

PRECISION FERMENTATION

THE NEXT-GENERATION FOOD PRODUCTION TECHNOLOGY

—INDUSTRY COLLABORATION ACCELERATING MARKET DEVELOPMENT—

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SUMMARY

- Precision fermentation is a technology that uses fermentation of microorganisms with specific gene insertions to produce target food ingredients, such as proteins and fats. It is attracting attention as a new food production technology to address the food crisis and environmental issues.
- Currently, precision fermentation ingredients are used mainly for animal-free dairy products and plant-based meat for vegan consumers. Some companies have efficiently developed expensive, high value-added ingredients derived from animals.
- Although there are regulatory and consumer acceptance challenges in each country, progress is being made toward market development with the formation of industry associations, partnerships with major companies, and active participation by leaders in this new field.

1. “PRECISION FERMENTATION” HAS BECOME A HUGE TOPIC UNDER THE FUTURE FOOD CRISIS AND ENVIRONMENTAL ISSUES

Precision fermentation is a technology that uses the fermentation of microorganisms with specific gene insertions to produce target food ingredients (proteins, fats, flavors, sweeteners, functional ingredients, etc.)¹ (Figure 1).

By 2050, it is estimated that global food demand will reach 1.7 times the number in 2010, especially demand for animal products (animal protein) forecast to increase to 1.8 times², thereby posing a threat to disrupting the food supply-demand balance. Moreover, the livestock industry uses enormous amounts of energy, land, and water and is a major source of greenhouse gas emissions. Given these circumstances, there is a need to increase food production through new food production technologies that have a low environmental impact, and precision fermentation is attracting attention as a technology towards achieving this.

According to a report by the US think tank, The Good Food Institute (GFI)³, the number of companies involved in precision fermentation jumped to 62 in 2022, which is 4.4 times the number in 2018. Accompanying this

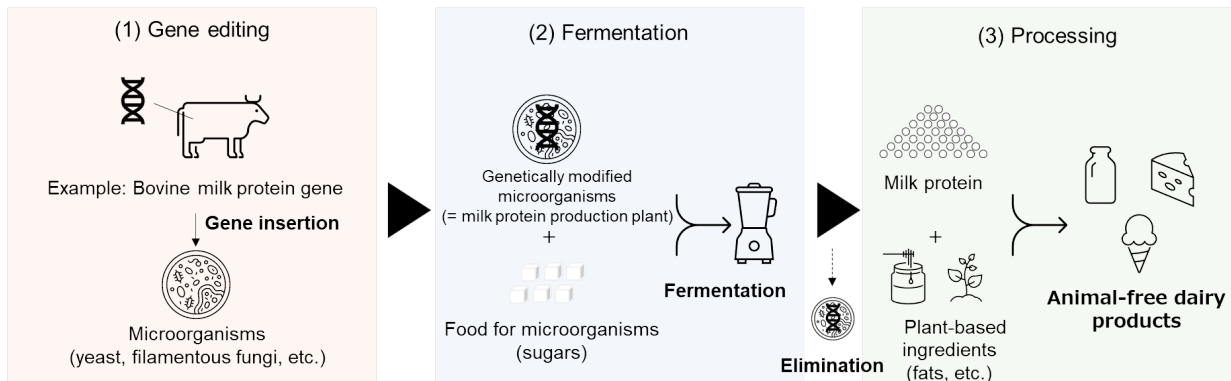
¹ Because genetically modified microorganisms are completely removed in the subsequent extraction process, in principle, the food is not considered to be a genetically modified food in the US.

