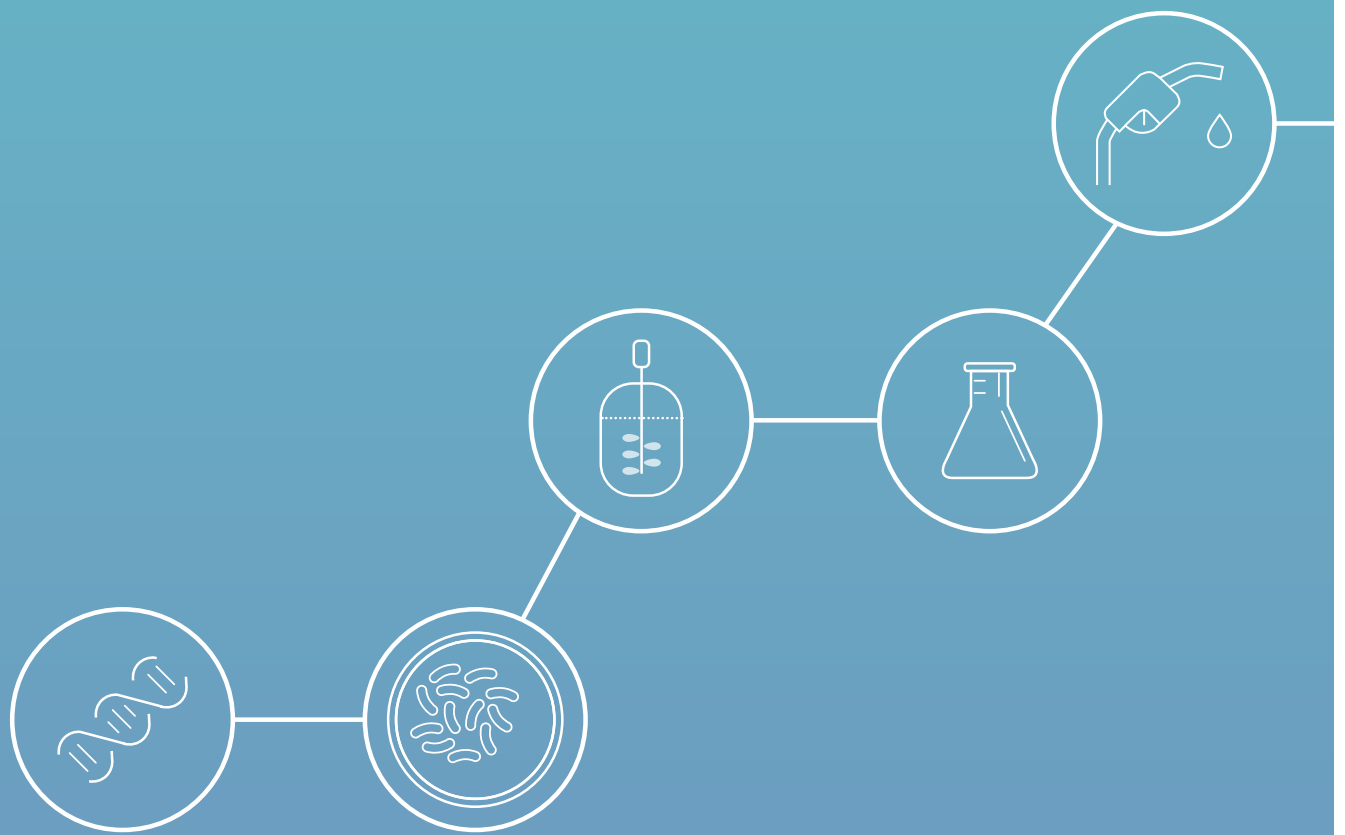


# PROGRESS

Priorities for Addressing Opportunities and Gaps of Industrial Biotechnology for an Efficient Use of Funding Resources



## Authors

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Bärbel Hüsing  
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# PREFACE

This brochure summarises the results of the research project “PROGRESS” – **P**riorities for Addressing **O**pportunities and **G**aps of Industrial Biotechnology for an Efficient Use of Funding **R**esources, a 15-month (2016–2017) project funded under the Horizon 2020-NMBP Work Programme of the European Commission. The content of this Brochure does not reflect the official opinion of the European Union.

The project had the objective to support and accelerate the deployment of Industrial Biotechnology (IB) in the EU by identifying high-value opportunities for IB and to propose actions how to address them successfully.

This brochure brings together the main elements of PROGRESS, ranging from the project's conceptual reasoning to the main results. On numerous occasions, PROGRESS has taken advantage of conceptual input and enlightening discussions with our peers in the IB community. We are also indebted to over 100 experts and stakeholders as well as the Advisory Group who were interviewed or participated in the project's workshops. Their advice and constructive feedback were essential for the project's key outputs and we are grateful for all the input we were given.

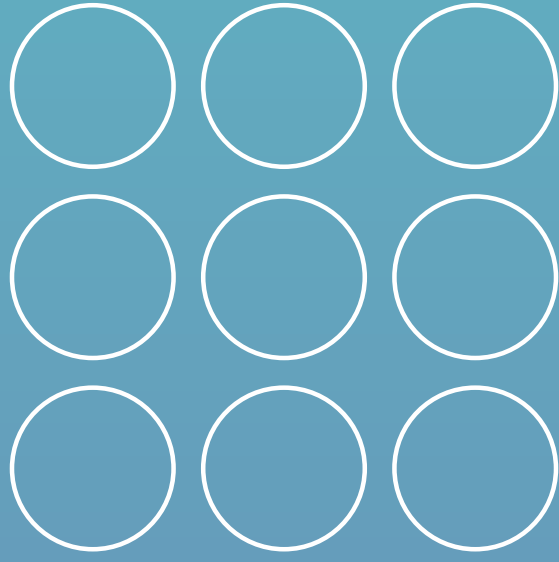
**Sven Wydra**

Project Coordinator

Karlsruhe, September 2017



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# EXECUTIVE SUMMARY

## BACKGROUND AND AIMS OF THE PROJECT

Industrial Biotechnology (IB) is a key enabling technology, supporting the transition from a fossil-based to a bio-based economy, contributing to a circular economy. It innovates especially the process industry by providing higher resource-efficient and climate-friendly production processes, as well as substituting environmentally harmful substances. However, the field of IB is heterogeneous, e.g. with respect to the stage of maturity, the type and applications of products or processes and the amount and type of biomass feedstock needed. In order to reduce uncertainty about the future development of IB and to harness its potential for the economy and society, the objective of PROGRESS, funded under the Horizon

2020-LEIT Work Programme of the European Commission, was to support and accelerate the deployment of IB in the EU by identifying high-value opportunities and to propose actions to address them successfully.

Several analytical steps including foresight, modelling and stakeholder consultations were carried out in the project. In particular, analyses of the current status of Industrial Biotechnology and future scenarios for six selected value chains were conducted: Lignocellulosic ethanol, bio-based plastics, enzymes, production of biopharmaceuticals, biotechnologically produced flavours and fragrances, microbiomes for food and healthy nutrition.

## STATUS TODAY AND FACTORS FOR THE FUTURE

In a nutshell, the current situation can be summarised as follows:

- The EU has a strong technology base in IB.
- Although adopting biotechnological methods in industry is and will in the near future remain confined to a few industrial sectors and firms with specific competencies, it must be emphasised that the share of value added by biotechnological production is actually much larger. IB has a clear enabling character for a broad range of industries through the provision of services, processes and products usually based on renewable resources.
- Internationally competitive innovation and commercialisation activities in IB are geographically highly concentrated within the EU: Some countries with world-leading activities in many segments as well as countries with selected priorities and activities in IB drive the future development.

The following factors significantly influence the future development of IB in Europe:

Advanced technologies play a crucial role in advancing IB further and in maintaining international competitiveness, both in research as well as in commercial production. Key trends comprise the increasing integration of biotechnology with other key enabling technologies for problem solving. Due to the need to increase biomass feedstock supply for IB without compromising food production, many new research topics arise from exploiting non-food feedstocks for IB, such as lignocellulose, side-streams in industrial production, waste and CO<sub>2</sub>. Technological improvements will be mandatory, but alone are not sufficient for a wide uptake of IB. Commercialisation activities are impaired by missing price competitiveness of IB processes and products compared to established fossil-based ones. In particular, the current low oil price is hampering the demand for those

bio-based products that heavily depend on feedstock prices (e.g. biofuels, bulk chemicals of drop-in character). Awareness of the environmental, economic and social benefits arising from IB processes and products and trust in the claimed benefits by the public as well as decision makers are necessary preconditions for the successful commercialisation of IB. Generally, the overall public attitude towards IB products is mostly positive, but may differ substantially depending on the target group, product segment, application, technologies used and perceived benefits. The significant contribution that IB could have towards sustainability and a circular economy is gaining importance and is key to the legitimacy of public and policy support. Product regulations have a significant impact on growth opportunities and innovation incentives in many IB segments. The present overall regulatory landscape for the whole IB is neither positive nor negative, but differs significantly between value chains.

## RECOMMENDATIONS

Key actions to shape general framework conditions for fostering the enabling role of IB across different sectors and value chains in the EU are the following:

### Supporting advanced technologies

R&D&I support for adopting and using advanced technologies is important for all value chains. In addition to value chain-specific R&D&I needs, cross-cutting research issues comprise pre-treatment of biomass, optimisation of production organisms and production processes, and the integration of life science technologies with other technologies (e.g. “green chemistry”, digital technologies/bioinformatics). Support of R&D&I should ensure that leading EU countries in IB stay at the cutting edge of international R&D&I and diversify into emerging IB industrial sectors while helping EU countries emerging in IB to adopt these technologies.

### Sustainable feedstock supply

The increasing industrial demand for biomass has to be satisfied without negative environmental and societal impacts. Therefore, the prioritisation of using biomass

for food (“food first”) has to be operationalised and implemented in practice. The following combination of approaches should be pursued: to raise the technological potential by using all fractions of food biomass and non-food biomass. To raise the economic potential, a monitoring system is needed which allows a consistent uniform assessment across the EU countries regarding the amount of available biomass potential and type of feedstock. Moreover, sustainability of biomass production has to become a key priority, requiring substantial efforts to establish internationally standardized approaches and tools to assess sustainability, and to certify sustainable biomass production schemes.

### Multidisciplinarity of skills

The multidisciplinary nature of IB requires teams of highly specialised experts. In order to interact synergistically and effectively in these teams, experts should not only be highly competent in their own field of expertise, but also have a basic understanding of other competencies, including business aspects. Additional efforts in education and qualification are needed to ad-

dress these needs (e.g. adaptations of curricula, specific Public Private Partnerships with training possibilities, cross-country exchanges of expertise).

#### **Transfer of R&D results into commercialisation**

As IB matures, the need to address the various – and well-known – barriers for commercialisation becomes even more pressing. Existing efforts to overcome these barriers have to be continued with a special focus on fostering competencies in commercialisation-relevant expertise (e.g. scaling up, market intelligence) of stakeholders, fostering the start-up scene and improving access to capital-intensive infrastructure. The latter comprises the set-up of pilot and demonstration plants as well as a more efficient network of existing infrastructures, which avoids duplicating activities, but rather offers synergetic services.

#### **Address public perception and acceptance**

Public concerns should be actively addressed in constructive stakeholder dialogues and public participation in order to develop commonly shared future visions for IB. It should be agreed on how IB R&D&I strategies should be tailored so that they are in concordance with the requirement of the relevant UN Sustainable Development Goals and the contribution of IB to achieving these goals is maximised. Moreover, value chain-specific critical issues of public perception and consumer acceptance should be addressed.

#### **Demand pull**

A higher demand pull could enforce the development of IB. The uptake of IB in the business-to-business sectors and public procurement of bio-based products should be supported for products and processes with improved sustainability. This requires substantial efforts to develop and implement standard sustainability criteria, assessment schemes as well as certificates and labels. Moreover, in order to also address the needs of the general public and end-users, education and dialogue measures should be implemented which facilitate an informed purchase decision. They should be specifically tailored to the needs and expectations of different target groups, using different communication channels.

#### **Co-evolution of regulatory environment and S&T development**

The co-evolution of S&T developments with regulations is of critical importance in highly innovative fields such as IB. The challenge is to align R&D&I policy with regulatory activities, both with respect to timeline and areas incentivised. Thereby, the regulatory environment has to balance incentives for industry and R&D&I with the interests of the public and consumers, thus contributing significantly to establishing trust and credibility and shaping the implementation of IB according to the UN Sustainable Development Goals.

#### **Collaboration along value chains**

Collaboration of actors from different stages of the value chain in R&D&I is a prerequisite for successfully transferring R&D results to commercialisation. Specific attention should be given to intensifying the cooperation between EU countries and sectors with a complementary strategic focus (e.g. biomass production and biomass conversion) and to establishing or strengthening emerging networks in emerging value chains (e.g. microbiomes) or in existing ones, where novel approaches enable an innovation push (e.g. Flavours and Fragrances).

#### **Collaboration across European countries**

Intensified collaboration between actors from different EU countries and integration of more countries into the various value chains should be strived for in order to build up critical masses, to combine complementary competencies and resources and to achieve a higher quality of R&D&I. On the one hand, collective efforts should be made to enable leading countries in IB to join forces to maintain their international leadership. On the other hand, R&D&I policy will have to be closely linked to cohesion policy in order to increase the potential contribution from EU countries that presently are only active in selected fields of IB. To overcome barriers for co-operations between leading and emerging IB countries, financial incentives and other forms of support in terms of providing information about competencies and potential synergies between European actors are needed.





