RÉPUBLIQUE FRANÇAISE
Liberté
Égalité
Fraternité

INRAE

INRAE's contribution to the EC's consultation on the European Biotech Act

EXECUTIVE SUMMARY

INRAE welcomes the European Commission's ambition to deliver a regulatory framework that can fully embrace the entire scope of biotechnology and enable the very significant opportunities embedded within it. We share below (and in the attached paper) our views and recommendations.

1. Need for a comprehensive Biotech Act – while biotechnology undoubtedly has a role to play in the health space, it can also play a major role in other sectors such as agri-food, environment and industry (chemicals, materials, energy…) while providing environmental services and contributing to the shift toward carbon neutrality. In particular, it must irrigate bioeconomy related sectors more explicitly. Support for biotechnology and biomanufacturing must recognize the cross-cutting nature of biotechnology and the whole range of application areas, each one requiring attention to ensure that public policy is adequate to stimulate market development and achieve EU strategic goals while taking in account biosafety, equity of access and maintenance of biodiversity aspects.

2. R&I as an essential lever for developing competitive biotech solutions – advances in 'omics' associated with innovation in data analysis offer high perspectives for the understanding of complex biological systems and for the development of synthetic biology to further develop, up-scale and commercialise innovations. Research must be supported through a continuum from basic research to market and consumers. Synergies in funding with national research programmes should be exploited.

3. Streamlining regulation and improving the competitiveness of biomanufacturing – the uneven competition with the petrochemical industry must be offset by subsidies and public procurement policy for biomanufactured products, ensuring that these meet sustainability criteria. Biotech is one of the key lever for EU scientific and industrial competitiveness and sovereignty. EU needs to balance innovation and regulation in a new way, by speeding up marketing authorisation procedures for innovations from biotechnologies while guaranteeing safety for end-users. In this purpose, regulatory sandboxes are interesting regulatory innovation. Supporting risk/benefit analysis with solid scientific evidence is one of the options.

4. Support start-ups and SMEs for scaling of bioprocess innovations – scaling biotechnology requires understanding of the research-development-innovation-industrialisation-continuum. Research infrastructures (RIs), especially hybrid entities (pre-industrial demonstrators) that support both applied research and technology development should help start-ups and SMEs to prototype processes and derisk business models before further scaling.

5. Developing skills – RIs play an important role in education and upskilling. Recognising Europe's rich RI landscape as a competitiveness factor is crucial to better integrate RIs into biotech research, promoting their use in MSCA and similar frameworks. Supplying RIs with the means to sustain long-term Transnational Access programmes providing access to early career professionals is vital.

6. Seizing opportunities offered by Artificial Intelligence (AI) – EU strategy regarding AI for biotechnology must focus on the development of robust data and metadata standards, and the development of smart, trusted organisations that favour data mutualisation (e.g. trusted innovation ecosystems) according to FAIR principles, generating the quantities of quality data necessary to train algorithms. Europe needs to better mobilise its assets through e.g., an EU biotechnology dataspace.

7. Raising public awareness of biotechnology – The Biotech Act should engage civil society to build trust in biotechnology solutions, by promoting transparency and education to foster understanding and demystify biotechnology applications. A large dedicated scientific dissemination programme at EU level should be set up capitalising on tools and actions such as those implemented in some HE projects.

1. Need for a Comprehensive Biotech Act

INRAE, the French National Research Institute for Agriculture, Food and Environment, welcomes the European Commission's ambition to **deliver a regulatory framework for biotechnology that can fully embrace the entire scope of biotechnology** and enable the very significant opportunities embedded within this domain. Unlocking its full transformative potential, especially within fields related to agriculture, food, chemicals, materials and fuels will be crucial for a **sustainable, competitive, and resilient Europe** where food security, decarbonised production systems, and geopolitically balanced supply chains must be the norm.

Support for biotechnology and biomanufacturing must recognise the cross-cutting nature of biotechnology and the whole range of application areas, each one requiring attention to ensure that public policy is adequate to stimulate market development and achieve European strategic goals.