² Ministry of Agriculture, Forestry and Fisheries, “World Food Supply and Demand Outlook for 2050” (in Japanese), https://www.maff.go.jp/j/zyukyu/jki/j_zyukyu_mitosi/attach/pdf/index-12.pdf (Last accessed January 29, 2024; same for all subsequent footnotes and figure references)

³ Good Food Institute, “2022 State of the Industry Report, Fermentation: Meat, seafood, eggs, and dairy”, <https://gfi.org/wp-content/uploads/2023/01/2022-Fermentation-State-of-the-Industry-Report-1.pdf>

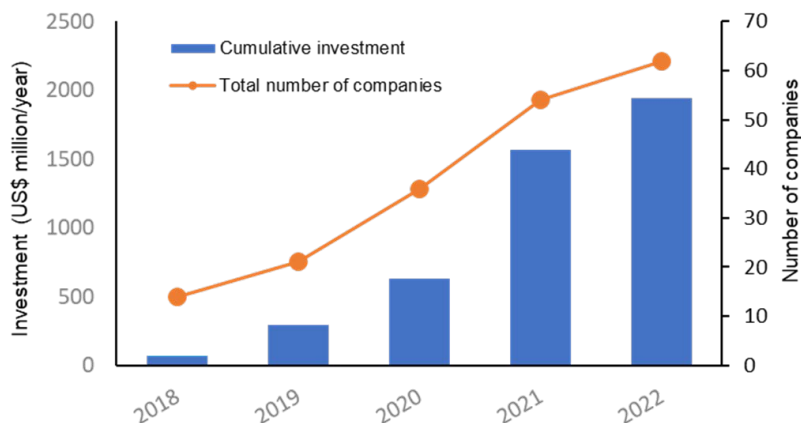
growth has been a steady increase in the amount of investment, which reached a total of approximately US\$2 billion from 2013 to 2022 (Figure 2).

Figure 1: Production process for precision fermentation food products



Source: Compiled by MGSSI based on materials on the website of Change Foods
<https://www.changefoods.com/blog/precision-fermentation-and-sustainable-animal-free-dairy/>

Figure 2: Number of companies and amount of investment in the precision fermentation industry



Source: Compiled by MGSSI based on the Good Food Institute's "2022 State of the Industry Report, Fermentation: Meat, seafood, eggs, and dairy"
<https://gfi.org/wp-content/uploads/2023/01/State-of-the-Industry-Report-Fermentation-2022.pdf>

2. EXAMPLES OF PRECISION FERMENTATION APPLICATIONS

Precision fermentation is currently being used primarily for vegan foods. Recently, however, the technology has also been adopted in the production of high value-added ingredients. Specific examples are described as follows.

2-1. Animal-free dairy products

Milk production by dairy farms is problematic in terms of water use, energy consumption, and greenhouse gas emissions. The US company Perfect Day has developed milk whey protein (β -lactoglobulin) using genetically modified fungi, and has used it to develop and launch a number of animal-free dairy products (milk, cream cheese, ice cream, etc.) in collaboration with its former subsidiary The Urgent Company (US) and major food companies (Figure 3). According to the results of the company's life cycle assessment, the use of this genetically modified whey protein can reduce water consumption by 96-99%, energy demand by 29-60%, and greenhouse gas emissions by up to 97% compared to using conventional bovine milk⁴.

⁴ Perfect Day, "The Life Cycle of Our Non Animal Protein" <https://perfectday.com/blog/life-cycle-assessment-of-perfect-day-protein/>

Figure 3: US company Perfect Day's animal-free dairy products using precision fermentation-derived milk whey protein

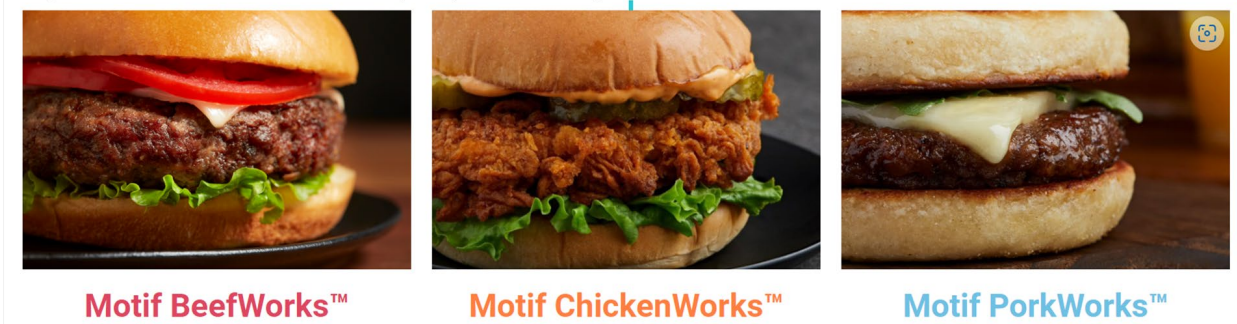


Source: Photo by the author at IFT FIRST Annual Event & Expo (July 16-19, 2023)