# 1 INTRODUCTION

Industrial Biotechnology (IB) has a significant impact on the European economy. IB enabled employment in Europe has been growing significantly in the last ten years and exceeded 200.000 jobs in 2013 (van de Velde et al. 2015). Furthermore, it is expected to continue growing in the future (EuropaBio 2016). Biotechnological production processes in IB offer numerous technological and economic advantages compared to classical chemical syntheses, for example products of superior quality or with novel functions, higher resource-efficient production processes and substitute environmentally harmful substances. Moreover, biotechnological production processes typically use renewable, non-fossil raw materials. In addition, IB enables the elaboration of products that are biodegradable or amenable to be reused or recycled. Therefore, IB products can contribute to cascade use and hence to circular economic concepts related to the bioeconomy, leading eventually to lower material consumption.

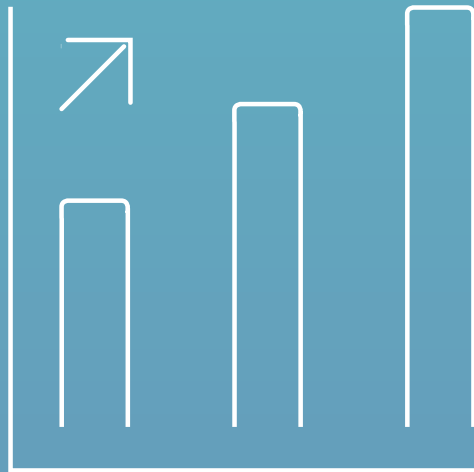
Europe has a strong technology base in IB. However, there is high uncertainty how to deploy IB and how to harness its potential for the economy and society. Especially, the contribution of IB to mitigate climate change and to achieve the UN Sustainable Development Goals is important.

Hence, the aim of PROGRESS is to support and accelerate the deployment of IB in the EU industry by identifying high-value opportunities for IB, related Research & Development & Innovation (R&D&I) needs and proposing necessary actions to address them.

The following analytical steps were carried out in the project:

- assessment of drivers for IB: market developments as well as innovation potentials of IB,
- assessment of current status of IB and future scenarios for six selected value chains, all representing high-value opportunities for IB,
- system dynamics modelling of two value chains to understand dynamic developments in IB,
- elaboration of potential common goals across the EU and identification of key opportunities and gaps for IB in Europe,
- providing recommendations for fostering the development of IB in the EU.

The following pages of this brochure will introduce the main findings of the project and give an overview of the key messages for the IB community in the EU.



# 2 TRENDS IN R&D&I, PRODUCTION AND MARKETS

## RESEARCH, DEVELOPMENT AND INNOVATION (R&D&I)

IB is one of the key enabling technologies (KETs), with a strong potential to facilitate new products and processes and to transform existing markets. IB can generate new growth, spur innovation, increase productivity, tackle environmental and climate challenges, and give rise to new applications, which contribute to opening up entirely new markets, or at least to shift product quality in existing markets to higher levels (EC 2009). As a consequence “the importance of staying competitive in these technologies cannot be overstated” (EC 2010, p. 9).

Moreover, IB is a key source of innovation in the concept of the bioeconomy, the gradual replacement of fossil resources by biological resources in order to contribute to societal goals such as mitigating climate change, lowering resource use, increasing food security, generating economic growth and securing jobs.

Significant efforts to foster R&D activities in IB in particular under the umbrella of the concept of the bioeconomy already exist. Examples are the funding of biotechnology projects in the LEIT in Horizon 2020, the establishment of the Public-Private-Partnership or the encouragement of specialisation strategies in the context of the European Structural Investment Funds (ESIF). Also in more and more EU countries bioeconomy

strategies have been elaborated and are in the process of being implemented (JRC 2017).

A comprehensive monitoring system for the transition from a fossil to a bio-based economy is still in the process of development. Therefore, EU-wide and comparable figures on R&D&I activities in IB are not yet available. However, our evidence suggests that IB innovation activities have been growing smoothly since 2005,<sup>1</sup> as can be deduced from patent statistics (Figure 1).<sup>2</sup>

Central European countries are dominant in patenting, in particular the larger countries Germany, UK and France: they cover about 75 per cent of all patent applications. The different EU regions develop in a similar way, with a slight upsurge of the shares of the Northern, Eastern and Southern European countries between 2005 and 2014. A few countries show a significant specialisation in IB such as the Netherlands, Belgium and Denmark (data not shown).

<sup>1</sup> The small downturn around 2010 reflects the impacts of the economic crisis on patenting activities.

<sup>2</sup> Central Europe comprises AT, BE, DE, FR, GB, IE, LU, NL; Eastern Europe comprises BG, CZ, HU, HR, PL, SK, SI, RO; Northern Europe comprises DK, EE, FI, LV, LT, SE; Southern Europe comprises CY, ES, IT, GR, MT, PT.

## PRODUCTION

IB is applied in many different products, processes and applications. The KETs Observatory estimates that production enabled by IB exceeded 100 billion euro in 2013 (van de Velde et al. 2015). However, it provides no specific information about the numbers or proportion of firms directly involved in IB production.

Therefore, the PROGRESS project takes an additional perspective by analysing the use of specific technologies within production at firm level. This provides an interesting picture of the adoption patterns for biotechnological and genetic engineering methods as tools within the production. Based on data from the European Manufacturing Survey (EMS) with a sample of over 3,000 firms from eight European countries (Germany, Austria, Spain, Croatia, Denmark, the Netherlands, Switzerland, Republic of Serbia), a reliable picture can be drawn of the share of the companies in an industrial sector that have adopted biotechnology (e.g. biocatalysis, bioreactors) and genetic engineering methods in their production processes, or plan to do so in the near future.

### Level of adoption and diffusion over time

An overall analysis of the eight selected countries shows that a significant adoption of biotechnology and genetic engineering methods in production processes started in the mid-1990s. This share is likely to increase in the coming years, as a significant number of firms have plans to introduce biotechnological or genetic engineering methods in their production processes.

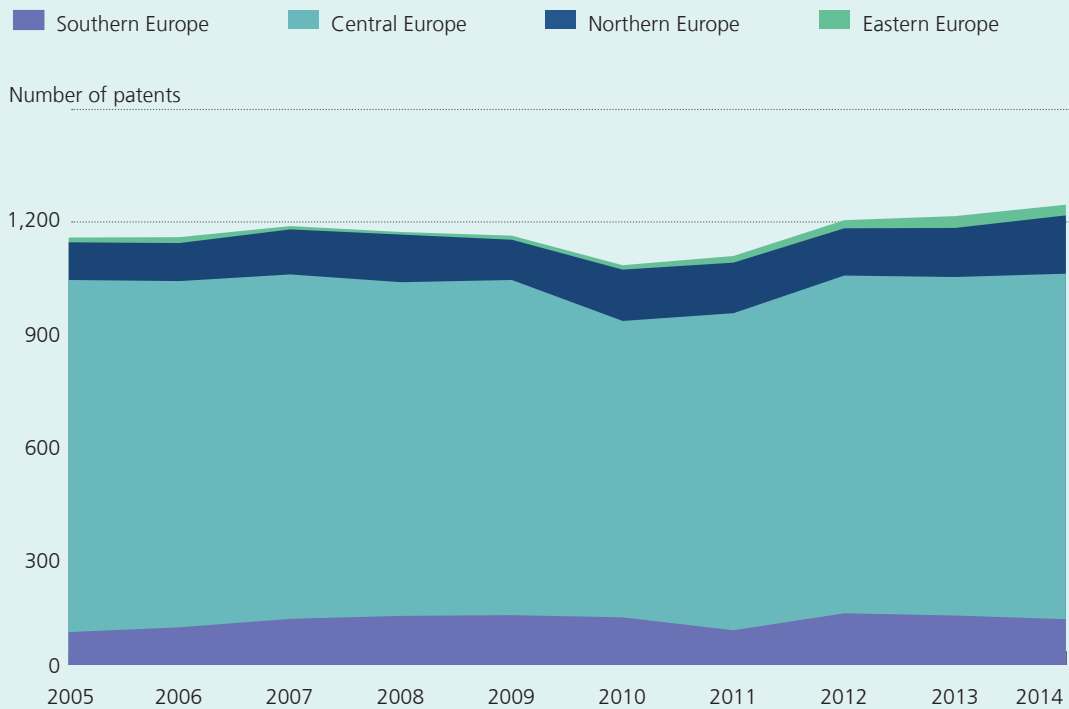
### Diffusion by sector and firm size

The differentiation by sector (Figure 3) shows that the leading sectors in respect to deployment of biotechnological production are the chemical industry (including the pharmaceutical industry) and the food sector. In addition, the use of biotechnological methods in production is widely dispersed over a broad range of sectors, albeit on a low level.

Figure 4 shows that the adoption rate differs considerably between firms of different sizes: Mainly large manufacturing sites use these technologies. The exception of the rule is the food sector where also small and medium-sized companies use biotechnological production methods.

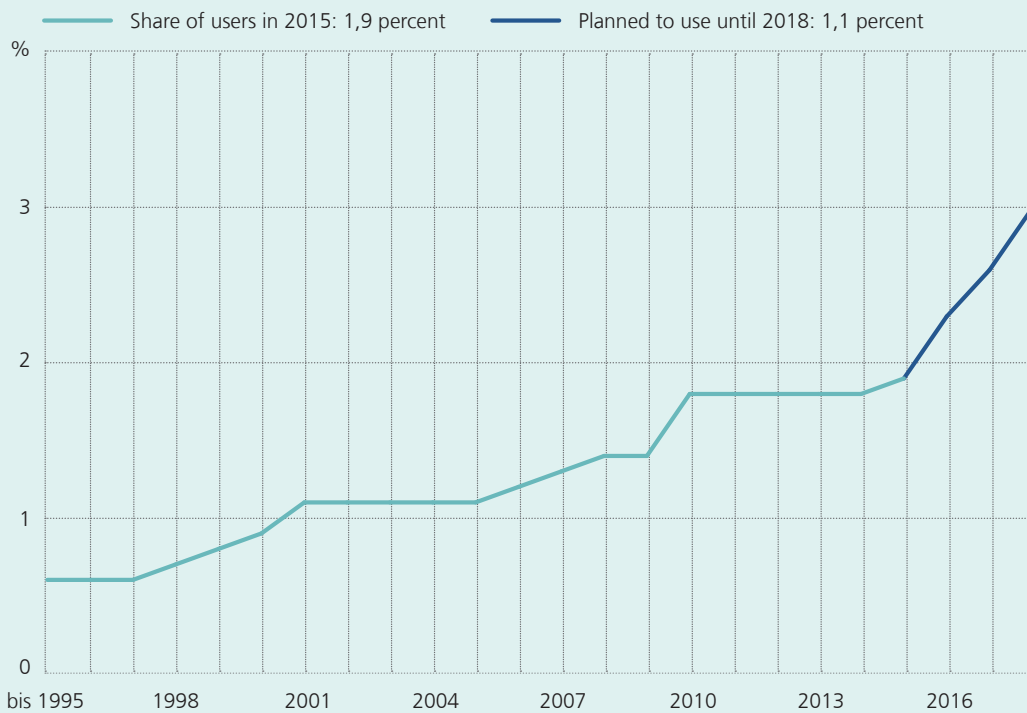
The fact that mainly large manufacturing sites use biotechnology in their manufacturing processes reflects first of all the uniqueness of several product groups (e.g. biopharmaceuticals) and secondly the need for dedicated production facilities, which have been specifically designed for biotechnological production processes with related high investments. Thirdly, the interdisciplinary competencies required to successfully develop and scale-up a process from the laboratory to commercial production. As biotechnology has its roots in the production of fermented food, it is no surprise that in the food industry food companies of all sizes use biotechnology.

**Figure 1: Patents in industrial biotechnology between 2005 and 2014 in European regions**



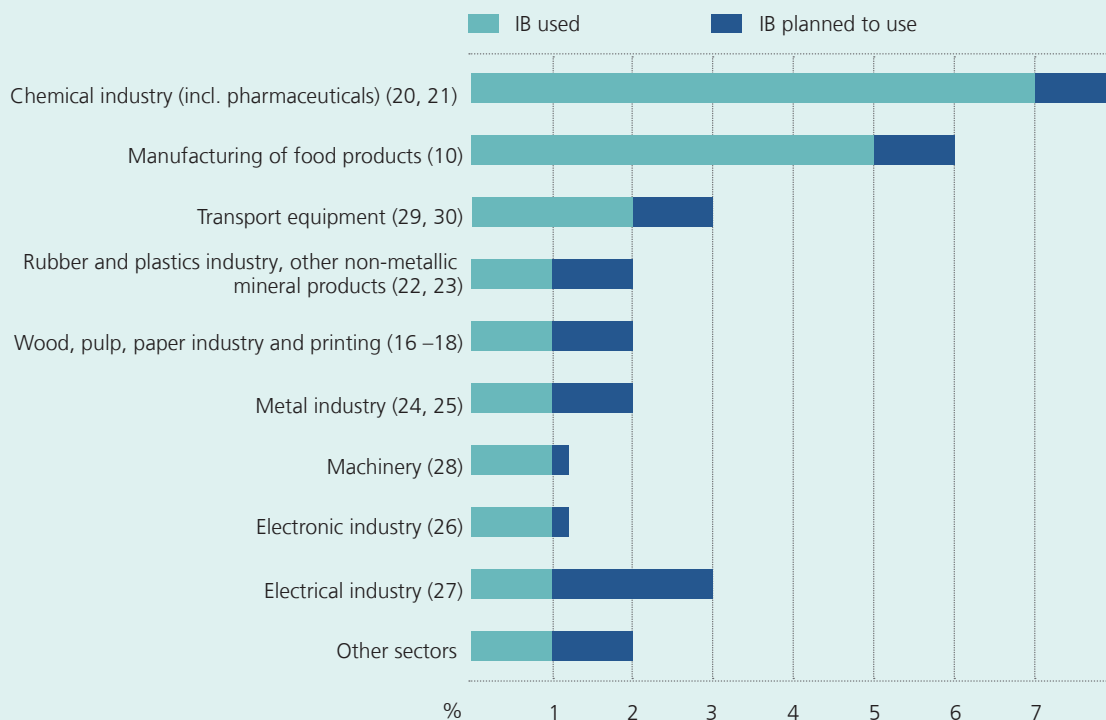
Source: Fraunhofer ISI based on World Patent Index

