Biotech4Food

D2.2 Value chain maps

Co-funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or the European Innovation Council and SMEs Executive Agency (EISMEA). Neither the European Union nor EISMEA can be held responsible for them.

PROJECT ACRONYM	Biotech4Food
GRANT AGREEMENT NUMBER	1011153135
PROJECT NAME	Acceleration of new promising circular agri-food value chains and sustainable industrial interregional investments in SMEs, by integration of advanced biotechnology
DELIVERABLE NUMBER & NAME	Deliverable 2.2 Value chain maps
DELIVERABLE RESPONSAIBLE	Flanders'FOOD
DELIVERABLE TYPE	R – Document, report
DISSEMINATION LEVEL	PU – Public

DOCUMENT VERSION HISTORY			
Version	Date	Modifications	Authors
1	20/12/2024		Ward Van de Velde, Lore Knaepen, Gus Verhaeghe, Anastasia D'hoore, Kim Hertegonne

ABSTRACT

The Biotech4Food project, funded by the EU, aims to advance circular agri-food value chains through biotechnological innovations. Deliverable D2.2 maps value chains for microbial protein, microalgae, and probiotic supplements, highlighting regional strengths, scaling challenges, and collaboration opportunities. Analysis reveals strong R&D in certain regions but bottlenecks in scaling and commercialization. Recommendations focus on fostering synergies with food systems, enhancing pilot facilities, and addressing regulatory barriers. Additionally, the deliverable emphasizes the role of societal acceptance, funding support, skilled talent, and ecosystem integration as critical factors for successful introduction of biotechnology. The deliverable validates prior findings, offering actionable insights for sustainable and innovative agri-food systems. These efforts support the project's goal of promoting regional and transregional collaboration in Europe's biotechnology sector.

TABLE OF CONTENTS

INDEX OF FIGURES

INDEX OF TABLES

1. OBJECTIVE AND CONTEXT

Objective

The objective of Deliverable D2.2 (Task 2.3 within the Biotech4Food project) is to produce detailed value chain maps for selected biotechnological applications in the agri-food industry. These maps provide a thorough understanding of key actors for each region, their interconnections, and the challenges and opportunities within the defined value chains. These are foundational for identifying strategic opportunities and enabling cross-border and cross-sectoral collaborations. This supports the overarching aim of Biotech4Food to accelerate sustainable and innovative biotechnological solutions in the agri-food sector across Europe.

Context

The *Biotech4Food project* operates at the intersection of biotechnology and the agri-food industry, emphasizing sustainability, circularity, and regional synergy. Funded under the I3-2021-INV2a initiative, the project involves diverse stakeholders, including SMEs, regional authorities, research organizations, and industry clusters, from 20 NUTS2 EU regions.

Task 2.3 plays a pivotal role in the project's strategic vision by combining regional insights and stakeholder inputs into actionable outputs, including value chain maps, a strategic implementation roadmap, and a business and investment plan.

Deliverable D2.2, the value chain mapping, builds upon insights from Tasks 2.1 and 2.2 where thematic priorities and implementation strategies for interregional collaborations were defined. This deliverable involves data collection, stakeholder engagement, analysis and visualization, and strategic recommendations. The maps are developed with input from Flanders.bio, expert in biotechnology in Flanders.

2. METHODOLOGY

This section outlines the methodology used to conduct a transregional value chain analysis. It encompasses a systematic approach that begins with the selection of three biotechnology cases relevant for commercial food applications. The aim is to provide insights into their value chains and their potential for scaling across diverse regional contexts in Europe. The second step involves the selection of eight regions to provide the diverse and representative contexts for the analysis. Factors such as geographical distribution of NUTS2 regions, and their cohesion index are taken into consideration to ensure a sample with economic and cultural differences.

The value chains of each case are studied. To obtain consistent and comparable data, they are used to develop robust data collection frameworks. These frameworks facilitate data collection in the eight regions and systematically study the value chain of each food biotechnology case, generating critical region-specific insights to inform the analysis.

The collected data is analysed with two primary objectives, herewith enabling the formulation of targeted recommendations:

1. To identify region-specific dynamics within the value chains, including local strengths, weaknesses, opportunities, and threats.

2. To explore opportunities for transregional collaboration in Europe, focusing on shared challenges and growth opportunities across regions.

Disclaimer: while every effort has been made to ensure reliability of the collected data, it is important to acknowledge certain limitations. The data is gathered using a scorecard system designed to minimize subjectivity and provide a consistent evaluation framework. However, the accuracy and comprehensiveness of the data are dependent on the regional ecosystem knowledge and input provided by each participating region.

We cannot guarantee that every scorecard has been completed with 100% accuracy or that all regional data fully captures the nuances of the respective ecosystems. Users of this data are encouraged to consider these factors when interpreting the results and making decisions based on this information.

2.1. Selection of cases

Three distinct biotechnology cases are selected to study their value chains across diverse regional contexts in Europe. The cases are:

1. Microbial protein
2. Microalgae
3. Probiotic supplements

These cases are chosen in consultation with the Biotech4Food consortium partners. The selection was guided by the following criteria:

- Focus on biotech food applications: all chosen cases maintain a clear link to the application of biotechnology within the food sector and were identified for their potential to address nutritional and sustainability challenges.
- Regional relevance: efforts were made to ensure that at least one case was directly relevant to each partner region, informed by regional surveys and input from cluster organizations that analyzed the "state of play" in their respective areas.
- Alignment with partner expertise: the selected cases reflect the expertise of the Biotech4Food partner SMEs.

Notably, all three cases represent a unique aspect of **microbial biotechnology**, excluding plant biotechnology, biocatalysis, or cultivated animal cells. These, too, are relevant biotechnologies for food applications but are not further included in the scope of this study.

- Plant-based biotechnologies - such as plant genetic engineering (or NGT in the EU-language) - focus on improving soil health, crop protection, and crop yield, stress resistance, and nutritional quality.
- Biocatalysis employs enzymes, nature’s catalysts, to facilitate highly efficient chemical reactions under conditions where high selectivity and mild environments are required.
- Cultivated or lab-grown meat and fish result from animal cell lines which are cultured in controlled bioreactors to produce meat and fish analogue products without the need for traditional livestock farming or fishing.

In contrast, the selected technologies are all fermentation-based systems. Fermentation technology is one of the main thematic priorities within the project but also for the I4CE partnership. Fermentation technology employs microorganisms (such as yeast, bacteria, fungi or microalgae) to produce whole cell biomass or valuable compounds on a large scale. Compounds include, amongst others : vitamins, proteins, carbohydrates, and specialty ingredients. They are typically more environmentally friendly than those produced through traditional chemical methods or animal-based processes, as microbial fermentation technology greatly supports a circular economy, where resources are reused and recycled rather than discarded. They are particularly relevant for addressing immediate food system challenges such as protein diversification, functional foods, and nutritional health applications. The scope of the three cases is elaborated in Table 1.