2-2. Replicating meat flavor and juiciness in plant-based meat substitutes

The market for plant-based alternatives is expanding not only due to demand from vegans, but also because the population of flexitarians⁵ is growing, especially in the US and Europe. However, it is difficult to reproduce the fully authentic taste of animal products with only vegetable ingredients. Consumers are not satisfied with the taste of plant-based meat in particular, and recreating the unique flavor, texture, and juiciness of meat is a major challenge. To address this, Motif FoodWorks (US) has developed a bovine myoglobin protein called HEMAMI™, a flavor component of meat, using genetically modified yeast, and is marketing it as a food additive for plant-based meat. In May 2023, the company announced the market release of a plant-based patty for the food service industry (Figure 4) containing HEMAMI™ and APPETEX™, a plant-based fat alternative that improves food texture and juiciness, and is beginning to strengthen its presence in the industry⁶.

Figure 4: Motif FoodWorks' lineup of plant-based patties



Source: Website of Motif Foodworks; <https://madewithmotif.com/products/finished-products/>

2-3. Efficient production of high value-added animal ingredients

While the use of precision fermentation technology to commercialize animal-free dairy products, plant-based meat substitutes and other such products is progressing, its monetization remains a key issue. TurtleTree (Singapore) has succeeded in producing bovine lactoferrin (a bioactive glycoprotein derived from milk) using genetically modified fungi, and aims to develop it as a functional food ingredient. In November 2023, the

⁵ Coined from the words flexible + vegetarian. A flexible vegetarian who basically eats plant-based foods, but sometimes also eats animal products such as meat and fish.

⁶ PR Newswire, "Motif FoodWorks Launches Plant-Based, Finished Format Portfolio at the National Restaurant Association (NRA) Show"

<https://www.prnewswire.com/news-releases/motif-foodworks-launches-plant-based-finished-format-portfolio-at-the-national-restaurant-association-nra-show-301819734.html>

company obtained self-GRAS⁷ status for its bovine lactoferrin in the US, and it is expected to release the product to the US market in 2024. Lactoferrin improves the intestinal environment⁸ and reduces visceral fat⁹, and is sold as supplements with function claims in Japan. However, since less than 100 milligrams can be obtained per liter of milk and the extraction process is complicated, the products are very expensive. The company claims it is possible to efficiently produce bovine lactoferrin that is bioidentical to that derived from milk¹⁰.

Figure 5: Major players in the precision fermentation industry (Companies in bold appear in the text)

Category	Company (country)			Main target products	End use
	US	Europe	APAC		
Protein	Perfect Day (US)			β -lactoglobulin (milk whey protein)	Dairy products
	Remilk (Israel)				
	Vivici (Netherlands) (founded by DSM and Fonterra)				
	ImaginDairy (Israel)				
	Zero Cow Factory (India)			A2 β -casein	
	New Culture (US)			Casein	Cheese
	Formo (Germany)				
	Better Dairy (UK)				
	Change Foods (US)				
	The EVERY Co. (US)			Ovomucoid (egg white protein)	Egg products
	Onego Bio (Finland)			Ovalbumin (egg white protein)	
	TurtleTree (Singapore)			Bovine lactoferrin (milk-derived bioactive glycoprotein)	Dietary supplements
	Geltor (US)			Type XXI collagen	
Helaina (US)			Human lactoferrin (bioactive glycoproteins from human breast milk)	Artificial breast milk	
Aromatics	Motif FoodWorks (US)			Bovine myoglobin	Plant-based meat substitutes
	Impossible Foods (US)			Soy leghemoglobin	
Fats	C16 Biosciences (US)			Palm oil	Dairy products
	Yali Bio (US)			Animal fats	
Sweeteners	ManusBio (US)			Rebaudioside M (rare sugars derived from stevia)	General purpose
	amyris (US)				

Source: Compiled by MGSSI based on various information

⁷ Abbreviation for Generally Recognized As Safe. To sell a food product with no prior history of consumption in the US, a company is required to obtain either an FDA-type GRAS, under which notification is made directly to the FDA, or a self-affirmed GRAS, under which experts and business operators voluntarily evaluate the safety of the food.

