Progress

Priorities for Addressing **O**pportunities and **G**aps of Industrial Biotechnology for an efficient use of funding **res**ource**s**

Project number: 723687
Programme: H2020-NMBP-CSA-2016
Contract type: Coordination & Support Action
Start date of project: August 1, 2016
Duration: 15 months

Deliverable D 4.1 Value Chain Workshop reports

Author: Sven Wydra, Bärbel Hüsing, Elna Schirrmeister, Aaron Rosa, Björn Moller, Heike Aichinger, Liliya Pullmann
(all Fraunhofer ISI)
Dissemination level: public
Deliverable type: report
Due date: 31.03. 2017
Submission date: 02.11.2017

This project has received funding from the *European Union's Horizon 2020 research and innovation programme* under grant agreement No 723687 This document does reflect the authors view only. The European Commission is not responsible for any use that may be made of the information the document contains.

About PROGRESS

PROGRESS is a coordination and support action for the European Commission and aims to support and accelerate the deployment of Industrial Biotechnology (IB) in the EU industry by identifying high-value opportunities for IB and proposing actions to address them successfully. For that purpose, we will first provide a comprehensive and dependable information base (including modelling and simulation approaches) which allows for plausible estimations on the future of IB in the EU in the short and medium-term. Second, in collaboration with stakeholders we will elaborate a future scenario and a common vision for IB in Europe containing the most promising value chains, related R&D&I needs and necessitated policies for IB in Europe. Based on these steps, we will provide strategic advice for research, industry and policy making regarding potential issues and topics for collaboration, future policy programmes, the required technological infrastructure, capabilities, and economic structures. A main focus will be to identify opportunities for collaboration between EU member states and proposed actions to increase awareness and incentives for those collaborations. For more information see www.progress-bio.eu

Contact: Sven Wydra
sven.wydra@isi.fraunhofer.de
+49 721 6809-262

Content

1 Introduction

In the following sections, the results from the workshop on value chain workshops from 7th-9th March are summarized. The selection of the value chains has been explained in Deliverable 2.1. The aim of the value chain workshops was to elaborate possible future pathways (scenarios) for each value chain in Europe in the next 10-12 years. The guiding question was how may the value chain in Europe look like in 2025-2030 from a technological, business, societal and policy perspective.

For each of the value chains between 7 and 13 experts participated. In total 64 experts attended the workshops. For each value chain the following steps were taken:

- Assessment of factors and current situation for technology, business, policy based on pre-analysis of the project team
- Priorization of key factors and imagination of alternative future developments for the key factors along the value chain
- Elaboration of three alternative scenarios by combining possible future developments for each key factor

In the following, for each value chain a short narrative describing a selection of potential alternative scenarios is described together with respective supporting tables. The tables contain the current situation for the critical factors that were identified and prioritized as well as the different future assumptions attributed to different scenarios. The narratives or story lines for the selected scenarios include links to the respective assumptions for the corresponding scenario as shown on the tables (the links T,B and P stand for Technology, Business, and Policy, respectively; the following number corresponds to the line in the table; and, A,B,C,D to the specific assumption).

Main conclusions are presented as a cross-value chain analysis for all 6 value chains in chapter 8. The conclusions for each value chain are being presented separately (Deliverable 6.6) as a result of combining the value chain analyses (Del 2.2) with the scenarios described hereby.

2 Scenarios for Lignocellulosic Ethanol

2.1 Story Lines for Lignocellulosic Ethanol scenarios

Scenario 1: Policy driven uptake

Seed: This scenario is characterized by demand-side policy measures (P4B), namely a modification of the current proposal of a new Renewable Energy Directive (RED II). The modifications provide strong incentives for advanced biofuels, but do not contain the currently planned significant reduction in first generation biofuels. As a consequence, existing producers or investors in bioethanol as well as potential new investors commit to advanced biofuels. The measure is integrated in a broader policy mix that comprises coordinated policy funding or tax incentives for private funders for high TRL-stages or commercial production (P6B). Different demand-side measures that aim to realize RED goals are introduced (e.g. Price guarantees via local tenders or exemptions for the use of lignocellulosic ethanol) (P5B).

On the technology side, significant progress is enhanced by specific R&D funding for ligno-cellulosic bioethanol projects throughout different TRLs. The leading production concept for lignocellulosic bioethanol will be few large-scale versatile biorefineries (T1B). They will use different types of feedstocks, which include among other tailored biomass crops. Significant advances will be reached for pre-treatment and hydrolysis (T2A). Optimized pre-treatment techniques are leading to higher yields and are limiting adverse effects of inhibitors.. More efficient enzymes through optimization or better re-use of enzyme combinations lead to lower production costs. Economic performance will be enhanced by favorable valorization of lignin and by-products (T3A). The integration of cellulosic bioethanol into biorefineries leads to highest value through broad spectrum of products as well as high value applications for lignin are broadly established. Here an important role of SMEs emerges in creating markets for by-products of ethanol; e.g. firms that are (independent from ethanol) active in lignin markets (B3B). They create new value products and settle the path for others to use the lignin coming out from lignocellulosic ethanol production to produce those goods.

On the user and investors side commitment for the use of second generation ethanol and to finance new facilities arises (B2A). The build-up of new facilities will lead to scale and learning effects that lead to a convergence of ligno-cellulosic costs to those of 1 generation bioethanol and fossil fuels (B1B).

In this scenario, prices of oil and biomass have no decisive impact on the total development of the market. The biomass prices will probably increase because of the increasing demand.

Scenario 2: Partial established production

Seed: This scenario presents a partial uptake of lignocellulosic ethanol. Rather favourable framework conditions with a rising oil price (P1A) and modest biomass price increases (P2B) go a along with only partial established demand-side policies that may foster the uptake of lignocellulosic ethanol. More concretely the current RED II proposal with binding mandates for lignocellulosic ethanol, but a significant cut in first generation biofuels come into place (P4C). Other demand-side policies or public/Private financing of commercial activities are only fragmented (P5A, P6A).

Regarding feedstock, agricultural/forest residues, organic (industrial/household) waste as biomass are increasingly used (T1A), often in nearby small scale production sites. Significant advances will be reached for pre-treatment and hydrolysis (T2A). Optimized pretreatment techniques are leading to higher yields and are limiting adverse effects of inhibitors. More efficient enzymes through optimization or better re-use of enzyme combinations lead to lower production costs. Economic performance will be enhanced by favorable valorization of lignin and by-products (T3A). The integration of celullosic bioethanol into biorefineries leads to highest value through broad spectrum of products as well as high value applications for lignin are broadly established. Here an important role of SMEs emerges in creating markets for by-products of ethanol; e.g. firms that are (independent from ethanol) active in lignin markets (B3B). They create new value products and settle the path for other to use the lignin coming out from lignocellulosic ethanol production to produce those goods.

However, due to reluctance on the use and investor side (T2B) and modest policy support, costs competitiveness is only achieved for very few pathways of LC Bioethanol and in certain regions, with favourable feedstock or political conditions. No major changes in industrial structure takes place, with large firms remain dominating.

Scenario 3: Stagnant development

Seed: This scenario presents a stagnant development of lignocellulosic ethanol. There is neither a development of an external framework, which may drive activities, nor significant policy commitment to bridge the phase and overcome missing cost competitiveness. More concretely, oil price remains low and comparable to current price levels (P1D), public financial support for R&D&I is falling (P3D), there are no binding mandates for lignocellulosic ethanol (P4A) or other demand-side policy (P5A) or strong financing of (near) commercial activities (P6A).

On the technology side, only incremental advances in the provision of sustainable lignocellulosic bioethanol occurs (T1D). Concepts based on straw and wood are further developed, but no major advances in cost reduction achieved. Regarding pre-treatment and hydrolysis, biotechnological conversion does not emerge as favourable option, but gasification of biomass to syngas becomes the predominant process (T2B). Regarding the use of lignin and by-products, energy production remains the most economic advantageous option (T3B).

On the business side, large companies and SME will remain reluctant (B3A), as neither user industry nor financiers provide long-term commitment to build up new plants (B2B). In consequence, rather few scale and learning effects will be realized and cost competitiveness to first generation bioethanol and fossil fuels not be achieved (B1A).

2.2 Overview of Factors and Future Assumptions –Lignocellulosic Ethanol

Scenario 1 (green): Policy driven uptake
Scenario 2 (yellow): Partial established production
Scenario 3 (red): Stagnant development

Scenario seeds:

Scenario 1: This scenario is characterized by demand-side policy measures, namely a modification of the current proposal of a new Renewable Energy Directive (RED II). The modifications provide strong incentives for advanced biofuels, but do not contain the currently planned significant reduction in first generation biofuels. As a consequence, existing producers or investors in bioethanol as well as potential new investors commit to advanced biofuels. The measure is integrated in a broader policy mix.

Scenario 2: This scenario presents a partial uptake of lignocellulosic ethanol. Rather favourable framework conditions with a rising oil price and modest biomass price increases go along with only partial established demand-side policies that may foster the uptake of lignocellulosic ethanol. More concretely the current RED II proposal with binding mandates for lignocellulosic ethanol, but a significant cut in first generation biofuels come into place.

Scenario 3: This scenario presents a stagnant development of lignocellulosic ethanol. There is neither a development of an external framework, which may drive activities, nor significant policy commitment to bridge the phase and overcome missing cost competitiveness. More concretely, oil price remains low and comparable to current price levels, public financial support for R&D&I is falling, there are no binding mandates for lignocellulosic ethanol or other demand-side policy or strong financing of (near) commercial activities.

2.2.1 Technology

T	Factor and Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
1	**Sustainable provision of lignocellulosic biomass** - Depending on the feedstock (agricultural residues, forestry, municipal waste), different machines, infrastructures and logistics for collecting biomass are under development; sustainability remains an issue - Alternative use of biomass as key influencing factor	2 **Waste and residues for small scale production** - Agricultural/forest residues, organic (industrial/household) waste as biomass for fuel production or chemicals - Small scale production close to raw material sources more widespread	1 **Tailored non-food crops for large scale production** few large-scale versatile biorefineries, using different types of feedstocks, among others tailored biomass crops	**Diversified biomass feedstock** - certain types of lignocellulosic biomass (e.g. straw) which are in principle available cannot be used in a sustainable way for ethanol production because their conventional use (e.g. soil improvement) cannot be re-placed → Additional biomass needed, e.g. - CO2 Fixation / Capture CCS - Marine based biomass (Blue biomass)	3 **Incremental advances** Mainly status-quo development, concepts based on straw and wood are further developed, but no major advances in cost reduction

T	Factor and Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
2	**Pre-treatment and hydrolysis** - Different options: Chemical, thermal, mechanical, biological pretreatment or a combination of these - Biological pre-treatment not very efficient yet (a lot of water and energy needed) and quite expensive - Enzymes break down cellulose and hemicellulose fractions to fermentable C5 and C6-sugars - Costs have decreased in the past, but are still significant	1 2 **Novel pre-treatment and hydrolysis steps** - Novel pre-treatment and hydrolysis steps broadly implemented - optimized pre-treatment techniques leading to higher yields and limiting adverse inhibitors' effects,e.g. through better fractioning and use of novel solvents; - less costly and more efficient enzymes through optimization of enzymes (modification/stabilization) or better re-use of enzyme combinations; up-scaling of enzyme production - enzyme costs of total production costs < 10 %	3 **Gasification** - Gasification of biomass to syngas becomes the predominant process	**Biological pre-treatment and hydrolysis** - Deployment of bio-based technologies for converting biomass which replicate natural processes - Complete biological processes by using optimized microbes, microorganisms and enzymes (mainly by synthetic biology) - Simplification of processes, e.g. simultaneous saccharification and fermentation	

T	Factor and Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
3	**Valorization of lignin and by-products** - Few high-value uses of by-products and residues, lignin mainly used in bioenergy production - Lignin can be applied both as material and aromatic chemical building block - Part of lignin will be used for process steam	1 2 **High value applications** - High value applications for lignin (e.g.: source of phenols in duroplastic and thermoplastic application) broadly established - Cellulosic ethanol production integrated into biorefineries; thus using multiple feedstocks and achieving highest value through broad spectrum of products - More advanced biorefineries would enable the production of purer and qualitatively better lignin - Lignin could be used for semi-bulk applications (e.g. as a glue for materials) - High-value uses for by products (extractives: tannins, lipids; fatty acids, bioactive compounds) established:	3 **Use for energy production** - By-products mostly used for energy production (= status quo)	**Less by-products** - Diversification of biomass used - Tailored use of biomass , reduction of by-products - Stronger valorization of biomass components - Use of marine biomass (salts, bioactives, antimicrobials)	

T	Factor and Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
4	**Fermentation using production organisms*** - Different production options: using yeast-based, bacteria-based systems, or chemical conversion of the produced acetic acid into ethanol - Current challenges: limited ability to ferment C6 and C5 sugars, sensitivity of microorganisms to inhibitors , achieved yields and final EtOH concentration	• Broad use of genetically modified, metabolically engineered microorganisms on commercial scale*	• Use of thermophilic archaea (e.g. tolerating 80°C) in order to combine pretreatment and ethanol fermentation in one process step *	• Broad use of tailored microorganisms designed by synthetic biology*	