Table 1: List of cases with detailed description

Name	Scope
Microbial protein	Microbial protein can be obtained through two distinct methods: **biomass production** (single-cell protein or SCP) and **precision fermentation** (cell factories), each serving different market needs and product channels. 1. **Biomass fermentation (SCP)**: In this method, microorganisms such as bacteria, yeast, or fungi are cultivated, and the entire microbial biomass is harvested. This biomass, which is rich in protein, can be used directly as a food ingredient or blended with other foods. The fibrous and dense nature of microbial biomass provides a **functional texture**, making it suitable for direct consumption or as a base in plant-based foods. SCP is primarily focused on the feed sector and **consumer-facing markets**, such as plant-based food products or protein supplements. 2. **Precision fermentation (cell factories)**: Precision fermentation, on the other hand, typically involves the genetic engineering of microorganisms such as bacteria, yeast, or fungi to produce **specific, high-value proteins** or other industrially relevant compounds, like carbohydrates or fats. These compounds are often used as **food ingredients** in industrial food production, such as dairy proteins (e.g., casein or whey) for non-dairy cheese or egg whites in vegan food. A major requirement to align with regulations on the European market is contained use, especially when the microorganisms were genetically engineered: no viable microbial cells can be present in the end product, else it would be regulated under the GMO-framework. Precision fermentation focuses on creating **exact molecular replicas of traditional animal-derived ingredients**, allowing manufacturers to integrate them into existing food systems. These products are positioned primarily in **ingredient markets** for large-scale food manufacturers or niche applications like alternative dairy and functional foods.
Microalgae	Microalgae are photosynthetic microorganisms grown for their rich nutrient profile, including proteins, lipids (such as omega-3 fatty acids), pigments (beta-carotene, astaxanthin), and antioxidants. Although **microalgae** can technically be classified as a form of **microbial protein**, the **production**

	technology and **organisms** differ from other microbial proteins like **bacteria, yeast, or fungi**. 1. Unlike bacteria, yeast, and fungi, which are typically grown in **fermentation bioreactors**, microalgae are cultivated in **open ponds** or **photobioreactors**, utilizing sunlight for photosynthesis. Although most microalgal species are grown under photoautotrophic cultivation, there are specific microalgae that can use organic matter – instead of light - as the primary energy and carbon source under heterotrophic or mixotrophic conditions. 2. Microalgae also naturally provide unique compounds, like omega-3 fatty acids and antioxidants, that are not typically found in other microbial cells. And while advances have been made, genetic engineering of microalgae is also **more challenging** than bacteria, yeast, or fungi. **Microalgae products** therefore tend to be whole biomass or natural bioactive compounds (high-value molecules) by nature present in the microalgae itself.
Probiotic supplements	Probiotics are live microorganisms (typically bacteria or yeast) produced via biomass fermentation. They provide specific health benefits, such as improving gut health, and are incorporated into food products (e.g. kefir, kombucha, miso, or yoghurt) or probiotic supplements. Health claims are validated through pre-clinical and clinical research, and the products are marketed for their functional benefits in **digestive and immune health**. This analysis focuses exclusively on probiotic supplements. This narrower scope is due to the advanced biotechnological processes involved in supplement production, such as synthetic biology, personalized formulations, and encapsulation technologies, which differentiate these products as "next-generation probiotics".

2.2. Selection of regions

For this analysis, all regions represented within the consortium are selected for data collection. Together, these regions have an adequate geographical diversity and include all three categories according to the European Union’s Cohesion Policy: more developed, transition, and less developed (see Figure 1), enabling their mutual comparison. Additionally, the selection is guided by the consortium partners’ knowledge of and outreach within their respective regional ecosystems.

Side note:
Valorial represents 3 NUTS1 regions, Brittany, Pays de la Loire and Normandie, all classified as a ‘in transition’ region. In the report this region is called ‘Western France’.

Innov’Alliance covers two NUTS 1 regions: Auvergne Rhône Alpes (FRK) and Provence Alpes Côte d’Azur (FRL). The Auvergne Rhône Alpes region comprises two NUTS 2 regions: Auvergne (FRK1), classified as a “transition” region, and Rhône-Alpes (FRK2), classified as a “more developed” region. For Provence Alpes Côte d'Azur, the NUTS 1 (FRL) and NUTS 2 (FRL0) levels are identical, covering the same administrative territory. The consortium partners have agreed to group the regions represented by Innov'Alliance under the label "South-East of France" and to designate this overall region as a "Transition" region for the purposes of this analysis. Important distinctions between the two NUTS 1 regions are highlighted during data collection to include in the conclusion and recommendations.

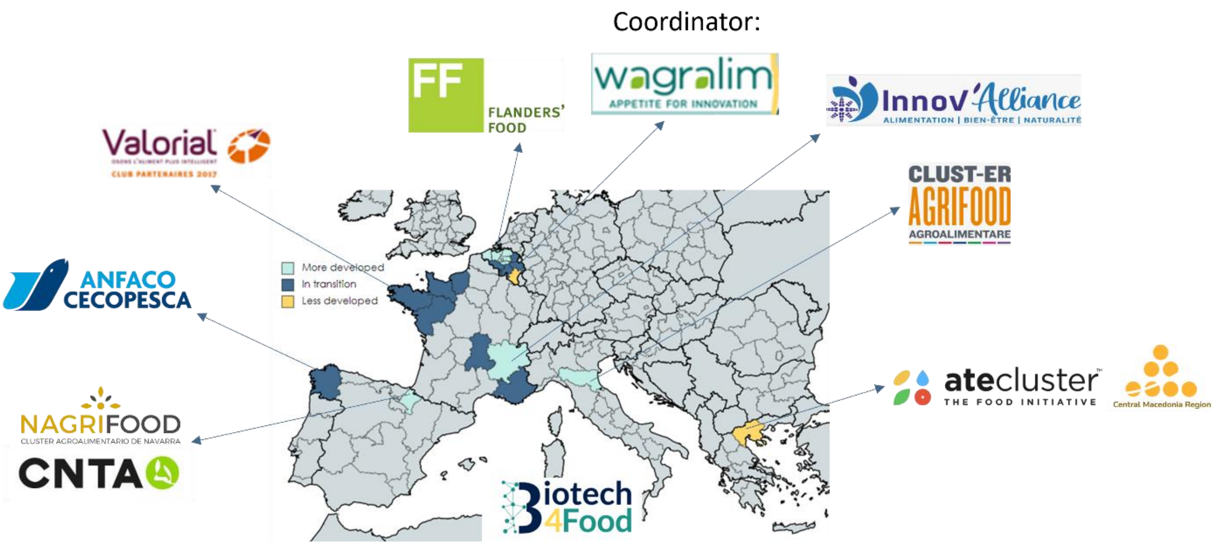


Figure 1: Overview of the Biotech4Food cluster and RTO consortium partners and their respective NUTS 2 regions

2.3. Data collection

<u>Step 1 - Generic value chains</u>: A value chain analysis is conducted per case. This establishes a common baseline for comparison across regions and ensures uniformity in data collection and analysis. It involves two main steps: (1) a high-level assessment to segment the value chain in distinct levels, and (2) a detailed evaluation of each level to identify the key contributors, initiatives, stakeholders, and their interconnections. These analyses are carried out through a combination of desktop research and discussions with experts within the biotechnology ecosystem.

The results of this high-level assessment for all three cases are depicted in

Table 2. In Table 3 an example is given of a detailed evaluation for value chain level 1 *'Strain discovery & selection (R&D)'* within the microbial protein case.