**Figure 2: Shares of manufacturers using biotechnology or genetic engineering methods in production or plan to do so until 2018**



Source: European Manufacturing Survey 2015, eight countries, compiled by Fraunhofer ISI, weighted data

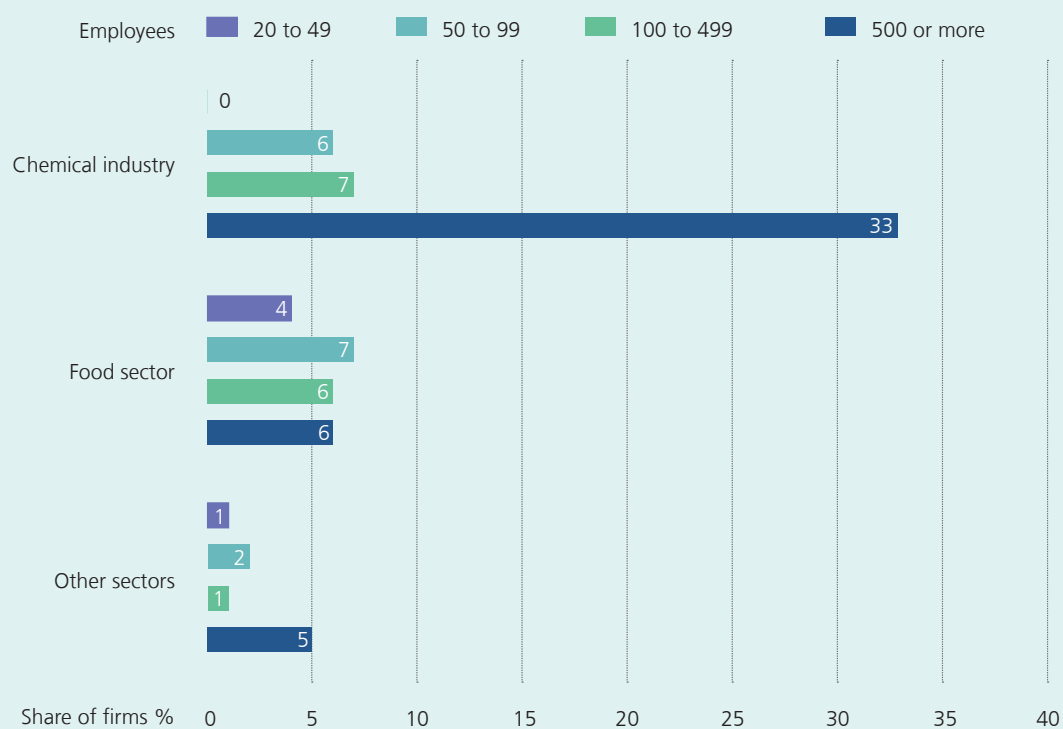
**Figure 3: Shares of manufacturers using biotechnology or genetic engineering methods in their production processes or plan to do so until 2018, by sector**



Note: figures in brackets refer to NACE, rev. 2

Source: European Manufacturing Survey 2015, eight countries, compiled by Fraunhofer ISI, weighted data

**Figure 4: Share of manufacturers using biotechnology in production, by company size**



Source: European Manufacturing Survey 2015, eight countries, compiled by Fraunhofer ISI, weighted data

These findings reflect:

- the enabling character of industrial biotechnology, which is relevant for a broad range of industrial sectors,
- that industrial biotechnology is traditionally and firmly rooted in the production of fermented food and beverages (e.g. milk products, bread, beer, wine) and therefore is used in food companies of all sizes,
- that the chemical industry holds a central role in the deployment of biotechnology for industry: This sector is leading in the biotechnological production of a broad range of different product groups of B2B and B2C products, from bulk to specialty and fine chemicals, of which some can only be produced by biotechnological methods (e.g. biopharmaceuticals). Moreover, large chemical companies have built up the interdisciplinary competencies required to successfully develop and scale-up a process from the laboratory to commercial production, and have the financial capacity to set up dedicated production facilities, which have been specifically designed for biotechnological production processes with related high investments. Finally, the chemical industry, together with the manufacturing equipment industry, is the main innovator for downstream sectors, (e.g. food industry, pulp and paper industry, textile industry) and therefore has a gatekeeper function for the deployment of industrial biotechnology in other industrial sectors.
- that SMEs, although they do not have a biotechnological production,<sup>3</sup> fulfil important roles in the value chain as they often provide biotechnological R&D services or test cutting-edge innovative approaches in early R&D and pilot stage levels which are later taken over by larger firms and developed to production maturity.

All in all, these results underline that IB will in the near future mainly be applied in firms with specific competencies, concentrated in a few industrial sectors. Although the number and share of the companies in the respective sectors may seem to be comparably small, it must be emphasised that the share of value added by biotechnological production may be much larger. Moreover, IB has a clear enabling character for a broad range of industries through the provision of critical services, processes and products in often long value chains, and through its potential to give rise to new value chains usually based on renewable resources.

<sup>3</sup> In statistics, firms without own production activities are classified in NACE codes which refer to R&D services. These codes are, however, not covered by the EMS.



## TRENDS AND CHALLENGES IN INNOVATION AND COMMERCIALISATION

While the presented numbers imply a steady, continuous development of IB, technological advances, framework conditions and challenges around IB evolve dynamically. Hence, it is crucial for the competitiveness of the EU to address the following developments and challenges:

### Advanced technologies

Advanced technologies, such as synthetic biology, genome editing, next generation sequencing etc. are perceived to have a high potential for the commercialisation of bio-based products. They may strongly contribute to reducing the costs and environmental impact of IB processes as well as enabling the provision of new functionalities. Moreover, the conjunction of biotechnology with different processing technologies & sciences (e.g. nanotechnology, information technology, chemical catalysis) as well as the use of biotechnology in fossil-based processes becomes of key importance.

### Skills

Industrial biotechnology is a highly specialised area with a need for a specifically skilled workforce (Bio-TIC 2015). It needs to change dynamically with new science and technology developments as well as increasing commercialisation activities. The multidisciplinary nature of industrial biotechnology requires that experts specialised in one field have additional understanding of other competencies, for example molecular biologists of bioinformatics or process issues and vice versa bioinformaticians or process engineers of biology issues. Moreover, specific skills for scaling-up processes from lab to production as well as business skills for commercialisation are increasingly needed.

### Technology transfer

While an increasing number of R&D projects gets to the mature stage, the transfer of innovations from R&D settings to commercial applications in Europe is gaining importance. Typical problems at that stage are becoming increasingly crucial for the whole value chain, such as:

- the high complexity of scaling up biotechnological solutions,
- the need for closer collaboration between academia and industry,
- unclear market perspectives from the view of potentials investors and consequently the lack of funding possibilities for pilot and demonstration activities,
- the lack of skilled people in scale-up (see "skills" above).

### Use of non-food feedstock

It is widely assumed that lignocellulose, side-streams in industrial production, waste and CO<sub>2</sub> bear a high, yet untapped potential of non-food feedstocks for IB. Technological and logistic challenges, including the heterogeneous and variable composition of many of these feedstocks, as well as their wide dispersal, need to be addressed in order to valorise these feedstocks.

### Collaboration across European countries

Currently, innovation and commercialisation activities in innovative biotechnology products and processes are geographically highly concentrated. This is because European regions are highly heterogeneous with respect to their technological capacities and resources (skills, biomass, etc.) in IB. Higher collaboration between the EU countries and integration of more countries into the various value chains may lead to a build up of critical masses and a better use of complementary competencies and resources that eventually leads to a higher quality of R&D&I. Moreover, a wider spread of economic and societal benefits of IB may be achieved.

Specific challenges lie in the appropriate combination of scientific-technical excellence and geographic coverage, pointing at the need for "smart specialisation" of regions and mutual learning, rather than supporting "me-too"-activities and duplication of efforts.

### Portfolio of IB products, processes and services

The potential product portfolio for IB ranges from high vs. low value products, from high to low volume products, from drop-ins (meaning that the bio-based

products have the exact same chemical structure as the fossil-based equivalent) vs. non drop-ins with new functionalities etc. It is controversially discussed whether the EU should take a more explicit focus on selected product segments. On the one hand commercialisation of the different segments is often highly dependent on external factors, such as resource prices or world-wide policies, which can hardly be influenced by EU policy. For example, the current low oil price is hampering the demand for those bio-based products that heavily depend on feedstock prices (e.g. drop-in chemicals, biofuels). On the other hand, only a broad product portfolio can address the many societal goals that are to be pursued by IB and is robust and flexible enough to cope with unfavourable or changing external factors and frame conditions.

#### **Sustainability as overarching goal**

As IB activities are understood to be an important part of the transition process to a sustainable bioeconomy, they are expected to contribute significantly to the respective Sustainable Development Goals of the UN. On the one hand, this implies that additional efforts must be taken for the “greening” of industrial biotechnology products and processes, especially by increasing their resource efficiency, minimizing emissions and striving for a Circular Economy. On the other hand, this has to be complemented by a broader perspective which takes

also for example the social dimension of sustainability into account. The difficulty is to assess all dimensions of sustainability through all segments of the value chain of bio-based products (from biomass production to end-use). The lack of a widely accepted mechanism to assess and confirm sustainability is still an important barrier (OECD 2011).

#### **Acceptance and perceived benefits of IB**

Awareness of IB products and trust in the claimed benefits by the general public as well as decision makers are necessary preconditions for the successful commercialisation of IB. Generally, the overall public attitude towards IB products is assumed to be mostly positive, but may differ substantially depending on the target group, product segment, application, technologies used, or benefits perceived: For example there is scepticism towards some advanced technologies and applications (e.g. for food, textiles). Moreover, for many product segments the “willingness-to-pay” of consumers for more healthy, more sustainable, natural products is still limited or restricted to small consumer groups. An important reason is the lack of awareness of the existence of IB products and in particular their benefits to consumers. While there are single best-practice cases, it is challenging to provide information and to communicate benefits for a broader range of products and processes.



# 3 VALUE CHAINS: CURRENT STATUS AND FUTURE SCENARIOS

## PURPOSE AND SELECTION

The field of Industrial Biotechnology is highly heterogeneous, for example with respect to the stage of maturity in innovation and commercialisation, the type of products or processes and their respective uses and applications, the amount and type of biomass feedstock needed and the level of competition with existing (fossil-based) products and processes. Against this background, a value chain perspective was chosen in the PROGRESS project. This perspective allows the differentiated, but integrated analysis of market needs, innovation potentials and the identification of (missing) European competencies and concrete bottlenecks affecting innovation and commercialisation. Six value chains with a high potential for innovation and for significant economic impact were selected which represent the heterogeneity of IB.

The selected value chains are:

- Lignocellulosic ethanol
- Bio-based plastics
- Enzymes (with specific reference to laundry and dishwasher applications)
- Production of biopharmaceuticals
- Biotechnologically produced flavours and fragrances
- Microbiomes for food and healthy nutrition

For each value chain, the current status was characterised and several scenarios of possible future developments of the respective value chain until 2025–2030 were elaborated. The results are summarised in Tables Annex 1 and 2. In the following, the different value chains are characterised and key insights of the cross-value chain analysis are presented.

## LIGNOCELLULOSIC ETHANOL

### Definition and delineation

Lignocellulosic ethanol, also often called second generation ethanol, refers to ethanol produced from non-food-crops with a high lignocellulose content, such as agricultural residues (e.g. straw, corn stover), other lignocellulosic raw materials (e.g. wood chips) or energy crops (e.g. miscanthus, switchgrass). In the PROGRESS analysis, the focus lies on the use of ethanol as a fuel, whereas its use as a chemical intermediate was not included in the analysis.

The value chain represents a potential mass-market product from a non-food feedstock, targeted at end consumers. It may represent a pilot product produced from lignocellulose, thus opening up this feedstock source also for other (non-fuel) bio-based products.

### Current status in Europe

Despite more optimistic expectations in the past, lignocellulosic ethanol is still in its early commercialisation phase. Globally, there are several first-of-its-kind commercial-scale lignocellulosic ethanol plants that represent around one per cent of the production capacities of total first and second generation ethanol. While European actors possess the technological capability to compete with other world regions, the EU has yet only a minor role in ethanol production. Only one full-scale commercial plant for lignocellulosic ethanol is operative

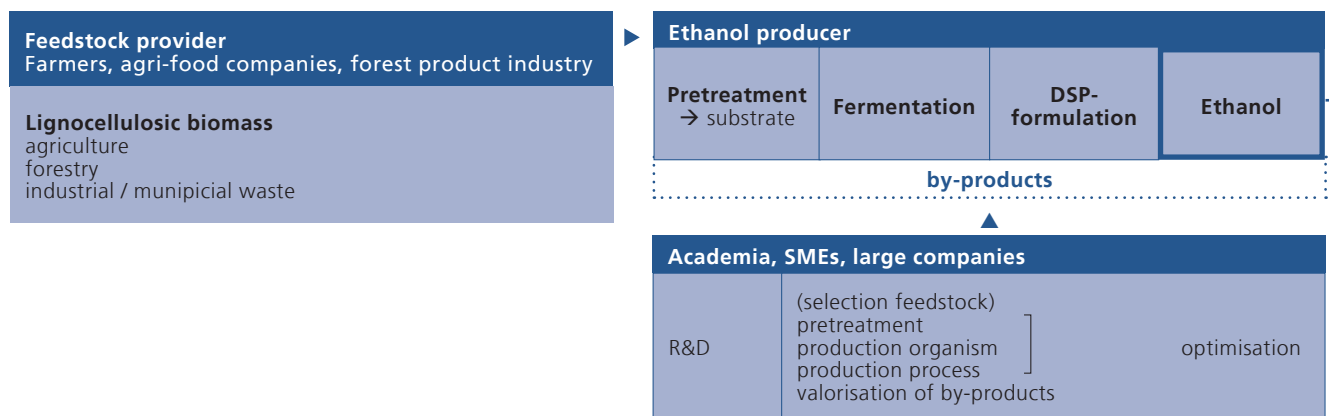
in the EU (Beta Renewables in Italy) and the European share of production lies beneath ten per cent.