Biotechnology holds the potential to provide new solutions for a range of challenges, securing sustainable growth and greater industrial sovereignty for EU Members states. While biotechnology undoubtedly has a role to play in the health space, it can also play a major role in many other sectors and is a key lever for novel environmental services. It has the potential to be a game changer contributing to the industrial shift toward carbon neutrality by supporting environment-friendly processes, products and services. **This is the reason why the forthcoming Biotech Act must integrate (circular) bioeconomy-related sectors explicitly.**

- In the **food** domain, biotechnology is a source of new ingredients and healthier, safer, more sustainable foods. Food fermentation has been used for millenars to naturally preserve foods, increasing the shelf life, diminishing the use of chemical preservatives and lowering the energy burden of food storage (check DOMINO project). Biotechnology can be of tremendous help in producing superstrains of microbes that could enable acceleration of fermentation processes, provide more efficient utilization of raw materials, and produce better-quality products. Precision fermentation can produce high quality ingredients such as proteins and lipids using conventional (sugars) or non-conventional resources, such as CO_2 (e.g., as a co-product of biomethane production).
- In **agriculture**, biotechnology can play a disruptive role, underpinning new strategies to protect crops (e.g., production of biopesticides), enhance plant breeding (e.g., genome-edited plants), stimulate plant growth (e.g., microbial soil amendments) and for environmental monitoring (e.g., biosensors to detect pathogens) (check MOBILES project).
- In the **environment** domain, biotechnology is crucial for water, wastewater and waste treatment, bioremediation and recycling strategies, in support to the development of a circular and sober bioeconomy (check LeAD project). Cutting-edge biotechnology includes the use of otherwise undesirable industrial CO_2-rich off-gases and the recycling of plastics.

A cross-cutting issue is the use of biotechnology approaches for **greenhouse gases capture** to achieve carbon neutrality.

Moreover, **biotechnology is deeply connected to biomass** (availability and conversion processes) and consequently to bioeconomy. Therefore, it is important to ensure the sustainable use of biomass, considering its finite resources and possible conflicts of biomass use between different sectors. In addition, biotechnology may provide ways to **broaden the spectrum of natural resources potentially available for use**. The use of underutilised and/or overlooked resources, in terms of biomass feedstocks, microorganisms and others, has an untapped potential to provide innovative and robust biotech-based solutions. Utilisation of novel, high-performance microorganisms; utilisation of residues and side streams; opportunities offered by biodiversity and by synthetic biology/gene edition; or

microbial chassis engineering, are examples of areas to further develop. In this sense, basic and applied research play a crucial role in providing promising new microorganisms for biotech start-ups and companies. Eventually, biotechnology and biomanufacturing can play an important role in achieving carbon neutrality and strengthening the bio-based economy. They address sustainability and climate change by: reaching net-zero emissions (CO_2 capture and sequestration), sustainable manufacturing, bio-based products, waste reduction, bioremediation, natural resources preservation, etc

Overall, the development of biotechnology solutions must consider:

- **Equity of access**: to ensure that biotechnological advances do not widen the inequality gap among populations.
- **Sustainable use of biodiversity**: to avoid over-exploitation of certain strains, breeds or species, as it may be the case in plant production.
- **Ethical and deontological requirements**: to ensure that all activities are performed while respecting the general principles of ethics and deontology, to avoid any misuse of technologies or applications.

2. R&I as an essential lever for developing competitive biotech solutions.

Recent and on-going progress in 'omics' (e.g., genomics, proteomics, metabolomics…) associated with innovation in data analysis and integration (e.g., AI tools) offer high perspectives for the understanding of complex biological systems. The corresponding data and knowledge may be mobilized through e.g., synthetic biology in order to further develop, up-scale and commercialize innovations. Taking in account the constraints of industrial processes as far as possible is a major prerequisite for innovation.

Research related to biotech must be supported following a continuum from fundamental research to market and consumers. This covers fundamental research to better understand biological mechanisms, but also the entire innovation path from transfer to industrial deployment. Through a voluntary policy of support to this continuum, the EU may generate added value in many different sectors, including agri-food.

We also see a need for the EU to put various kind of resources (regulatory framework, facilitating tools, etc.) into the process of **coordinating national initiatives**. The outcomes and impacts of research may be amplified through synergies with national programmes such as, for example, the French Plan France 2030 (see Box 1) with massive public investments in research on societal challenges.

