴ JRC (2007) - Consequences, Opportunities and Challenges of Modern Biotechnology for Europe
 ¹⁵ Based on: M. Kircher (2010) - Trends in Technology and Applications. Discussion paper at the OECD workshop: Outlook for Industrial Biotechnology (Vienna 13-15 January 2010)

Table 2: Strengths

	EU	USA	Japan	BRIC
Drivers of industrial biotechnology	chemical industry, ecology, added value products	energy and chemical industry; start ups, venture capital	chemical industry, ecology, added value products	commercialisation of biorenewable carbon sources
Compentence in R&D	strong in biotechnology and chemistry in academia, industry, highest regional R&D density	strong in biotechnology and chemistry in academia, start-ups, industry	strong in biotechnology and chemistry in academia, industry, high regional R&D density	
Public acceptance		GMOs and transgenic plants well accepted	society willing to accept new products	GMOs and transgenic plants well accepted
Availability of biorenewable carbon sources	production of sugar beet, potatoe starch, cereal starch	large production of corn and soy; leading in lignocellulosic ethanol	tradition in marine culture	large production of corn, sugar cane and soy

Table 3: Weaknesses

	EU	USA	Japan	BRIC
Drivers of no relevant		bioenergy	no relevant	industry early in
industrial	technology provider	dominates too much	technology provider	value chain
biotechnology	in bioenergy		in bioenergy	
Compentence in	technology transfer,		technology transfer,	only few centers of
R&D	not enough start-ups		not enough start-ups	compentence
Public acceptance	GMOs and			
	transgenic plants			
	not accepted			
Availability of	limited due to lack	limited due to lack	insufficient due to	
biorenewable	of land, importer	of water	lack of land,	
carbon sources			importer	

Table 4: Opportunities

	EU	USA	Japan	BRIC
Drivers of industrial biotechnology	chemical industry seeks feedstock flexibility	chemical industry may add another driver	export bioenergy technologies	development of biorefineries
Compentence in R&D	accelerate partnering and technology transfer, build entrepreneurial culture	licencing technologies	intensify cooperation with more global regions	improvement of academic compentence
Public acceptance	improve acceptance of GMO and transgenic plants as industrial carbon sources			
Availability of biorenewable carbon sources	special plant-based precursors for niche markets	algae cultivation, large scale production of lignocellulosic carbon sources	develop marine biotechnology	become the world's producer of biorenewable carbon

Table 5: Challenges

	EU	USA	Japan	BRIC
Drivers of industrial biotechnology	investments in early technologies	establishing ecology as a driver in politics	investments in early technologies	infrastructure
Compentence in R&D				technology transfer into BRIC countries
Public acceptance	resistance against GMO and transgenic plants			
Availability of biorenewable carbon sources	land use for industrial plant cultivation	focus on chemical usage beside bio- ethanol	domestic availability of renewable carbon sources	free trade conditions in all regions

6. Industrial biotechnology research in Europe

6.1. Funding of Industrial Biotechnology research¹⁶

The OECD estimates that approximately 75 percent of the future economic contribution of biotechnology and significant environmental benefits are likely to come from applications derived from agricultural and industrial biotechnology¹⁷. However, these sectors currently receive less than 20% of all research investments made by the private and public sectors. Therefore there is a pressing need to boost research in agricultural and industrial biotechnologies by increasing public research investment, reducing regulatory burdens and by encouraging private-public partnerships.

Besides individual companies, bio-based products related research in Europe is today mainly funded via various public sources:

- European Union level: the 7th Framework Programme for Research and Technological Development, running from 2007-2013, is the EU's main instrument for funding research in Europe. The Framework Programmes for Research have two main strategic objectives: to strengthen the scientific and technological base of European industry, and to encourage its international competitiveness, while promoting research that supports EU policies. Calls such as the KBBE 2011 (Knowledge Based Bio- Economy 2011) within FP7 could continue to be supported and their financing could be increased in FP8.
- Member State level: Specific public research funding for industrial biotechnology is very limited in the EU Member States. Only a few countries are running dedicated research programs. Some are funded via general research programs or supported via parallel programs (such as energy, agriculture, etc.)¹⁸. Funding is provided by the regional and/or national Research Councils.
- In addition, several Member States try to coordinate their research via **ERA-NET schemes** (e.g. the ERANET for Industrial Biotechnology). Under the ERA-NET scheme, national and regional authorities identify the research areas of common interest, and launch

¹⁶ http://www.era-ib.net/

¹⁷ OECD (2009) - The Bioeconomy to 2030

¹⁸ See member state reports at <u>www.bio-economy.net</u>

collaborations via joint calls for projects. The national partners in these actions are programme 'owners' (typically ministries or regional authorities defining research programmes) or programme 'managers' (such as research councils or other research funding agencies managing research programmes), The partners usually have an extended collaboration with relevant national research institutes and other national and international professional organizations and governmental authorities. The scope, aims and deliveries are defined by the partnership in the ERA-NET.

Europe and individual Member States should use the rich varied potential that this continent offers in terms of knowledge, industrial activities and academic research institutes. The European Union distinguishes itself by a fragmented approach across the different Member States. Every country has its own programmes and initiatives in various research areas, with little EU-level coordination. Research funding played an important role in stimulating academic/industrial collaboration, though the processes are not always easy and transparent, and the regulatory environment poses some problems for collaboration between actors in various countries. International collaboration through joint calls could be seen to be essential to future functioning of research in industrial biotechnology in Europe.

To ensure increased pan-European collaboration in the area of research and development, it is recommended that the ERA-NET scheme and different partner countries/institutions strengthen the focus on a productive and sustainable societal development using bio-based products. Such strengthened pan-European collaboration will contribute to reducing the current fragmented approach of research funding across the different Member States - where every country has its own programmes and initiatives in various research areas - and optimize the outputs and benefits of the respective national and European research funds available. International collaboration through mapping of research and joint calls in the ERA-NET is regarded as essential in Europe. Improved coordination and collaboration between Member State, regional and European public programmes for research and innovation is the only way to avoid overlap and fragmentation and to keep pace with the massive research programmes in the United States and in Brazil, Russia, India, and China. In addition, a Joint Programming Initiative or another operational framework should be established in order to facilitate the assembly of European, national, and regional funds to ensure European cooperation and competitiveness in this area. This should be done in conjunction with improvements in the cooperation between the private and public sectors.