⁸ Shoko Uesaki, et al., “Effects of Lactoferrin Supplementation on Immunoglobulin A Secretion, Enteric Environment, and Sleep Quality in Healthy Adults –Randomized, Placebo-controlled, Double-blind Study–”, Japanese Pharmacology & Therapeutics (JPT), vol. 44 no. 9 2016

⁹ Tomoji Ono, et al., “Potent anti-obesity effect of enteric-coated lactoferrin: Decrease in visceral fat accumulation in Japanese men and women with abdominal obesity after 8-week administration of enteric-coated lactoferrin tablets” British Journal of Nutrition. 2010-08-09 Dec,104 (11),1688-95

¹⁰ PLUG AND PLAY JAPAN, “Food & Beverage Report 2023: Challenges and Latest Technologies for Alternative Raw Materials” (In Japanese)



https://japan.plugandplaytechcenter.com/ebooks/vr_foodbeverage2023/

3. EYES ON INDUSTRY TRENDS TOWARDS MARKET EXPANSION

3-1. Formation of industry associations: Pursuing regulatory frameworks and market expansion

The formation of the Precision Fermentation Alliance (PFA), an industry association of nine US-based precision fermentation startups, was announced in February 2023¹¹. The PFA was established to promote consumer understanding, optimize the value chain, work with regulators, and facilitate public-private partnerships, to accelerate market development in the US. In Europe, meanwhile, the establishment of Food Fermentation Europe (FFE), an industry association of five precision fermentation startups based in Europe, was announced in March 2023¹² (Figure 6). As one of its main founding objectives, the FFE cites reforming EU regulations on precision fermentation to be more transparent. Currently, the sale of novel foods with no history of consumption in Europe requires prior approval through a cumbersome and unclear review process, whereas corresponding regulations are relatively easy and clear in the US. The FFE initiatives reflect the European company's impatience to catch up with the US, where investment in the precision fermentation industry is converging and a number of precision fermented foods are already on the market.

Figure 6: Memberships of each industry association and purpose of establishment

	Precision Fermentation Alliance (PFA)	Food Fermentation Europe (FFE)
Participating companies		
Vision	Leading companies in the precision fermentation field are taking the lead in promoting precision fermentation as a reliable solution to achieve adaptable and sustainable food systems worldwide	Precision fermented food companies in Europe are taking the initiative to create a global sustainable food system and leading the rapid development of innovative food products in Europe
Objectives	<ul style="list-style-type: none"> Establish safety of precision fermented foods (promote consumer understanding) Build and optimize the value chain Cooperate with regulatory authorities and public-private partnerships (promote efficient market adoption of precision fermented foods) 	<ul style="list-style-type: none"> Establish a sustainable food system in Europe (environmental considerations and food security) Promote market uptake of precision fermentation-derived protein (promote consumer understanding) Make recommendations for a transparent and efficient regulatory framework (promote the efficient development of precision fermented foods)

Source: Compiled by MGSSI based on the following materials: Precision Fermentation Alliance, https://www.pfalliance.org/wp-content/uploads/2023/04/PFA_All_Logos-scaled.jpg, Business Wire, <https://www.businesswire.com/news/home/20230216005362/en/Food-Tech-Leaders-Come-Together-to-Form-the-Precision-Fermentation-Alliance-to-Champion-a-More-Resilient-and-Sustainable-Future>, Food Fermentation Europe, <https://static1.squarespace.com/static/63fc99009958ca6e316067e2/t/64a3eaa5e281e906a3f387da/1688464039933/Food+Fermentation+Europe%E2%80%99s+Vision+on+the+upcoming+Sustainable+Food+Systems+Framework.pdf>