Given the insights from

Table 2, some similarities and differences are worth highlighting. Notably, all cases share coherence in both upstream processes (such as microbial strain selection, process optimization, and production) and downstream processes (including biomass harvesting, compound extraction, and processing). This overlap can be explained thanks to their common technology: microbial fermentation.

However, key differences emerge as well. The case of 'probiotic supplements' differentiates itself from 'microbial protein' and 'microalgae' by levels 3 and 4 – preclinical and clinical studies respectively – which are essential for substantiating health claims. Additionally, production methods differ as well: while 'microalgae' production frequently relies on open pond and photobioreactor systems, particularly when phototrophic, both 'microbial protein' and 'probiotic supplements' typically utilize bioreactor systems for fermentation.

Table 2: High-level analysis for the three value chains

	Microbial protein	Microalgae	Probiotic supplements
1	Strain discovery & selection (R&D)	Strain discovery & selection (R&D)	Strain discovery & selection (R&D)
2	Strain development & process optmization (Lab to pilot)	Strain development & process optmization (Lab to pilot)	Strain development & process optmization (Lab to pilot)
3	Production - fermentation (Pilot to commercial - USP)	Production - fermentation (Pilot to commercial - USP)	Preclinical studies
4	Production - harvesting/extraction (Commercial scale - DSP)	Production - harvesting/extraction (Commercial scale - DSP)	Clinical trials
5	Processing to food ingredients	Processing to food ingredients	Production (UpStreamProcessing & DownStreamProcessing)
6	Formulation to food product	Formulation to food product	Formulation to food product
7	Final product to consumer	Final product to consumer	Final product to consumer
8	Overall value chain suppor*	Overall value chain support*	Overall value chain support*

* **Overall Value Chain Support** includes ecosystem enablers such as clusters and non-profit organizations that facilitate internationalization, funding access, knowledge sharing, and talent attraction; incubators and innovation hubs that host R&D companies to boost local innovation and ecosystem visibility; and dedicated agri-food investors, including venture capital firms, public agencies, and private equity players, actively supporting regional SMEs and start-ups.

Table 3: Detailed analysis of stakeholders in level 1 of the microbial protein case

Microbial protein – Level 1: strain discovery & selection (R&D)
Dedicated research groups (from universities and research institutes)
Dedicated biotech R&D companies
Dedicated Contract Research Organizations (CROs)

Step 2 - Data collection frameworks: Using the generic value chains as input, a tailored data collection framework is developed for each case and shared with the eight selected regions. These frameworks serve as standardized tools to ensure that the regional partners collect data using consistent metrics, and a structured approach. This standardization facilitates direct comparison across the regions.

An example of a data collection framework is illustrated in Table 4. Within this framework, a score (Z) is assigned to each level of the value chain. This score is not arbitrary nor subjective, but calculated as a weighted average from data collected for each level.

To compute these scores, unique scorecards are created for each level of the value chain to evaluate the presence and relative importance of key contributors, initiatives and stakeholders in the region. They are identified through the detailed evaluation conducted earlier in this process (mentioned above). Each regional partner conducts an ecosystem analysis to complete its respective scorecards, providing region-specific inputs for the study. An example of such a scorecard is presented in Table 5, showcasing how the weighted average score is calculated to assign as Z-score for level 1 *'Strain discovery & selection (R&D)'* in Table 4. The Z-score of 6.3 is calculated as the weighted average:

$$\text{Z-score} = \frac{(3 \times 25\%) + (4 \times 25\%) + (14 \times 25\%) + (4 \times 25\%)}{25\% + 25\% + 25\% + 25\%}$$

Side note: given the time and knowledge constraints of this study, the scorecard system is adopted as a practical alternative to a detailed, more comprehensive ecosystem analysis. This approach still allows for the collection of valuable region-specific input without relying on arbitrary scoring or requiring a full comprehensive, and detailed catalog of each regions' ecosystem.

Table 4: Data collection framework of the microbial protein case

Region	Region type (X)	Value chain level (Y)	Score (Z)
Flanders	More developed	Strain discovery & selection (R&D)	6.3
Flanders	More developed	Strain development & process optimization (Lab to pilot)	[redacted]
Flanders	More developed	Production - fermentation (Pilot to commercial - USP)	[redacted]
Flanders	More developed	Production - harvesting/extraction (Commercial scale - DSP)	[redacted]
Flanders	More developed	Processing to food ingredients	[redacted]
Flanders	More developed	Formulation to food product	[redacted]
Flanders	More developed	Final product to consumer	[redacted]
Flanders	More developed	Overall value chain support	[redacted]

Table 5: The scorecard for VC level 1 of the microbial protein case, region Flanders

Count	Weight	Description	Examples in Flanders
3	25%	# Universties in top 200 (top 1%)	KU Leuven, Ghent university, Antwerp University,
4	25%	# Dedicated research institutes	VIB, ILVO, VITO, Flanders Make,
14	25%	# R&D companies	Paleo, Those Vegan Cowboys, Bolders Foods, Naplasol, AB InBev (Biobrew), Puratos, BASF, Cargill, IFF (Genencor, DuPont), Danone (Alpro), NovelYeast, Citribel, Calidris Bio,
4	25%	# CROs	Bio Base Europe Pilot Plant, Avecom, Biolynx, ILVO Food pilot,
6.3			

2.4. Data analysis

For the analysis of the collected data, all Z-scores are compiled to compare the regions and the clustered region according to the EU's Cohesion Policy type at each level of the three value chains. Results of this analysis are discussed in the following section.

3. TRANSREGIONAL DATA ANALYSIS

This exercise studies three distinct biotechnology value chains to evaluate their potential and identify gaps and opportunities across different regions in Europe.

To present the findings effectively, the calculated Z-scores are compiled and visualized. Two types of visualizations are created for each case separately:

1. **Heat maps**: these enable comparison between the three EU's Cohesion Policy categories at each level of the value chain, highlighting strengths and weaknesses among more developed, transition, and less developed regions in a clear, intuitive format.

2. **Radar maps**: these allow comparison of the regions themselves, showcasing their performance across all levels of the value chain and offering insights into regional capabilities and gaps.

An overview of all collected Z-scores can be found in the Appendix of this document. They are depicted per case, per value chain level, and per region.

3.1. Comparison among the EU's Cohesion Policy index

A key observation is that the EU's Cohesion Policy categorization does not directly correlate with the level of biotechnology development in a given NUTS 2 region. The analysis indicates here that biotechnology development is highly case-specific, as illustrated by the following examples:

- Flanders and Navarre: despite being categorized as more developed regions according to the Cohesion index, Flanders is a frontrunner in microbial protein, while its performance in microalgae reflects a lower focus, mainly due to regional climate conditions. Navarre meanwhile scores well for the probiotic supplements case.
- Southeast of France and Western France: both regions are labelled as Cohesion transition regions, yet they perform well across all three biotechnology cases. Similarly, Wallonia, another transition region, scores well overall but, like Flanders, reflects a lesser focus on the microalgae case.
- Galicia: in contrast, although a transition region, scores low across the entire value chain for all three biotechnology cases, demonstrating a notable difference compared to the other abovementioned transition regions.