Box 1. France 2030 Plan:

Since 2021, the France 2030 Plan has been a flagship initiative of the French government designed to support innovation and its leading actors across the nation. Among other tools, Priority Research Programmes and Equipment (PEPR) and Acceleration Strategies (AS) aim to bolster French research and innovation in strategic scientific fields that are pivotal/crucial to technological, economic, social, health and environmental change. These programs are completed by applied programs with a deployment capacity. As an example, the "*Bioproductions* (PEPR B-BEST): *Biomass, Biotechnologies, and Sustainable Technologies for Chemistry and Fuels*" research program is part of the AS "*Bio-based Products and Industrial Biotechnologies - Sustainable Fuels*". Co-led by INRAE and IFPEN, this program started in 2023 and will run for 7 years, with a budget of 65 M€.

A balanced vision is key to maintain the EU's scientific excellence and to expand the knowledge base, while taking steps to close the investment gap in strategic technologies (in comparison with the US and China). It is essential to strike a balance between the production of actionable knowledge and the

deployment of innovation, so as not to 'dry up' the innovation pipeline. For reconciling the objectives of production, human and environmental health, life sciences are of paramount importance.

3. Streamlining regulation and improving the competitiveness of biomanufacturing

Europe has strong assets to be at the forefront of biotechnology R&I. However, a huge economic potential is currently being lost, while competitors from USA, UK, Australia and Asia are seizing opportunities by massively investing in this emerging field. For example, the EU's Novel Foods Regulation hampers the wider and fast adoption of microbiome & biotech-based solutions (up to 5-7 years). The EU regulatory framework on synthetic biology is also critically slowing down the adoption of precision fermentation innovations. Beyond regulation, better access to fermentation substrate and lower energy cost are two other key success factors for industrial developments.

Both the OECD (Organisation for economic cooperation and development) and IEA (International Energy Agency) have shown that the incumbent **petrochemical industry** benefits from significant direct (subsidy) and indirect (non-payment of negative externalities) fiscal advantages amounting to 7 trillion US$ per annum. These unfairly handicap the development of the biomanufacturing sector. This uneven playing field must be offset by subsidies and public procurement policy for biomanufactured products, ensuring that these meet sustainability criteria.

A EU Biotech Act embedding agri-food, bioeconomy and health dimensions is an opportunity to reduce hurdles in deploying research-based innovations and support EU leadership in these very strategic fields.

Europe needs to balance innovation and regulation in a new way. It is essential to speed up marketing authorisation procedures for innovations from biotechnologies while guaranteeing safety for end-users. This implies providing sufficient resources (financial and workforce) to European agencies to speed up product assessment. At the same time, the EU must provide the means to control the safety of products imported from outside the EU, particularly those resulting from innovations in life sciences that are not yet authorised or in the process of being authorised in the EU.

A **regulatory sandbox** is an interesting regulatory innovation of its own. If used smartly, it can benefit both consumers and the economy. However, regulatory sandboxes come with a risk of being misused or abused, and need the appropriate legal framework to succeed (e.g., ensuring that modified organisms do not cause ecological disruption or uncontrolled proliferation in natural ecosystems). Therefore, **extreme caution is required when it comes to deploying regulatory sandboxes for innovations stemming from biotechnology**. Past failures in downgrading existing regulations, such as the mad cow crisis or H1N1, demonstrate the need for the utmost precaution. It would be preferable to provide the necessary resources to produce a robust ex-ante risk analysis through research (economic analysis, health of regulations) to reduce risks.

The creation of a more favourable regulatory framework is certainly required to stimulate innovation and spur the delivery of new technologies, processes and products, while favouring the emergence of related EU-based companies and start-ups. One aspect of achieving this is to support risk/benefit analysis with solid scientific evidence.

4. Support start-ups and SMEs for scaling of bioprocess innovations

There is a need to better support start-ups to allow them to stay in Europe and to grow. This implies financial support, stimulating entrepreneurship as well as simplification and changes in regulation (as

discussed in section 3); supporting industrial developments with better access to biomass feedstocks and lower energy costs; devoting more resources to collaboration between research organisations and risk assessment agencies to speed up the adaptation of regulation framework.