* This factor and assumptions haven't attributed to scenarios in the workshop

2.2.2 Business: Selected Factors

B	Factor and Current-Situation	Future Assumption A	Future Assumption B	Future Assumption C
1	**Cost Competitiveness** - ligno-cellulosic ethanol is not cost competitive compared to fossil fuel and bioethanol 1 generation - Still a significant cost gap exist, literature assumes around 25-30% higher costs	3 **No cost competitiveness** - No cost competitiveness compared to1st gen. bioethanol and fossil fuels	1 **Increasing cost competitiveness** - Ligno-cellulosic costs converge to those of 1st generation bioethanol and fossil fuels - Preconditions: RED mandate for significant 2nd LC-Bioethanol; financing for new facilities available; scale up of facility and build up of at least 20 facilities	2 **Cost competitiveness for selected pathways** - Costs competitiveness only achieved for very few pathways of LC Bioethanol and only economic viable in certain regions - Preconditions: Favourable regulation (e.g. such as CO_2 tax in Sweden) and feedstock supply advantage in a region

2	**Commitment of users and financiers**
	- Large uncertainties regarding revenues, as
	  - no long-term commitments/contracts from user industry, as there is no advantage or must for them to provide fixed acceptance guarantees
	  - depends on policy mandates for LC bioethanol, which are unclear
	- consequently raising funding for build up of new plants is difficult
		1
		Increasing commitment
		- Blenders give long-term commitment
		- More financing programs for building plants available
			2 3
			Very limited commitment
			- Neither user industry nor financiers provide long-term commitment to build up new plants	

B	Factor and Current-Situation	Future Assumption A	Future Assumption B	Future Assumption C
3	**Industry Structure** - Large companies are dominating the market (for ethanol, not necessarily fuels) - SMEs are present in different roles, some as technology developer, as producer or as service provider (e.g. engineering concepts)	3 **Large firms and SME struggle** - Markets of large companies are declining → these firms move into new markets, - Small firms may not step in as market conditions are unfavourable - → less industrial dynamic in the ethanol sector	1 2 **SMEs on the rise** - SMEs become more and more successful and take shares of large companies → these become more agile and fruitful market concurrence emerges - SMEs are also active in creating markets for by-products of ethanol; e.g. firms that are (independent from ethanol) active in lignin markets. They create new value products and settle the path for other to use the lignin coming out from lignocellulosic ethanol production to produce those goods	**Large firms dominate (Status-Quo)** - Large firms are still dominant - As SMEs are not assumed to have a special role in this sector this may not necessarily hinder further developments, but market is highly dependent on large companies decisions

2.2.3 Policy and Framework Conditions

P	Factor	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
1	**Oil Price** - 50 US$/bbl	2 **111 US$/bbl** - (From IEA New Policy Scenario)	**127 US$/bbl** - (From IEA Current Policy Scenario)	**85 US$/bbl** - (From IEA 450 Scenario)	3 **60 US$/bbl** - (From Expert Workshop)
2	**Biomass Price** - Varying between regions in feedstock in EU, prices for straw and wood in a range of around 50-70 €/t – 100€/t - Biomass Prices will to some extent follow oil prices in the long run	3 **Constant/slight declining prices (up to10%)**	2 **Moderate Price increase (10-25%)**	1 **High price increase (> 25%)**	
3	**R&D&I Policy** - Considerable funding for lignocellulosic bio-ethanol available	**Public funding at constant level** - Funding opportunities for R&D remain at a comparable level.	1 **Extensive public funding made available for specific purposes** - Specific funding for lignocellulosic fuel projects throughout different TRLs	2 **Extensive public funding made available more generally** - Stimulation of general replacement of oil-based products (not only fuels)	3 **Less public financial support available**

P	Factor	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
4	**Renewable Energy Directive** - Indicative target for 2nd generation biofuels of 0,5 % and double counting to quota - Sustainability criteria: 60% GHG emission saving for new installations, 50% GHG emission saving for existing installations (from 2018 on)	3 **Continuation of existing RED goals until 2030** --> no stimulation of new investments in lignocellulosic ethanol	1 **Amendment of existing RED goals** - Continuation of 10% share for biofuels - introduction of obligatory mandate for lignocellulosic ethanol	2 **EC proposition for RED II** - cap on the contribution of food-based biofuels to declining to 3,8 % in 2030; - submandate for advanced biofuels (3.6 %) - Mandatory quotes would give a market with price pressure - Higher sustainability criteria (70% GHG savings for advanced biofuels) Policy Targets vs. penalties very important	
5	**Demand side measures** - Public Procurement/Price Guarantees hardly introduced yet	2 3 **Very limited demand side measures** - Very few, fragmented activities to support demand for 2nd gen. biofuels	1 **Broad range of demand side measures** - Price guarantees, e.g. via local tenders - tax exemptions for lignocellulosic ethanol - Fossil fuel tax	**Climate protection tax**	

P	Factor	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
6	**Financing of (near) Commercial Activities** - Public/private investors are reluctant; rather low incentives for investment - Approach of banks important	2 3 **Limited financing** - Predominance of the status quo development	1 **Increasing public/private financing** - Comprehensive, coordinated policy funding or tax incentives for private funders for high TRL-stages or commercial production		

Workshop participants gave written comments to the policy factors. Some of these comments have been integrated into the factors listed above. The other comments can be summarized as follows:

- The need for several public support instruments was expressed as necessary
- For some instruments (e.g. mandates) the characteristics of the penalties are of key importance for the functioning of the instrument
- Also instruments should be considered that reach beyond fuels and the lignocellulosic feedstock, e.g.
  - Stimulate the replacement of oil-based products, not only fuels
  - R&D&I policy innovation on flexible processes that can be applied to using CO2 / sugars / syngas / other as biobased raw materials

3 Scenarios for bio-based Plastics

3.1 Story Lines for bio-based Plastics Scenarios

Scenario 1: “Derisking strategy“

There is a comprehensive, coordinated policy (P4B) regarding biobased plastics: while funding for R&D remains considerable at the status quo level (P3A), additional financing of risky business with strategic importance is implemented (P4B). This takes the form of e.g. flagship projects, public-private partnerships or investment financing and specifically address private funders and higher TRL stages (e.g. pilot/demonstration scale, near commercialization) (P4B). In addition, coordinated market pull measures (e.g. public procurement, tax exemptions etc.) are implemented in the EU (P6B). Moreover, labels and transparent information about bio-based plastics and their benefits (e.g. indicating bio-based content, biodegradability, recyclability) are widespread (P5B).

As a consequence of these coordinated policy efforts, many new market opportunities arise: Bioplastics become increasingly competitive in a wide range of applications (B2C) and are incorporated into a greater diversity of products from a number of industries (B4B). Brand-owners drive the demand for biobased plastics. In these market segments, some biobased plastics achieve commodity status and earn more than 1 % of the overall commodity market (B5C). Regarding the share of drop-ins vs. new materials, price, policy and functionality all play an important role (T4C). Due to the diversity of products on the market, bio-based plastics are produced both in large and small scale processing plants (T2B) via many production pathways (T5B). Due to the high production volume of bio-based plastics, more feedstock is drawn to this market with the risk of feedstock shortage. Therefore, the use of a wide diversity of feedstocks is required (T1C, B1C), depending on regional capacities, product specifications etc. The positive market development is further supported by awareness and positive perception in the population (B3A). No special attention is given to plastic waste, so that incineration of plastic waste (both fossil- and biobased) predominates (T3A).

Scenario 2: High oil price, no additional specific policy measures

The oil price rises considerably (e.g. to 127 €/bbl or even 200 €/bbl) (P1B) and thus creates much more favourable market conditions for biobased plastics than today, making certain biobased plastics, mostly drop-ins, marginally competitive as commodity (B2B). Price determines the share of drop-ins in the overall plastics market (T4A). Brand owners (e.g. Coca Cola, LEGO) become the primary drivers of producing and bringing biobased plastics to the markets (B5A). However, the spectrum of products remains limited (B4C) and the demand for biobased plastics is mainly determined by the brand owners demand (B3C). Production of few biobased plastics in large amounts takes place in large scale plants (T2A) via few production pathways (T5A), using conventional feedstocks (mainly sugar, starch, fats and oils) (B1A, T1A). No special attention is given to plastic waste, so that incineration of plastic waste (both fossil- and biobased) predominates (T3A).

Scenario 3: (Micro)plastics receive high attention by policy and consumers

There is very high awareness and concerns of (micro)plastics in the environment. This creates a climate in which much stricter policies regarding plastic use and plastic waste are enforced (P6C): there is a trend to ban short-lived plastics which do not degrade readily under

environmental conditions. On the one hand, this creates novel niche market opportunities for certain, biodegradable biobased plastics (T3B, B2A). They can be easily identified via transparent and widespread labels (P5B). Moreover, recycling of plastics becomes a priority (T3C, T3D), and in addition, water treatment technologies are implemented to remove plastics from water. Functionality, in this case biodegradability, determines the share of biobased plastics (T4B). On the other hand, there is social resistance to biobased plastics which do not degrade readily (B3B), and innovation in this field is stifled (B3C). As only few biobased plastics fulfill all the requirements, the bioplastics markets stagnate or even contract (B4A). Brandowners drive the demand for biobased plastics (B5A). Production mainly takes place in small-scale plants (T2C). Due to the recycling-friendly climate, waste is used as feedstock (T1B, B1B), in addition to conventional feedstocks (e.g. starch) (T1A, B1A). As a consequence of feedstock variety and small processing plants, a multitude of production pathways are used (T5B).

3.2 Overview of Factors and Future Assumptions – bio-based Plastics

Scenario 1 (green): “Derisking strategy” scenario
Scenario 2 (yellow): High oil price scenario
Scenario 3 (red): Niche market scenario: Recycling of plastics as a priority, ban of short-lived plastics

Scenario seeds:

Scenario 1: De-risking strategy: there is a comprehensive, coordinated policy which finances risky business with strategic importance, e.g. via flagship projects or investment financing. In addition, coordinated market pull measures (e.g. public procurement, tax exemptions etc.) are implemented in the EU. Moreover, labels and transparent information about bio-based plastics and their benefits (e.g. indicating bio-based content, biodegradability, recyclability) are widespread. Many new market opportunities arise. As a consequence, more feedstock is drawn to the bio-based plastic market, with the possibility of feedstock shortage. Brand owner roadmaps to bio-based plastics (including lignocelluloses sugar) become attainable.

Scenario 2: Favourable oil price (127 €/bbl), market pull measures remain status quo (=Standardisation/information about biobased plastics, labeling: functionalities and benefits remain unclear or are partly unknown)

Scenario 3: (Micro)plastics in the environment receive high attention by consumers and policy. Recycling of plastics becomes a priority, and water treatment technologies to remove plastics from water are implemented. There is a trend towards the ban of short-lived plastics which do not degrade readily under environmental conditions, and water treatment technologies to remove plastics from water are implemented. However, there are only few niche applications for bio-based plastics which degrade under environmental conditions. In addition, new solutions for textiles are needed

3.2.1 Technology

T	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
1	**Type of feedstock** (= biomass used for the production of bioplastics) The factor refers to the respective shares of feedstock type. A certain flexibility in feedstock use is required (e.g.: start now with future assumption A, adapt to market, then switch to other feedstock). Efficient feedstock use is a prerequisite (expressed as e.g. kg bio-based plastics / ha)	2 3 **Sugar/ starch and fats/oils dominate as feedstocks** as they also have the following characteristics: - The feedstocks are globally available in large quantities, they are transportable, storable, they have a constant quality, - A high grade of preprocessing is required	3 **Nonfood feedstocks play a major role** Dominating feedstocks are - A: wood, reed, straw, hay - B: fresh biomass, e.g. green grass, and waste: from the food industry, municipal waste, agricultural waste Characteristics of these feedstocks are A feedstocks have similar characteristics as the feedstocks in Future Assumption A B feedstocks have the following characteristics: The feedstocks are locally available in small quantities, they are fresh, have a high water content, and require immediate processing There is the option that high value substances can be isolated from feedstock fractions	1 **A wide diversity of feedstock is used** - All the feedstocks listed in future assumptions A and B are used - In addition, gasous feedstocks are used (CO, CO_2, H_2, CH_4, exhaust gases, gasification of waste)	

T	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
2	**Infrastructure for feedstock provision, processing and logistics** The factor refers to the type of biomass processing plants where bioplastics or building blocks are manufactured, and the required supply chains and logistics Sustainable feedstock provision is a prerequisite	2 **Large scale plants processing plants** - Processing of feedstocks takes place in large scale plants, where only a few products are manufactured. This is state of the art and will be continued (business as usual) - They are part of global supply chains - Technology is improved continuously	1 **Large and small scale processing plants** - Technologies for the pretreatment of biomass, which meet bioprocess requirements, become cost-competitive - Logistics for waste collection and waste pretreatment are established - Processing of feedstocks T1A may take place in larger scale plants - Processing of feedstocks T1A and T1B takes place in small scale conversion plants	3 **Small scale processing plants** - Processing of feedstocks takes place in small scale conversion plants	

T	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
3	**Recycling technology for biobased plastics**	1 2 **Thermal use of plastic waste predominates** - Bioplastics remain a disaster for recycling - Mixed plastic waste is incinerated or converted to fuels	3 **Degradation of plastic waste** - Environmental degradability becomes mandatory for short-lived plastics	3 **Recycling established for certain plastic products or types of plastic** - Collection systems and recycling technologies are established for certain plastic products which make a “bottle-to-bottle” recycling possible (example: PET bottles) - Technologies are established which allow to recover high quality plastics from recycling (e.g. no smell, high chain length, etc.)	3 **Recycling established for all types of plastics** - All plastic materials can be separated or sorted by types of plastics. They are channeled into high value (re)-uses
4	**Share of drop-ins vs. share of new materials**	2 **Price determines the share** - Drop-ins dominate the bio-based plastics segment, they compete by price with fossil-based plastics	3 **Functionality determines the share** - New bio-based materials dominate the bio-based plastics segment because drop-ins cannot compete with fossil plastics on a cost basis	1 **Price, policy and functionality play an important role** - The share of drop-in bio-based plastics in the bio-based plastics segment is determined by price and/or market uptake policy measures - The share of new bio-based materials in the bio-based plastics segment is determined by performance and functionality	

T	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
5	**Production pathway** - Different pathways for bioplastics production, e.g. direct production from feedstock (e.g. PHA), or intermediate steps, where monomers (e.g. platform biochemicals) are formed	2 **Few production pathways** - Few pathways a established for few large scale production processes/plants	1 3 **Many production pathways** - A multitude of production pathways coexist		

3.2.2 Business

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
1	**Feedstock** - Currently, Sugar and Starch based feedstock have market dominance for Bioplastics. - Alternatives (like lignocelluloses) remain ineffective or cost prohibitive. - First generation feedstock is inherently unreliable in regards to their performance consistency. Though second generation feedstock are under development, it is likely that most will go to the production of bio-fuels (not plastics).	2 3 **Continue to use traditional feedstock (sugar and starch) for production of most industrial Bioplastics.**	3 **Major switch to non-food biomass** - This would require a major technological and procedural breakthrough, but if successful would radically shift the balance. - Many researchers are currently experimenting with lignocelluloses technologies.	1 **Wide diversity of conventional and non-food feedstock are used.** - Dependent on regional capacities and policy, - Product specifications, - Other factors.