The USA and Japan are Europe's major competitors in industrial biotechnology. According to statistics, the **US** is strongly supporting industrial biotechnology and is spending nearly ten times as much as member states of the European Union on research in this field. Also China and other emerging countries like India are developing in this area rapidly becoming a major threat to European Industrial Biotechnology. The United States administration has decided to stimulate industrial biotechnology as part of its governmental programme and allocated a substantial budget to draft a plan to facilitate further development and implementation of the use of this form of biotechnology. Major R&D programmes are in place in the areas of biofuels and biomaterials and to a lesser extent on biochemicals. The American vision of development till 2020 is structured around a coherent strategy aimed at becoming less energy dependent. Federal Agencies in the USA give priority to bio-based products that have been approved and legislation is being changed rapidly to coordinate federal programs promoting the use of industrial biotechnology products. Budgets are being set aside for research programmes on enzyme and biomass technologies as well as biobased products and bioenergy. Research and development expenditures in biofuels increased 400 % from 2004 to 2007, reaching \$152.5 million, a rate three times the conventional R&D spending. Research and development expenditures for biobased chemicals were much larger than for biofuels, reaching \$3.4 billion.

Japan takes biotechnology very seriously considering that the old biotechnologies have played a critical role in Japanese industry in the last decades. In the past, Japan had tried to select technologies and industries relevant to its future and had instituted bureaucracies to support this redirection. However, now it initiated mergers of government ministries to form super ministries in an attempt to provide more integrated and consistent approaches to change across government.

Biotechnology in **China** is based on a solid domestic research base, strongly connected with foreign networks and benefiting from the scientific competence of those Chinese that came back from abroad. The Chinese government has a developed framework of science and technology policy structured in three main programmes and the government also invests in quasi-venture capital companies to support start-up firms, to attract private investment into life science through tax incentives etc. Local governments develop high tech parks and attract funds through matching investments and marketing campaigns aimed at foreign investors.

6.2. Identification of essential research priorities

Since 2004, several Technology Platforms were set up (such as SusChem¹⁹) and have developed their Strategic Research Agenda (SRA), giving recommendations on priority R&D topics to be pursued to support the long-term development of their respective sectors. The implementation of the SRAs started at the EU level with the 7th Framework Program and in the Member States and associated countries via their national research programs where some of them integrated in ERA-nets. The development of the KBBE (Knowledge-based bio-economy) as a concept and the creation of the KBBE-net by the European Commission helped to significantly stimulate awareness at an EU and Member State level.

In order to make full use of the biomass, for food as well as for non-food applications, it is important to develop **efficient and robust enzymes**, particularly for the conversion of lignocellulosic material from a variety of feedstock.

Synthetic biology and metabolic pathway engineering are examples of emerging technologies that will significantly increase the diversity of biotechnological processes and products, driving the development of innovative products. These techniques lead to the development of the so-called "microbial cell factories", which are production hosts that produce desirable products in high yields and with high productivity.

However, some of these biorefinery products will require further chemical processing and unless these chemical processes are made available there will be no market for these precursors. Therefore dedicated research on the **combination of technologies** such as biochemical and chemical processes should also be given a special attention.

It is also crucial to secure a sustainable **supply of feedstock** for the KBBE. This will require further research into methods of improving feedstock yields and/or the composition of biomass for optimal conversion efficiency. This research will involve both plant genomics and new breeding programmes, and also research into efficient crop rotation, land management and land-use change issues.

The ERA-Net Industrial Biotechnology²⁰ recently organized a survey on national research programmes, and the current and future use of industrial biotechnology by manufacturers.

¹⁹ http://www.suschem.org/

²⁰ http://www.era-ib.net/

Comparing the areas of interest of industry and research programmes (Fig. 7), it was concluded that there are areas where funding is not compatible with industry needs.

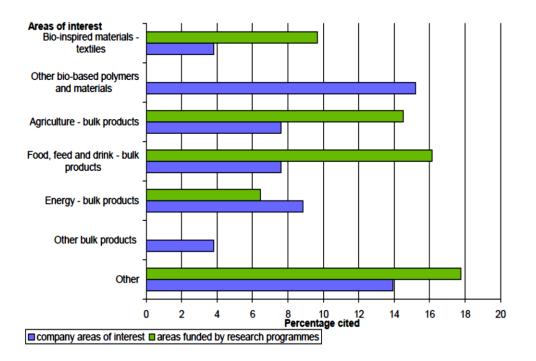


Fig. 7: Comparison of areas of interest

6.3. Industrial Biotechnology research in Europe: SWOT analysis²¹

-					
		- -	rich carried potential of research in many different areas companies active in many areas of interest government funding of industrial biotechnology research programmes (or areas linked with IB) exists in all European countries quality of research is an important criteria both for government funding and industry collaborations	-	eaknesses lack of coordination on European level of research funding cultural and language barriers in collaboration many fragmented small companies lacking capital for development facing large multinationals company areas of interest and research funding is
					not coherent
-	portunities possible European coordination of research programme funding and directing the areas of interest international collaboration is accepted by most companies in order to develop	- -	hancing opportunities joint calls may allow the various areas of expertise of research institutions and areas of interest of companies in several countries to meet international collaboration should be promoted between the European IB actors		trengthening eaknesses a pan-European approach to research funding is necessary with deeper coordination collaboration will allow capital sources to reach underfunded companies
-	reats rapid development of Chinese and Japanese industrial biotechnology reduced funding due to a worsening financial situation in Europe	Re	educing vulnerability choosing research gaps to develop and fund which may not be yet the interest in other countries	-	educing threats collaboration helps use the economies of scale to overcome reduction of profits

²¹ Study performed by Era-Net Industrial Biotechnology (<u>http://www.era-ib.net</u>)

6.4. The importance of clusters and public-private partnerships

Building on the successes of the European Technology Platforms (ETPs), FP7 and national research programmes, Europe needs to mobilise sufficient resources to **support a Europe-wide coordinated research programme by means of a public-private partnerships**. This type of joint undertaking would achieve a pooling of resources, thus allowing, among others, to set more ambitious goals in terms of reducing the time-to-market and for the industry to adopt long-term investment plans in the field of biobased products, taking into account the market perspective. The elaboration of market perspectives for non-subsidised bio-based products should be a central part of the coordinated R&D programme. If this Europe-wide research programme takes place, special attention should be given to keeping the administrative burden at a minimal level.