3-2. Leading company speeding up supply of precision fermentation food ingredients

In July 2023, industry leader Perfect Day, which has developed several brands of animal-free dairy products through its group company The Urgent Company, announced the sale of The Urgent Company and its exit from the consumer-oriented business¹³. The company has indicated its intention to focus on the B2B food ingredient supply business, and this policy change is seen as a positive strategy to avoid competing in the end product markets with food giants who are expected to become customers for precision fermentation food ingredients. Perfect Day has already entered into a long-term partnership with Bel, a major French dairy products

¹¹ Business Wire, “Food Tech Leaders Come Together to Form the Precision Fermentation Alliance to Champion a More Resilient and Sustainable Future”

<https://www.businesswire.com/news/home/20230216005362/en/Food-Tech-Leaders-Come-Together-to-Form-the-Precision-Fermentation-Alliance-to-Champion-a-More-Resilient-and-Sustainable-Future>

¹² Onego Bio, “Food Fermentation Europe launches, calling on EU to speed up in global race on sustainable food innovation”

<https://www.onego.bio/press/our-news/food-fermentation-europe-launches-calling-on-eu-to-speed-up-in-global-race-on-sustainable-food-innovation>

¹³ Green Queen, “New Food Tech Co Superlatus Agrees To Acquire Perfect Day’s The Urgent Company Brands for \$1.25 Million”

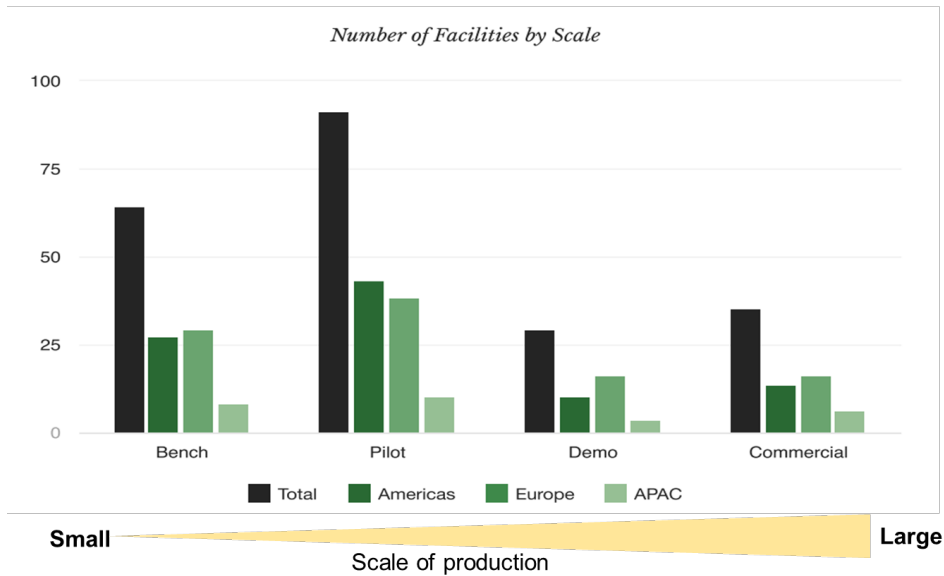
<https://www.greenqueen.com.hk/new-food-tech-co-superlatus-acquires-perfect-days-the-urgent-company-brands-for-1-25-million/>

manufacturer, and started marketing animal-free cream cheese in the US in January 2023. In addition, the company is considering large investments in food manufacturing facilities in the US and is in discussions with some food giants such as PepsiCo (US).

3-3. Scale-up support companies helping with commercialization

Large fermentation plants are required by startups to make the price of their precision fermentation products competitive, but the majority of existing fermentation plants are small to medium in size¹⁴ (Figure 7). Large-scale fermentation plant construction requires a significant amount of financial investment, and this has been a bottleneck. In this environment, contract development and manufacturing organizations (CDMOs), which help companies scale up from lab prototyping to commercial production, are helping to solve the problem. For example, Liberation Labs (US) has announced that it will build the first large-scale fermentation plant for food products in the US in Indiana¹⁵. The company aims to begin operating the plant by the end of 2024, and if realized, it will mark the emergence of a CDMO capable of producing large volumes of precision fermentation foods in the US.