As such, the Cohesion index will not be considered further in this analysis, as it does not provide meaningful insight for comparing regional biotechnology development. Instead, the regions will be analysed in greater depth, focusing on the specifics of each biotechnology case.

Figure 2: Heat map of microbial protein. The Z-scores are visualized per Cohesion index

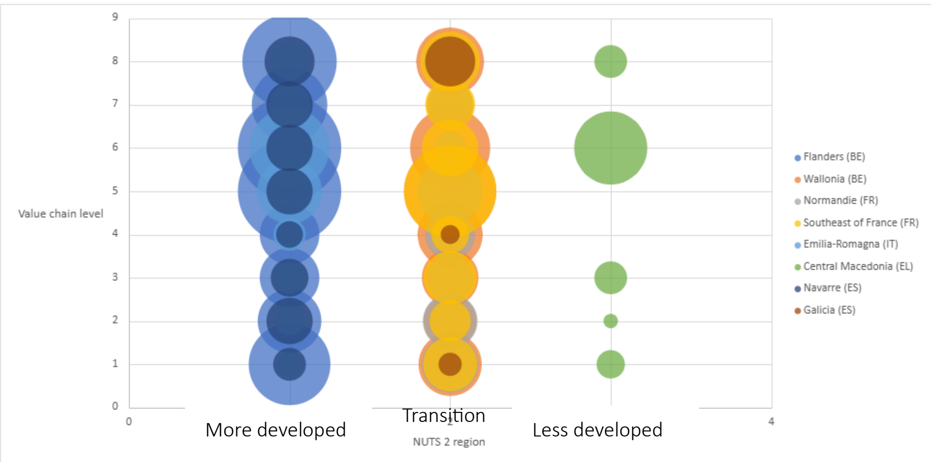


Figure 3: Heat map for microalgae. The Z-scores are visualized per Cohesion index

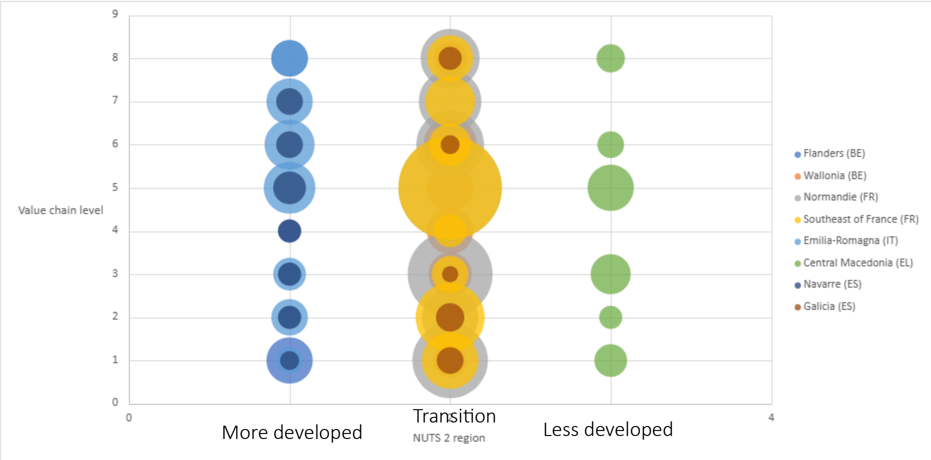
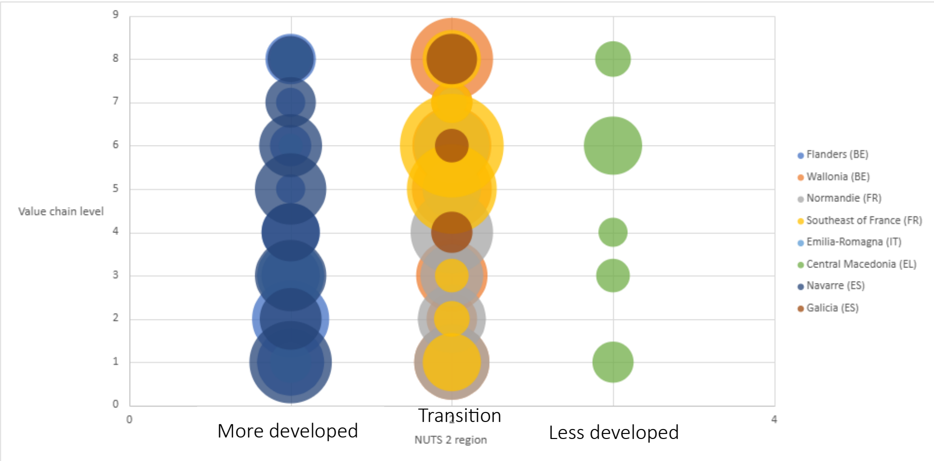


Figure 4: Heat map for probiotic supplements. The Z-scores are visualized per Cohesion index



3.2. Transregional analysis: microbial protein

The following observations are noted from the microbial protein radar map in Figure 5.

Regional trends:

- Galicia, Central Macedonia, and Navarre: these regions show lower overall performance. However, regional specialization is notable, such as "Formulation to food product" in Central Macedonia and "Overall VC support" in Galicia. For the latter, despite ecosystem support, the region yields limited results, suggesting knowledge exists but lacks translation into tangible outcomes due to regional bottlenecks.
  In Navarre there is the IRIS innovation pole which, sponsored by the regional government, is setting up lab facilities and advanced equipment for molecular biology and synthetic biology services (e.g., custom DNA printing, bioreactors, etc.). They are not yet included in the score cards since they will kickstart their activities in Q1 2025. The pole will play a key role in Navarra's near future. These facilities, combined with the advanced data processing pipeline already present within the pole, will help support and expand the research network in Navarra, including its biotech companies (current and to be established), positioning it as the forefront of research and innovation.

- Flanders, Wallonia, and Southeast of France: these regions consistently score high across the microbial protein value chain:
    - Flanders and Wallonia: perform exceptionally well at all levels of the value chain and can be considered as frontrunners or expert hubs.
    - Southeast of France: displays strong capabilities in "Processing to food ingredients", presenting opportunities to further exploit synergies with the established food (ingredients) supply chain.