This should include (financial) support of relevant research, education, and international programmes with the aim to **remove bottlenecks** that limit the contribution that bio-based products can make to Europe's bio-economy. The main objectives of such projects are to **share the risk** of the development of innovative bio-based products and processes through support for research of a more "pre-competitive nature", covering the entire value chain (from crop to bio-based product), and to **facilitate innovation** in this sector and encourage the uptake of research results by the industrial partners. In such a research programme, the entire value chain of the bio-based economy should be covered. This means that projects should be considered in their full scope: from plant engineering, harvest and local processing, logistics, processing at the biorefinery through pre-treatment, enzymes, fermentation organisms, recovery, secondary manufacturing, including integration of subsequent chemical synthesis steps, compounding, shaping, side product valorisation and product recovery, with research to improve the yield and sustainability of new crops for raw material supply. Indeed, one of the industry's major challenges is to translate research to products, including the development of new product applications. Such projects could also include research on the social acceptance of the technology and products.

Because of the high R&D investments needed to develop an innovative bio-based product, we see a growing number of public-private partnerships developing. Cooperation in cluster structures rather than in single-company partnerships is significantly accelerating the development of processes and their penetration into the industry. Fig. 8 shows a schematic example for the bio-based products sector.

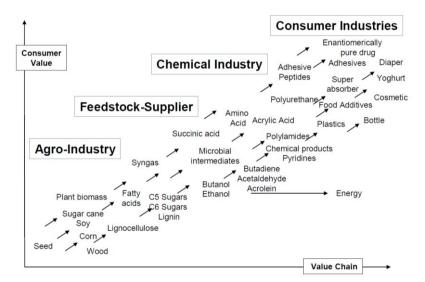


Fig. 8: Production-oriented value chain (CLIB2021)

Some examples:

- In 2010 in the Netherlands, knowledge institutes, the Dutch government and industry decided to cooperate more intensively and at international level to speed up the introduction of the bio-based economy via the **BE-BASIC** consortium²² (Bio-Based Ecologically Balanced Sustainable Industrial Chemistry), by placing the emphasis on scale-up research, an open innovation model and a proactive role for the financial sector. This initiative includes a R&D budget exceeding 120 million Euro, of which 60 million is made available by the Dutch Ministries of Finance and Economic Affairs. BE-Basic also plans a multi-purpose facility for scale-up research.
- A different model is represented by the five German industrial biotech clusters, initiated by the German Federal Ministry of Education and Research. The clusters started in 2007. Among these clusters is CLIB2021²³ with 32 founding members. Since then the cluster grew to include up to 70 academic institutes, companies and investors, launched R&D projects with a total volume of 50 million Euros, founded 5 start-ups and attracted 10% international members. Another cluster is BioM WB²⁴ with two demonstration plants for cellulosic ethanol and acetic acid, a new multi-purpose pilot plant for and a degree program of industrial biotechnology at the Technical University of Munich.
- **BioHub**²⁵ is a cereal-based biorefinery in Lestrem, France targeting on platformchemicals like succinate and isosorbide. Partners include Roquette, DSM and the University of Georgia (USA) amongst others. The project is funded by the French Industrial Innovation Agency. The isosorbide demonstration plant has been launched in July 2009.

7. From research to market

7.1. The time-to-market timescale

Typical research in the area of industrial biotechnology can take 2 to 4 years before obtaining an new process that can be upscaled and commercialized. Upscaling the process until commercial scale takes often another 2 years, and building a new production plant takes an additional 2 years. Finally end users have to develop specific applications before the new product can enter the market. We have to add the fact that the industrial biotech value chain includes different stakeholders or industries (feedstock producer, fermentation industry, chemical industry, end-user), which means a longer and more complex innovation chain. So generally it takes up to 6 à 8 years before a product can be commercialized.

²² http://www.be-basic.org

²³ http://www.clib2021.com/

²⁴ http://www.biom-wb.de/

²⁵ http://www.biohub.fr/

7.2. Some key barriers

There are at least 5 barriers²⁶ impeding the translation of R&D to the markets:

- **Understanding** the technological and business potential of academic R&D results needs adequate competence in the targeted industries at least in the lower and middle management and support from the top. The same is true *vice versa* for academics who often do not have sufficient understanding for industrial process and market demands.
- Strong competitiveness must be given for the foreseeable future. When competing against a running process based on fossil carbon sources, the alternative process must ensure competitiveness also in scenarios of high energy- and feedstock-cost volatility. Part of this criterion is the investment into the plant especially if the new one competes against a depreciated this might be a strong barrier. For a SME such an investment is an even stronger hurdle. The actual conventional production processes have the chance being optimized during a long period, and as such biobased products often have higher production costs in more complex value chains.
- Multiple product bio-refinery models include a complex network of individual process chains starting from biorenewable feedstocks to different intermediates and ending in diverse bio-and chemical endproducts. If the biorefinery is seen at first as a provider of feedstocks like lignocellular carbon sources and platform chemicals the business model is quite clear: Lignocellular sugars and platform chemicals serve the similar and transparent markets of carbon sources and precursors. However, the more transformation steps and products are added the more complex the business model becomes because its various products target different markets all with their own dynamics. Therefore a multiple product biorefinery needs an effective mass flux flexibility to be able to adapt to different market situations. Such flexible processes are not available yet.
- Academia and SMEs often contribute **intellectual property** (IP) early into the development of a complex process giving them only a reduced time of IP-revenues after launching the final process. Both parties should receive a fair share of the produced value. As late income from IP might be especially a problem for SMEs the promotion of early IP fees might be discussed. IP and patenting are crucial issues in the biorefinery era. IP strategies and policies should be improved in order to make them able to protect the inventors of the specific steps of the quite complex and integrated biorefinery pathways. Further, patent costs are often prohibitive for SMEs and therefore, policies addressed to reduce such costs are needed.
- As stated before at least some of the biorefinery products will need further chemical processing. As long as such chemical processes are not available these precursors will find no market. Therefore R&D on the **bio/chemo process** interface addressing resource efficiency should get special attention.
- A more general barrier is the availability of well-educated scientists (biology, chemistry, botany) and engineers (plant- and process engineering).

²⁶ M. Kircher (2010) - Trends in Technology and Applications. Discussion paper at the OECD workshop: Outlook for Industrial Biotechnology (Vienna 13-15 January 2010)

7.3. The need for pilot plants and demonstration projects

For some time now it has been clear that Europe's relatively poor record on innovation is due only in part to its not spending a sufficiently high percentage of GDP on research and development, and in addition the public funding is too fragmented in Europe. Though this is a factor, a bigger problem is that we take too long to transform research results into innovative, marketable products. Indeed, much of the knowledge resulting from European research leads to the commercialization of products by European companies in other parts of the world.

In order to turn research into products, a crucial step is to establish a proof of concept and test it under industrial conditions. Because often full-scale manufacturing facilities or even pilot plants are not accessible to researchers, the concepts developed in R&D are not immediately applicable nor necessarily economically feasible on a larger scale. It is therefore necessary to have access to scaleup and pilot infrastructures during the research and development stage to develop and test industrial processes, thus reducing both lead time and investment. This can also facilitate the establishment of stronger cooperation between the academia and the industry, in order to facilitate the translation of research into industrial innovation through the prototype phase.