Because of missing cost competitiveness compared to fossil fuels, the ethanol market is mainly driven by the obligation of the Renewable Energy Directive. According to the current regulation, incentives for advanced biofuels such as lignocellulosic ethanol are small. There is no obligatory mandate specified for this kind of biofuel, only an indicative target of 0.5 per cent of total fuels. Moreover, there is a double-counting system for advanced biofuels, meaning that advanced biofuels count twice to fulfil the mandated quota for biofuels.

### Potential future developments and drivers

On the one hand, significant R&D efforts will be required in order to further improve the cost competitiveness and the environmental performance of second generation ethanol. This includes the optimisation of the whole production chain from feedstock logistics, to pre-treatment, more efficient enzymes and production organisms. On the other hand, as long as fossil oil prices remain on the current low level, these efforts will be necessary, but not sufficient to gain a needed market share for second generation ethanol. Rather, production and market penetration will depend heavily on the framework conditions set by policies in order to create a long-term and stable outlook. This is required

Figure 5: Value chain for lignocellulosic ethanol



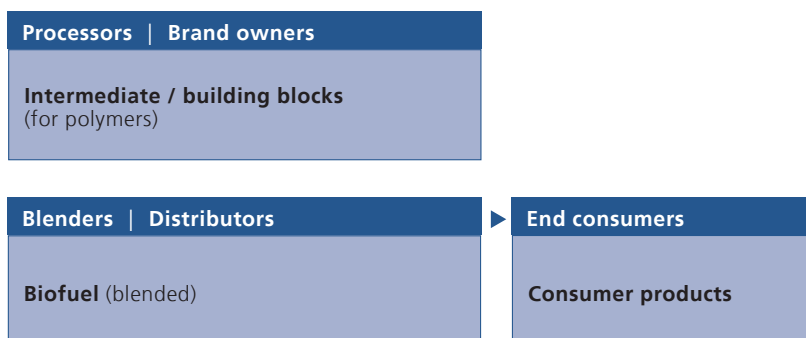
to support significant investments in new production facilities. According to expert opinions, a policy mix will be necessary to build up a whole ecosystem and stimulate investments into new production facilities: in this mix, an amendment of the Renewable Energy Directive (RED II) will be required,<sup>4</sup> but must be complemented by supportive framework conditions for further investments.

If a considerable number of production facilities are built, significant scale and learning effects are expected, possibly leading in the longer run to a higher cost competitiveness to other bio- or fossil fuels (see Box 1).

<sup>4</sup> A recent proposal by the European Commission aims at switching from first to second generation biofuels, by introducing a cap for first generation biofuels at 3.6 per cent and a mandate for second generation biofuels of 3.8 per cent. See [http://ec.europa.eu/energy/sites/ener/files/documents/1\\_en\\_annexe\\_proposition\\_part1\\_v6\\_0.pdf](http://ec.europa.eu/energy/sites/ener/files/documents/1_en_annexe_proposition_part1_v6_0.pdf)

An issue that was controversially discussed by experts involved in the PROGRESS project is the overall availability of lignocellulosic feedstock. Knowledge gaps regarding the availability of the required amounts, possible unintended and harmful environmental impacts, as well as unintended impacts on other markets related to this feedstock exist and should be closed in order to provide a sound knowledge base for strategic and political decisions.

Moreover, the PROGRESS scenarios showed that such a dynamic development of lignocellulosic ethanol is just one possible future path, which could be supported by favourable policy decisions for lignocellulosic ethanol. Should the support by policy makers be weak or the policy mix incomplete, either stagnation or the establishment of lignocellulosic ethanol in niches may occur. For example only in certain regions with favourable feedstock supply and/or supportive regional political conditions, the lignocellulosic market is established.



## Box 1: System dynamics modeling of lignocellulosic ethanol demand

To analyse the dynamics of second generation ethanol demand based on interactions of policy incentives and learning effects as a result of production capacity changes, a System Dynamics model was elaborated for the ethanol value chain in the PROGRESS project. Main features of the model are learning effects due to the expansion of production capacities, leading to lower process costs, which cause a feedback loop to higher demand via lower prices. Moreover, the impact channels of various policy instruments are considered. With the aid of this model it is analysed how the dynamics of policies and learning effects influence the demand for lignocellulosic ethanol in Europe. Therefore, the qualitative scenarios have been simulated:

### Stagnant development scenario

The current indicative quote of 0.5 per cent for lignocellulosic ethanol is achieved in 2030, no further political measures from the supply or demand side to foster commercial activities. Market growth is limited, only low learning effects are achieved and costs remain high.

### Partial established production scenario

An obligatory mandate of 1.8 per cent was assumed. Considerable cost decreases by learning effects are achieved, but no cost competitiveness compared to fossil fuel or first generation ethanol occurs.

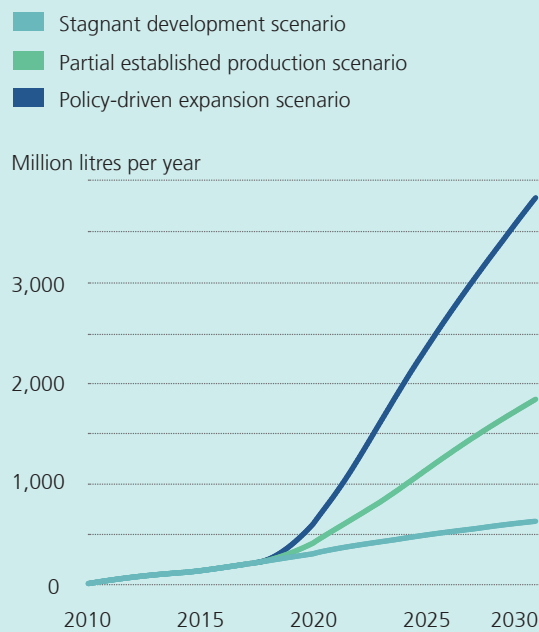
### Policy-driven expansion scenario

Strongly supportive policy mix with an obligatory mandate of 3.6 per cent, financial support to build up new commercial production facilities. As a result, markets increase considerably, while costs and mar-

ket prices decrease significantly via learning effects despite higher feedstock prices.

The results on market demand in the EU until 2030 are summarised in Figure 6. The volumes in the respective scenarios are close to the assumed quotas, as price competitiveness will be reached only at the end of the period for the policy-driven scenario.

**Figure 6: Simulation of market demand for lignocellulosic ethanol in the EU until 2030**



Source: Fraunhofer ISI

## Box 2: System dynamics modeling of bio-based plastics demand

System dynamics modelling (see Box 1) is used to simulate the development of bio-based plastics demand. It is assumed that expanding the production capacities will have effects on costs and prices due to scaling and learning effects. We also analysed the effects of the price competition between the bio-based and fossil-based plastics. For the sake of easiness the model logic stands for those segments where bio-based plastics compete mostly directly as a drop-in for certain applications and competition can be approximated by the relative costs between the fossil and bio-based alternative. Three scenarios for bio-based plastics were simulated:

### Baseline scenario

Incremental advances in technology and market awareness as well as no policy changes were assumed. Such a development leads to a rather slow adoption, resulting in limited learning effects. Price competitiveness is not achieved in the regarded time period.

### High oil price scenario

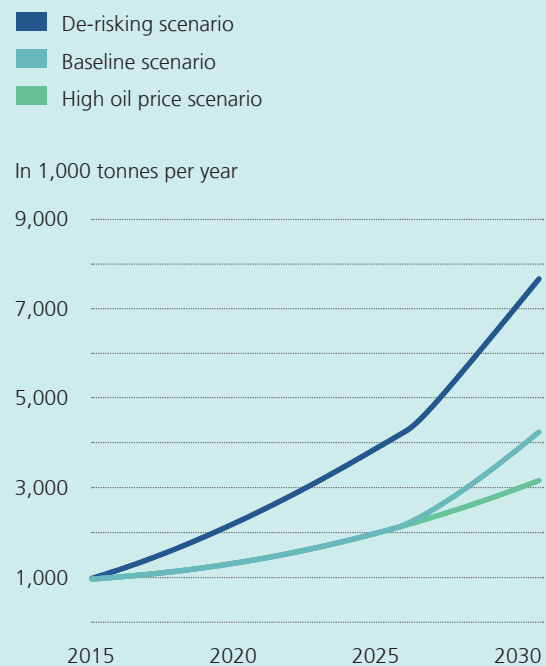
A steady rise of oil prices to 127 US dollars per barrel in 2030 was assumed, together with no significant policy measures. The model shows a modest effect on market demand, and it will take still some years until the cost competitiveness to fossil based products is achieved. Only when the tipping point of price competitiveness has been reached, the market will grow more rapidly.

### De-risking scenario

substantial policy support for commercial activities, tax exemptions as price lowering effects as well as a higher demand by consumers were assumed. The simulation results show a dynamic development by self-reinforcing feedbacks and the market grows significantly over the time period.

The results on market demand in the EU until 2030 are summarised in Figure 8.

**Figure 8: Simulation of market demand for bio-based plastics in the EU until 2030**



Source: Fraunhofer ISI



## BIO-BASED PLASTICS

### Definition and delineation

In the PROGRESS project the term bio-based plastics is used for plastics, which are – at least in part – produced from renewable biomass as feedstock and there is a biotechnological step in the production. They may be biodegradable or durable.

Bio-based plastics represent an important value chain of IB (Figure 7), comprising high-volume products in Business-to-Business and Business-to-Consumer markets, which the public associates with bioeconomy or industrial biotechnology and therefore has a signalling function for other IB-based developments.

### Current status in Europe

Currently, bio-based plastics still represent a niche with a share of about one per cent of the 300 million tonnes of plastic produced annually. However, the market has grown considerably in the last five to ten years at rate of about 20 per cent per year (Bio-TIC 2015; European Bioplastics 2017). European actors are technologically highly competitive; the EU-28 is leading in patenting. Moreover, the EU possesses considerable production capacities with a share of 27 per cent of world-wide capacity. However, there is strong global competition regarding the setting up of new facilities and policy incentives are provided across the world.

### Potential future developments and drivers

While bio-based plastics are established in niches, reducing production costs, increasing contributions to sustainability in non drop-in markets and providing new functionalities are needed for further market deployment. Among the technological challenges are:

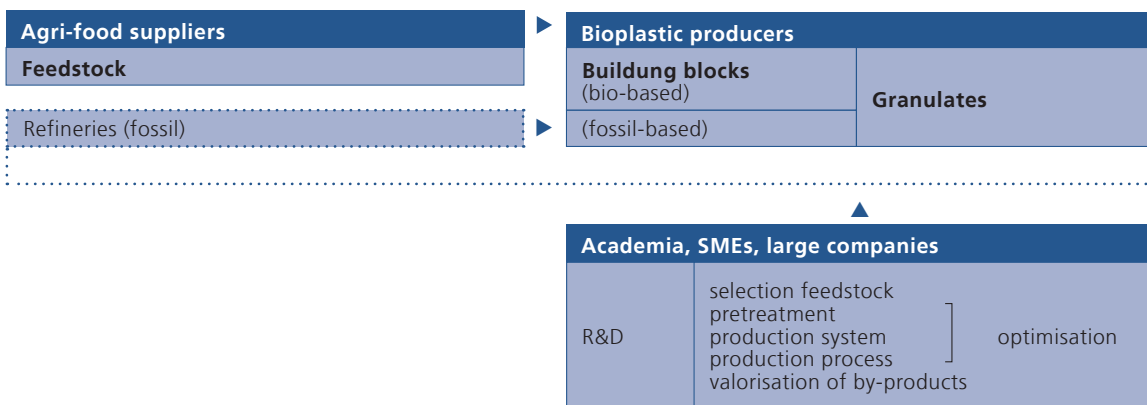
- the setting up of novel bio-based processes for new bio-based plastics building blocks,
- the switch from food to non-food feedstocks,
- delivering constant plastics quality despite fluctuating feedstock quality,
- making production organisms more robust and productive under production conditions,
- avoiding undesired plastics properties (e.g. smell, colour),
- and combining fossil- and bio-based building blocks to plastics with the desired properties.

However, technological challenges are not the main bottleneck for market development. Instead, the following conditions shape market growth profoundly and influence which applications or types of bio-based plastics (e.g. drop-ins, readily degradable plastics, etc.) dominate in the future:

### Policy

According to the bio-based plastics community a policy-mix of different instruments would be needed for a

Figure 7: Value chain for bio-based plastics



significant uptake of bio-based plastics in the coming years. Such a policy-mix would comprise:

- additional funding or tax incentives for private funders of large-scale demonstration plants or commercial production,
- coordinated market pull measures (e.g. public procurement, tax exemptions etc.),
- widespread use of labels and transparent information about bio-based plastics and their benefits (e.g. indicating bio-based content, biodegradability, recyclability).

Moreover, regulation like bans on fossil-based plastics for certain applications may have a major impact on bio-based plastics. The effects will depend on the precise regulation. If, for example, the stricter regulation concerns the fossil resource itself (e.g. ban on fossil-based bags), bio-based products may benefit widely. If, however, plastics that do not degrade readily are banned for certain applications, the bioplastics markets may stagnate, as only few bio-based plastics currently fulfil the latter requirements.