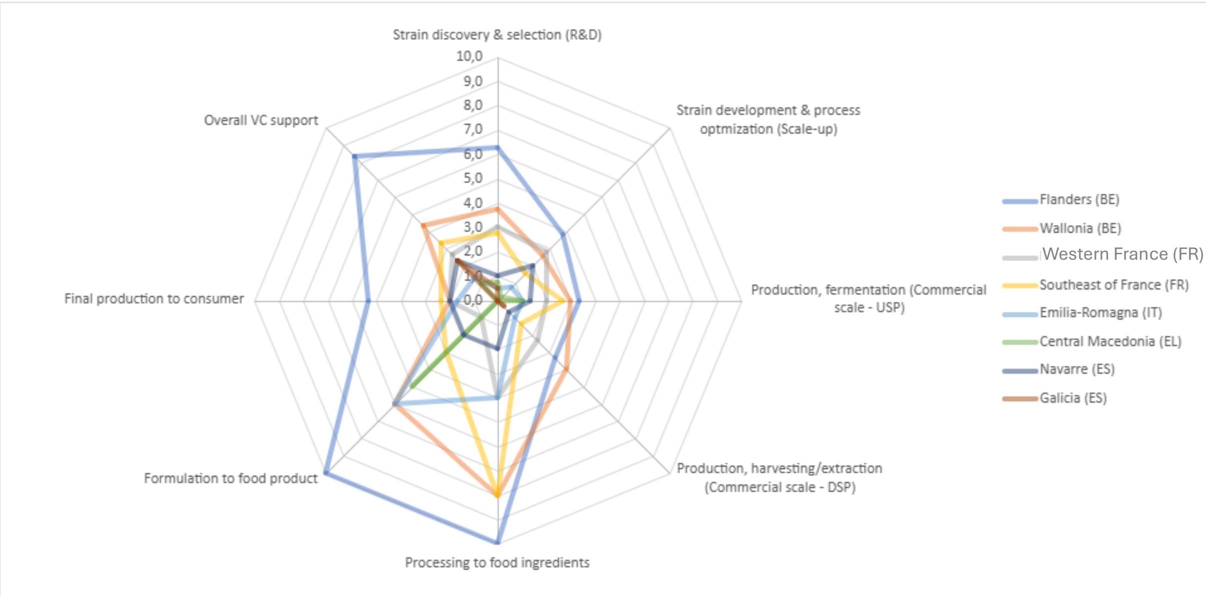
- Western France and Emilia-Romagna: both regions show average scores across the value chain, with Western France scoring higher early in the value chain (R&D intensive) and Emilia-Romagna scoring higher later in the value chain (less R&D intensive, more reliant on the food supply chain).

Value chain trends:

- Lab-to-Pilot-to-Commercial (Scale-up & USP), DSP and "Final product to consumer" score consistently low across regions, indicating bottlenecks in scaling and final market delivery.

- "Processing to food ingredients" and "Formulation to food product" show the highest scores, emphasizing a strong regional focus on transforming microbial protein into consumer-oriented products. This also highlights the importance of leveraging synergies with the (trans)regional food (ingredients) supply chains.

Figure 5: Radar map for microbial protein. The Z-scores are visualized per region



3.3. Transregional analysis: microalgae

The following observations are noted from the microalgae radar map in Figure 6.

Regional trends:

- Western France: the region excels across the entire value chain, with particular high scores in "Production (USP)" and "Processing to food ingredients". Notably, the region's Z-score falls back completely at the level of "Production, harvesting/extraction (DSP)", indicating either the lack of activities or their integration into the neighbouring, high-scoring levels.

- Southeast of France: the region scores particularly high in "Strain development & process engineering" and "Processing to food ingredients", showing the region's R&D strength but lack of translation to commercial production. In addition, this highlights the possibility to leverage synergies with the food ingredients supply chain.

  Emilia-Romagna and Wallonia: both regions showcase average scores in the microalgae value chain. Emilia-Romagna appears less active in in early and mid-value chain levels (R&D intensive) while Wallonia excells in "Production (DSP)", suggesting the microalgae industry as emerging in the region.

- Flanders and Central Macedonia: While these regions show lower activity across most stages of the value chain, there is some presence, particularly in "strain discovery and selection" for Flanders and Central Macedonia. This suggests a focused but niche involvement with transregional collaboration opportunities.
- Navarre and Galicia: These regions score lower overall, primarily due to cloudy and rainy climates that limit outdoor microalgae production reliant on natural light. The lack of investor interest further hampers development.

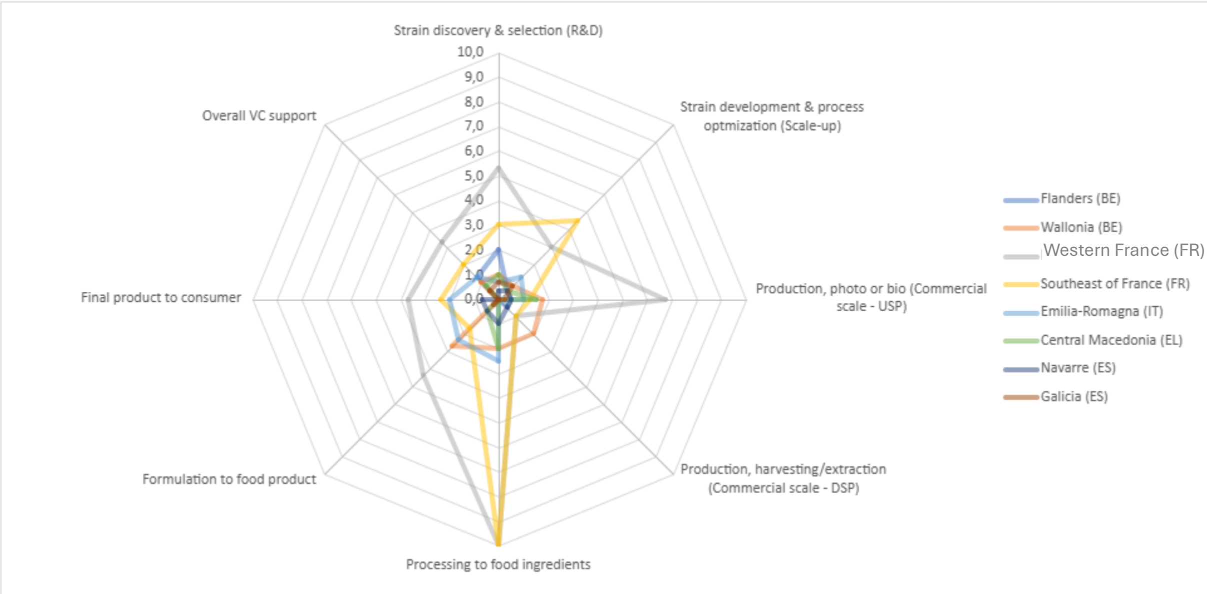
Value chain trends:

- "Processing to food ingredients" is again the highest scoring category with a total Z-score of 27,5 across all regions. With "Formulation to food product" scoring in total less than half this value, questions are raised on the incorporation of microalgae ingredients into food products. From the results of this analysis, it seems that microalgae are mostly sold as ingredients.

- "Production (DSP)" is surprisingly the lowest scoring category, while prior and subsequent value chain levels indicate regional activities. This step is likely not considered a standalone level in the microalgae value chain.

- Just like the microbial protein case, "Final product to consumer" scores consistently low across regions, indicating bottlenecks in final market delivery.

Figure 6: Radar map for microalgae. The Z-scores are visualized per region



3.4. Transregional analysis: probiotic supplements

The following observations are noted from the probiotic supplements radar map in Figure 7.

Regional trends:

- Wallonia, Western France and Navarre: these three regions score best across the entire value chain, with Wallonia leading the pack. Similar to Southeast of France, Wallonia excels in commercial-scale production of probiotics. However, unlike the French region, Wallonia also demonstrates strengths early in the value chain, leveraging its R&D expertise and preclinical capacity. This is further driven by the region's robust "Overall VC support" system. While Navarre and Western France follow similar trends, they lack Wallonia's strong regional support structures. Notably, Western France stands out as the only region with clear expertise in clinical trials for probiotics, providing it with a unique competitive edge.