Pilot infrastructures to demonstrate the technologies and to test new feedstocks and pretreatment processes already exist to some extent but need to be complemented by larger-scale demonstrators to verify scale-up of processes. The initial construction of biorefinery pilot and demonstration plants is not only a costly undertaking but it also involves bringing together market actors along new and highly complex value chains. This includes the diverse suppliers of biomass raw materials (farmers, forest owners, wood and paper producers, biological waste suppliers, producers of macro- and microalgae etc.); the industrial plants that convert the raw materials and industries providing them with the necessary technologies; and the various end users of intermediate or final products.

It is difficult to access public money for public-private partnerships and for demonstration projects (e.g. biorefineries) in Europe. Addressing this must be treated as a priority if the EU is to move beyond a situation in which the benefits of research carried out here are felt predominantly through the roll-out of innovative technologies elsewhere. The high additional investments for process safety concerns for these so called first-of-its-kind production plants - also reference or flagship plants - have to be taken into account. To bring this new technology to the market, investors need to pay the same price for a first production plant as they would for future plants. This gap has to be financed by public-private partnerships to prepare the ground for a successful market entry of bio-based products in the EU. Ambitious demonstration programmes with significant amounts of funding in other parts of the world have already attracted many European companies in this way. As an example, the USA has recognized this gap for advanced biofuels such as cellulosic ethanol and has given more than 1 billion in this "pre-commercial" full-scale production plants.

Countries like the US, Brazil, China and others are increasing investments into research, technology development and innovation, and supporting large-scale demonstrators, illustrating there is a clear sense of urgency to change the situation in Europe. There is a need for a concrete timeline and action plan if Europe wants to reach its 2020 targets. Some examples of initiatives being taken outside of Europe include:

 On 5 May 2009 the US Government's Department of Energy (DoE) announced plans to provide USD 786.5 million from the American Recovery and Reinvestment Act as additional funding for commercial-scale biorefinery and cellulosic ethanol demonstration projects. DoE anticipates making 10 to 20 awards for the construction of new refineries of a variety of scales and designs with the aim of having them up and running within a three year period. The projects selected will work to validate integrated biorefinery technologies that produce advanced biofuels, bioproducts, and heat and power in an integrated system, thus enabling private financing of commercial-scale replications. A further USD 176.5 million will be used to increase the federal funding ceiling on two or more demonstration - or commercial-scale biorefinery projects. In December 2009, they announced an additional investment of USD 600 million in advanced biorefinery projects.

 In February 2010 the Brazilian government announced the launch of the Brazilian Bioethanol Science and Technology Laboratory (CTBE) in São Paulo. The new research centre aims at strengthening the country's leadership in the sustainable production of sugarcane ethanol and clean energy innovation and its advanced laboratory equipment and pilot plant will enable a joint effort in research and development from around the world in the production of ethanol from biomass. With an initial investment of USD 40 million, research programmes will focus on sustainability, agriculture, virtual bio-refineries and basic science, including the development of second generation biofuels.

Lessons learnt from existing biorefineries teach us that the construction of demonstration activities is a crucial step towards developing a fully-fledged bio-refining industry. Demonstration activities are able to close a critical gap between scientific feasibility and industrial application. They enable us to measure actual operating costs, and specific strengths and weaknesses of technological processes before costly, large-scale facilities are built. They dramatically reduce the risk of introducing new technology on an industrial scale and therefore make a biorefinery venture much less risky for investors. Stimulating the construction of demonstrators via public-private partnerships is therefore one of the most important measures that can be taken in the development of the bio-economy. Some European programmes, such as the Structural Funds or the Rural Development Programme, can play a key role in converting knowledge to commercial success stories. It is recommended that information on possibilities to support technology transfer through demonstration plants/projects are conveyed more efficiently to interested parties.

Bio-based products that are not "drop-in" materials can offer new characteristics in an existing application that are unique and therefore help to differentiate them in the market, which, in turn, is often a prerequisite to be considered for adoption. However, due to the fact that they are not dropin materials, companies that consider their adoption are required to go through a complete application development cycle in order to define the optimum processing equipment (or changes to an existing installation) processing conditions. This investment and associated risks constitute a hurdle towards the adoption of bio-based materials. Financial support mechanisms such as government funding or business angels could help companies to mitigate that risk and associated investments and would weigh favourably in any decision regarding the adoption of bio-based materials. The Ad-hoc Advisory Group for Bio-based Products has developed following recommendations in its "Financing Document" :

- Set up a programme to facilitate access to existing flexible research-oriented pilot- and scale-up
 infrastructures during the development stage to develop and test industrial processes, and
 promote collaboration between existing pilot- and demonstration plants to the benefit of
 industries
- Increase public funding for demonstration projects and stimulate the construction of demonstrators via Public Private Partnerships:
 - In the short/mid-term: Stimulate "coordination and joint use of funding" (EIB, member states, structural funds, FP7 including ERA-Nets, etc.) for demonstration activities, thus reducing fragmentation of research efforts and funding
 - In the mid/long term: Set up a specific "EU Innovation fund" in parallel to the Framework Programme for research to shorten time from research to market. It is important that such fund provides opportunities for producers of new bio-products and the potential end-users to work together to develop products, as this will lead to a strong market pull for the bioproducts. The fund could also serve to aid the transition of the results achieved in FP7 to fullscale implementation and to the marketplace.
- Establish a programme to accelerate and alleviate risks of transforming knowledge into commercial products, by supporting financially access to pilot and demonstration facilities and by integrating production processes.
- All programmes in Structural Funds and Rural Development, which are used to support and implement bio-energy and biofuels, should be opened to bio-based products, and all criteria for funding should be handled equally.

7.4. Examples of efficient deployment efforts in Europe

Successful examples are Sunliquid (Germany), BioHub (France), Bio Base Europe (Belgium), and BE-BASIC (The Netherlands). They also go back to governmental public funded programs but are focused on specific product segments (BioHub: succinate; Sunliquid: cellulosic ethanol)

- **Sunliquid** (Germany): since 2010 a cellulosic ethanol demonstration plant with straw as feedstock is built at the center for renewable resources in Straubing. One of the target products are cellulosic ethanol and lignin. Partners are among others Süd-Chemie AG, TU Munich and several other academic and industrial partners. The project is funded by the German Federal Ministry of Education and Research (BMBF), the Bavarian state government and the German agency for renewable resources (FNR). The demonstration plant will be operable in 2011 and will subsequently operate with other feedstocks and other products.
- **BioHub** (France) is a cereal-based biorefinery in Lestrem (France). It targets on platformchemicals like succinate and isosorbide. Partners are among others Roquette, DSM and the university of Georgia. The project is funded by the French Industrial Innovation Agency. The isosorbide demonstration plant has been launched in 07/2009.