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
2	**Competitiveness of „Drop-Ins“** - Due to currently low oil prices, cost competitiveness of Bioplastics has been impeded, and some bio-based companies have struggled to remain in operation and/or to move up the value chain. - This status is also closely linked to various policy threads, including national and international policy regarding sustainability. - There is steady interest in Drop-ins that can alter functionality and safety or result in novel materials within current production infrastructures.	3 **Limited or Constricted Competitiveness.** - The increasing availability of shale-oil based products could severely limit the growth potential for Bioplastics, and continue to push the industry into smaller niche provider directions. - If C2 based Drop-Ins (which are largely the product of shale-oil) continue to grow in quantity, Bioplastics could be pushed out of commodities entirely. Actors then will focus their efforts on other areas of the value chain and niche markets.	2 **Marginal Competitiveness**. - With strong, brand-owner led demand, Bioplastics could become marginally competitive as a commodity***. - Such demand could support a growing infrastructure for Bioplastics production, but it is likely that such development would occur in regions or nations where it was most fiscally profitable. - It was also put forth that Bioplastics could become increasingly competitive within niche or minor industries (aromatics, etc). (***It was estimated that, specific for C2 plastics, 1% of the commodities markets for plastics could equal upwards of 300 million tons)	1 **Broadly Competitive.** - Bioplastics might become increasingly competitive if demand can be encouraged through changes to policy and/or a heightened public awareness of their potentials. - Increasingly stringent policies (rooted perhaps in carbon caps) could greatly benefit the Bioplastics industry both as it exists and its future development. - As the public becomes more aware of Bioplastics and their range of functionality, they might be more insistent on such products in the market, and push for further policy reform.

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
3	**Societal Awareness and Actions -** - Currently, social awareness of Bioplastics seems restricted to their capacity to biodegrade – a concept both misunderstood and radically limiting of Bioplastics potential. Raising consumer awareness also carries the danger of public fear (for example public reactions to GMO products and the resulting legislation). - There are also few policies in place to differentiate Bioplastic products and incentivize consumer purchases. Official certification programs to promote consumer awareness and /or policy that impacts pricing of non bio-based plastics could have a strong impact on consumer decision making.	1 **Bio Plastics could see major expansion if an increased level of social awareness can fuel a growing demand in both B2B and B2C markets.** - Waste Policy that favors certain functionality from plastic products could create growth in Drop-in and Non-Drop-In production and development. Coupled with awareness raising campaigns regarding technological breakthroughs and advanced functionality of Bioplastics, social demand for bio-based products could be radically increased. - If Climate Change continues to shape social perception regarding product life cycles and their environmental impact, growing social awareness and demand for public and private Bioplastics consumption could greatly benefit the industry.	3 **Falling Demand for Bioplastics could arise from different social movements and policies.** - If food security becomes a growing social concern, then land usage policy could reduce feedstock availability by limiting its production. - Alternatively, resistance to new products (both by industrial and individual consumers) might prove an important obstacle to garnering public favor, and could be detrimental to existing Bioplastic markets..	2 **Demand for Bioplastics could reach a plateau in the coming years due to many converging factors.** - If Bioplastics either fail to deliver on publicly perceived functionality promises, they could come to be viewed as a “fad” technology and fall out of the public imaginary. This perception might not eliminate incumbent Bioplastic technologies or industries, but could reduce the amount of funds available for research, development, and innovation. 3 - Alternatively, if public policy and regulation raises functional requirements too high, Bioplastics innovation could be stifled (both by established large firms, and in SMEs/startups).

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
4	**Markets for New Materials and „Non-Drop-Ins“** - Currently, the majority of bio-based products are Drop-Ins for existing mass markets. These are cost-competitive with fossil based counterparts, particularly during times of higher oil prices. - B2B opportunities typically dominate the industry, though B2C opportunities are growing alongside consumer awareness.	3 **Contracting Bioplastics Markets** - Multiple factors could lead to a contraction of the overall Bioplastics market and the variety and quantity of products offered. - Continued low (or lower) oil prices can undermine what little competitive advantage Bioplastics once held. - Concerns over Food Security fuel a social movement regarding land usage for non-food bio production.	1 **Greater diversity of Products could come from a number of industries.** - For Bioplastics that can exhibit the required functionality, growing interest from architecture, industrial design (including automotive), and other high-volume markets for traditional fossil plastics could lead to competitive parity for bioplastics within certain niches. - Such interest could spurn R&D&I for more diverse Bioplastics as both building blocks and as finished products.	2 . **Stagnant Product Evolution** - This could be the result of a variety of factors, but primary drivers include continued low-oil prices, restrictive policies, or the development of alternative processes to achieve carbon neutrality. - The CO2 process that is currently being developed and marketed by the Coca Cola Co. is one such instance of a competing process that undermines the stability of Bioplastics.
5	**Brand Owner Strategies**	3 2 **Brand Owner Driven Demand for Innovation** - If brand owners (LEGO, Coca Cola) become the primary drivers of demand for new products and functions - Bioplastics R&D&I institutions from academia to SMEs is likely to grow in scope and overall production. - It is possible that Brand Owner driven demand can help bio plastics pass critical tipping points, and become ever more competitive with fossil based alternatives across a growing variety of plastic types.	**As an extension of the status quo, Brand Owners continue to drive the market for all non-food biomass based products.** - Under such conditions, novel innovations in Bioplastics and their functionality remain specialized and marginalized in regard to the wider market.	1 **Brand owner driven demand for Bioplastics could result in commodity status, with some bio-based products earning more than one percent of the overall commodity market (a very large amount).**

3.2.3 Policy

P	Factor and Current Status	Future Assumption A	Future Assumption B	Future Assumption C
1	**Oil Price** - 50 USD/bbl	- 111 €/bbl (IEA New Policy Scenario)	2 - 127 €/bbl (IEA Current Policy Scenario)	- 85 € /bbl (IEA 450 Scenario)
2	**Biomass Price** Varying between regions in feedstock in EU, prices for straw and wood in a range of around 50-70 €/t, white sugar 470€/t	- Constant/slight declining prices (up to10%)	- Moderate Price increase (10-25%)	- High price increase (> 25%)
3	**R&D&I Policy (EU + national)** Considerable funding for biobased plastics available	1 - Status Quo: Funding opportunities for R&D remain at a comparable level.	- Extensive public funding made available	- Less public financial support available
4	**Financing of (near) Commercial Activities** Public/private investors are reluctant; rather low incentives for investment	2 - Mostly status quo development	1 - Comprehensive, coordinated policy funding or tax incentives for private funders for high TRL-stages or commercial production	
5	**Standardization/Information about Bio-based Plastics, Labelling** Terms (e.g. “green”, “bio-degradable”, “biobased”, “bioplastics”, etc. are not well defined Some EU standardization initiatives	2 - Functionalities and benefits unclear/partly known	1 3 - Transparent and widespread labels /information about bio-based plastics and their benefits (e.g. indicating bio-based content, biodegradability, recyclability)	

P	Factor and Current Status	Future Assumption A	Future Assumption B	Future Assumption C
6	**Market pull measures** Various measures debated (bans, mandates, public procurement, tax exemptions, etc.) Fragmented national policies for bans/procurement; no market uptake incentives	2 - Status quo, few fragmented national activities	1 - Market uptake measures (public procurement; tax exemptions etc.) coordinated in the EU	3 - Short-lived plastics, which do not degreade readily under environmental conditions are more and more banned - Recycling of plastics as a priority

Participants' comments for the Policy measures/factors and future assumptions:

- Oil price: Non-linear effects of oil prices should be taken into consideration, regarding plant size, fuels, and commoditization of specialities
- Biomass price: constant or slightly declining prices are expected for 2nd generation feedstocks; moderate price increases are expected for competitive pricing without subsidies
- R&D&I Policy: both EU and national policies should be taken into consideration
- Financing of (near) Commercial Activities: Flagship projects, Public-Private Partnerships and financial instruments for a "derisking strategy" are suggested. These instruments could target pilot and demonstration units in the EU (e.g. like in BBI), upscaling and implementation.
- Standardization/Information about Bio-based Plastics, Labelling: A clear distinction should be made between "bio-based" and "biodegradable". There are CENTC4II standards on bio-based products. Standards and certification should be for sustainability. It is warned against "over-marketing", as it bears the risk that no-one believes in "green" anymore.
- Market pull measures: Bioeconomy and bio-based products have important roles in the EU circular economy strategy. Bioplastics and market uptake measures have/should have a role in the upcoming EU plastics strategy. Market pull measures should be part of a coherent supportive policy framework. Life cycle thinking and the performance of new biomaterials should be taken into consideration. Green public procurement is expected to create a critical mass with the market.

4 Scenarios for Production of Biopharmaceuticals

4.1 Story Lines for Production of Biopharmaceuticals Scenarios

Scenario 1: Increasing Demand for Biopharmaceuticals

Seed: This scenario is mainly market/ demand driven with a dynamic growth for biopharmaceuticals (in absolute numbers, but also in market shares) that demands for increasing production (B1B). Stratified medicine is widespread and will lead to a diversification of the product and service portfolio, as the development of respective biomarkers and devices as well as testing will be provided complementary to the biopharmaceuticals.

On the technological side, the current “one line, one product” setup stays the predominant production mode for larger volume products (T1B); flexible multiple product operations are only established slowly, as they require too high quality control efforts. The availability of data available in real-time will grow enormously (T3A). Related infrastructure will be set up and related knowledge for data interpretation will grow cumulatively.

Breakthroughs will be reached in terms of more productive upstream methods via new improved organisms (e.g. plants, insects) (T2A). Moreover, respective downstream process are established to improve the process (continuous production, process intensification, new methods). Those advances in manufacturing, e.g. establishment of continuous manufacturing, will lead to slightly declining prices, which will be requested by the moderately continuation of cost containment pressures.

Regulation for biopharmaceutical manufacturing will continue to get stricter, but a higher transparency and growing consensus between regulators and manufacturers enables for a more efficient addressing of regulatory requirements (P3A). In particular, new biopharmaceuticals will receive considerable price reimbursement when they can prove high medical value. (P2C).

Europe is able to take advantage of this development. The number of biopharmaceutical facilities increases smoothly, while the output increases significantly (B1B). The share in production capacities in the EU remains constant and technological expertise can be secured in the EU (B2B). But also the markets and production in emerging countries may grow, as technological innovation and reduction of production cost enables to deliver products to patients there that cannot afford those medicines yet.

Scenario 2: Status Quo Development

Seed: This scenario reflects incremental evolution in the production of biopharmaceuticals with rather slow technological progress and a rather modest market growth (B1A).

While the manufacturing of existing product groups (e.g. monoclonal or derived antibodies) with known production organism continues to work smoothly, difficulties in manufacturing processes for new types of product arise (T1A, T2C). This may lead to that the market entry of some new product groups is significantly delayed and hampered. Regarding process analytics advances regarding real time and online monitoring will be achieved, but not all data will be available online (T3B).

The market for biopharmaceuticals grows steadily, but no high growth rates will be achieved (B1A). An important reason is the increasing cost containment pressure for biopharmaceuti-

cals around the world (P2B). Incentives for biosimilars production are enforced, but to a lesser extent for the production of new biopharmaceuticals. For production, this may mean that the demanded volume (but not necessarily turnover because of falling prices) may rise, but also the pressure for more cost efficient solutions will rise. Because of limited probability especially for new products pharmaceutical companies will be rather reluctant in biopharmaceutical production, as the financial outlook is too modest to build capacities for new biopharmaceuticals in development. Flexible CMOs will step in; here, new firms from other fields (e.g. firms such as the already active firms Samsung Biologics, Fujifilm) will increasingly enter the market (B3A). Globally, Asia will catch up and increase their production capacity enormously (B2C). In Europe, the production capacities will fall in absolute numbers and world-wide share. Moreover, the advantages in technological expertise in Europe can hardly be preserved.

Scenario 3: Gene Therapy Breakthrough[1]

Seed: This scenario is characterized by the establishment of gene therapies in clinical routine, enabled by advances of CRISPR / CAS methods (T1C). This could change medical delivery profoundly: for example, in mono-genetic diseases a one time treatment could become possible compared to medical treatment (e.g. enzyme replacement therapy) over a period of time or even life-long. New therapy forms with new manufacturing requirements will gain importance. While the industry structure will not change profoundly, new SMEs active in gene therapy enter the market (B3B).