- Southeast of France and Flanders: both regions have an average overall score of respectively 17,5 and 13,7. For Southeast of France, its performance is mainly driven by peak scores in "Production (USP & DSP)" and "Formulation to food product", highlighting a more mature probiotics industry compared to other regions. In contrast, Flanders strengths at the earlier stages of the value chain, particularly in “Strain discovery & selection (R&D)” and “Strain development and process optimization”, showcasing its strong foundation in biotechnology R&D. Additionally, Flanders performs relatively well in “Preclinical studies” and “Clinical trials”, largely due to synergies with its well-established pharma and medical biotechnology industries.

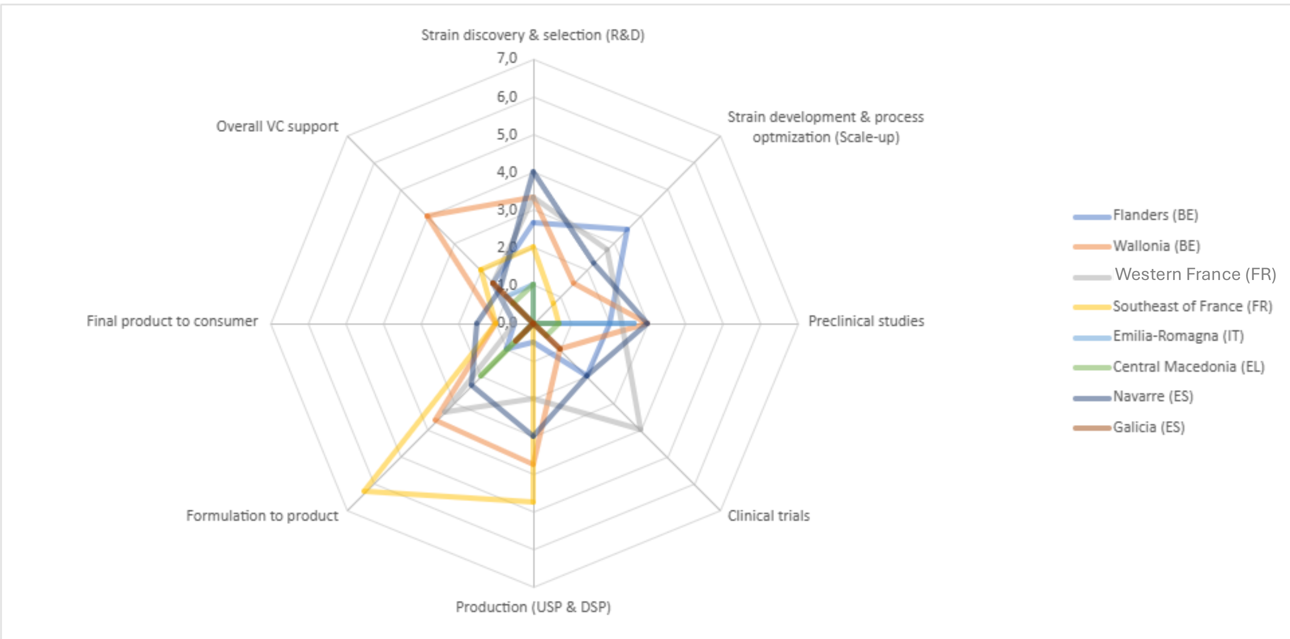
- Galicia, Emilia-Romagna and Central Macedonia: these regions underperform across most stages of the probiotic supplements value chain.

Value chain trends:

- “Preclinical studies” scores are relatively balanced, hinting at trends toward more *in vitro* and *ex vivo* trials. This is especially the case for regions that show great R&D expertise. The same trend can be observed for “Strain development and process optimization”. This could indicate a growing area of innovation.

- “Final product to consumer” is by far the lowest scoring level of the value chain, with only five out of eight regions indicating some – although very low - level of activity here.

Figure 7: Radar map for probiotic supplements. The Z-scores are visualized per region



4. GENERAL CONCLUSIONS

4.1. Case-specific findings and recommendations

4.1.1. MICROBIAL PROTEIN

1. For frontrunner regions, particularly their SMEs, a bottleneck exists in scaling from pilot to commercial production (both USP and DSP). This difficulty can stem from limited access to Contract Manufacturing Organizations (CMOs), insufficient capital expenditure (CAPEX) for building proprietary infrastructure, and a gap in forming strategic partnerships with established biomanufacturing companies.

- The compatibility between SMEs and **CMOs** depends on technical factors like strain compatibility, process needs, and scale-specific expertise. However, finding the right CMO is complex, especially for unique or novel strains and processes.
- **Self-manufacturing** remains an appealing option for SMEs, as proprietary manufacturing facilities can offer greater control over production and IP retention. However, the high CAPEX involved in constructing bioprocessing infrastructure often makes this route unattainable without substantial financial backing.
- **Partnerships**, such as with biomanufacturers or other commercial players, require convincing evidence of commercial-scale viability to justify corporate investment or collaboration. SMEs often lack the resources (e.g. a CMO match) to demonstrate this, making it a critical hurdle in forming partnerships. In addition, licensing deals demand robust IP - such as patents.

“Strain development and process optimization” - the lab-to-pilot level – received a lower overall score as well. In addition to funding, this step is crucial for SMEs to overcome the infamous ‘valley of death’. However, there is a lot of ongoing progress to minimize this step as a bottleneck in scaling the technology. For example, all existing open access pilot and demonstration facilities across Europe are mapped in the open access Pilots4U database (https://biopilots4u.eu/).

Recommendation 1: there is an opportunity for underperforming regions to focus on market integration and mid-value-chain activities, such as CMOs and pilot-to-commercial scale facilities to complement frontrunner’s innovation efforts. Especially when work force and energy cost are lower to allow for a more cost-effective production. By transforming these regions into biotechnology contributors, they can build R&D expertise gradually.

2. "Processing to food ingredients" and "Formulation to food product" are the highest-performing stages, emphasizing a strong focus on transforming microbial protein into consumer-oriented products.

4.1.2. MICROALGAE

1. “Processing to food ingredients" is the highest-performing category indicating a strong focus on transforming microalgae into intermediate ingredients for food-related applications. However, the lower score for "Formulation to food product" suggests that microalgae are now primarily sold as ingredients (for e.g. dietary supplements and nutraceuticals) rather than fully integrated into food products. This is also a finding by Araújo, et al., 2021. For their commercial applications, microalgae can be segmented into low-value (bulk) and high-value (Araújo, 2021).

This is linked with their cultivation method: open pond, photobioreactor or fermenter. The choice depends heavily on the availability of light, as light energy is crucial for phototrophic or mixotrophic microalgae growth. Light can be provided by sunlight or artificial light. While artificial light increases productivity, it also raises the cost associated with microalgae cultivation (Blanken, 2013).

- Sunlight and optimal weather conditions are, therefore, important for the cost-effective large-scale production of microalgae bulk ingredients in open-pond systems.