• **Bio Base Europe** (Belgium) is a joint initiative by Europe, Belgium and the Netherlands to build an open innovation Pilot Plant and a Training Centre for biobased products and processes with a budget of 21 million euros. The Bio Base Europe Pilot Plant is a flexible and diversified pilot plant, capable of scaling up and optimising a broad variety of biobased processes up to the 10 m3 scale. These facilities are open for all players of the biobased economy and will start operations in 2011. This European research and training infrastructure is an important building block for the development of the biobased economy in Europe.

8. Gaps in Innovation Skills, Higher Education and Training

In general, there is a lack of awareness of IB potential both in the manufacturing industry and amongst policy makers, consumers and even investors²⁷. To facilitate the long-term development and implementation of the technologies, a strategy for communication and stakeholder involvement is necessary. This would help to raise awareness of the technologies and their benefits and would also help to develop insight into the long term objectives, applications and products needed by society in general.

Stakeholders must be involved and engaged in order to raise further awareness. Indeed, in its recent bio-economy report, the OECD²⁸ suggests creating an ongoing dialogue between regulators, citizens and industry, as many of the policies to support the bio-economy and its sustainability will require the active participation of these groups. From previous experience it is clear that information and communication are not synonymous with public acceptance. Instead, a long-term process needs to be developed by industry and governmental organisations in order to build trust through a transparent process of engagement on values, risk management and critical self-evaluation. Sustainability, characterised by the triple bottom line of People, Planet and Profit, should be made more visible as the core value driving the development process.

Improving education in order to develop a highly skilled workforce is one of the recommendations of the Becoteps²⁹ white paper. For a successful bio-economy, it is necessary to have a multi- and interdisciplinary work force, remaining up-to-date on new knowledge and developments. To achieve this multidisciplinary education, good international training programmes and efficient lifelong learning will be necessary. In addition, due to a gap in education, biotechnology and chemistry are still too often perceived as "competing technologies" instead of as being complementary³⁰.

²⁷ EuropaBio (2006) - Industrial or White Biotechnology: a policy agenda for Europe

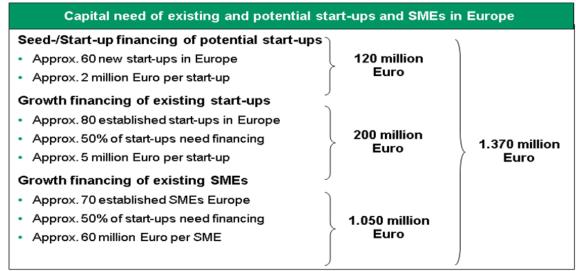
²⁸ OECD (2009) - The Bioeconomy to 2030

²⁹ Becoteps White Paper (2011) – See: http://www.becoteps.org

³⁰ EuropaBio (2010) – Building a bio-based economy for Europe in 2020

9. Access to Finance and Risk Capital

SMEs, and start-ups in particular, are confronted with three types of risk: technological risk, resulting from the explorative nature of R&D and production of high-tech goods; market risk, as a result of the uncertainty in the high-tech product market; and financial risk, as high-tech innovation usually requires huge investment. In general, most high-tech start-ups lack long-term investment capability. If we take industrial biotechnology as an example, capital requirements for start-ups and SMEs are calculated separately for Europe using a different approach: Festel Capital recently calculated that the capital need of existing and potential start-ups and SMEs in the field will be almost 1.4 billion Euro. The operational income is the most important financing source for industrial biotechnology start-ups. Financial resources through private investors are rather small and not sufficient for further growth, hence the need to improve access to finance for SMEs.



Source: Market Study on Financing Strategies in White Biotechnology of FESTEL CAPITAL from April 2005 / Market Study on Financing and Investment Trends in Industrial Biotechnology of FESTEL CAPITAL from February 2009

Spin-offs and high-tech SMEs are key for technology and knowledge development, and investing in research and innovation is the only way for these enterprises to survive. For these SMEs it is very important to improve access to finance as, due to the worldwide credit crunch, venture capital and private equity funding have become even tougher to access.

Without larger scale validation, it remains very hard for SMEs to attract the large industrial partners or other private investors that they need to reach sustainability. Developing grants for "Proof of Concept" studies for sustainable technologies could help partially overcome this problem. Consideration should also be given to the creation of grant foundations, such as the ones operating in the U.S. Such foundations could have a mandate to give preference to industrial applications listed in a regularly reviewed hierarchy of industrial "hot spots" relating to key enabling technologies in order to provide maximum economic, social and environmental benefits. Such action would also help significantly in attracting new investment. In addition, existing national schemes could also be used as an example, such as the small scale Dutch Small Business Innovation Research (SBIR) pilot programme inspired by the US SBIR programme . Here, contracts are awarded based on the three key criteria of feasibility, research and commercialisation.

One of the weaknesses of many SMEs is that many of them do not have the in-house technical skills necessary to absorb the results of cutting edge research and to take up the results of innovation. Supporting tech transfer or stimulating SMEs to participate in "open innovation" programmes could be one way to overcome this problem.

The European Commission mentioned *access to finance* as an important issue in its Communication on the Lead Market Initiative. For this reason, the Advisory Group developed a set of concrete recommendations to improve the access to finance for SMEs to increase their operational income, by

- Improving access to public finance for "proof-of-concept studies¹" for environment-friendly technologies (e.g. consider developing a grant foundation to give preference to industrial applications with optimal economic, social and environmental impact).
- Attracting new investors through communication campaigns and developing a database with "players of excellence"
- Developing an adapted investment model at EU level between loans and private equity to increase the availability of risk capital
- Evaluating existing market instruments on their ability to finance the development of biobased products.

10. Market Pull Measures

10.1. Regulatory Framework Conditions

Bio-based products are affected directly or indirectly by a large number of legal acts and public policies at EU, national or even local level. The Ad-hoc Advisory Group for Bio-based Products³¹ has analysed the impact of existing legislation and policies on products made from renewable raw material. The analysis has focused on all the different steps in the production and supply chain, including:

- the supply of renewable raw materials,
- the production of intermediate chemicals, materials and components,
- the manufacture of assembled products,
- retail market conditions,
- the use of bio-based products,
- the disposal of bio-based products as waste, through re-use, recycling, recovery or other options.