Figure 7: Number of fermentation plants by size and region



Source: Compiled by MGSSI based on Capacitor's report on the "State of Global Fermentation Capacity", released in February 2023

4. OBSTACLES TO EXPANDING THE MARKET FOR PRECISION FERMENTATION FOOD PRODUCTS

4-1. Different regulations by country

Each country has its own regulations regarding the safety of novel foods (foods that have no history of consumption) and conducts pre-market reviews (Figure 8), and differences in regulations are affecting the progress of market development in each country. The review process by the US Food and Drug Administration (FDA) is relatively tolerant, with a short review period of six months to one year. To date, many novel foods have been approved, including the bovine myoglobin developed by Motif FoodWorks and β -lactoglobulin by Perfect Day. In contrast, the EU's European Food Safety Authority (EFSA) is very strict, and the process is not clear. In fact, the US company Impossible Foods has yet to receive approval for its 2019 application for soy leghemoglobin¹⁶. The Singapore Food Agency (SFA) also conducts pre-market reviews. In accordance with the

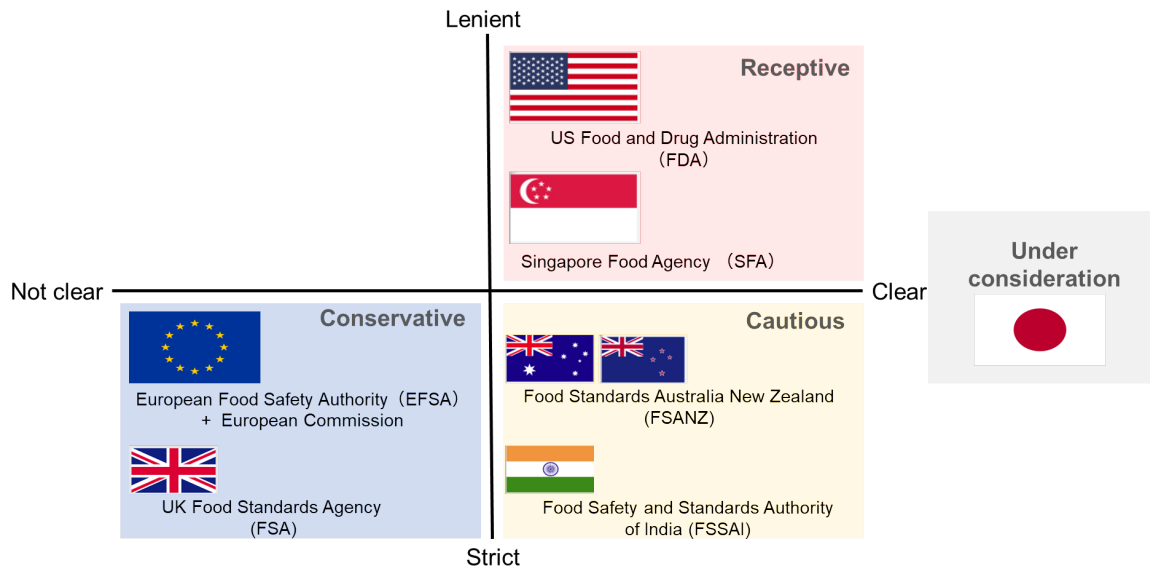
¹⁴ Capacitor "Trends Reports" <https://capacitor.bio/trends>

¹⁵ AgFunderNews, "Liberation Labs bags \$30m in to kit out biomanufacturing hub in Indiana"

¹⁶ Open EFSA , <https://open.efsa.europa.eu/questions/EFSA-Q-2019-00651>

government's "30 by 30" goal of increasing food self-sufficiency to 30% by 2030¹⁷, Singapore is actively promoting the commercialization of novel foods, and many have been approved so far. As for Japan, regulations