### Customers

The rather low awareness and willingness of consumers to buy bio-based plastics and to pay a premium still presents a major hurdle. Instead, consumer brand companies that aim to build up more sustainable value chains may create a stronger market pull: different brands already use bio-based plastics. Further uptake depends – among others – on which contributions to sustainability can be achieved by bio-plastics, and how they can be measured and transferred into communicable messages.

### Oil prices

An upsurge of oil prices would improve cost competitiveness of bio-based plastics compared to fossil-based alternatives. In particular, drop-ins in mass markets would benefit from such developments because of higher cost-sensitivity. However, it is unlikely that an increasing oil price alone will lead to a highly dynamic market development for the whole bio-based plastics segment if other favourable framework conditions (e.g. policies, higher consumer awareness) are not in place (see Box 2).



# ENZYMES

## Definition and delineation

Enzymes are proteins that act as macromolecular biocatalysts, either in living cells or in isolated form. They are used in a broad range of different industries and applications for biotransformations. Their specific strength – as compared to chemical catalysts – lies in their high specificity and selectivity and their ability to work in ambient conditions.

There is a demand for novel and/or improved enzymes to enable economically competitive and more sustainable solutions and production processes (van de Velde et al. 2013, Adrio 2014). The application of enzymes is a cross-cutting competence which bears a high innovation potential in all industrial sectors of the process industry. Moreover, in these industrial sectors, the use of enzymes is a key enabler for the substitution of fossil resources by renewable feedstock, and for optimising the environmental performance of industrial wet chemistry processes.

Enzymes represent (intermediate) products, which can only be produced by biotechnology. They cover a broad spectrum from low-value-high-volume products to high-value-low-volume products, delivered to B2B and B2C customers. A key characteristic is the high added value in final products which are produced by enzymatic processes.

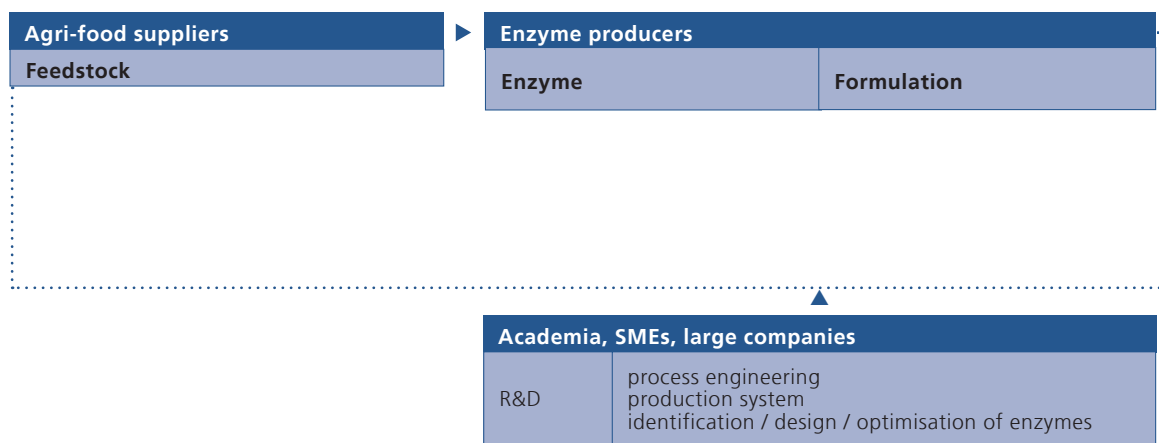
## Current status in Europe

The global enzyme market has grown considerably in recent years. It is estimated that it was over four billion US dollars in 2015 (Grand View Research 2016, Freedonia 2016). Europe is the largest market for industrial enzymes after North America with roughly around 20 per cent market share. A few large firms dominate the market. They have production sites in Europe, the US, Latin America and Asian-Pacific countries. However, Europe is the only net exporter of enzymes. Moreover, a considerable number of SMEs is active as technology and service providers or specialised in screening and designing enzymes.

## Potential future developments and drivers

The global enzyme market will grow, for example Freedonia (2016) expects a market growth of four per cent per year between 2015 and 2020. Main reasons for considerable growth expectations are the increased wealth in developing countries where the emerging middle class shows a high demand for products containing enzymes (e.g. laundry detergents) or bio-based products produced with the help of enzymes. The market in industrialised countries is close to saturation. However, additional market growth and demand pull for enzymes is triggered by framework conditions which favour the substitution of fossil resources by biomass feedstock (e.g. high oil prices), favour resource-efficient industrial production processes (e.g. saving of energy,

Figure 9: Value chain for enzymes

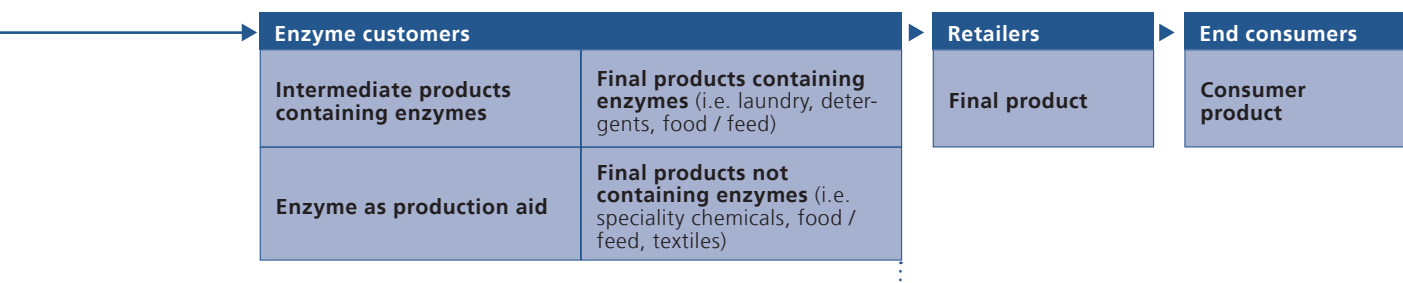


less waste, valorisation of side and waste streams) and which aim at reducing the emission of greenhouse gases.

The presently leading position of European enzyme companies is challenged by emerging players, for example in Asian-Pacific countries, especially in the production of enzymes which have gained commodity status. One possible option for the European enzyme industry to maintain its leading international position is a focus on technological excellence and innovative enzymes, enzyme-catalysed processes and innovative products, eventually specifically tailored to customers' needs. Relevant scientific-technological trends, among others, are innovative approaches in miniaturised high-through-put screening of novel or optimised enzymes, using combinations of evolutionary and rational design for the optimisation of enzymes, establishing alternative production hosts or concepts (e.g. cell-free production) for enzyme production, development of novel enzyme-catalysed process concepts (e.g. reaction cascades, artificial multienzyme complexes, co-factor-dependent reactions), expanding the scope of

industrially relevant enzymes to non-hydrolase enzyme classes, and developing novel enzyme applications. The required scientific-technological competencies are present within the companies or their networks, respectively. However, the collaboration of academia and the enzyme industry in publicly funded projects may be hampered by the reluctance of the enzyme industry: under the current IP frame conditions their freedom to operate may be challenged.

Moreover, alternative scenarios for the enzyme industry are plausible. For example, it cannot be ruled out that the presently positive perception of enzymes and regulations may change in the future. Issues of concern may be for example the use of genetically modified production organisms and genetically engineered enzymes, in particular for applications such as food. In such a scenario the use of enzymes would be limited to certain segments. There would be increasing competition of enzymes with non-enzymatic alternatives on a case by case basis, depending on labelling requirements, public concern and other factors (such as the oil price).



## PRODUCTION OF BIOPHARMACEUTICALS

### Definition and delineation

Biopharmaceuticals are pharmaceutical drug products from biological sources. The focus is on engineered macromolecular products like protein-based drugs (e.g. hormones, antibodies) often of human origin, which are manufactured in specifically engineered organisms. Here we refer to the often-neglected stage of the manufacturing of biopharmaceuticals, either for clinical trials in phase III of the R&D process, or for the commercial production of approved biopharmaceuticals.

The value chain represents very high-value very low volume products which can only be produced biotechnologically and tackle diseases, where usually no alternative treatment options are available.

### Current status in Europe

Production of biopharmaceuticals is well established in the EU: one third of the world-wide biopharmaceutical production capacities are located in Europe. However, Europe is still behind the US, with around one half of the global market. While many EU countries have at least one facility, there is a clear concentration of most facilities towards Western European countries.

The global market of biopharmaceuticals exceeds 200 billion US dollars. The expected annual growth rate for the biopharmaceutical market for the next few years is between 8 per cent and 15 per cent (BioPlan

Associates Inc. 2016; Mc Kinsey & Company 2014) and thus above the average economic growth.

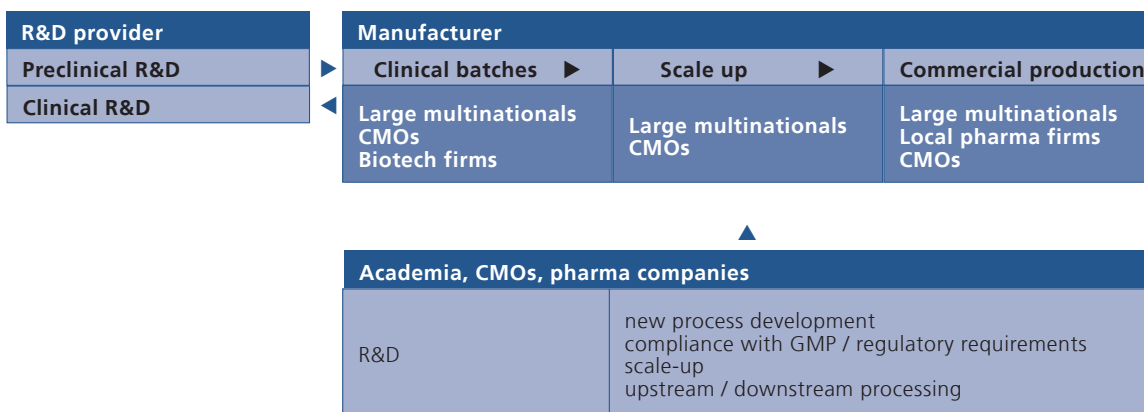
Although lower-end biopharmaceuticals and biosimilars are increasingly manufactured in Asian countries, highly industrialised countries – despite their higher labour costs – still have a competitive advantage in the manufacturing of high-value biopharmaceuticals. This is due to the complexity of the production process, and the regulatory requirement to comply with the highest quality standards in Good Manufacturing Practice. Currently, no finished biopharmaceutical produced in China is allowed to be exported to the EU or the US because of lack of compliance with authorisation requirements (Qing et al. 2016).

### Potential future developments and drivers

The production volume and manufacturing capacity for biopharmaceuticals directly depends on the development of the biopharmaceuticals market. Although this market is likely to grow globally, the overall global biopharmaceutical market will change dynamically with respect to product portfolio, major countries and major industrial players.

Key factors for market expansion are a growing demand in emerging countries with growing GDP and the approval of new biopharmaceuticals, which address unmet medical needs. Factors leading to shrinking biopharmaceutical markets (for European producers) are:

Figure 10: Value chain for production of biopharmaceuticals



- competition from emerging non-EU producers and novel players entering the market,
- reimbursement practices and cost containment regulations of national health care systems,
- the emergence of novel production systems (e.g. cell-free production, production in genetically engineered crop plants/“pharming”),
- competition by emerging novel therapeutic principles (e.g. advanced therapies such as gene therapy, cell-based therapies, immune therapies),
- framework conditions for the development of the biosimilars market.

As a consequence, the product portfolio will undergo dynamic changes: Established biopharmaceuticals are likely to require reduced production volumes. Several developments will contribute to this, including: increased competition by biosimilars, by alternative emerging treatments and novel production concepts. Moreover, the share of stratified biotherapeutic therapies targeted at smaller patient groups (“precision medicine”) increases, so that smaller batches of a larger number of different biopharmaceuticals will be needed. In addition, there is a need to develop novel production processes and concepts for emerging novel therapeutic concepts, such as advanced therapies.

Against this background, there is a high demand for technological advances in biopharmaceutical manufac-

turing in response to the market and product portfolio changes listed above, in order to maintain the competitive edge. In particular have the improvements in the following aspects are a priority:

- process analytical technologies, especially with respect to real-time data and their interpretation, single-cell analysis,
- complementing or replacing the currently dominant “one line, one product” production mode by flexible multiple product operations, for example in the form of single-use bioreactors,
- continuous production of biopharmaceuticals,
- developing novel production processes for novel therapeutic concepts (e.g. gene therapy, immune therapy, patient-individual therapeutics),
- complementing or replacing the currently dominant production in genetically engineered mammalian cell cultures by cell-free production, production in transgenic crop plants or livestock.

All in all, the strong position of EU countries in the production of biopharmaceuticals will be challenged in the future. Maintaining this competitive position will depend on the development of the global biopharmaceuticals market and on technological advances, which keep EU players ahead of competitors.



## BIOTECHNOLOGICALLY PRODUCED FLAVOURS AND FRAGRANCES

### Definition and delineation

Biotechnology provides additional options to produce Flavours and Fragrances (F&F) in addition to the extraction from natural sources and chemical synthesis. They can be biotechnologically produced by biosynthesis (e.g. from sugars), by enzymatic biotransformation of precursors, or by bioconversion. Flavours and fragrances are used in a wide range of different industries such as food & beverages, perfumes and cosmetics, household products, etc. While the use of biotechnology in the F&F market is far from new, it holds a still unexplored potential for biotechnological innovations, which at the same time satisfy the consumer demand for “natural” F&F.