This analysis is complicated for two reasons: many legal acts at different levels influence the manufacture, sale and disposal of bio-based products; and bio-based products are not one uniform product group, but a broad range of products with completely different characteristics, qualities and uses.

³¹ <u>http://ec.europa.eu/enterprise/policies/innovation/policy/lead-market-initiative/biobased-products/index_en.htm</u>

At present, the drivers for bio-based products – especially plastics - differ substantially: in the US, resource security and utilisation are the main drivers, while in Japan, there is a strong drive towards products with a green image. In Europe, resource utilisation, GHG emissions, and compostability are the important drivers in developing supporting policies.

However, in contrast to biofuels, there is currently no European policy framework to support biobased materials. As a result, these products suffer from a lack of tax incentives or other supporting regulations. Although the Ad-hoc Advisory Group for the Lead Market Initiative for Biobased Products has developed a series of recommendations to stimulate market uptake and development these measures still have to be implemented. Other demand-driven policies focus on the sustainability agenda (including green public procurement) and are often implemented as a mix of public procurement procedures, legislation and direct financial incentives.

However, such policy frameworks have been developed in other parts of the world³²:

- In the **US**, The BioPreferred³³ program aims to increase the purchase and use of renewable, environmentally friendly biobased products.
- In Japan, in 2002 the government initiated the Biomass Nippon Strategy, requiring that 20% of all plastics consumed in the country be sourced renewably by 2020. This prompted Toyota, NEC and others to accelerate levels of R&D into bio-based plastics and to raise the bio-based content of their products. Bio-based chemicals and bioplastics benefit from usage, waste management, and labelling legislation.
- In **China**, industrial parks for chemical R&D are being established, and specific projects for liquid biofuels and bio-based products are funded by a national high-tech R&D program. Feedstock prices are regulated, reportedly held below international levels, and sometimes frozen. Support for bio-based chemicals includes numerous incentives for producers and a preferential tax treatment for selected firms in emerging biochemical industries. In addition, since 2005 a specific programme promotes production and consumption of biodegradable plastics.
- In Korea, government-funded research institutes are developing technologies to produce chemical raw materials from biomass, and scaling-up R&D for biochemical and production technologies. The Korean government also supports the use of biodegradable materials in refuse bags and fishing nets. One-time use products cannot be made from conventional plastics, and polystyrene is banned in food packaging.

A different situation is the **biofuel** market. Due to the high potential of surplus straw and other lignocellulosic feedstocks in the EU for cellulosic ethanol and other advanced biofuels, the sole measure of the double counting for biofuels made from lignocellulosic material or waste is not sufficient to give investors the necessary security and to get cellulosic ethanol into the market. Further incentives are needed to ensure investment and conclusively the achievement of Europe's goals in climate and nature protection as well as independence from fossil resources.

• Funding of R&D research programs: besides some activities in the FP7 for biofuels, a clear focus is needed for advanced biofuel research and development, such as lignocellulosic

³² David Batten (2010) - International Policy Approaches and Challenges in Industrial Biotechnology. Discussion paper of the OECD workshop on "Outlook on Industrial Biotechnology", Vienna, 13-15 January 2010

³³ http://www.biopreferred.gov

ethanol, butanol and other biofuels in the next funding programs on EU level. Furthermore the combination of this topic with agricultural science and economics is needed.

- Funding of demonstration and first commercial plants: fundamental obstacles to bring a
 new technology into the market are the high additional costs for safety concerns. Therefore,
 funding of demonstration plants and first production plants (so called first-of-its-kind,
 reference or flagship projects) is an essential task. For first-of-its-kind plants, construction is
 planned in a way, that all risks concerning the never before realized up scaling of this
 technology are taken into account. Those additional costs account for up to 100% of the total
 plant costs for completely new technologies. To bring new technologies such as Cellulosic
 Ethanol to the market, investors need to pay the same price for a first production plant as
 they would for future plants. Technology providers cannot cover this gap in the development
 alone and will need support from public authorities.
- Subsidies for the agricultural sector: incentives are also needed for farmers to collect agricultural residues and thus ensure feedstock supply for cellulosic ethanol production plants. Per hectare agricultural land, the EU currently pays funding of about € 250 per year. Part of this funding could be connected to the delivery of a proportion of the produced straw to a cellulosic ethanol plant. Hence, a high security of supply of up to 30% of the current EU fuel demand could be covered medium term by cellulosic ethanol as biofuel. In the EU, an estimated 1.000 to 2.000 cellulosic ethanol plants would be needed to start operation to exhaust the total straw potential. A rather small number compared to currently about 4.500 biogas plants just in Germany. In the US a similar approach is already being taken. The Biomass Crop Assistance Program establishes so called matching payments for producers of eligible material meaning particularly also lignocellulosic agricultural residues if they sell it to biomass conversion facilities for conversion to heat, power, bio-based products, or advanced biofuels. In practice this means, that feedstock suppliers get the same amount, they got from the purchaser again as subsidy from the state.
- Mandatory blending quotas and tax incentives: mandatory blending quotas are an efficient tool to ensure cellulosic ethanol can enter the market. It offers security to investors and producers as the demand for cellulosic ethanol is foreseeable. Blending quotas for biofuels already exist and experience shows us how effective they are. The bioethanol market has been booming over the last years. Now we need to make the next step, clearing the way for advanced biofuels like cellulosic ethanol, to overcome the problems of first generation biofuels. Other very effective tools are tax incentives that are also stated on in the Fuel Quality Directive. Through tax incentives higher production costs can be covered to make sure cellulosic ethanol can be sold for a competitive price.

10.2. Public Procurement

The potential for increasing demand for bio-based products through public procurement is huge, as European public authorities spend almost €2000 billion, or 16% of GDP, on goods and services yearly. Almost all product areas could potentially feature products made entirely or partly from renewable raw material. Likewise, the production of almost all types of services could potentially benefit from bio-based inputs. By introducing requirements for sustainability in tender specifications, the demand from public authorities could significantly increase the market for green or sustainable products and drive technological innovation. Member States have given political support to an increase in Green Public Procurement (GPP). However, the improvements have to be accomplished through action at

the national, regional and local level. This may be supported by normative measures (e.g. national targets or requirements for green public procurement). The difficulty in providing an inventory of public procurers at all different levels makes it inefficient to rely only on a bottom-up approach; normative measures can hence be helpful.