In addition to advances in gene therapy, there will be significant advances in biopharmaceutical production, especially in process analytics (T3A). The availability of real-time data will grow enormously (e.g. CO_2 / O_2 / pH values available in real time). Related infrastructure will be set up and knowledge for interpretation will grow cumulatively. Further advances may come from cell-free synthesis, implemented for biopharmaceuticals production on industrial scale (T2B). The distribution of R&D activities increases all over the world (B2A). Emerging countries will increase their R&D activities along with production capacities. Instead, Europe suffers some decline in share of production capacities.

The market for biopharmaceuticals grows will grow (B1C), but the product portfolio becomes more diversified due to advanced therapies Cost containment pressure will continue with significant efforts to link price setting to the additional medical benefit (P2A). Overall, prices will remain high.

[1] This scenario was considered as very unlikely by some participants, because of high technology challenges and unclearness of technology design.

4.2 Overview Factors and Future Assumptions – Production of Biopharmaceuticals

Scenario 1 (green): Broader Access to Biopharmaceuticals
Scenario 2 (yellow): Status Quo Development
Scenario 3 (red): Gene Therapy Breakthrough

Scenario 1:

Market demand leads to a dynamic growth for biopharmaceuticals (in absolute numbers, but also in market shares) that demands for increasing production.

Scenario 2:

Incremental evolution in the production of biopharmaceuticals with rather slow technological progress and a rather modest market growth

Scenario 3:

Gene therapies become established in clinical routine, enabled by advances of CRISPR / CAS methods (T1C). This will change medical delivery profoundly with one time treatment compared instead of medical treatment with pharmaceuticals over a period of time or even life-long. New therapy forms with new manufacturing requirements will gain importance.

4.2.1 Technology

T	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
1	**Technologies for new products** - Solutions for rare diseases gain importance - protein therapeutics -gene therapy - Push to develop technologies for true personalized approaches at affordable cost; e.g. oncology, diagnostics, orphan drugs - Maintaining expertise in microbiology (in academia – SME – large companies as challenge)	2 **Manufacturing difficulties for new products** - Difficulties in manufacturing process for new type of products. Market entry of some new product groups is significantly delayed and hampered - Monoclonal or derived antibodies still on the market	1 **One line- one product set-up** - current “one line, one product” setup stays the predominant production mode; flexible multiple product operations require too high quality control efforts - Single-use systems are suited - Virology + brain / nerves as important areas	3 **Gene Therapies established** - Gene Therapies more widely established by CRISPR / CAS - Drug device combinations (insulin)
2	**Production organisms for biopharmaceuticals** - Most biologicals are manufactured in bacteria or mammalian cell cultures. New production platforms (e.g. cell-free synthesis of recombinant proteins) are mainly in lab to pilot scale and are predominantly used in the research phase, but not yet in manufacturing - Important developments - - Improved cell lines (e.g. secreting cell lines) - New production organisms (e.g. plant cell lines, - Alternatives to engineered cell lines (e.g. transgenic crop plants or transgenic animals (“pharming”))	1 **Break through: more productive upstream methods** - new and/or improved production organisms (e.g. plants, insects) -> reduce downstream hurdles(-> GMP)	3 **Cell free synthesis established**	2 **Incremental Advances**

T	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
3	**Process analytics** Relevant aspects: - real time monitoring - - online analytics, single use - "Data integrity", Data management - Data evaluation - Process control for continuous production - Advanced models - Data handling - Need to understand / control the process: in-process analytics development	3 . 1 . **All data available in real time** - All Data (CO_2 / O_2 / pH values) available in real time - IT-infrastructure available - Knowledge for interpretation available - Process control for continuous processes - Intercellular devices - Molecular sensors"	2 . **Some data available offline**	

4.2.2 Business

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
1	**Market for new Biopharmaceutical Products** Mixed market developments for new biopharmaceuticals, which determine the needed production capacities and its utilization: - Unmet clinical needs and personalized medicine favor biopharmaceuticals - Payer pressure on cost of drugs increase - From the cost side, approval of product becomes increasingly expensive. This may hamper the R&D and commercialization of new products - Blockbuster model is losing importance	2 **Slow growth** - Market grows steadily, but no high growth rates	1 **Dynamic growth** - Market for of biopharmaceuticals (in absolute numbers, but also in market shares) grows very dynamically - Stratified medicine widespread - The value chain for the products will broaden significantly, as the development of respective biomarkers and devices as well as testing will be provided complementary (e.g. companion diagnostics) Cost reduction for companion diagnostics via improved methods in DNA sequencing	3 **Dynamic growth, diversified product portfolio** - Market for of biopharmaceuticals (in absolute numbers, but also in market shares) grows very dynamically - New therapy forms with new manufacturing requirements gaining importance
2	**Localization of R&D and production** - Europe strong in technology and production capacities - Increasing importance of emerging markets for (bio-)pharmaceuticals - Trend of localized production in many countries and also costs are very low in some locations	3 **World-wide distribution** - Increasing R&D distribution all over the world - Share of emerging markets in biopharmaceuticals rises significantly; - Emerging countries increase production capacity for these products - Europe suffers some decline in share of production capacities	1 **EU holds position** - The number of biopharmaceutical facilities increases smoothly, while the output increases significantly - The share in production capacities in the EU remains almost constant - Technological expertise can be secured in the EU	2 **Asia catch-up** - Asia will catch up and increase their production capacity enormously - In Europe, the production capacities will fall in absolute numbers and world-wide share - Significant technological expertise in Europe is lost

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
3	**Division of Work** - Increasing importance of CMOs, new firms from other fields entered the market (e.g. Fuji Films, Samsung) - Some large firms with production of own-developed pharmaceuticals and production for other firms - Some biotech firms with production capacities for clinical batches; role for CROs and SMEs in the production process unclear	2 **CMOs importance continues to rise** - Reluctant activities of large pharmaceutical companies - Flexible CMOs sill step in; here, new firms from other fields will increasingly enter the market	3 **SMEs on the rise** - Increasing importance of SMEs (in Europe) - New research areas are not occupied by big pharma; hence, fruitful fields of activities for SMEs exist	**Large companies dominate** - Status-Quo development Diversified landscape of actors, but large pharmaceutical companies have still a dominating role in the market

4.2.3 Policy

P	Factor	Future Assumption A	Future Assumptions B	Future Assumptions C
1	**R&D&I policy*** - Considerable funding for production technologies for biopharma available	**Status Quo: Funding opportunities for R&D remain at a comparable level.**	**Extensive public funding made available** - for R&D funding , but partly also for clinical trials	**Less public financial support available**
2	**Price regulations** - Increasing cost containment measures for (bio-) pharmaceuticals	3 **Significant cost containment, price regulations adjusted** - Price will be fixed according to additional medical benefit	2 **High cost containment, biosimilars incentives** - Incentives for biosimilars production, but to a lesser extend for the production of new biopharmaceuticals	1 **Moderate cost containment, new biopharmaceuticals favoured** - favourable reimbursement of new biopharmaceuticals
3	**Regulation for manufacturing** - GMP regulation sets up high requirements for manufacturing - Some discrepancies between regulators and manufacturers arise - Emerging compounds have to fulfill GMP when produced globally	1 **More Transparence and Consensus** - Transparent, partly more strict regulation - Growing consensus between regulators and manufacturers	2 **Less harmonization** - Less harmonization of regulations across world regions	**Much stricter regulations** - Increasingly strict regulations: Local advantages for industrialized countries due to a favourable regulatory framework and abundant endowment with advanced production factors

* Not identified as important driver in the various scenarios

5 Scenarios for Enzymes

5.1 Story Lines for Enzymes Scenarios

Scenario 1: Technology push, everything is optimal

Seed: Substantial technological progress, higher than in Scenario 2, new options (e.g. production hosts, cell-free systems, rational improvement) are quickly developed and taken up by industry (T1C, T2B, T3C, T4B, T5B, T6C, T7aB, T7bC). The IP framework supports intensive cooperation of academia, SMEs and large enzyme companies (B3C/D).

New enzymes and new applications thrive. Markets expand in all segments (B1A/B, B2A/B, B5A). Europe maintains a leading position in enzyme innovation (B6C), in production (B4A) - there is even relocation of enzyme production from Asia to Europe (B4D)! Enzymes are perceived positively by customers and end-users (B7B). Regulation becomes clearer and more transparent without limiting enzyme applications (P3B).

Scenario 2: Coordinated bioeconomy policy, but global competition

Seed: Rather favourable conditions for R&D (P1A), market pull measures = market expands (P2A), but increasing competition from Asia (B6A, B5B, B4B, B4C). This competition remains limited, because European players can maintain certain market shares due to their technological excellence (T7abB).

Rather favourable conditions for R&D result in good progress in R&D, both in academia and industry. There is a moderate knowledge transfer between the big enzyme industry and innovative SMEs, but not between academia and big enzyme companies because of the IP framework (B3B). R&D efforts result in moderate broadening of industrial production platforms, but established ones remain most important (T1B). Random approaches for optimization of established enzymes increase significantly (T2C) due to progress in high throughput screening (HTS); another option is, that rational optimization also increases due to favourable conditions for R&D (T2B) and increasing competition from other players/countries. The identification of new enzymes receives a push from screening technology breakthroughs (T3B). There is also progress in formulations through computational tools and knowledge-based understanding (T4B). New enzymes are evaluated for their potential applications, especially/for example for valorization of wastes and by-products (T5B). Process development remains a challenge, but market pull creates sufficient incentives to overcome hurdles (T6B). European players have a competitive advantage over Asian competitors because they use new processes, e.g. enzyme cascades or continuous processing at industrial scale (T7B) or use synthetic biology, the latter having, however, a minor role for industry (T7B).

There is a considerable extension of the market for enzymes, both for industrial as well as laundry enzymes, because the replacement of chemicals by enzymes is favoured by high oil prices and environmental concerns/regulations (B1B). New industrial processes using established and also newly developed enzymes are implemented (B2B). Moreover, positive perception of enzyme use by end-users has an additional positive impact (B7B), the favourable perception of enzymes is partly due to awareness raising campaigns which focus on the innovation aspect and the positive environmental impacts. Due to growing wealth in developing countries, emerging players in developing countries get big enough to become global players and compete with present leaders (B5B). Present market leaders loose shares of the (ex-

panding) market to Asian competitors (B4C); European producers especially withdraw their production from Asian countries, but still distribute their products globally (B4B). Saturation in Western markets triggers R&D into customer-specific solution, e.g. through novel combinations of laundry components, and into novel product forms (e.g. lower water content) (B1B). With respect to R&D investment, talents and competencies, Europe and USA remain among the leading countries, but China/Asia catch up quickly and obtain a leading position in certain segments (e.g. commodity enzymes) (B6A). Safety aspects of enzyme exposure are no major issue; it is being dealt with by standard operating procedures in industry (B8A).

Scenario 3: High oil price, but consumer concerns

Seed: The oil price is high and thus creates favourable conditions to replace fossil-based chemicals and processes by enzymes (P2C, B2C). However, there is growing concern of consumers of genetically modified organisms and adverse health effects of enzymes (B7A). NGOs run anti-enzyme campaigns. As a consequence, regulations for enzymes become stricter (P3A).

The progress in R&D and innovation is less than in scenario 1, because there is less revenue from the markets and thus less private investment in R&D (e.g. T3D, T5C, T1A, T2A, T4A, T3A). Public funding of R&D remains on a comparable level as today and is focused on certain fields (P1B, T2D). The high oil price favours R&D bioeconomy initiatives (P2C). The R&D focus shifts to fields which are compatible with the enzyme regulations and public concern, especially to non-GMO production, natural production processes, synthetic chemistry, non-sensitizing enzymes and their formulations, and cell-free production systems for enzyme applications close to end-consumers (T4B, T2D). In fields which are hampered by negative public perception (e.g. synthetic biology) (T7bA), enzyme development is significantly slowed down, redirected or moved to other countries (T1D, T2D). The enzyme industry sticks to the established expression systems (T1A). The high oil price favours the replacement of chemicals by enzymes in industrial processes, but the full potential cannot be exploited due to negative public perception (T3A). Process development is improved for industrial processes not hampered by public perception. It remains on status quo level in the other segments (T6A). There is certain progress in academic R&D in rational optimization of enzymes, but is not taken up by industry (T2A). One of the reasons may be that big enzyme companies reduce their cooperation with SME and academia (B3A).

The market also becomes segmented: applications develop positively, where the high oil price drives enzyme use and which are not significantly impaired by negative public perception and regulation: here, new enzymes are introduced, also for new applications (B2C). Enzyme applications close to consumers and of public concern decrease, e.g. food and drink, personal care products (B1D). There is increasing competition of enzymes with non-enzymatic alternatives on a case by case basis, depending on labeling requirements, public concern, oil price and benefits from enzyme use (B1A, B1D). New applications of new enzymes are being developed in certain segments (B2C). With respect to the geographical distribution of activities, Asia takes over in R&D because investment, talents and competencies are developed and supported in the whole enzyme field whereas Europe focuses strongly only on certain segments and has given up development in other segments (B6B). Emerging enzyme producers in developing countries become global players, replace present leaders in certain segments (B5C) and compete with them in other segments (B4C). Production of enzymes mainly takes place in Asia, the share of Europe and US decreases (B5C).

5.2 Overview Factors and Future Assumptions – Enzymes

Scenario 1 (green): Technology push, everything is optimal
Scenario 2 (yellow): Coordinated bioeconomy policy, but global competition
Scenario 3 (red): High oil price, but consumer concerns

Scenario 1:

There is substantial technological progress: Enzymes can be designed on demand due to powerful prediction technologies. Enzymes can flexibly be produced by in vitro expression on large scale. Generation 3.0 enzyme production hardware is established.