The value chain represents high value low volume products with a broad application potential for which biotechnological production may have competitive advantages over current production methods. Moreover, many F&F substances show additional biological activity and may find additional high value applications as health food ingredients, colours, pharmaceuticals etc.

### Current status in Europe

Although the market for biotechnologically produced F&F has grown steadily in the last decades, it still represents a niche market: with the overall market estimated slightly below 500 million US dollars (TMR 2017), the share of biotechnologically produced flavours is well

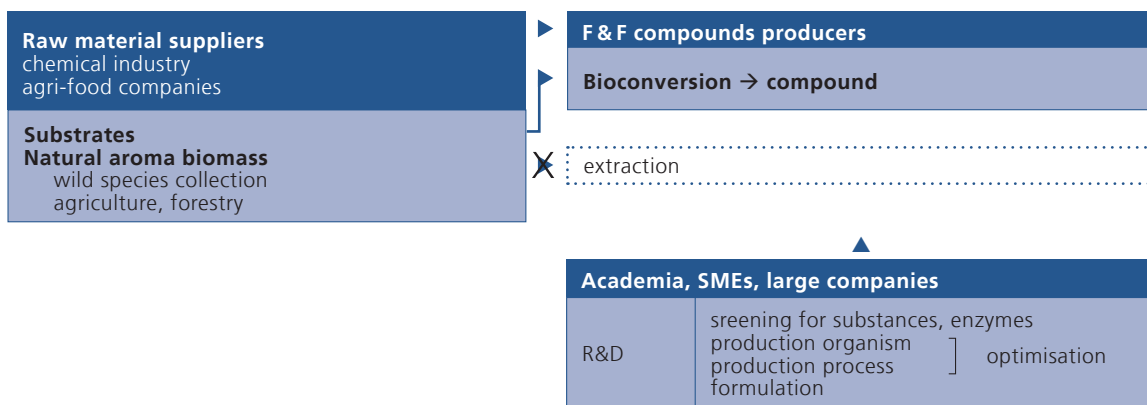
beneath < 5 per cent.<sup>5</sup> The share of biotechnologically produced fragrances is assumed to be lower.

Europe holds a strong position in global competition with a market share of around 30 per cent as well as the presence of some leading globally F&F supplier firms and related biotechnology firms. However, experts estimate strong activities in the biotechnological production of flavours and fragrances in the US and in China, with the EU facing immature networks and collaboration across Europe as well as lack of financing, so that the currently strong position of EU industrial players is challenged.

The key potential value of the biotechnological production of flavours from natural raw materials by microbial or enzymatic methods is – compared to chemical synthesis – in many cases that the respective flavour can be labelled as “natural” in the US and Europe. No specification regarding the exclusion of certain biotech methods (e.g. use of genetically modified organisms) are used. Consumers in general prefer products with “natural” flavours and are more interested in products that contain “natural” rather than chemically synthesised flavours. In addition to these economic reasons, biotechnological production may have advantages as

<sup>5</sup> The Flavours and Fragrances industry is estimated to around 25 billion US dollars globally. The market is almost equally split between Flavours and Fragrances (Tully & Holland 2014).

Figure 11: Value chain for biotechnologically produced Flavours and Fragrances



the availability of the natural source of the flavour may be limited or fluctuating due to seasonal, environmental and (geo)political conditions, or the use of the natural source may have negative impacts on biodiversity. In consequence, biotechnological production of F&F is an interesting option for producers, regarding products that are either hardly available or costly by natural extraction.

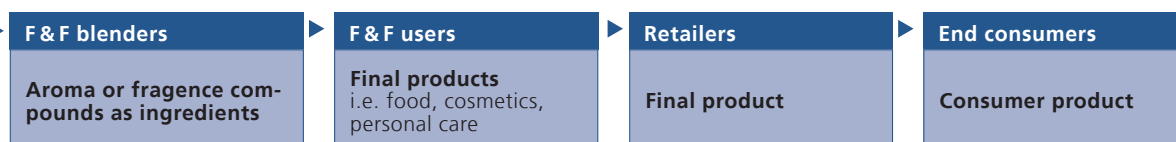
### Potential future developments and drivers

The systematic application of recent scientific-technological knowledge and know-how bear the potential to expand the number of biotechnologically produced flavours and fragrances significantly. This includes screening of natural substances, optimisation of biosynthetic pathways by metabolic engineering, systems biology and synthetic biology, optimisation of bioprocessing technologies and combining bio- and chemosynthesis. Several synthetic biology firms have recently turned their focus to flavours and fragrances, and first products have been already commercialised. Still, technological bottlenecks in scaling-up have to be resolved, and many more biosynthetic pathways should be the focus of R&D activities, as the current focus lies on only very few biosynthetic pathways.

The future development path of biotech F&F will depend on the interaction of technological progress with interaction of key market drivers, such as price,

demand/regulation for natural F&F, sustainability of F&F production. Should regulation and consumer behaviour remain unchanged, a rising demand in the “natural ingredient”-segment would be foreseeable, where biotechnological production is in cost and price competition with other production methods. Here, the application of systems and synthetic biology could enable the achievement of cost competitiveness with the extraction from natural sources.

It is hard to predict, whether consumers and the general public will accept biotechnologically produced flavours and fragrances as “natural” if they are produced with the help of highly engineered microorganisms, and whether the regulation for “natural”-claims will remain as it is. Against this background, scenarios are plausible, in which GMOs as production organisms or certain technologies (e.g. synthetic biology) will not be accepted or will not be allowed in the “premium” segment with natural claims. Under these conditions, the challenge for the EU actors would be to successfully adopt alternatives to the currently dominant production paradigm: such alternatives could be for example breeding and growing plants with a high content of the respective F&F substances.





## MICROBIOMES FOR FOOD AND HEALTHY NUTRITION

### Definition and delineation

Microbiomes is the term given to the collective genomes of mixed microorganism populations. In recent years, scientific-technological progress in genome sequencing and other -omics technologies as well as in the bioinformatic analysis and interpretation of the data has opened up the opportunity, to better understand the composition of (often uncultivable) microbial communities, the functions and interaction of their members, and their interaction with their environment (e.g. soil) or hosts (humans, animals, plants).

In the PROGRESS project, the focus is on human microbiota (e.g. microorganisms that normally inhabit the skin, mouth, nose, digestive tract, and vagina of the human body), the microbiota-host-interactions in health and disease and on human microbiome engineering in nutrition, via food and food ingredients and in products that are available without medical prescription, for example over-the-counter pills.

The value chain represents an emerging science- and technology driven field, at the interface of health/disease, nutrition/medicine, life-style & prevention/treatment. It bears the potential of novel products which can only be produced by using industrial biotechnology or novel services which are enabled by biotechnology. They are likely to be positioned as products in the medium to high-value-low-volume range, delivered to B2B and B2C

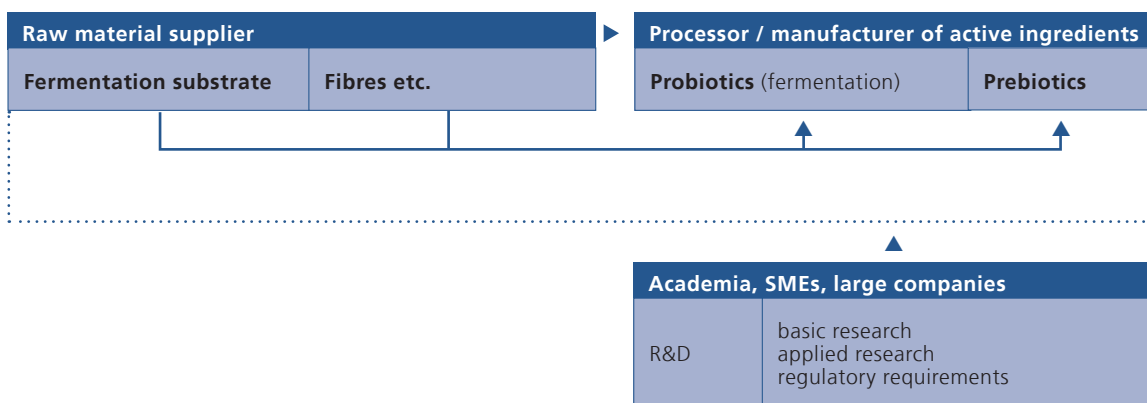
customers. The approaches and technologies of human food-related microbiome research can also be applied in other fields of microbiome research, dealing with livestock health, crop plants, or soil microorganisms. This research also bears large potentials for the bioeconomy, but is outside the scope of this PROGRESS project.

### Current status in Europe

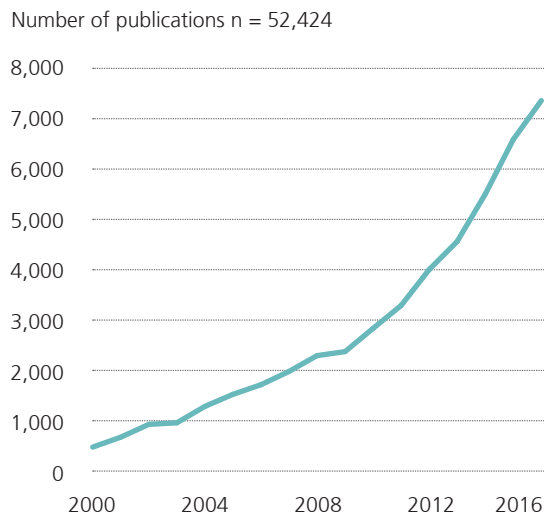
While the focus of activities regarding microbiomes is still on (academic) research in order to build the required knowledge base, various industrial players (e.g. biotechnology companies, technology service providers, food ingredient producers, consumer goods companies, medical device companies) engage in the field with the aim to commercialise services and products. Especially scientific publication activities have grown dynamically in recent years (see Figure 13), but patent applications show increasing microbiomes research results in recent years.<sup>6</sup> The EU is the leading world region regarding scientific publication activities and patent applications, which are most active in microbiome research, together with the US and Asian countries, especially China.

<sup>6</sup> Scientific publications and patent applications have been analysed in the PROGRESS projects (see Deliverable 3.2). Please note that only transnational patent applications at the European Patent Office or the WIPO, respectively, limited to pharmaceutical or food applications, were analysed. A significant number of patent applications refers simultaneously to the food and the pharmaceutical field.

Figure 12: Value chain for microbiomes for food and healthy nutrition



**Figure 13: Scientific microbiome publications worldwide, 2000–2016**



Source: SCOPUS database, search terms in title, article, keywords: microbiome\* OR prebiotic\* OR probiotic\*

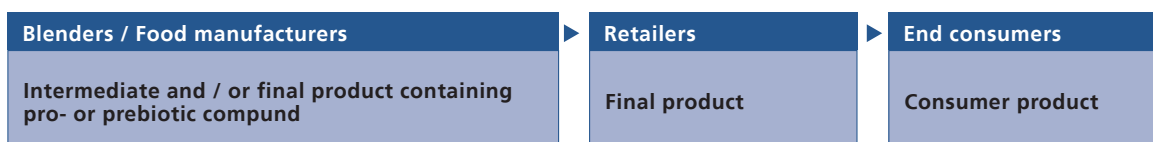
While the potential for novel applications, products and services has been outlined and recognised, the industrial application is still at an infant stage. The potential portfolio ranges from analytics and diagnostics (e.g. microbiome profiling, biomarker-based screening and health monitoring) to novel active food ingredients (e.g. probiotics, prebiotics, phages, metabolites, signalling molecules) or microbiota-addressing functional food with or without health claims to dietary supplements. It would be complemented by services, such as dietary

advice and education, personalised nutrition plans, personalised food and diet solutions and related devices (e.g. for point-of-care testing and monitoring).

#### Potential future developments and drivers

Drivers for future developments in the field are scientific-technological advances. These depend significantly on related publicly and privately funded R&D activities, the establishment of the required R&D resources (e.g. biobanks, cohort studies, facilities for data collection, analysis and interpretation, networks of relevant players, standards) and forms of organisation which support translational research, taking basic research findings to applications and products. A cross-cutting issue in these R&D activities is the need to combine interdisciplinary expertise, coming from microbiology, molecular biology/genome sequencing, bioinformatics, manufacturing, industrial biotechnology and food technology, health apps and point of care testing.

The future economic development will depend to a certain extent on whether academia-industry and cross-industry collaborations (e.g. biotech – food – pharma/medical devices) and knowledge transfer can successfully be established. Presently, spin-off and start-up SMEs play an important role as innovators, technology and service providers in this high-risk field in addition to (a few) large multinational companies which are also active in R&D, but could also acquire successful start-ups.



In early stages of commercialisation, target groups are especially health-conscious consumers with high socio-economic status. To which extent broader groups of the population could be reached, depends on the level of a positive attitude of consumers towards microbiota-addressing food and the willingness to pay. Specific education of consumers may be necessary. Presently, it is unclear which level of scientific evidence for the effectiveness of microbiota-addressing food will be demanded both by consumers and regulators, and an appropriate balance between different interests has to

be found: From a company point of view, very stringent requirements may hamper the commercialisation of respective food innovations due to an unfavourable return of investment. From a consumer and public health perspective science-based evidence for the safety and efficacy should be demanded for food with respective health claims. All in all, an early integration with health policy would be required to achieve not only economic benefits and individual well-being, but also positive public health effects.

## IMPLICATIONS OF THE VALUE CHAIN ANALYSES

The analyses and scenarios for these six value chains point out that for a favourable development of IB in Europe a set of different factors has to evolve positively, such as maintaining competitiveness in future technological developments, aligning supply to customer needs, adjusting policy instruments, etc. While some factors are similar across the value chains (e.g. pressure to reduce costs) others differ (e.g. role of regulation). In the following, those main insights are summarised, and a differentiated picture for the general factors and challenges for IB (given in Section 2) are drawn.