The Green Public Procurement Guidelines now include criteria that allow bio-based products to be given preference in tender specifications. The European Commission cooperates with Member States and stakeholders to set common GPP criteria for endorsement in national action plans. The fact that a product is bio-based is not alone a proof of its sustainability; a range of other factors need to be considered (e.g. health, safety, environmental effects, waste). By integrating the requirement for bio-based content with other common GPP criteria and by applying the EU Ecolabel to products complying with a minimum level of bio-based content set for that product category, public procurers may be able to distinguish the products that should be eligible for preferential selection.

National GPP programmes can have a significant effect on the uptake of bio-based products. For instance, the Netherlands have legislated that 100% of the procurement should select sustainable goods and services. Although this should lead to an increased demand for bio-based products, the buyer may lack essential information:

- Is there a sustainable bio-based alternative available on the market?
- Is the performance as good as that of similar products?
- Is there a suitable European standard for bio-based products?
- Have the environmental claims been certified?
- What is the minimum level of renewable content to call the product "bio-based"?
- How to compare recycled material with bio-based material?

10.3. Standards-Related Issues

The current absence of standards for bio-based products causes difficulties for European companies who have developed bio-based products. Downstream, the lack of standards creates uncertainty for companies willing to use bio-based components, for distributors and for retailers. In turn, the consumers cannot distinguish between conventional plastic and bioplastic, because of the lack informative product labels (that are based on standards). In addition, bio-based products may have specific characteristics, e.g. biodegradability, recyclability, low toxicity, etc.

10.4. Incentives Policy, such as Taxation or State Aid Measures

Competitiveness must be a key focus for the future. When competing against a running process based on fossil carbon sources, the alternative bio-process must also show competitiveness in scenarios with high energy- and feedstock-cost volatility. Additionally, investments required for building a new bio-industrial facility - especially if it competes with the conventional one – might present a significant barrier. For SMEs, such investment might represent an insurmountable hurdle which is of critical importance since the development of new technologies and products often starts in niche-markets served by SMEs prior to their wider distribution amongst customers.

In addition, it has become even more difficult to obtain bank loans and funding required for investing into building new full-scale commercial plants and infrastructure as result of the worldwide credit crunch. Governments too tend only to provide financial support and incentives on a relatively short-

term basis, while pathway to success for many enterprises is a long term process. For this reason governments interested in supporting biorefineries for reasons of environmental protection, energy security and innovation leadership need to support market growth, and to carefully regulate the industrialisation process in order to trigger private sector investments

Producing chemicals through bio-chemical routes is currently still more expensive compared to traditional production routes. In addition, existing production facilities for chemical syntheses cannot be converted to biotechnological production without massive new investments, and in many cases there are clear economic restrictions in biotechnological production processes due to higher operating costs and higher levels of R&D costs and investments.

In the US – at Federal as well as at State-level - numerous programs have been set up to stimulate the construction of new plants (producing advanced biofuels or bio-based products) and/or new biorefineries, e.g.

- in USA (federal incentive):
 - mandatory blending of 10% bioethanol,
 - producer tax credit, ca. 1 USD/gal,
 - Blender tax credit, ca. 0,5 USD/gal,
- in Kansas: tax incentives for cellulosic biorefinery construction
- in New York: specific grants for biorefinery construction: New York Farm Bureau said that the finalisation of the Bio-Fuels Production Tax Credit and a recently announced \$20 million state funding proposal for cellulosic ethanol will position New York as a national leader in biofuel production. The Bio-Fuel Production Tax Credit makes companies eligible for a tax credit for each gallon of renewable fuel they produce.

The European Commission and its Member States could support the development of such tax incentives in order to support the industry that wants to invest in such greener and more sustainable production processes, complementary to incentives proposed in the Commission's report "Taking bio-based from promise to market"³⁴. Due to differences in national tax policies, the industry and policymakers on both European and national levels should evaluate if such incentives could be developed.

The US is currently evaluating the option of opening the bioenergy and biofuel tax policies, programs and carbon legislation for other bio-based chemicals and products. In this context, the US Biotechnology Industry Organization (BIO) published recently the report "Bio-based chemicals and products: A new driver of US economic development and green jobs³⁵". The report has two main statements:

- "Bio-based products can offer significant growth to the US economy and confer a competitive advantage in the chemicals and plastics industry. The industry can create tens of thousands of green jobs and provide a range of additional societal benefits to the United States, including a reduction in CO2 emissions and reduced dependence on foreign oil."
- "... to foster the growth of its bio-based products sector, federal policy should provide strong support for research, development, and commercialization of innovative bio-based products, including grants and loans for construction of biorefineries, a strong bio-based markets program, and tax incentives for pioneering commercial production."

³⁴ Taking Bio-Based From Promise To Market - Measures to promote the market introduction of innovative biobased products (EC, 2009)

http://ec.europa.eu/enterprise/sectors/biotechnology/files/docs/bio based from promise to market en.pdf ³⁵ http://www.bio.org/ind/20100310.pdf

The report is discussing in detail several instruments that could support a bio-based economy, such as

- Provide product parity and early-stage support in biorenewables tax policy , e.g. via a production tax credit (PTC) for bio-based products, or by opening the section 48C advanced energy manufacturing credit to renewable chemical and bio-based product biorefineries
- Increase funding through grants and other programs for non-fuel bio-based products, e.g. by opening existing DOE and USDA loan guarantee programs to bio-based product projects, or by establishing grants and loans to help struggling biorefineries to add high-value chemical production
- Ensure that bio-based products are incentivized in climate change/carbon legislation.

10.5. Recommendations proposed by the Ad-hoc Advisory Group for Biobased Products

Europe is well-placed to become a world leader in the market for innovative bio-based products, building on its strong technological and industrial position in the field. The European Commission's Lead Market Initiative for bio-based products³⁶ is a good example of a synchronised approach to stimulating demand for these innovative new products. It should be further developed and built upon. In 2008, the Commission set up an expert group composed of representatives from national governments, industry and academia, entitled the Ad-hoc Advisory Group for Bio-based Products. End of 2009, the Ad-hoc Advisory Group agreed unanimously on measures³⁷ relating to legislation, policies, standards, labels, certification and public procurement.

The Advisory Group's main recommendations to promote bio-based products

Legislation promoting market development

- The biological/biobased carbon contained in biobased products shall be deducted in the calculation of the total CO2 equivalent emissions of the products.
- Consider setting indicative or binding targets for certain bio-based product categories, drawing on the experience from biofuel quotas in the EU.
- Allow Member States to reduce taxes for sustainable bio-based product categories.