Scenario 2:

There is a coordinated bioeconomy policy in Europe, which invests in R&D and establishes market pull measures. The regulation supports the replacement of chemicals by enzymes, the use of biomass, the saving of energy, environmental protection. Countries in the Asia/Pacific region advance significantly in enzyme-related skills as well as enzyme production, thus challenging the EU leadership in enzyme R&D/innovation as well as enzyme production.

Scenario 3:

The oil price is high (100 Euro/barrel). There a growing concerns of consumers of genetically modified organisms and adverse health effects of enzymes. NGOs run anti-enzyme campaigns. As a consequence, regulations for enzyme use become stricter.

5.2.1 Technology

T	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
1	**Expression Systems for Production (Production Host Systems)** - A small set of highly optimized production organisms (e.g. Bacillus, Trichoderma, Aspergillus) is used for most enzymes - Multinational enzyme companies often hold their proprietary technology. - New production systems provided by SMEs and academia.	3 **Established expression systems (**e.g. Bacillus, Trichoderma, Aspergillus**) predominate** and determine which enzymes can be produced on an industrial scale. E. coli as cloning system has the advantage of high flexibility.	2 Established expression systems remain the most important hosts, but a **larger choice of host systems** becomes industrially available.	1 **New expression systems are in widespread and growing use across multiple industrial applications.** Among them are - **Cell-free in-vitro protein expression**, which has the advantage of very high process flexibility. - **Whole cell biocatalysis using optimized enzymes** enters industrial applications.	3 **Curtailment of Enzyme Process Development, including some of the established production organisms**. - Negative public attitude impacts use of some of the established production organisms. - Development in certain segments put on hold until public perception can be redirected. - R&D focus shifts to enzymes in fields with few public concerns (e.g. enzymes in industrial processes, manufacturing of intermediates)

T	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
2	**Optimization of Established Enzymes** - Mainly hydrolases (E.C.3) are in use for industrial and commercial applications. - The exploitation of other enzyme classes is hampered by o technical challenges (e.g. co-factor recycling) o lack of basic enabling technologies, including bioinformatics tools, HTS biochemical characterization, and databases of structural/functional knowledge.	3 . **Rational optimisation expands in academia, but doesn't scale and is rarely used for industrial enzyme optimisation.** - Rational optimization is applied to enzymes from all enzyme classes - has substantial impact on general understanding of enzymes - This progress in science and research leads to slow, but well understood, development of new enzymes.	1 2 . **Rational optimisation increases for most use cases** (random approaches for optimization are applied only in special cases). - Bioinformatics and data processing capacities lead to multiple breakthroughs. - more efficient or effective enzymes can be constructed with reasonable effort	2 . **Random optimisation increases for most use cases,** based on high-throughput-systems (HTS) - Bio-informatic capacities remain insufficient, enzyme modeling is too complex. - Bio-informatics research is hindered by access and non compatible data sets.	3 . **Optimization of established enzymes is slowed down and/or takes place only in certain segments** - Major shift to natural production processes - R&D focus shifts to non-sensitizing enzymes and/or non-sensitizing formulations

T	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
3	**Identification of New Enzymes** **There are bottlenecks between finding and using new enzymes:** - Evaluation of molecular diversity for potential applications - Genome Mining becomes a basic bioinformatics tool in new enzyme identification - Development of new functions is more difficult than optimization. - Software based forecasts and predictive models of expectable outcomes and risk assessments.	**Status Quo: Mainly hydrolases are used in industrial applications.** - Hydrolases continue to grow in applications like biomass conversion & bulk processes. 3 . - The use of new enzymes in industrial applications is limited due to cost and risk of R&D, and limited integration into industrial processes.	2 . **Screening Technology Breakthrough** - In-silico enzyme screening and design, in-vitro synthesis and automated HT enzyme analytics become routine. - Bioinformatics development enables in-silico promiscuity screening even for hydrolases - Fine-tuned biochemical characterization of enzymes, and evaluations of molecular diversity of new production enzymes are enabled through HTS.	1 **Identification of enzymes diversifies** - De novo design becomes feasible for first applications in industry. - Enzymes are designed according to predefined characteristics including non-natural reactions. - Technical difficulties are overcome enabling dream reactions through the discovery or design of new enzymes. - Enzymes from all classes see widespread industrial adoption and a broad range of new applications.	3 . **Reduction in new enzyme research.** - Funding for new enzyme R&D dries up - R&D focus shifts to non-sensitizing enzymes and/or non-sensitizing formulations
4	**Formulation** - Formulation for enzyme applications in detergents - Addressing safety and effectiveness aspects by formulation (e.g. encapsulation) - Proprietary delivery systems	3 . **Trial & Error formulation development remains the primary research mode**. - Better formulation is achieved through HTS approaches (allowing greater efficiency in testing).	1 2 . - an increasing understanding of underlying principles makes more rational, knowledge-based research possible. More efficient formulation development is supported by computational tools	3 . - **Formulation research slows to a halt** with a wide shift back to synthesis.	

T	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
5	**Enzyme Applications** - High development costs are a major hurdle. - Typically, the different steps within the R&D process are carried out independently resulting in a high risk of late-stage-failure. - Integrated approaches are also in place in industry, (especially for improving existing development processes) - Always a question of Host Ambivalence vs. Host Speciality	3 . **Lack of evaluation tools** - The use of new enzymes in new applications is hindered by a lack of evaluation tools.	1 2 . **New enzymes are evaluated for their potential applications**. - Potential use of co-products - Enzymes for use in the waste management industry, and waste management of the IB enzyme industry itself.	3 . **R&D&I efforts slowed down** Reductions in funding sources and market demand slow R&I efforts in new application development.	

T	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
6	**Process Development/Development time and cost** - High development costs are a major hurdle. - Typically, the different steps within the R&D process are carried out independently resulting in a high risk of late-stage-failure. - Integrated approaches are also in place in industry, (especially for improving existing development processes) - Always a question of Host Ambivalence vs. Host Speciality. - Expressability and Culturability factors - Space/time yield efficiency create conditions for technological and business development.	3 - **Process development is improved for some industrial applications**, but remains on status quo in other applications/market segments	2 **Process development** remains a challenge, but there are **sufficient incentives to overcome hurdles**	1 **The complexity in process development process becomes manageable.** **Water removal becomes new barrier or limitation** because enzyme technologies and technics are so far advanced.	
7a	**Production Processes** - Currently underrepresented in R&D&I, even though downstream benefits can be significant.	3 **New process designs (e.g. enzyme cascades, continuous processing) are not or only rarely implemented in industrial processes**	1 2 **New process designs (e.g. enzyme cascades, continuous processing) are implemented in industrial processes**		
7b	**Production Processes**	3 **Synthetic biology is not used by industry**	2 **Synthetic biology plays a minor role for industrial processes**	1 **Synthetic biology is important for industrial processes**	

5.2.2 Business

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
1	**New applications for established enzyme** - Industrial processes - today are based on chemistry, physics - could be biological (environmental friendly, more specific (chiral), more cost effective) - Reduced use of chemistry/chemicals, economics and environmental concerns drive growth of enzyme use - Scope to use enzymes in new applications is often limited by safety considerations (e.g. use in open systems) - Regarding both technology and business, there are fundamental differences between industrial enzymes and "specialty" enzymes (very high value	1 **Enzymes are in competition with chemical catalysis** - **Industrial enzymes:** Enzymes replace chemical catalysis/chemicals on a case by case basis if their use saves raw materials, saves energy, reduces by-products - **Laundry enzymes:** the driver for replacement of chemicals by enzymes are the formulators' needs; they want fast acting enzymes with broad specificities, replacement takes place if these needs can be met by enzymes - REACH effects are ambivalent; can either favour or disfavor use of enzymes (see also future assumption C)	1 2 **Extension of the market for enzymes** - **Industrial and laundry enzymes** Chemicals are replaced by enzymes in new applications (e.g. cleaning applications such as hand dishwashing, spray; in personal care products which are only in short contact with the skin, or use of proteases in peeling - Synergistic action of chemicals and enzymes can be exploited - A new process/product/solution becomes possible without existing predecessor, e.g. in biopharmaceutical production - High oil prices favour the replacement of chemicals by enzymes - Environmental concerns and strict environmental regulation favour the replacement of chemicals by enzymes - Saturation in Western markets triggers customer-specific solutions, e.g. novel combinations of laundry components, or novel product forms. As a consequence, enzymes become commodities and enzyme prices fall	**Market for established enzymes decreases** - **Industrial enzymes** Clean chemistry, chemical catalysis and certain chemicals outcompete enzymes, they are cleaner, well-defined, and cheaper - Low oil price disfavours enzyme use 3 - **Laundry enzymes**: Enzymes are used less in laundry detergents, because… - …New washing machine concepts without water are broadly introduced - …New synthetic fibres and functional clothes become more important than cotton - …Clothes have a shorter life time and therefore need less washing	3 **Use of enzymes in non-consumer products is favoured** Use of enzymes in food, drink, textiles, personal care decreases Laundry formula are changed in order to comply with labeling requirements

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
2	**New applications for new enzymes** - Enzymes are remarkable for their specificity - New applications for new enzymes exploit enzyme specificity; especially for high value products - Enzymes in Biocatalysis: value of enzyme is low!	1 **Enzymes are in competition with chemical catalysis** See above	1 2 **Extension of the market for new enzymes** - Generation 2.0 production systems for enzymes become available, so that new enzymes can be produced on industrial scale which cannot be produced with the current microbial hosts - A new process/product/solution becomes possible without existing predecessor, e.g. in biopharmaceutical production - New complex compounds (e.g. peptide antibiotics) made by new enzymes - Synergies between chemicals and enzymes can be exploited (also: see above)	3 - Enzymes replace chemicals/chemical catalysis in Industrial processes in certain segments/applications, because they save raw materials, save energy and reduce by-products	
3	**IP Framework** - High barrier to entry for SME to supply directly "ready to use" enzyme ingredients	3 **Big enzyme industry hardly cooperates** - Big industry reduces their collaboration with SME and academia to protect their IP / freedom to operate	2 **Big enzyme industry/SME collaboration** - Big enzmye industry collaborates with SMEs but not with academia in order to protect their IP/freedom to operate	1 **Swiss model for cooperation:** Big enzyme industry collaborates within publicly funded projects with academia, because the generated IP will be owned by the companies	1 **Alternative ways for co-creation/cooperation** - Ways are found for co-creation (open innovation) - Joint development by large companies, SMEs and academia - Patent protection 10 instead of 20 years

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
4	**Geographical distribution of activities: Production** - Western Europe is the only net exporter of enzymes.	1 **Global production by present market leaders** - Western Europe and USA remain market leaders, they produce globally	2 **Glocal production** - Enzymes are produced locally (= in a few leading countries, e.g. by present market leaders), but are distributed globally (as in the chemical industry))	2 3 **Production in Asia** - Enzymes are produced in Asia; the share of Europe and the USA decreases (as in steal industry)	1 **Relocation to EU** - Relocation of enzyme production from Asia to Western Europe due to rising prices in Asia
5	**Geographical distribution of activities - Market** - Detergent/laundry enzyme use in Europe is a mature sector - Growth potentials lie in export to emerging markets - Specific adaptation to non European wash processes (e.g. non-soaking) and local markets required	1 **Globalisation 1** - Developing countries as major growth markets: detergents are produced by local companies. These local companies are the major customers of big global enzyme producers or are even bought by the global players	2 3 **Globalisation 2** - Developing countries as major growth markets: emerging players in developing countries get big enough to become global players and compete with present leaders	3 **Globalisation 3** - Emerging players in developing countries become global players and replace present leaders in certain segments	**National isolation** Global trade is severely impaired by national isolation strategies (e.g. USA/ Trump, EU breaks apart, tariffs)
6	**Geographical distribution of activities - R&D** - with respect to R&D investment, talents, competencies Europe and USA leading, China is emerging - Specific adaptation to local markets required (for laundry enzymes), is partly carried out locally	2 **Europe, USA and China leading** Europe and USA remain leaders, but China also obtains a leading position in certain segments	3 **Asia is world leader in industrial enzymes innovation**	1 **Europe is world leader in industrial enzymes innovation**	

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
7	**End-user-demand / perception** - For detergents cold-active detergents are a major trend	3 . **Negative impact of end-user demand/perception on enzyme use** - User gut feeling could switch a process - Non-bio-formulations due to consumer health concerns of enzymes 3 . - Awareness raising campaigns are required	1 2 . **Positive impact of end-user demand/perception on enzyme use** - User gut feeling could switch a process - Awareness raising campaigns support positive attitude		
8	**Safety aspects of enzyme exposure**	1 2 . - Enzyme Exposure Limits			

5.2.3 Policy

P	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
1	**R&D policy** - Considerable funding opportunities in Europe and from national agencies.	1 2 - Funding opportunities for enzyme R&D increase	3 - Status Quo: Funding opportunities for enzyme R&D remain at a comparable level as today - Efforts are focused on specific fields	- Funding opportunities for enzyme R&D decrease.
2	**Bioeconomy policy** - Bioeconomy as a strong driver for enzyme technology. - Various initiatives exist at European and national level. - Instruments differ between various applications.	1 2 - European industry greatly benefits from the R&D investments and market-pull policy. New applications for enzymes with high value-added arise in Europe.	- Bioeconomy policy is losing importance.	3 - R&D Bioeconomy initiative continue to exists and are frequently revised resulting in a strong R&D base in Europe. - No/only few corresponding market incentives are implemented.
3	**Regulations and Standards** - Regulatory framework for enzyme applications depends on their applications. - SOPs for production safety are implemented	3 - Regulations concerning enzymes become stricter and more transparent. - As a result access to certain applications and markets also becomes restricted.	1 - Regulations concerning enzymes become clearer and more transparent without limiting applications of enzymes significantly. - As a result of higher certainty applications and markets for enzymes grow/open up.	- Status Quo: Regulatory framework differs between applications and is not always well defined. - Effects are unclear.