### Cost reduction

A key challenge for technological development and economic activities in all value chains is the reduction of cost. This applies even to those value chains without direct competition to chemical synthesis or fossil-based products, for example, the production of biopharmaceuticals and some applications for enzymes where regulatory or market pressures exist to reduce the costs.

### Advanced technologies

For the production of biopharmaceuticals, enzymes, bio-based plastics and lignocellulosic ethanol, advanced technologies have important potential for increasing the (cost)- efficiency and environmental performance of production processes. For the value chains Flavours and Fragrances and microbiomes the potential is even more impressive: Advanced metabolic engineering, systems and synthetic biology in the case of Flavours and Fragrances and next generation geno-

me sequencing and bioinformatics in the case of microbiomes are of major importance for the further advancement in these value chains. However, the use of certain technologies in applications “near the human body” (e.g. Flavours and Fragrances and enzymes in personal care, textiles, food) may evoke negative perceptions in parts of the public and certain consumer groups.

### Feedstock

Biomass feedstock availability and relative prices compared to fossil fuels are most important for mass products such as lignocellulosic ethanol and bio-based plastics. In addition, the further market uptake of enzymes is indirectly dependent on feedstock prices and availability as many potential application markets are influenced by them. For the other value chains analysed, feedstock issues are of minor importance.

### Role of R&D&I support

R&D&I support for the adoption and use of advanced technologies is important for all value chains to the extent outlined above. Moreover, additional R&D&I support efforts are required in a value chain-specific manner in certain innovation phases or issues. Examples are the establishment of an interdisciplinary, internationally integrated microbiome research community and the related microbiome research infrastructure; the specific support of EU-wide academia-industry collaboration in Flavours and Fragrances, the support of higher TRL (Technology-Readiness-Level) development

activities and demonstration plants in lignocellulosic ethanol and bio-based plastics. Other issues in need of R&D&I support are cross-cutting issues of relevance to all value chains, for example studies for taking stock of the available land and biomass in the EU, attitudes of population groups towards different IB applications, technologies and products, and related dialogue and communication formats, skilled workforce, collaboration along value chains and across industries and sectors. However, only in the value chains microbiome and Flavours and Fragrances, R&D&I support seems to be the crucial factor for the dynamic development of the value chain. In the other value chains, other factors have a stronger influence, for example demand side policies for lignocellulosic ethanol or bio-based plastics, reimbursement practices in the case of production of biopharmaceuticals, R&D priorities of large companies less dependent on public funding (e. g. enzymes, biopharmaceutical production).

### **Regulatory environment**

Product regulations have a significant impact on growth opportunities in all six value chains. The effects of regulations are often complex and not positive or negative *per se*. Moreover, effects can differ between being short and long term as incentives for actors in the markets may change. Value chain-specific regulations, which create a rather favourable environment for commercial activities exist in the value chain biopharmaceuticals (securing a competitive advantage for EU players over competitors due to high requirements), Flavours and Fragrances (opening opportunities for IB to produce substances which can be claimed as being “natural”), and enzymes (no need for labelling and/or interme-

diated products with enzymes produced in genetically modified organisms). It is an open question to which extent this rather favourable commercial environment will be maintained in the future. On the other hand, in three value chains, amendments of existing or even novel regulations are called for: In the microbiome value chain, it is being discussed whether existing regulations regarding both food for specific nutritional purposes or medicinal products should be amended in order to specifically address microbiome products at the borderline between food and medicinal products, clarifying the requirements and procedures for health claims for the respective products. In the case of lignocellulosic ethanol and bio-based plastics, demand-side regulations such as mandates, tax exemptions or bans of competing products are called for.

### **Effective collaboration networks**

The current status and challenges for effective collaboration networks differ between the value chains. For example, on the one hand for the value chains Flavours and Fragrances and microbiome European-wide networks still have to be firmly established and expanded. On the other hand, for the value chains production of biopharmaceuticals and enzymes collaboration networks are well established. However, the question arises whether they are sufficiently open to address the challenges from alternative, competing concepts (e.g. cell-free production, advanced therapies). For enzymes, collaboration between large companies and academia has decreased, because of IP issues. This may represent a hurdle for taking up R&D impulses from academia into commercialisation.



# 4 RECOMMENDATIONS

## INTRODUCTION

Concepts of support of the future development of IB in Europe have to consider the substantial heterogeneity of IB and the different barriers that exist throughout the IB innovation ecosystem. A broad product portfolio of IB products and processes should be envisaged for the EU: it is robust and flexible enough to cope with unfavourable or changing external factors and frame conditions allows the full exploitation of IB and can contribute to mastering the grand challenges. In order to achieve critical mass, and to efficiently allocate resources for R&D&I, production and marketing it is recommended to continuously support roadmapping activities or related analyses to identify areas of strategic importance, such

as the value chains analysed in the PROGRESS project. These areas should become a focus of support. Selection criteria could be signalling functions for other IB areas, high potential for innovation, supporting competitiveness of the EU in key resources (e.g. skills, feedstocks) and contributions to the grand challenges.

Moreover, the PROGRESS value chain analyses have revealed an important role of R&D&I policy, but such policy has to be embedded in a wider set of suitable framework conditions. In the following, key actions are proposed for fostering the enabling role of IB across different sectors and value chains.

## SUPPORTING ADVANCED TECHNOLOGIES

Advanced technologies play a crucial role in advancing IB and in maintaining international competitiveness, both in research and in commercial production. Support of R&D&I should ensure that leading EU countries in IB stay at the cutting edge and to diversify into emerging IB industrial sectors while helping EU countries emerging in IB to adopt these technologies. While established and emerging advanced life science technologies remain core competencies, significant progress is expected from the integration with other

technologies, especially with environmentally benign chemical processes (“green chemistry”) and with digital technologies and bioinformatics. In addition to value chain-specific R&D needs<sup>7</sup>, the following cross-cutting R&D and technology issues are relevant to IB in general:

<sup>7</sup> Detailed R&D&I needs for the different value chains are included in Deliverable 5.1. See <http://www.progress-bio.eu/progress-bio/results/deliverables.php>

The pre-treatment of biomass to yield fermentable substrates requires continued R&D efforts to develop robust, low cost processes for a large diversity of non-food feedstocks of variable qualities without compromising the following production processes. Combinations of physical, chemical and biotechnical technologies for pre-treatment, information and communication technology approaches for feedstock logistics, and model-based adaptation of process parameters to feedstock quality may offer solutions.

Significant advances in tailoring production organisms and biocatalysts to bioprocess requirements are expected from systems metabolic engineering in a high throughput manner. This is the integrated application of metabolic engineering with bioinformatics and systems and synthetic biology in iterative design-build-test cycles. The synergistic and coordinated combination of these competencies remains a challenge. Further R&D efforts are required in bioinformatics for data mining, data interpretation and for modelling the complexity of relevant pathways and properties, in synthetic biology, and in debottlenecking the test phase of the cycle. Moreover, R&D should address cost-competitiveness

by optimising organisms with respect to yield, product concentration and productivity, to simplifying the overall process, and to improving their robustness under production conditions.

In production processes, R&D topics are scale up and further optimisation of production processes with respect to biotechnical, economic, ecologic and safety or quality parameters. Digital technologies also bear potentials for optimising production processes, e.g. by further automatisation and integration of unit operations, by process analytical technologies and by coupling them with process modelling. Moreover, R&D efforts should be targeted at further developing and optimising integrated biorefineries.

Hence, advanced technologies have a key role for IB development that must continue to be reflected in future research Work Programmes.<sup>8</sup> To which extent the possible contribution of advanced technologies for the deployment of IB can really be exploited, is closely linked to actions taken in the areas outlined below.

## SUSTAINABLE FEEDSTOCK SUPPLY

In IB bulk product value chains (e.g. biofuels, bio-based plastics and platform chemicals) an increased industrial use of biomass is expected which might have negative impacts for food security, on water resources and soil fertility, biodiversity, and net energy use.

In order to prioritise food use, effective concepts for the realisation of “food first” have to be developed and implemented. Sustainability of biomass production also has to become a priority: The UN Sustainable Development Goals should be implemented consistently with regard to cultivation and use of biomass. In a globally linked economy, there is an urgent need to strive for European and international agreements on standard definitions of sustainable production of feedstocks, and the related tools and indicators for measuring sustainability.

To satisfy the growing demand for feedstock, different approaches have to be pursued or intensified in combination with each other: First, the technological potential of land use in the EU has to be raised by using all fractions of biomass and by tapping non-food biomass sources (straw, wood, industrial and municipal waste, CO<sub>2</sub>, aquatic resources) as well as applying the cascading principle. The related technological and logistic challenges, e.g. the heterogeneous and variable composition of feedstocks, as well as their wide dispersal, have to be addressed.

Second, knowledge gaps should be closed regarding the economic potential of land use and biomass availability, possible unintended and harmful environmental impacts of increasing use, as well as unintended impacts on other markets. In order to provide a sound knowledge base for strategic and political decisions, a

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<sup>8</sup> See [www.ec.europa.eu/research/participants/data/ref/h2020/wp/2018-2020/main/h2020-wp1820-leit-nmp\\_en.pdf](http://www.ec.europa.eu/research/participants/data/ref/h2020/wp/2018-2020/main/h2020-wp1820-leit-nmp_en.pdf) for the topics of the NMBP Work Programme 2018-2020

study or monitoring system is needed which allows a consistent uniform assessment of the available biomass and type of feedstock across the EU. This could be complemented by mapping and characterizing different use paths of biomass in order to direct activities to products and processes with high resource efficiency and value added.

Moreover, in order to exploit synergies between the bioeconomy and the circular economy, the revision of waste regulation such as the EU Waste Framework Directive should be considered. In order to overcome existing legal restrictions to exploit the potential of waste as feedstock for IB, it should be clarified which types of waste could be allowed to be used further for recycling.

## **ADDRESS PUBLIC PERCEPTION AND ACCEPTANCE**

Generally, IB has a rather positive public perception because of its potential to contribute to mitigating climate change and substituting fossil fuels. However, attitudes and acceptance differ substantially depending on stakeholder group, application, and technologies. Particularly sensitive areas are the potentially negative environmental impacts, distribution of socio-economic benefits and burdens of IB, and scepticism towards advanced technologies in certain applications.

Against this background, IB R&D&I strategies should be tailored in a way that they are guided by the UN Sustainable Development Goals. Moreover, constructive

stakeholder dialogues and public participation should be continued in order to develop a commonly shared future vision for IB and to address value chain specific concerns. It should be ensured that these involvement processes may have the consequence that certain areas may no longer be funded publicly, that regulations may have to be amended, that presently neglected R&D topics may become more important, and that sufficiency concepts could be taken into consideration. The PROGRESS scenario analyses show that such strategies, although they may at first sight seem to be counterproductive for the advancement of IB, also bear significant potential for IB in international competition.

## **DEMAND PULL**

Despite substantial scientific-technological progress, achieving cost-competitiveness in IB will remain difficult for many IB products in times of low prices for fossil resources. Therefore, a higher demand pull would be needed to enforce the development of IB. Although the broad range of IB products makes it very challenging to reach consumers, efforts should be taken to increase their awareness, to communicate the benefits of IB products and thus facilitate informed purchasing decisions. Special attention should be given to dialogues, to specific approaches tailored to the needs and expectations of different target groups, as well as to establishing different communication channels to inform about IB products in a balanced way.

As the impact of measures targeted at influencing rational purchase decisions in consumers is limited, increased attention should be given to nudging approaches by targeting the Business-to-Business sector, in particular large brands. While several brand owners have switched to bio-based products, even more actors could be sensibilised for IB solutions, especially as a means to improve corporate sustainability performance. The communication of IB success stories could help to convince decision makers in industry.

In order to establish a level playing field between IB solutions and other competing options to improve corporate sustainability, the scientific underpinning of measurements of sustainability, the development and



implementation of respective sustainability assessment tools, and European and international standardisation of sustainability labels and certificates, e.g. for IB products and processes, should be publicly supported.

Finally, a public procurement programme should be taken into consideration. It could be comparable to the US BioPreferred Program, but should be more ambitious by including only IB products and processes with superior sustainability performance.

## **MULTIDISCIPLINARITY OF SKILLS**

The multidisciplinary nature of IB requires teams of highly specialised experts. In order to interact synergistically and effectively in these teams, experts should not only be highly competent in their own field of expertise, but also have a basic understanding of other competencies.

opportunity for scientists from academia to gain industry relevant experiences. R&D centres with an infrastructure for applied research and scaling-up could gain a more important role in skill formation, or dedicated facilities for training in IB-relevant disciplines may be set up.

The portfolio of instruments should comprise, among others, adaptation of curricula in higher education, universities and vocational training, cross-country exchanges of expertise, public-private partnerships as an

As IB is a rather small field in the overall economy, coordinated efforts of industry, academia and governments should be taken to position IB among talented students as an attractive field of operation.

## **TRANSFER OF R&D RESULTS INTO COMMERCIALISATION**

As IB is entering more mature stages the need to address the various – and well-known – barriers to commercialise IB products and processes becomes even more pressing. Existing efforts to overcome these barriers have to be continued, e.g. by continuously supporting the collaboration between academia and industry, by the early integration of industry into R&D projects in order to focus on market-driven developments, by fostering the start-up scene, including financing and venture capital. A special focus should be on the following issues: First, the development of teams with commercialisation-relevant expertise (e.g. scaling up, market intelligence) should be improved by actively bringing different experts (researchers, investors, intermediaries) closer together.

Second, presently, there is a temporary lack of personnel specifically qualified in scaling up bio-processes. While this can be solved in the longer term by amending curricula accordingly, short-term options are attracting such experts to IB from related industrial branches, e.g. the pharmaceutical or chemical industry. Moreover, access to capital-intensive infrastructure should be improved by setting up pilot and demonstration plants, and by improving access to and services of existing infrastructures: they should offer commercialisation consulting services even for actors in early stages of R&D, and duplicating activities should be avoided. Rather, synergies are expected if these R&D infrastructures offer complementary services and if access to the specific services is facilitated.