Figure 8: Regulatory trends in each country



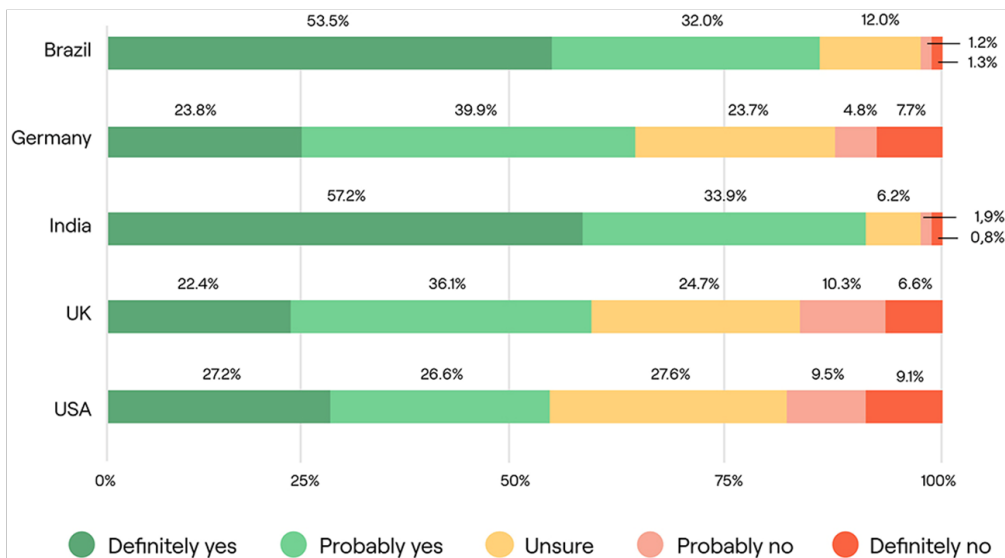
Source: Compiled by MGGSI based on the Good Food Institute's "2022 State of the Industry Report, Fermentation: Meat, seafood, eggs, and dairy"

are presently under consideration, and this is proving a barrier to market entry.

4-2. Acceptance by consumers

The results of a survey on consumer acceptance of cheese made with precision fermentation, which was conducted in five countries (Brazil, Germany, India, the UK, and the US), found that more than 50% of

Figure 9: Consumer attitudes towards buying animal-free cheese by country



Source: Frontiers. "Don't Have a Cow, Man: Consumer Acceptance of Animal-Free Dairy Products in Five Countries" <https://www.frontiersin.org/articles/10.3389/fsufs.2021.678491/full>

¹⁷ Singapore Food Agency, "30 by 30, Strengthening our food security" <https://www.ourfoodfuture.gov.sg/30by30/>

consumers expressed an intention to buy the product (Figure 9). In addition to "sustainability", "taste" also emerged as a key factor influencing consumer acceptance¹⁸.

5. FUTURE OUTLOOK

Within the next one to two years, many food companies are expected to introduce animal-free dairy products by obtaining supplies of ingredients from leading companies. Market development will first proceed in the US, where regulations are more tolerant, but is also expected to accelerate in Europe, where there is a strong awareness of sustainable animal welfare, although it will depend on regulatory revisions.

Partnerships from upstream to downstream will be the key factor to successful commercialization. Societal acceptance of these novel foods is expected to progress as a result of collaboration between R&D-type companies with strengths in microbial design and fermentation process optimization, and major food companies with strengths in final product development and branding, and also CDMO companies with capabilities to support scale-up operations. For example, New Culture (US) has entered into a partnership with ADM, a leading US food ingredients company, to launch a mozzarella cheese containing precision fermented casein by 2024. The result of one survey indicates that consumers have a strong desire for improved quality in plant-based cheese alternatives¹⁹, and the practical application of casein derived from precision fermentation is expected to greatly accelerate market formation. In the future, developing alternatives to animal fat, which is a crucial component in the taste of food products, will also be a major focus.

¹⁸ Frontiers, "Don't Have a Cow, Man: Consumer Acceptance of Animal-Free Dairy Products in Five Countries" <https://www.frontiersin.org/articles/10.3389/fsufs.2021.678491/full>

¹⁹ Nature Biotechnology "Cow-less milk: the rising tide of animal-free dairy attracts big players" <https://www.nature.com/articles/s41587-022-01548-z>