Workshop participants gave written comments to the policy factors. Some of these comments have been integrated into the factors listed above. The other comments can be summarized as follows:

- The EU bioeconomy strategy should be updated and/or revised.
- Several instruments for R&D funding are suggested:
  - significant funding of basic research, as this is the foundation for innovation;

  - synergistic combination of different funding instruments
  - specific funding instruments for SMEs; e.g. > 50 % public funding for SMEs
  - tax reductions for R&D&I investments within EU projects
  - in calls for project proposals, higher transparency which project volumes will be funded, perhaps separate calls depending on project volume (e.g. < 300 k€; 300-700 k€; 700 k€-1,5 mio., >1,5 mio.)
  - funding of company R&D at lower TRL stage (< TRL 6)
- The IP policy in the EU regarding academia is a disincentive for industry to cooperate with academia, leading to industrial R&D being carried out “in isolation". Novel connections would be desirable.
- Regulations should be specific for the targeted products or fields.
- Globalisation might lead to more permissive regulations in order to be able to stay competitive internationally.
- It is unclear which effort has to be taken by industry in order to comply with national regulation beyond REACH
- It is a realistic estimate that the status quo of the regulatory framework will remain, so that the framework differs between applications and is not always well defined.

6 Scenarios for Microbiomes

6.1 Story Lines for Microbiomes

Scenario 1: optimal future development
Seed: The regulation is changed. Publicly funded core studies are performed (long term cohort studies plus intervention studies) and a biobank is publicly financed over the long term. Thus, better data are generated, and the public perception is positive.

Technology development is driven by significant public funding of research (P1B). Moreover, specific measures are implemented to support international collaboration (B3A), public-private cooperation, IP protection for companies and SME support (B4A) so that an active, diverse innovation landscape develops. R&D&I is characterised by the following aspects:

It becomes possible to define certain features of healthy and unhealthy microbiomes over the entire life span (T1A/C) and to establish evidence-based interventions for engineering the microbiome. Next generation microbiome products are developed which comprise well-known bacteria, a broad spectrum of probiotic bacterial strains, phages and parasites, prebiotics, and also active molecules etc. (T6D). Many modes of action are exploited; it even becomes possible to engineer microbiomes and maintain the engineered microbiome for a long time (T7A/B/C). Several evidence-based interventions become personalised (T5C). This progress is to a large extent due to research infrastructure (e.g. biobanks), international collaboration in large-scale projects, small-scale projects, an appropriate balance between flexibility, openness and innovativeness in research on the one hand (T2C) and comparability and standardisation on the other hand (T2A/B/C). Large epidemiological cohort studies and clinical intervention trials of highest standards are performed (T4A/B/C).

There are many opportunities for companies. Large research-intensive companies as well as highly specialised SMEs are active. Microbiome addressing foods and interventions are perceived very positively and consumer demand is high (B1A/B), both in the premium segment with official health claims (B1B) and in the segment where official health claims are of little importance (B1A). Social media, peer-to-peer advice and DIY microbiome monitoring play a significant role (B5C). Frame conditions support collaborations between academia and companies (B3A), the development of SMEs and start-ups (B4A) and thus contribute to product development. Multiple new regulatory categories are implemented (B6C). Regulations for health claims are clear (P3C), harmonized within the EU (P2B) and moves towards a global regulatory framework (B2A/B) which opens new market opportunities but at the same time increases competition from producers in non-EU-countries.

Scenario 2: Focus on publicly funded research
Seed: The regulation is not altered and remains as it is (B6B, P2A, B2 = status quo) and differences in terminologies prevail (P3A). However, public R&D funding in the EU is significantly increased (P1B) and allows intensive US-EU-Asia R&D cooperation. The data generated must be made publicly available. This increases the generation of basic knowledge about microbiomes considerably. Companies do not play an active role in the generation of this knowledge base, as the requirement to make the data publicly available is not attractive for them. Companies, however, use the publicly available knowledge base for product development.

Technology: Due to considerably increased public funding, the knowledge about healthy and unhealthy microbiomes and ways to modify them deliberately is significantly expanded (T1A/C/D). This deeper understanding of microbiome functions is to a significant extent due to global cooperation in research (EU–USA–Asia) and the integration of different –omics-data (T3C). Significant contributions to this integration stem from the standardisation of data acquisition, analysis and interpretation on a level that depends on the innovation phase (T2A/B/C): in research, comparability (e.g. sharing samples) is more important than extensive standardisation (T2A), and research has a high degree of flexibility in order to develop new technologies, algorithms and approaches, whereas in applications outside research, SOPs for sampling and data collection are implemented (T2C). But not only preclinical laboratory work is being publicly funded. Significant research budgets are also allocated to population studies and targeted human intervention studies (T4B/C). A set of validated biomarkers is established (B2A) In addition, citizen science projects contribute to sample and data collection (T4C). As a consequence, a broad spectrum of probiotic bacterial strains is being developed which go beyond the established well known bacteria and also comprise GMO and novel prebiotics (T6A/B). The mode of action is modification of the microbiome and also maintaining the altered microbiome (T7A/B). There is also a trend towards personalisation of interventions. While life style and demand driven interventions with unproven health effects dominate (T5A), few evidence-based interventions are also personalised (T5C). Research is predominantly carried out in academia. Data and findings from publicly funded research must be made publicly accessible which is not attractive for companies.

Business: Microbiome addressing food gains broad positive perception and is readily consumed (B1A). Official health claims are of little importance (B1A) for marketing. Companies use the publicly available research data to develop a broad range of products (B2A) which are in part personalised (T5A), but not necessarily evidence-based, as official health claims do not play a major role for consumer behaviour (B1A). There are significant efforts in marketing (high profile marketing campaigns, celebrity usage) which bear the risk that market success is only a short-term hype cycle but not sustainable (B5B).

Due to lingering IP issues, industry mainly focusses on product development but not on basic knowledge generation (B3C). Public R&D&I Policy implements new forms of public-private cooperation in order to address this hindrance to knowledge transfer, innovation and product development (B3A). These measures also specifically address SMEs and start-ups (B4A). However, there is global competition in the research and supply services offered by SMEs, making the situation for EU-based SMEs nonetheless difficult (B4C).

Scenario 3: Favourable regulation, but negative public and consumer perception

Seed: In regulation, the FSNP category with widened scope[2] is established for microbiome targeting food/products (P2B; B6A). NGOs transmit, however, a negative perception (B5A). Public R&D funding remains at a comparable level (P1A); increase cannot be justified due to negative public perception.

2 It has not been specified in the workshop in which way the scope is widened. We assume that due to negative public perception, rather strict consumer-oriented issues (privacy/data protection; regulatory oversight, level of evidence for claims) will be implemented.

Regulation: the (improved) regulation is shaped significantly by consumer/public concerns and therefore has mixed impacts: on the one hand, the more clearly defined regulations support the development of microbiome products and services. On the other hand, requirements to comply with the regulation and obtain market approval/official health claims are high and in addition differ within the EU. As a consequence, the ratio of pre-marketing efforts to market size is unattractive for more advanced products and services. Companies therefore focus their efforts on only few (well-known) product categories for which a health claim can be readily obtained and on countries with more permissible regulation. The company landscape is dominated by few large, multinational or highly specialised players; SMEs play a minor role.

Research: Public funding remains on a comparable level and scope as today. Funding budgets cannot be increased due to public concerns. However, funding is focused on certain issues which relate to the health claim regulation, e.g. definition of microbiome functions..., standardisation, large cohort studies. Regulations in the category “Food for Specific Nutritional Purposes (FSNP)” require compliance with Standard Operating Procedures (SOPs) for sampling and data collection for dossiers; there is also a high level of standardisation in research, which hampers innovation (T2D).

In the FSNP category, a positive definition is given for certain functions or metabolites (T1C); a comprehensive definition of a healthy microbiome remains, however, scientifically impossible (T1B). Regulation in the FSNP category is backed by knowledge from large cohort studies, for which funding has been made available (T4C). However, additional research into causal associations mainly remain restricted to case-control studies. Due to public concerns, rather strict consumer-related aspects are enforced, among them a strict data protection policy/regulation for microbiome data (P4A). As a consequence, only highly professionalized players can integrate omics data which have appropriate privacy/data protection procedures established (T3B). Moreover, the regulation protects against unsafe or misleading services or products (T5B). Although the scope of the regulation is rather broad and comprises also microbiome-targeting products beyond bacteria, and more clearly defined regulations support the development of products, the efforts focus on only certain product categories (B3A): e.g. market approval is only readily obtained for well-known bacteria with GRAS status (T6A) or well-established prebiotics; there are only few products on the market which make use of a broader spectrum of probiotic bacterial strains or novel prebiotics (T6B) because the requirements to provide evidence for this broader spectrum are too high in relation to the size of the market segments. Therefore, the dominating mode of action is modification of microbiota (T7A). Due to the public concerns, EU-wide regulation is complemented by additional national (in part even stricter) regulations so that a common EU market does not fully exist (B2C).

Business: The market is divided: on the one hand, there is a high demand by health conscious consumers who prefer food with official health claim labeling and pay premium prices (B1B); on the other hand, large population groups reject microbiome-addressing food because it is perceived as unnatural (B1C); this negative public perception can be knowledge-based or not (B5A) and influences markets, regulation and public and private R&D funding. Due to the public concerns, EU-wide regulation is complemented by additional national regulations so that a common EU market does not fully exist (B2C). This fuels divergence in regional development and marketing of products because national/regional actor networks develop primarily products specific to local/national market demands and regulatory frame-

works (B3B). The uneven development also impacts SME and start up scene negatively (B4B).

6.2 Overview Factors and Future Assumptions – Microbiomes

Scenario 1 (green): Favourable regulation, positive public perception, science-based product development
Scenario 2 (yellow): Focus on publicly funded research
Scenario 3 (red): Favourable regulation, but negative public perception

Scenario 1:

The regulation is changed. Publicly funded core studies are performed (long term cohort studies plus intervention studies) and a biobank is publicly financed over the long term. Thus, better data are generated, and the public perception is positive.

Scenario 2:

The regulation is not altered and remains as it is. However, public R&D funding in the EU is significantly increased and allows intensive US-EU-Asia R&D cooperation. The data generated must be made publicly available. This increases the generation of basic knowledge about microbiomes considerably. Companies do not play an active role in the generation of this knowledge base, as the requirement to make the data publicly available is not attractive for them. Companies, however, use the publicly available knowledge base for product development

Scenario 3:

In regulation, the FSNP category with widened scope is established for microbiome targeting food/products. NGOs transmit, however, a negative perception

6.2.1 Technology

	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
T1	**Knowledge Base/** Healthy microbiome - "what is healthy microbiome over the entire life span"	2 1 . **"Negative" definition given (= definition of an "unhealthy microbiome")** - Unhealthy microbiomes can be defined for certain diseases	3 . **No definition possible** - Healthy microbiomes can never be defined due to heterogeneity and complexity dynamics host-environmental interactions	3 . 2 1 . **"Positive" definition given for certain functions or metabolites** - For certain mb functions & metabolites a "healthy state" can be defined -	2 **Healthy microbiome as basis for personalized medicine** Understanding of healthy microbiomes is basis for personalized medicines
T2	**Bio Informatics, Role of standardisation**	2 1 . **Standardisation vs. comparability** Comparability (e.g. sharing samples) more important than extensive standardization	2 1 . **Implementation of standardization depends on innovation phase** - In the development of bioinformatics standardisation is counterproductive - In the use of bio informatics: standardization is implemented	2 1 . **Medium level of standardisation** - High flexibility for evolving technologies - SOPs for sampling + data collection	3 . **High level of standardization** - Most approaches (sampling, data analysis) are standardized - But: stagnation
T3	**Causal associations** **-Role of integration of omics data**	**Not helpful** - Integration of –omics data leads to more confusion	3 . **Highly professionialised players required** - Integration of omics data requires big data / bio informatics statistics companies (who owns the data?)	2 1 . **Very helpful** - Integration of –omics leads to deeper understanding of microbiome functions	-

	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
T4	**Causal associations** - Role of studies and methodologies for investigating causal associations	3 . **Case-control-studies** - Remains restricted to case – control - studies	2 1 . **Targeted interventions** - Targeted interventions (from n=1 to larger group)	3 . 2 1 . **Large cohort studies** - large long-term prospective cohort studies are performed, funding is made available - (citizen science)	-
T5	**Personalisation**	2 **Life style and demand driven interventions** - Personalized interventions are offered - Not evidence-based, health effects unclear gadget /life style driven	3 . **Regulatory protection against unsafe procedures** - Regulatory oversight to prevent unsafe / misleading services / products	2 1 . **Evidence-based interventions become personalised** - Host microbiome analysis and integration with personalized medicine, is basis for personalized Nutritional advice and subsequent intervention	-
T6	**Next generation microbiome products** - Need for “new” probiotics and bacterial products - Live biotherapeutic products (single strains, mixed strains)	3 . 2 **Well-known bacteria and prebiotics** - Lactobacilli and Bifidobacteria probiotics (GRAS) - Fructans etc	3 . 2 1 . **Broad spectrum of probiotic bacterial strains and prebiotics** - Broad spectrum of probiotic bacterial strains (genus, physiological functions), also GMO - Broad spectrum of prebiotics, also novel ones	1 . **Broader definition, beyond bacteria** - Probiotics comprise bacteria, microbial phages, parasites, …	1 . **Broadest definition, beyond organisms and prebiotics** - Microbiome products comprise every active ingredient which modifies the microbiome