Product-specific legislation

- Allow bio-based plastic to enter all waste collection and recovery systems, including composting, recycling and energetic recovery (depending on the type of plastic and compliance with applicable standards). Bio-based plastics certified compostable according to EN 13432 should gain unhindered access to biowaste collection.
- Study the possibility of mandating the use of biolubricants and hydraulic fluids in environmentally sensitive areas. This could be implemented e.g. via soil protection and water protection legislation.
- Bio-based construction materials (foams for insulation, composite material, mortar, and concrete made of vegetative aggregate particles)
 have now become sufficiently advanced to offer a real alternative. The Construction Products Directive should promote the specificities of
 biobased products. In addition, new and transparent standards showing the product capabilities are needed to help demonstrate that biobased materials comply with construction legislation.

Legislation related to biomass

- Legislation and policies must allow renewable raw materials for industrial use to be available in sufficient quantity of good and guaranteed quality and at competitive price.
- Increase investments in developing and optimising infrastructures and logistics for an optimal use of all available biomass (including waste).

Encourage Green Public Procurement for biobased products

Encourage contracting authorities in all EU Member States to give preference to bio-based products in tender specifications. A
requirement or a recommendation to give preference can be laid down in a national action plan adopted by the government. Preference
should be given to bio-based products unless the products are not readily available on the market, the products are available only at
excessive cost, or the products do not have an acceptable performance.

Standards, labels and certification

- Develop clear and unambiguous European and international standards. The standards will help to verify claims about bio-based products in the future (e.g. bio-degradability, bio-based content, renewable carbon, recyclability, and sustainability).
- The sustainability assessment should be based on all three pillars of sustainability: environmental, social and economic. While we need (to develop) tools to assess sustainability of products, we need to ensure the tools used will stimulate and not limit the development and implementation of bio-based products.
- Begin a reflection process on what types of specific product labels are suitable for bio-based products and what information to be given to the consumer.

Financing and funding of research

 Continue to stimulate and enhance technological innovation and the development of technology: setting up demonstration projects via public-private partnerships

³⁶ http://ec.europa.eu/enterprise/policies/innovation/policy/lead-market-initiative/biobased-products/index_en.htm

http://ec.europa.eu/enterprise/sectors/biotechnology/files/docs/bio_based_from_promise_to_market_en.pdf

³⁷ TAKING BIO-BASED FROM PROMISE TO MARKET: Measures to promote the market introduction of innovative bio-based products. See:

11. The importance of communication

Communication is about informing different stakeholders of bio-based products, their characteristics, their benefits and their contribution to sustainable production and consumption. Communication should be based on scientific facts and should help to increase transparency both within the market and towards the wider public.

The term "bio-based products" comprises a great variety of innovative products in ubiquitous applications. However, due to the fact that no external, perceptible characteristics differentiate biobased products from traditional products made with petrochemicals, most bio-based products cannot be easily recognised as such by users and consumers, due to the fact that no external, perceptible characteristics differentiate bio-based products from traditional products made with petrochemicals. Thus, the specific features of bio-based products are mostly invisible to the purchaser. Today, this lack of awareness and knowledge represents a major obstacle to increased market uptake of bio-based products. Recently, the Ad-hoc Advisory Group for Bio-based Products³⁸ has formulated a set of recommendations:

The LMI Advisory group recommendations concerning "communication":

What to communicate?

1. As life cycle assessment techniques and standards are evolving rapidly, a pragmatic approach needs to be taken, first using characteristics/criteria that are well defined and standardised. In a second step, other characteristics could be added.

Communication towards professionals (businesses or procurers)

- 2. Develop a simple and pragmatic operational Reference Life Cycle Data System (such as through ILCD product category guidance for bio-based products) for industry, especially SMEs.
- 3. Raise awareness of existing targeted life cycle assessments, eco-efficiency, environmental product declarations and sustainability assessments, and facilitate further industrial agreements on communication guidelines.
- 4. Promote and use harmonised certification and labelling schemes for bio-based products.
- Make use of existing networks to improve the effectiveness of communication with SMEs in different languages.
- 6. Develop an official tool for monitoring market development by building on existing national surveys on production and consumption.

Communication towards the public – education and bio-literacy

- 7. Develop and promote harmonised labelling schemes.
- 8. Build alliances with the major "green and consumer associations" communicating with and through the public, in collaboration with other strong communicators).
- 9. Design a communication strategy involving all partners in the value creation chain and all other stakeholders to achieve coherent messages on bio-based products.
- **10.** Involve well-known brands and retailers in the communication process.

³⁸ <u>http://ec.europa.eu/enterprise/policies/innovation/policy/lead-market-initiative/biobased-products/index_en.htm</u>

12. Need for a coherent policy for industrial biotechnology

Whilst a number of sectoral policies and funding mechanisms have been put in place to support the development of industrial biotechnology and bio-based products in Europe, these exist to an extent in isolation from one another. At EU level, the European Commission's Directorate General (DG) for Research promotes and finances research into industrial biotechnology through the Seventh Framework Programme and the knowledge based bioeconomy (KBBE); DG Enterprise's biotechnology unit is seeking to facilitate the early adoption of new bio-based products as part of the 'Lead Market Initiative'. All of these initiatives are extremely important, but for the moment the whole is not greater than the sum of the parts. A more integrated, strategic approach is needed if Europe is to get serious about developing a globally competitive bio-based economy within the next decade.

Europe has the potential to lead the world in transitioning to an economic model which uses renewable resources sustainably not only for energy production but also for industrial sectors like chemicals and materials. Such a goal would be fully in line with the aims of both the European Economic Recovery Plan and the new Europe 2020 agenda but it demands a holistic strategy involving both the European Commission and EU member states, as well as key players in industry and academia.

A holistic approach is all the more urgent since the bio-based economy will need a supportive policy framework in numerous areas. These include climate change, energy security, renewable feedstock supplies, research and innovation, agriculture, the environment and trade.

According to the OECD, in order to achieve a competitive bio-economy, broad approaches, such as creating and maintaining markets for environmentally sustainable products, funding basic and applied research, and investing in multi-purpose infrastructure and education will be necessary. In addition, these will need to be combined with shorter term policies such as the application of biotechnology for improving plant and animal varieties, improving access to technologies for use in a wider range of plants, fostering public dialogue and increasing support for the adoption and use of internationally accepted standards for life cycle analysis together with a range of other incentives designed to reward environmentally sustainable technologies.

EuropaBio, the European Association for BioIndustries, recently published a policy guide³⁹ setting out such requirements and calling for a more integrated and strategic approach, with supportive policies in the areas of climate change, energy security, renewable feedstock supplies, research and innovation, the environment and trade.

³⁹ http://www.bio-economy.net/reports/files/building-a-bio-based-economy-for-Europe-in-2020.pdf