  Most of the European regions have sub-optimal climate conditions - due to rainy and cloudy conditions - for these large-scale outdoor microalgae production facilities (Vigani, 2015). It’s hence no surprise that only 19% of microalgae production in Europe employs ponds (European Commission, 2021)

- In contrary, for the production of high-value specialty compounds like astaxanthin, beta-carotene, and omega-3 fatty acids more advanced photobioreactor systems or hybrid setups can be used as the increased production costs related to the use of artificial light may here be acceptable (Blanken, 2013).

  The transregional analysis shows that France and Italy are leading the way. However, the studied regions in Spain don’t belong to the frontrunner group, despite being in the top 3 producers according to Araújo, et al., 2021. It is however noted that there is limited interest by investors because of their less suitable climate.

In addition, microalgae production in Europe remains limited by a series of technological, regulatory and market-related barriers. Only a minor share of the naturally occurring microalgae species are exploited commercially as new species need to be authorized under the EU Novel Food regulation before they can be placed on the food market. This is a lengthy and expensive registration procedure.

Recommendation 2: underperforming regions, particularly in Northwestern Europe, can overcome their less favourable weather conditions by capitalizing on their strengths “Strain discovery and selection (R&D)” and other innovation capabilities. These regions have the potential to excel in advanced technologies, including proprietary photobioreactor systems and high-yielding strains for specialty ingredients. Circumventing the need for favourable weather conditions. Important to note is that an enabling regulatory framework is necessary.

2. “Production, harvesting/extraction (DSP)” is weakest category across regions. This stage likely lacks standalone activities, as the flow between upstream and downstream processing does not seem to be disrupted. This reflects robust downstream capabilities and highlights the importance of leveraging synergies with transregional food supply chains.

4.1.3. PROBIOTIC SUPPLEMENTS

1. The probiotics industry seems to be most mature in the regions Southeast of France, Western France, Wallonia, and Navarre. Their historical prevalence of dairy and fermentation industries offer a natural foundation for probiotic product development.

Recommendation 3: underperforming regions with strong R&D expertise in microbiome research - especially in "Strain discovery & selection (R&D)" and "Strain development and process optimization" - can leverage these to contribute to next-generation probiotics, while utilizing the well-established probiotics production capacity of frontrunners.

- New applications in food: probiotics are most commonly found in dietary supplements. They are also naturally present in foods like fermented yogurts, kefir, kimchi, and kombucha. There is also a growing trend toward using probiotics in functional foods, especially non-dairy options (Min, 2019).
- Preclinical assessment: there is a trend toward more *in vitro* and *ex vivo* analysis to assess parameters such as stability, efficacy, site of action and engraftment of new strains and effectiveness of probiotic formulations (Kiepś, 2022).
- New probiotic strains: almost all probiotic formulations use lactobacilli with GRAS status. Finding new strains in the untapped microbial space, can lead to new – more personalized – formulations.

2. Probiotic based dietary supplements require scientific evidence to substantiate health claims, particularly in the EU, where regulatory frameworks like EFSA are stringent. Regions with access to preclinical and clinical testing services are better positioned to meet these requirements.

- Synergies with well-established biopharmaceutical and nutraceutical sectors are essential for scale and distribution: partnerships provide access to expertise and services in clinical trials, encapsulation, stability testing, and dosage formulation, which are critical for supplement production.

3. "Final product to consumer" remains the weakest value chain level, with only limited activity observed across five regions. However, as many regional governments are promoting healthy habits and nutritional products to promote overall health, there is a rise in the health-conscious consumer group & awareness of health benefits associated with probiotics. This implies that consumer demand eliminates the need for consumer acceptance campaigns.

4.2. Overall observations

1. Knowledge and skilled talent: the biotechnology sector is very knowledge intensive and thrives in regions with a skilled workforce, excellent research institutions, and effective technology transfer initiatives.

- Importance of tech transfer: while dedicated research groups are foundational to fostering innovation in biotechnology, they alone are not sufficient for a robust biotechnology economy. The critical element lies in technology, which serves as a bridge between academic research and industry. It ensures that groundbreaking discoveries in biotechnology are transformed into tangible, commercially available products and services, ultimately driving economic growth. A prime example is the Flemish research Institute of Biotechnology (VIB) in Flanders. They set up Biotope, an incubator program which supported over 30 biotech startups, cementing Flanders' position as a global biotech leader in life sciences and agrifood biotechnology.

2. Ecosystem support: regions with strong innovation ecosystems that foster cross-sector collaboration, knowledge sharing, and coordinated advocacy and internationalization efforts, gain a competitive advantage.

This advantage is catalysed by ecosystem support from dedicated biotechnology and food innovation associations, startup accelerator programmes, as well as bio-incubators with dedicated lab and research infrastructure. Moreover, fostering interaction between regions creates opportunities which can enhance the collective strength of ecosystems across Europe. By leveraging regional expertise and synergies, ecosystems can address shared challenges more effectively and accelerate innovation on a broader scale.

3. Regulatory support: an enabling EU legislation is crucial to the commercial success of novel foods in the EU. Harmonized regulatory frameworks facilitate uniform compliance. Distinct national regulations can complicate market entry and create competitive (dis)advantages among regions.

Underperforming regions in Europe often lack the regulatory expertise needed to navigate EU compliance processes. Capacity-building initiatives, including training and resources for local regulators, can enable these regions to participate effectively in the biotech landscape. This heavily depends on shared advocacy efforts, supported by dedicated biotechnology associations.

- Example of a competitive advantage: in 2023, The Netherlands introduced its own 'Code of Practice', allowing Dutch companies to request an official tasting panel limited to cultivated meat, and recently microbial protein as well, making it the first and only country in the European Union to enable tastings before official EFSA approval of the novel food. This was achieved thanks to strong coordinated cross-sector advocacy, led by the Netherlands' biotechnology association HollandBIO.

4. Funding support: access to financial resources such as EU grants, private investments, and regional subsidies is pivotal for scaling operations, e.g. cutting-edge research, advanced infrastructure, IP protection, and regulatory authorization.

In addition, the percentage of GDP that a region invests in R&D serves as an indicator of its innovation-driven capacity (Table 6). Regions with higher R&D investment demonstrate a stronger commitment to building knowledge-intensive industries like biotechnology. Moreover, consistent R&D investment attracts top talent, fosters collaborations between academia and industry, and enhances the overall ecosystem's ability to innovate.

Table 6: The percentage of GDP invested in R&D by EU member states based on most recent data (European Commission, 2023).

Country	% of GDP invested in R&D
Belgium	3.32%
France	2.17%
Greece	1.49%
Spain	1.49%
Italy	1.31%

Furthermore, many SMEs in biotechnology face the “valley of death”, a critical phase where promising innovations struggle to bridge the gap between research and commercialization. During this stage, insufficient funding can prevent companies from scaling their promising technology into commercial products. In addition to funding, the presence of pilot plants and demonstration facilities in the ecosystem plays a critical role in addressing this challenge.

5. Integration with the existing food ingredients supply chain: synergies with established food supply chains (access to processing of food ingredients, their formulation to food products, packaging, distribution, and retail networks) facilitate scalability. When well-organized, they provide efficient pathways for introducing biotechnological innovations into markets.