	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C	Future Assumption D
T7	**Mode of action of microbiome products (microbiome addressing food)**	3 . 2 1 . **Modification of microbiome** Next generation products that modify microbiota to improve health	2 1 . **Maintaining altered microbiome** Next generation products that maintain altered microbiota	1 . **Engineering microbiomes and maintaining the engineered microbiome** Xenobiotics to eliminate microorganisms in dysbiosis and establish modified microbiota	-

6.2.2 Business

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
B1	**Consumer Demand** - Current consumer demand trends point to an increasing share of consumers with higher awareness and demand for healthy food. - While 'probiotics' tended to encapsulate much of the early Microbiome related consumer products, and still frames much of the popular understanding, more nuanced, specific, and impactful information is (slowly) gaining public awareness	2 1 . **Microbiome addressing food gains broad positive perception and is readily consumed, official health claim labels are of little importance.**	3 . 2 1 . **High demand of particularly health conscious end-consumers who prefer food with official health claim labeling and pay premium prices.**	3 . **Microbiome-addressing food is perceived as unnatural (ie. Infant formula) and therefore rejected by large population groups.**

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
B2	2 **Regulatory Issues** - The status quo in which regulations exist but are unclear and or too broad. - Under such conditions R&D remains a more open, and uncertain, endeavor. Without guideline to establish viable marketable products, R&D&I practices must cast a wide net (resource intensive) with fewer guarantees of success (higher risk).	1 . Clearly stipulated and evidence-backed procedures and cooperation standards established by the ENA/EFSA - Heightened focus to research - Companies to pursue more viable Microbiome-effecting products. - Enables the establishment of a set of validated biomarkers – a lynchpin issue for the R&D&I community.	1 . Movement towards a Global Regulatory framework. - Enable extension of industrial development of new products - Reach into new markets, - Increase in competition from producers in Asia, North America.	3 . Fragmented Regulation - Regulations and standards are developed on a national or geographic basis, - Increased complexity for product development. - Increase risk and uncertainty in R&D&I - New products might not be applicable to sufficient markets resulting in overall losses and fewer investments.
B3	**Collaboration and Knowledge Transfer** - Current trends show that collaboration between industry and academic or pure research institutions is declining. - In part this is due to issues of Intellectual Property regarding product development and sales based on research findings. - Knowledge transfer, between public and private research organizations, is inconsistent and adheres to few standards. - This slows down innovation and product development.	3 . 2 1 . **Increased EU wide collaboration clearly linked to faster product development could take two forms.** - On one side, more clearly defined regulations concerning IP produced in public/private partnerships could create Win-Win conditions for 2-party collaborations. - Alternatively, funding policies could be developed to encourage multi-party, transnational consortiums between industry actors and public research facilities. This alternative could favor more general acceptance of Microbiome-addressing foods and products, as it would encourage general awareness raising.	3 . **Collaboration that is divided among national lines could benefit the development of national Microbiome industry ecosystems.** - This would fuel divergences in regional development (likely favoring those nations with pre-existing, competitive industries. - It would also fuel the creation of national or regional actor networks, and develop more products specific to local market demands and regulatory frameworks.	**Reduced collaboration as a results of one or more of the following factors:** - 1 - Less public funding available - 2 - Less R&D funding available - 3 - Negative consumer perception - 4 - Lingering IP concerns 2 - 5 - Regulatory issues

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
B4	**Role of SMEs** - There is currently a considerable SME scene, primarily focused on providing research or supply services to larger industrial actors - Some research firms operate independently, and have even diversified their services to allow for the acceptance of VC funds, without threatening their daily operations.	2 1 . **Growth in SMEs and Startups** - "Incubator" programs increase opportunities for private equity and pharmaceutical companies to invest in early stage, higher risk research. New EU policies streamline processes to initiate and fund startup and incubator programs in Microbiome research. - In addition, the utilization of university programs as startup launch platforms (with shared IP) could further expand the SME space within the industry. - Open innovation approach becomes a new model for SME development – with open access to data and research being exchanged for EU funding, and community support through Creative Commons licensing.	3 . **Large Variation in Regional industrial biotechnology development** - If policies concerning regulation, funding, or VC investment vary wildly across national or regional borders, **an increasing variegation in the SME and Startup scene** could emerge. - While the biotechnology industry in general, and the Microbiome research specifically, would certainly be impacted, it does not lead to large overall growth. Rather, **growth prospects become unevenly distributed** according to regional or national conditions.	2 **The number of SMEs and the amount of services they are able to legitimately offer could decrease** - Based on **differing interpretations** of the standards and **mechanistic regulations** that might be passed to encourage growth in the overall bioeconomy. - Alternatively, **competition could come from overseas operations**, making the environment for EU-based SMEs more difficult.

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
B5	**Information and Education** - Currently there exist some significant gaps in the various communication channels between actor groups in the Microbiome-addressing research, producers, providers, and consumers. - Translating the science and knowledge of Microbiome-based studies and products to consumers is of highest concern, as this shapes public perception and consumer demand. - Also important is education and training of healthcare professionals (doctors and nutritionists) such that they can better assess patient microbiomic needs and suggest appropriate dietary and lifestyle changes. - A larger issue regarding health benefits vs. health claims looms over the industry as a whole. Without critical regulations and standardized metrics, health claims remain suspect and possibly deleterious to public perception (when products fail to improve health).	3 . **Public Perception Turns Negative** One or more of the following influential factors could negatively sway public opinion of Microbiome-addressing products: - **NGO's transmit a negative view** of Microbiome products (seen as comparable to the No-GMO movement and policies from the past 15 or more years). - **Meta-analysis publications** in peer-reviewed journals can provide negative viewpoints, without providing substantial evidence of their claims. - **Mass media** can sway public opinion quite dramatically, and often pick up on "attention-grabbing" research articles, regardless of their legitimacy. Any of these factors, acting alone or in conjunction with one another, could have an immediate impact on sales and consumer perception. It was also thought that any setbacks to public perception would take years to repair.	2 **Short-term Product-Use "Hype" Cycles** - It is possible that the industry sees a boom/bust cycle develop through a mixture of high-profile consumers, marketing, and misunderstanding of Microbiome-addressing products and processes. - **Celebrity usage** of a product could be a boon to fueling high consumer demand, particularly when used with high profile **marketing campaigns**. - However, while this could have a short-term dramatic increase in Microbiome-addressing product consumption, if such use is **not paired with appropriate shifts in diet and lifestyle**, it is likely that many consumers will see less than satisfactory results. **Consumer disappointment** then leads to a retreat in consumer demand, even if the products themselves were functioning properly. - While the "hype" cycle marketing and sales can fuel short-term growth, it also represents a threat to the industry's reputation and longevity.	1 . **Broad & Positive Public Perception** - Optimally, the public comes to regard Microbiome-addressing products as essential to their consumer habits. - If the public taboo on discussing **gastro-intestinal issues** recedes, and people feel like they can **share their G.I. experiences**, and treatments, more openly, public awareness and consumer demand could benefit from social network effects. - Citing similar studies in diet and lifestyle changes, **peer-to-peer advice and support** is seen as the most reliable form of creating long-term consumer awareness and demand. This can be facilitated by **educating NGOs**, and **pairing Microbiome-addressing products to overarching changes in lifestyle and diet.** - The development of **DIY Microbiome monitoring devices and analytics** could further fuel consumer demand. This would be facilitated by a set of clearly defined **validated biomarkers** (approved by EFSA, or another governing institution).

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
B6	**Commercialization & New Product Category** - Currently the R&D, production and sales costs for new Microbiome products are significant, making it difficult for industry leaders to diversify their products offerings and setting harsh conditions for SMEs to enter the market. - This difficulty is compounded by the lack of a clearly defined new product category that could streamline the process for classifying and regulating Microbiome products.	3 . **With the establishment of a "For Specific Medical Purposes" category by a governing institution (EFSA/EHA), R&D efforts (and costs) can be more streamlined**. - This would lead to a greater diversity of Microbiome products, and open the market to focused SMEs. - This new category helped move increases in insurance coverage for certain Microbiome products, and established a more legitimized position for these products as a part of a therapeutic/treatment regime.	2 **Persistence of no new product category** - Due to disagreements among governing institutions, no new category that can encompass Microbiome-addressing products. - This has continued to discourage any increase to investment in R&D, but has also set the conditions in which broad ranging research has led to some surprising discoveries.	1 . **Development of multiple new regulatory categories could evolve in different ways.** - It is possible that governing institutions establish multiple new categories that apply to Microbiome R&D&I. (For instance, topical treatments, preventative products, or "medical devices" for non-metabolizing organisms.) Such a development leads to multiple opportunities for SMEs, startups, and established industry leaders. - Alternatively, if a single new category is established, but differentiates along national or regional governance, the industry could be faced with higher market uncertainty due to regulatory nuances. This could lead to radically uneven development of the industry, and would work against single market economic policies.

6.2.3 Policy

	Factor	Future Assumptions	Future Assumptions	Future Assumptions
P1	**R&D&I Policy** - Considerable funding for microbiome R&D available	3 . **Status Quo: Funding opportunities for R&D remain at a comparable level**.	2 1 . **Extensive public funding made available**	**Less public financial support available**
P2	**EU Regulation for Nutrition and Health Claims** - Claims only allowed when listed on a so-called positive list - Terminology and categories not sufficiently clarified - Health claims that modulate the gut microbiome have had little success in obtaining approval in Europe	2 **Status-Quo development Limited clarifications**	3 1 . Improved clarification of terminology and categories - Food regime retains some differences to pharma - Some claims possible without intensive efficacy proving	High adaption to pharma regulatory regime - Usually clinical testing on to demonstrate the health claims needed - More extensive post-marketing surveillance
P3	**Global Harmonization of Health Claim Regulations** - Differences in terminologies between countries (e.g. probiotic has health claim in EU, but not in US)	2 Differences in terminologies prevail	Rather high harmonization of terms; related health claims are limited	1 . High harmonization of terms; Key terms are linked to strong health claims

P4	**Safety and Ethical Issues** - Legal status of microbiome data is not defined - Scientific discussion about the importance of protection of microbiome data	3 . Microbiome data is treated equal to patient data A Strict regulatory framework to protect these data is established	2 1 . Microbiome data is not considered personal data therefore no further regulations are implemented	

Participants gave comments to the policy factors. They can be summarised as follows:

R&D&I Policy: Participants felt that considerable public funding is only available for basic science whereas for future R&D funding, a shift of focus is suggested: suggestions comprise funding of smaller projects and programs, funding of explorative industrial R&D, sufficient (=extensive) funding of clinical trials, linking public R&D funding to health benefits and business development. Standardization/harmonisation of diagnostics, protocols and microbiome profiles in R&D is needed. R&D funding should take the very fast progress in technological development into account. Bioinformatics, access to data and open source software are important.

- EU Regulation for Nutrition and Health Claims: Participants favour a new product category between pharma and food. Several comments stress the importance of impacts on microbiomes, health and health outcomes rather than on biomarkers. It cannot be deduced from the comments whether this is compatible with the suggested new product category between food and pharma. In other comments it is expected that a pharmaceutical-like regime will be implemented because this is seen as the only option to convince users and guarantee safety. Postmarketing surveillance are seen as important.
- Global harmonisation of health claim regulation: Comments point out that economic benefits are a prerequesite for global harmonisation, otherwise differences will remain. Moreover, it should be kept in mind that there are geographical differences in microbiomes which must be reflected in the harmonised claims.
- Safety and ethical issues: it is pointed out that science-based products and services and any personalisation of treatments, food/nutrition, products such as probiotics/prebiotics requires access to microbiome data sets/microbiome profiles from a large study population. However, a strict data protection regulation is seen as “most likely”.

7 Scenarios for biotech Flavours & Fragrances

7.1 Story Lines for biotech Flavors & Fragrances Scenarios

Scenario 1: Price driven scenario

Scenario seed: This scenario is characterized by price driven market developments. While regulations stay mostly unchanged (P2B), technology is optimized mainly regarding cost reduction (T1C).

An increased level of R&D funding (P1B) will support the development of basic tools in synthetic biology and the understanding of fundamental metabolic and regulatory processes and the application of synthetic biology approaches to new biosynthetic pathways (T3B). Moreover, problems in the transfer of results from lab to production are increasingly solved (T2C). This will lead to increasing cost competitiveness for biotech products, which is enhanced by the fact that costs for plant-derived ingredients are increasing (B4A).

The considerable extension of the biotech F&F market is driven by the key importance of the price for the consumers, also for the "natural ingredient" segment (B1aC, B1bC). And on the same side, regulations will continue to allow flavors claimed to be natural (P2B) even if they are produced by modern biotechnological methods. This is accepted by the consumers: they do not necessarily link the biotechnologically produced compound to the natural ingredients isolated from fruits or plants. However, the price is most important, and the similar aroma is regarded as sufficient. From a geographical point of view, the U.S. will gain a leading position, as the higher availability of Venture Capital leads to strengths in commercialization of synthetic biology (B3B).

Scenario 2a: non GMO scenario – alternative niches for the EU

Scenario seed: In this scenario GMO produced flavors are either not accepted as natural by the consumers or are not allowed to use this claim due to an amended regulation (B1aA, B1bA, P2A). While this hampers the diffusion of biotech in the F&F markets there are quite some successful attempts of European actors in advances in non-GMO biotech fields.