## **CO-EVOLUTION OF REGULATORY ENVIRONMENT AND S&T DEVELOPMENT**

The regulatory environment has a significant impact on IB growth opportunities and innovation incentives in many IB value chains, but cannot be assessed as

being generally positive or negative for IB: In some value chains, rather favourable regulatory conditions already exist for industry, whereas in other value chains,

a significant deployment of IB is rather unlikely without regulatory change. Moreover, relevant regulations and the implemented or proposed regulatory instruments differ highly between value chains and are often value chain-specific.

Against this background, the PROGRESS scenarios show that co-evolution of S&T developments with regula-

tions is of critical importance. The challenge is to align R&D policy with regulatory activities, both with respect to timeline and areas incentivised. Regulations should also be seen as instruments for establishing trust and credibility in IB by balancing incentives for R&D and industry with – potentially differing – interests of the public and consumers.

## **COLLABORATION ALONG VALUE CHAINS**

The collaboration of actors from different stages of the value chain in R&D&I is a prerequisite for successfully transferring R&D results to commercialisation.

Although many new collaborations and networks of communities have been established in IB in the last few years, fostering networks remains a key issue in emerging value chains (e.g. microbiomes) or in existing ones, where novel approaches enable an innovation push (e.g. Flavours and Fragrances). Suitable instruments comprise R&D projects that include actors along the value chains and from different countries, national and cross-border cluster policies. Efforts should be di-

rected at even better linking the various instruments to generate more synergies, and to improve coordination among agencies in funding and investment.

In order to strengthen the presently comparably weak linkage of biomass production and supply on the one hand and biomass conversion on the other hand, R&D funding should more explicitly address research questions that require closer cooperation between these sectors (e.g. quality of biomass for certain industrial uses and applications, decentralised small scale biorefineries), logistics concepts, and digitisation as a tool to link the sectors.

## **COLLABORATION ACROSS EUROPEAN COUNTRIES**

Intensified collaboration between actors from different EU countries and integration of more countries into the various value chains should be strived for, in order to build up critical masses, to combine complementary competencies and resources, to achieve a higher quality of R&D&I and to contribute to more balanced, more sustainable regional development within the EU. On the one hand, efforts should be targeted at enabling leading countries in IB to join forces, to maintain their international leadership, and to team up with countries with complementary strengths. On the other hand, R&D policy and cohesion policy should jointly increase the potential contribution from EU countries, that have presently low activities in IB by addressing low visibility and network competency of actors from countries

with few IB activities, their integration into existing networks, and the joint development of strategies for cross-country collaboration, e.g. between feedstock providers and converters.

In order to support collaboration across European countries, a combination of financial incentives with other forms of support is needed. A pan-European wide mapping of relevant IB competencies could be established as an information base and first step. This should be followed by activities, which bring the relevant stakeholders together to explore their interests and resources for collaboration and to elaborate actions for creating win-win-situations in the respective countries.



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**Table Annex 1: Characterisation of the analysed value chains in the PROGRESS project\***

Value Chain	Characteristics			State of Biotech
	Potential volume	Price	Quantity of feedstock	
<b>Lignocellulosic ethanol</b>	very high	low	very high	Early commercialisation phase
<b>Bio-based plastics</b>	mostly high	mostly rather low	high	Niche market (~1 per cent), with considerable market growth
<b>Enzymes</b>	low	mostly high	very low	Established markets, but new application opportunities
<b>Production of biopharmaceuticals</b>	very low	very high	very low	Significant market size and dynamics for biopharmaceuticals Biosimilars in rather early commercialisation phase
<b>Biotech Flavours and Fragrances</b>	low	rather high	low	Biotech still a niche (< 5 per cent), rising steadily New impulses by synthetic biology
<b>Microbiomes</b>	low	high	very low	Mostly in R&D phase, few commercialisation activities yet

\* The patent shares refer to the time period 2010–2014. For production the data for the last year available, usually 2015, has been taken. Sources for patent share are analysis of Fraunhofer ISI with World Patent Index, for production share various market studies. More information on results and sources are provided in Deliverable 3.2

\*\* Number refers to market share for flavours, no information for fragrances and production shares available

EU competitiveness (% shares of world output)		Main factors for future deployment in Europe
Patents	Production capacities	
32 %	9 %	<ul style="list-style-type: none"> <li>• Cost competitiveness to fossil fuels and 1 gen biofuels</li> <li>• Feedstock availability</li> <li>• Mandates for use of advanced biofuels</li> <li>• Perception and acceptance by policy and the public</li> </ul>
43 %	27 %	<ul style="list-style-type: none"> <li>• Cost competitiveness to fossil-based plastics</li> <li>• Oil price impacts competitiveness to fossil-based products tremendously</li> <li>• Acceptance and willingness-to-pay, strategies of brand-owner companies as gatekeeper for the demand side</li> <li>• Demand-side policies</li> </ul>
36 %	40 %	<ul style="list-style-type: none"> <li>• Keeping the global competitive advantage over competitors, especially through scientific-technological excellence, innovative products and applications, customer-specific solutions</li> <li>• High oil price and strict environmental regulations are favourable frame conditions for the industrial use of enzymes</li> <li>• Competition with novel technologies for conversions and enzyme production concepts (e.g. cell-free production)</li> </ul>
n.a.	31 %	<ul style="list-style-type: none"> <li>• Cost containment policies for biopharmaceuticals</li> <li>• Regulatory requirements (“Good manufacturing practices”)</li> <li>• Technological hurdles for manufacturing of new products</li> <li>• Set of ongoing technological challenges (continuous manufacturing, single-use systems, process analytic technologies)</li> <li>• Competition with novel production concepts (e.g. cell-free production, pharming) and with advanced therapies with novel therapeutic concepts</li> </ul>
31 %	30 %**	<ul style="list-style-type: none"> <li>• Advances and acceptance of synthetic biology</li> <li>• Regulation of “natural” claim</li> <li>• Collaboration across EU-borders</li> <li>• Facilities for small-scale production and scale-up</li> <li>• Rapidly changing fashions in user markets vs. long R&amp;D periods</li> </ul>
41 %	n.a.	<ul style="list-style-type: none"> <li>• Major advances in the fundamental understanding of microbiota, their functions in health and disease, their modes of action and in ways to manipulate and engineer microbiota</li> <li>• Establishment and expansion of internationally linked, cross-sectoral R&amp;D&amp;I collaboration networks</li> <li>• Translational research into services and products</li> <li>• Regulation, required evidence for health claims</li> </ul>

**Table Annex 2: Future scenarios for the analysed value chains in the PROGRESS project**

Value Chain	Scenario 1
<b>Lignocellulosic ethanol</b>	<p><b>Policy-driven uptake</b></p> <ul style="list-style-type: none"> <li>• High binding target for advanced biofuels</li> <li>• Only slight slowdown for first generation biofuels</li> <li>• Strong support for new commercial plants</li> <li>• Price competitiveness to fossil fuel and first generation ethanol in 2030</li> <li>• Optimisation of the whole production chain from feedstock logistics, to pre-treatment, more efficient enzymes and production organisms</li> </ul>
<b>Bio-based plastics</b>	<p><b>“De-risking strategy”</b></p> <ul style="list-style-type: none"> <li>• Financial support for risky business decisions</li> <li>• Coordinated market pull measures implemented in the EU, labels and information are widespread</li> <li>• Many new market opportunities arise</li> <li>• Bio-based plastics produced both in large and small scale processing plants via many production pathways</li> <li>• Possibility of feedstock shortage</li> </ul>
<b>Enzymes</b>	<p><b>Technology push</b></p> <ul style="list-style-type: none"> <li>• Substantial technological progress, new options (e.g. production hosts, cell-free systems, rational improvement) are quickly developed and taken up by industry</li> <li>• Enzymes are perceived positively by customers and end-users</li> <li>• Markets expand in all segments</li> <li>• IP framework supports intensive cooperation of academia, SMEs and large enzyme companies</li> </ul>
<b>Production of biopharmaceuticals</b>	<p><b>High demand for biopharmaceuticals</b></p> <ul style="list-style-type: none"> <li>• Considerable price reimbursement for new biopharmaceuticals if they can prove high medical value</li> <li>• Stratified medicine is widespread and will lead to a diversification of the product and service portfolio</li> <li>• Higher transparency and growing consensus between regulators and manufacturers</li> <li>• High technological progress in upstream and downstream efficiency, continuous manufacturing as well as process analytics</li> </ul>
<b>Biotech Flavours and Fragrances</b>	<p><b>Price driven market</b></p> <ul style="list-style-type: none"> <li>• GMO produced flavours accepted and used widespread</li> <li>• High advances in synthetic biology</li> <li>• Strong position of the US firms due to favourable investment climate</li> </ul>
<b>Microbiomes</b>	<p><b>Optimal development</b></p> <ul style="list-style-type: none"> <li>• Publicly funded R&amp;D infrastructure and research</li> <li>• Favourable conditions for public/private cooperation in R&amp;D</li> <li>• Favourable market conditions through amended regulation and positive public perception</li> <li>• New regulatory categories for microbiota addressing food</li> </ul>

Scenario 2	Scenario 3
<p><b>Partial established production</b></p> <ul style="list-style-type: none"> <li>• Considerable binding target for advanced biofuels</li> <li>• Slowdown of first generation biofuels</li> <li>• Economically attractive for some pathways/feedstock/national regulations at specific locations</li> <li>• Waste and residues for small scale production of increased importance</li> </ul>	<p><b>Stagnant development</b></p> <ul style="list-style-type: none"> <li>• No binding target for advanced biofuels</li> <li>• No price competitiveness to fossil fuel and first generation ethanol</li> <li>• Limited commitment of blenders and investors</li> <li>• Rather modest technological progress</li> </ul>
<p><b>High oil price, no additional policy measures</b></p> <ul style="list-style-type: none"> <li>• High oil price (127 Euro per barrel), creates favourable conditions to replace fossil-based plastics by bio-based alternatives</li> <li>• Market pull measures remain status quo</li> <li>• Mostly drop-ins that are marginally competitive as commodity</li> <li>• Production of few bio-based plastics in large amounts takes place in large scale plants</li> </ul>	<p><b>High attention for (micro)plastics</b></p> <ul style="list-style-type: none"> <li>• Very high awareness and concerns of (micro)plastics in the environment</li> <li>• Regulation bans short-lived plastics</li> <li>• Bio-based plastics become established in few niche applications and markets</li> <li>• Processing of wide diversity of feedstock</li> <li>• Production in small scale conversion plants</li> </ul>
<p><b>High oil price, but consumer concerns</b></p> <ul style="list-style-type: none"> <li>• High oil price creates favourable conditions to replace fossil-based chemicals and processes by enzymes</li> <li>• Full potential of enzyme use cannot be exploited because negative public perception and resulting strict regulation disfavours use of enzymes in certain applications</li> <li>• R&amp;D focus shifts to fields which are compatible with the enzyme regulations and public concern</li> <li>• Big industry reduces their collaboration with SME and academia to protect their IP/freedom to operate</li> <li>• Europe focuses strongly only on certain segments</li> <li>• Production of enzymes mainly takes place in Asia</li> </ul>	<p><b>Coordinated bioeconomy policy, but global competition</b></p> <ul style="list-style-type: none"> <li>• Coordinated bioeconomy policy in Europe, which invests in R&amp;D and establishes market pull measures</li> <li>• Moderate knowledge transfer between the big enzyme industry and innovative SMEs, but not between academia and big enzyme companies because of the IP framework</li> <li>• R&amp;D efforts result in moderate broadening of industrial production platforms</li> <li>• Countries in the Asia/Pacific region advance significantly in enzyme-related skills as well as enzyme production</li> <li>• European players can maintain certain market shares due to their technological excellence</li> </ul>
<p><b>Gene therapy breakthrough</b></p> <ul style="list-style-type: none"> <li>• Establishment of gene therapies in clinical routine, enabled by advances of CRISPR/CAS methods</li> <li>• Product portfolio becomes more diversified</li> <li>• New therapy forms with new manufacturing requirements will gain importance</li> </ul>	<p><b>Stagnant development</b></p> <ul style="list-style-type: none"> <li>• Cost containment pressure for biopharmaceuticals around the world leads to modest market growth</li> <li>• Increased focus on biosimilars</li> <li>• Rather modest technological progress</li> <li>• Difficulties in manufacturing processes for new types of product arise</li> </ul>
<p><b>Alternative niches for the EU in non GMO production</b></p> <ul style="list-style-type: none"> <li>• No acceptance or allowance for use of GMO in production to claim it naturally</li> <li>• Use of conventional methods in the EU instead of synthetic biology</li> <li>• Technological advances in high-content plants and alternatives to scale-up</li> <li>• EU is strong in some segments</li> </ul>	<p><b>Carbon footprint as market driver</b></p> <ul style="list-style-type: none"> <li>• Sustainability will increasingly determine purchase decisions taken by consumer</li> <li>• New label with a positive connotation for favourable environmental footprint</li> <li>• Increasing use of waste as feedstock</li> </ul>
<p><b>R&amp;D focus</b></p> <ul style="list-style-type: none"> <li>• Public funding targeted at building a sound knowledge base in academic research</li> <li>• Companies use this knowledge base for product development, private R&amp;D limited to certain fields</li> <li>• Status quo regulatory framework</li> <li>• Demand side not specifically addressed by policy</li> </ul>	<p><b>Supporting regulation, negative public perception</b></p> <ul style="list-style-type: none"> <li>• Amended regulation implemented which favours product development and marketing</li> <li>• Products perceived negatively for several reasons (e.g. GMO, data protection, safety and efficacy...) this limits market penetration</li> </ul>





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