In addition, synergies with other industries can provide a competitive advantage as well (e.g. the pharmaceutical and nutraceutical industries for probiotic supplements). There is an opportunity here for life sciences and agrifood clusters to collaborate and identify these synergies.

6. Societal acceptance: market delivery of biotechnological food products faces persistent bottlenecks, which are influenced by multiple interlinked factors, including societal acceptance. Consumer acceptance of biotech food products depends on perceived safety, health benefits, and ethical concerns. A lack of understanding about biotechnology can lead to scepticism or resistance. Furthermore, acceptance varies heavily across regions based on cultural norms, dietary habits, and previous exposure to biotechnological innovations. Regions who actively work on transparency, consumer education, trust-building, and openly addressing of potential risks, tend to increase societal acceptance and market delivery of biotechnological food products.

However, societal acceptance is not the sole factor. Other challenges which are discussed previously, such as limited funding, regulatory complexity and integration into existing food systems also contribute to these bottlenecks.

In addition, for biotechnological food ingredients to gain traction, they must be competitive with existing alternatives in key areas like cost, performance, and supply chain integration.

7. In general, the findings and recommendations presented in this value chain analysis validate and reinforce the insights from the first ecosystem analysis (Deliverable 2.1), which outlined general opportunities, challenges and needs within the agri-food sector. The value chain mapping highlights key areas for intervention, including talent development, regulatory clarity, funding support, and ecosystem integration which were also identified as critical in the ecosystem analysis of deliverable 2.1.

Together, these deliverables provide a cohesive foundation for strategic actions that address shared challenges and unlock opportunities for regional and transregional collaboration. By validating these focus areas and offering a detailed mapping of value chain dynamics, this deliverable provides guidance for the next stages of biotechnology implementation.

5. BIBLIOGRAPHY

Araújo, R. V. (2021). Current status of the algae production industry in Europe: an emerging sector of the blue bioeconomy. *Frontiers in Marine Science*, p. 626389.

Blanken, W. C. (2013). Cultivation of microalgae on artificial light comes at a cost. *Algal Research*(4), pp. 333-340.

European Commission. (2021, 3 8). *Knowledge Centre for Bioeconomy*. Opgeroepen op 12 18, 2024, van https://knowledge4policy.ec.europa.eu/bioeconomy/algae-production-industry-europe_en

European Commission. (2023). *https://ec.europa.eu*. Retrieved 12 6, 2024, from https://ec.europa.eu/eurostat/statistics-explained/index.php?title=R%26D_expenditure

Kiepś, J. &. (2022). Current trends in the production of probiotic formulations. *Foods*(15), p. 2330.

Min, M. B. (2019). Non-dairy probiotic food products: An emerging group of functional foods. *Critical reviews in food science and nutrition*(16), pp. 2626-2641.

Vigani, M. P.-C. (2015). Food and feed products from micro-algae: Market opportunities and challenges for the EU. *Trends in Food Science & Technology*(1), pp. 81-92.

6. APPENDIX

Table 7: All Z-scores per value chain level and per region for microbial protein

	Southeast of France (FR)	Central Macedonia (EL)	Emilia-Romagna (IT)	Flanders (BE)	Galicia (ES)	Navarre (ES)	Western France (FR)	Wallonia (BE)	Total
Strain discovery & selection (R&D)	2,8	0,8	0,5	6,3	0,5	1,0	3,0	3,8	**18,5**
Strain development & process optimization (Scale-up)	1,6	0,2	0,8	3,8	0,0	2,0	2,8	2,6	**13,8**
Production, fermentation (Commercial scale - USP)	2,7	1,0	1,0	3,3	0,0	1,3	2,0	3,0	**14,3**
Production, harvesting/extraction (Commercial scale - DSP)	1,3	0,0	1,0	3,3	0,3	0,7	2,3	4,0	**13,0**
Processing to food ingredients	8,0	0,0	4,0	10,0	0,0	2,0	4,0	8,0	**36,0**
Formulation to food product	3,0	5,0	6,0	10,0	0,0	2,0	1,0	6,0	**33,0**
Final production to consumer	2,3	0,0	1,7	5,3	0,0	2,0	2,0	2,0	**15,3**
Overall VC support	3,3	1,0	1,3	8,3	2,3	2,3	2,7	4,3	**25,7**
Total	**25,0**	**8,0**	**16,3**	**50,4**	**3,2**	**13,3**	**19,8**	**33,7**	**169,6**

Table 8: All Z-scores per value chain level and per region for microalgae

	Southeast of France (FR)	Central Macedonia (EL)	Emilia-Romagna (IT)	Flanders (BE)	Galicia (ES)	Navarre (ES)	Western France (FR)	Wallonia (BE)	Total
Strain discovery & selection (R&D)	3,0	1,0	0,7	2,0	0,7	0,3	5,3	1,0	**14,0**
Strain development & process optmization (Scale-up)	4,5	0,5	1,3	0,5	0,8	0,5	3,0	0,8	**11,8**
Production, photo or bio (Commercial scale - USP)	1,3	1,5	1,0	0,5	0,3	0,5	6,8	1,8	**13,5**
Production, harvesting/extraction (Commercial scale - DSP)	1,0	0,0	0,0	0,5	0,0	0,5	1,0	2,0	**5,0**
Processing to food ingredients	10,0	2,0	2,5	0,0	0,0	1,0	10,0	2,0	**27,5**
Formulation to food product	1,7	0,7	2,3	0,0	0,3	0,7	4,3	2,7	**12,7**
Final production to consumer	2,3	0,0	2,0	0,0	0,0	0,7	3,7	0,0	**8,7**
Overall VC support	2,0	0,8	1,3	1,3	0,5	0,0	3,3	1,0	**10,0**
Total	**25,8**	**6,4**	**11,0**	**4,8**	**2,5**	**4,2**	**37,3**	**11,2**	**103,1**

Table 9: All Z-scores per value chain level and per region for probiotic supplements

	Southeast of France (FR)	**Central Macedonia (EL)**	**Emilia-Romagna (IT)**	**Flanders (BE)**	**Galicia (ES)**	**Navarre (ES)**	**Western France (FR)**	**Wallonia (BE)**	**Total**
Strain discovery & selection (R&D)	2,0	1,0	1,0	2,7	0,0	4,0	3,3	3,3	**17,3**
Strain development & process optmization (Lab to pilot)	0,8	0,0	0,0	3,5	0,0	2,3	2,8	1,5	**10,8**
Preclinical studies	0,7	0,7	2,7	2,0	0,0	3,0	2,3	3,0	**14,3**
Clinical trials	0,0	0,5	0,0	2,0	1,0	2,0	4,0	1,0	**10,5**
Production (USP & DSP)	4,8	0,0	0,0	0,5	0,0	3,0	2,0	3,8	**14,0**
Formulation to food product	6,3	2,0	0,3	1,0	0,7	2,3	3,3	3,7	**19,7**
Final product to consumer	1,0	0,0	0,0	0,5	0,0	1,5	0,5	1,0	**4,5**
Overall value chain support	2,0	0,8	1,0	1,5	1,5	1,3	1,5	4,0	**13,5**
Total	**17,5**	**4,9**	**5,0**	**13,7**	**3,2**	**19,3**	**19,8**	**21,3**	**104,6**