Conventional Biotechnologies will continue to dominate the biotech developments (T1B). In particular, the combination of chemical synthesis + enzymes becomes more powerful. However, dedicated funding support for alternative pathways to GMO in Europe leads to some interesting developments: Growing high-content plants are more and more established as alternative for IB (T3C). On the production side, hurdles in scale-up are avoided by the establishment of either small scale production sites or even 3-D printing approaches that lead to widespread production activities (T2A). Europe may gain from such opportunities as it is less focused only on advances in GMO modified production than the U.S. actors (B3A).

On the market side, biotech F&F suffer most from limited cost competitiveness compared to ingredients extracted from natural sources and to chemical synthesis (B4B). Hence, biotech is mostly relevant in niche markets (B3B), e.g. when it is not possible to extract ingredients from natural sources in sufficient quantity or in sustainable ways. Regarding regulation, a new label will be established that declares the use of biotechnology (P2A). Although products with this label will in total be less popular among consumers compared to products with natural claims, higher transparency may lead to an acceptance in the described niche markets.

Scenario 2b: non GMO scenario – status quo development

Scenario seed / outline: In this scenario GMO produced flavors are either not accepted as natural by the consumers or the regulation is amended in a way that it is no longer allowed to use this claim for this type of products (B1aA, B1bA, P2A). This leads to a continuation of incremental advances of biotech in F&F markets, but rather slow growth.

Conventional Biotechnologies will continue to dominate the biotech developments. In particular, the combination of chemical synthesis and enzymes becomes more powerful (T1B). Focus of research keeps on the known pathways (T3A), among others as funding opportunities for new approaches are not sufficiently available (P1A). Problems regarding the scale-up prevail (T2A), leading to missing investments for biotech in this sector. As a consequence, expertise in Europe in bio-processes / downstream processing is lost while respective expertise is built up in Asia. In particular China may profit from this development, and use its strength in conventional Biotech expand its market shares (B3C).

On the market side, biotech F&F suffer most from limited cost competitiveness compared to ingredients extracted from natural sources and to chemical synthesis (B4B).

Scenario 3: Carbon footprint scenario

Scenario seed / outline: In this scenario, environmental concerns will gain significant importance as a driver of changes and rules in the market (T1A, B2A). Environmental footprint of F&F will become a major issue, which is usually favourable for biotech (at least compared to natural extraction from plants, but also to chemical synthesis). The trend to valorize waste may lead to new feedstock possibilities for biotech F&Fs.

An increased level of R&D funding (P1B) will support the development of basic tools in synthetic biology and the understanding of fundamental metabolic and regulatory processes and the application of synthetic biology approaches to new biosynthetic pathways (T3B). Moreover, problems in the transfer of results from lab to production are increasingly solved (T2C). This will lead to increasing cost competitiveness for biotech products (B4A). However, the main market driver for biotech will be environmental concerns. Sustainability will increasingly determine purchase decisions taken by consumer (B2A). Overall, market diversification for F&F will continue and considerable markets will evolve for Natural Identical (non-biotech), for natural ingredients (biotech) and organic ingredients (non-GMO biotech) (B1aB, B1bB). Regarding regulation, a new label will be established that declares of use of biotechnology (P2A). This label will have a positive connotation for favourable environmental footprint, but also enforce the pressure to find alternative values such as sustainability for biotech F&F, as the advantage to use the same natural claim as for extraction of ingredients from natural sources applies in fewer product cases than currently.

7.2 Overview Factors and Future Assumptions – Flavors and Fragrances

Scenario 1 (green): price driven scenario
Scenario 2a (yellow): non GMO scenario – alternative niches for the EU
Scenario 2b (turquoise): non GMO scenario – status quo development
Scenario 3 (red): Carbon footprint scenario

Scenario 1:

Prices drive market developments. While regulations stay mostly unchanged, technology is optimized mainly regarding cost reduction.

Scenario 2:a

GMO produced flavors are either not accepted as natural by the consumers or are not allowed to use this claim due to an amended regulation. While this hampers the diffusion of biotech in the F&F markets there are quite some successful attempts of European actors in advances in non-GMO biotech fields.

Scenario 2b:

GMO produced flavors are either not accepted as natural by the consumers or are not allowed to use this claim due to an amended regulation. This leads to a continuation of incremental advances of biotech in F&F markets, but rather slow growth.

Scenario 3:

Environmental concerns will gain significant importance as a driver of changes and rules in the market (T1A, B2A). Environmental footprint of F&F will become a major issue, which is usually favourable for biotech (at least compared to natural extraction from plants, but also to chemical synthesis). The trend to valorize waste may lead to new feedstock possibilities for biotech F&Fs.

7.2.1 Technology

T	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
1	**Drivers and Motivation** Biotech-driver for Flavors (90% natural) higher than for fragrances (90% cost reduction) For both segments environmental footprint is a driver for biotech F&F	3 **Environmental concerns** - Environmental footprint is major issue - Advantage for BioTech (compared to natural flavours obtained via extraction from plants) - Valorisation of side and waste streams (politically motivated) - more undefined raw material - more used for F&F - just for feedstock	2a 2b **Conventional Technologies dominate** - Combination of chemical synthesis + enzymes becomes more powerful - No GMO is allowed	1 **Low Price or new functionality** - Chiral compounds could be produced by Biotech (chemical synthesis expensive – even in China) - New products possible by Biotech for fragrances (is an option for high-value fragrances, but not for low price commodity fragrances))
2	**Scale up & Production** Key challenges: - Downstreamprocessing for volatile compounds - Scale-up capabilities not as advanced as microbe optimization capabilities - Suitable production capacity (for fermentation) often not available - Toxicity of ingredient for micro-organism -> Downstream processing technologies - Scale-up from research to production	2b **Research doesn't leave the lab** - no scale-up, no investment in Biotech, no customer - US-Biotech companies with focus on F&F fail - negative impact for use of biotech in the whole F&F sector - Loosing leading position in expertise of bio-process / downstream engineering in Europe to Asia	2a **Low hurdles to production, scale up of minor importance** - Small scale becomes economical - Increasing flexibility - Advanced technology is "easy to use" for everybody: "Fragrance brewery in the backyard" -	3 1 **Scale-up capabilities available** - Technical problems from lab to production are solved

T	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
3	**Knowledge & Research** - Focus on limited number of biosynthetic pathways - Knowledge for synthetic biology / enzymatic achievements has risen, but full potential remains to be unlocked - Cross sector cooperation important for exploiting additional pathways	2b **Focus kept on the known biosynthetic pathways and substance classes** - Not enough research for new pathways, e.g blocked by IP on basic methodology/ tools	3 1 **Many different pathways possible** - Synthetic Biology enables to produce desired products - More fundamental understanding of metabolic and regulatory processes thanks to more research	2a **Breed and growing plants with high content of F&F compounds as alternative for IB** - This development is enabled by knowledge accumulation

7.2.2 Business

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C

1a	**Consumer Preferences for Flavors**
	
	User companies are willing to pay a premium for ingredients that allow them to market their products with "natural" claim. Regarding consumer trend one has to divide between organics, natural and natural identicals
	- Natural flavors market is growing faster (7% p.a.) than natural identiticals market (4 % p.a.)
	- Trend to organics in Food Flavouring (in particular in U.S.)
	
	For consumers it is often not clear what "natural claim" for products means. Moreover, there is confusion among consumers between biotechnology processes and GMO (e.g. whether end product contains GMO)
	
	Societal perception of synthetic biology and derived F&F products from it, is not clear yet
		2a 2b
		
		No demand for GMO produced flavors
		
		- GMO produced flavors are not accepted (by the consumer) or are not allowed (by regulation)
		- Key drivers:
		  - New technologies implemented that enable to check, whether the flavor compounds are natural (e.g. company Eurofins in France)
		  - Bloggers are disseminating the results
			3
			
			High diversification of markets
			
			- considerable markets will evolve for natural identicals, for natural ingredients and organic ingredients (not GMO)
				1
				
				High demand for GMO produced flavors
				
				- GMO methods are fully allowed and accepted to produce flavors
				- Main driver in the market is the price and sustainability
				- Consumer do not link the compound to the naturals fruits or plants, but the similar aroma is regarded as sufficient

1b	**Consumer Preferences for Fragrances** The main drivers for biotech fragrances are potential price or sustainability advantages. Natural claim is less important.	2a 2b **No demand for GMO produced fragrances** - Natural fragrances will be demanded similar to flavours → GMO produced fragrances are not accepted by the consumer	3 **High diversification of markets** - Natural fragrances will be demanded similar to flavors - Diversification into different markets: Markets for natural identicals and natural products and organic products	1 **Price and sustainability dominating drivers** - The market driver are not consumer preferences of naturality etc., but the price and sustainability issues dominate

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
2	**Environmental Impact** 1. Availability of feedstock for plant-derived ingredients is quite often limited 2. Carbon footprint of biotech F&F is potentially lower than for petrochemicals or plant extraction In those cases higher prices are payed in the markets → less cost sensitive	3 **High environmental awareness in demand** - Significant change from synthetic compounds to natural plants is not sustainable → for <u>many compounds</u> biotechnologically produced F&F are favourable - The technology is similar to which is used already today, as not breakthrough needed	2a 2b **Considerable environmental awareness in demand** - Significant change from synthetic compounds to natural plants is not sustainable → for <u>some compounds</u> biotechnological production is most favourable	
3	**Geographical distribution of activities** - Europe is strong in technology and possesses considerable production capacities, but activities are more fragmented compared to the U.S. - Both U.S. and EU have several actors with capabilities and experiences in synthetic biology - U.S. has advantages in exploitation of synthetic biology advances due to more access to Venture Capital - In the EU, “organic” product-based growth prevails - China has some strong players in the F&F industry - Europe has strong F&F user industry	2a **Europe is improving its competiveness in certain segments** - One key driver is the establishment of a network (of academia, F&F producers from different countries) in the EU	1 **U.S. dominates in GMO biotech**	2b **China dominates in non GMO-biotech**

B	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
4	**Costs: Competitiveness and volatility** - High volatility for prices of natural resources => may lead to advantages (if plant derived flavors get more expensive) or disadvantages for biotech F&F (if biomass source prices get more expansive and /or unpredictable) - Markets are fragmented into many products as well as within the EU => R&D costs have to be covered by small product markets - Production cost for biotech conversion are often somewhat higher than for plant-derived ingredients and often significantly higher compared to chemical synthesis of F&F - Synthetic biology offers significant potential for cost reduction and may lead to lower costs compared to plant-derived ingredients	3 1 **Higher cost competiveness via synthetic biology** - Advances in synthetic biology leads to higher cost competitiveness - Costs for plant-derived ingredients are increasing - Increased cross-sector collaboration (e.g. transfer of methods for the pharmaceuticals to F&F) and common target selection	2a 2b **Limited cost competitiveness** - Synthetic Biology is not sufficiently competitive - Costs for biotech produced F&F remain higher compared to plant-derived ingredients and synthetic compounds	

7.2.3 Policy

P	Factor und Current Situation	Future Assumption A	Future Assumption B	Future Assumption C
1	**R&D&I Policy**	2b **Status Quo: Funding opportunities for R&D remain at a comparable level.**	3 1 **Extensive public funding made available** - More PPP's	2a **Less public financial support available for synthetic biology, but more for other methods**
2	**EU regulation for "Natural Products" claims for flavors in food** - EFSA regulation concentrates on process, accepting a limited list of procedures - Regulation on flavors is already uniform in all European countries (EC1334/2008), but implementation still differs between EU member states - Natural label for GMO produced F&F challenged by NGOs	2a 3 **Explicit declaration of use of biotechnology** - New regulation on adding the prefix "bio-" to the name of the flavor compound to inform that biotechnological approaches have been used	1 **Status Quo-Regulation** - Regulations principally allowing modern biotechnological produced flavors claimed to be natural	2b **Stricter regulations regarding use of advanced technologies** - Products with advanced process methods (e.g. from synthetic biology) not accepted as natural products

8 Conclusion

A cross-value chain analysis of these different value chains has been conducted to delineate the key factors for future development of the value chains. The scenarios point out that for a favourable development of IB in Europe a set of different factors have to evolve positively, in order to maintain competitiveness in future technological developments, aligning supply to customer needs, adjusting policy instruments, etc. While some of the key factors are similar across the value chains (e.g. pressure for reducing costs) others differ (e.g. of the need to amend current regulations or not). In the following, those main insights are summarized.

Cost reduction: A key challenge for technological development and economic activities in all value chains is the reduction of cost. This applies even for those value chains without direct competition to chemical synthesis or fossil-based products, e.g, 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 flavors & fragrances and next generation genome sequencing and bioinformatics in the case of microbiomes are of major importance for the further advancement in these value chains. However, use of certain technologies in applications "near the human body" (e.g. flavors & 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 analyzed, 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 flavors & fragrances, the support of higher TRL (Technology-Readiness-Scale) development activities and demonstration plants in lignocellulosic ethanol and bio-based plastics. Other issues in need of R&D&I support are cross-cutting needs of relevance to all value chains, e.g. 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 flavors & 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, e.g. demand side policies for lignocellulosic ethanol or bio-based plastics, reimbursement practices in the case of production of biophar-

maceuticals, R&D priorities of larger companies less dependent on public funding (e.g. enzymes and biopharmaceutical production).

Regulatory environment: Product regulations have 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 short and long term as incentives for actors in the markets may change. Value-chain specific regulations, which create a rather favorable environment for commercial activities exist in the value chains biopharmaceuticals (securing a competitive advantage for EU players over competitors due to high requirements), flavors & fragrances (opening opportunities for IB to produce substances which can be claimed "natural"), and enzymes (no need for labelling end or intermediate products with enzymes produced in genetically modified organisms). To which extent this rather favorable commercial environment will be maintained in future is an open question. 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 for public procurement, 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. E.g., on the one hand for the value chains flavors & 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 to take up R&D impulses from academia into commercialization.