Scaling biotechnology requires understanding of the research-development-innovation-industrialisation continuum. Nurturing European innovation at an early stage is vital.

The EC should recognise and support the crucial role of hybrid entities such as preindustrial demonstrators, as well as research infrastructures, that bridge gaps and mobilise public-private partnerships to nurture the early stages of innovation pipelines. In fact, there is a need to design technological capabilities to support innovation throughout the value chain and at different scales.

Research infrastructures (RIs), such as IBISBA (see Box 2) are provided with the means to partner with commercial entities. For this, ESFRI regulations must be clear and financial support to provide access to early stage enterprises should be considered (e.g., a RI access voucher scheme).

Box 2. European Research Infrastructure IBISBA:

IBISBA is the only European distributed Research Infrastructure dedicated to Industrial Biotechnology and Biomanufacturing. It provides a single access point to researchers from academia and industry to integrated services for end-to-end bioprocess development. It bridges a gap at the interface of research, technology and innovation and supports both fundamental scientific excellence and innovation. IBISBA operates biofoundries and other automated experimental platforms, pilot-scale facilities for fermentation-based processes and equipment for various upstream and downstream operations. Finally, it develops advanced computational resources (Decision Support Systems, digital twins, etc).

Hybrid entities, such as pre-industrial demonstrators, support both applied research and technology development, helping start-ups and SMEs to prototype processes and derisk business concepts before further scaling. In the last 15 years French Government has been launching and financing this type of hybrid entities (see Box 3) which have greatly contributed to the translation of research into innovation by supporting SMEs and start-ups.

Box 3. Examples of French pre-industrial demonstrators contributing to scaling of biotech innovations:

Ferments du Futur, is a French Public-Private Partnership gathering 42 members (companies, higher education and research institutions, branch organisations, technical institutes, trade unions and competitiveness clusters). It was launched in 2022 to accelerate research and innovation in ferments, fermented foods and bio-preservation. In 2024, this was supported by the opening of a unique Ferments du Futur Innovation Centre on the Paris-Saclay cluster with cutting edge equipment. It has received a funding of 48 M€ for 10 years.

Toulouse White Biotechnology (TWB) is a demonstrator forging links between basic research and industry. It offers collaborative public/private R&D projects and services while it also supports start-ups in order to accelerate their launch and development. The projects are based on a continuum of expertise for innovation: from research and proof of concept to pre-industrial development and industrial technology transfer including business creation. TWB activities foster the creation and design of biological tools (enzymes, microorganisms, microbial consortia) for use in innovative and profitable industrial processes. Launched in 2012, it has received a funding of 27 M€ for 15 years.

MetaGenoPolis (MGP) is a demonstrator on microbiome analysis and implications in health & nutrition, offering cutting edge state-of-the-art equipment for biobanking, DNA extraction, sequencing, screening, bioinformatics, and data visualization. Launched in 2012 it has received a funding of 25 M€ for 13 years.

Making room for public-private partnerships to scale-up industrial deployment of biotech-based innovations. The interactions between the two sectors may allow innovation in life sciences to reach the market more rapidly. It could be especially interesting to develop public-private partnerships for pre-industrial demonstrators to mitigate risks: co-financing, with public funding for the riskiest upstream part, and private access to demonstration. EU and National Public-Private Partnership such as CBE-JU or Ferments du Futur (see Box 3) are good examples for supporting and accelerating R&I translation into market applications.

5. Developing skills

The role of research organisations and universities role should be recognised in the Biotech Act since they educate the next generation of scientists, bioengineers and entrepreneurs. This is particularly important in complex and fast-evolving fields such as biotechnology. They also provide crucial access to excellence-based research infrastructure and testbeds to validate and scale new biotech companies.

Training is an intrinsic mission of RIs. In this regard, European RIs, such as IBISBA, provide access to a range of expertise and cutting-edge equipment for early career scientists and other professionals, for examples working in SMEs, requiring training in the field of biotechnology. So that RIs can contribute to training it is vital to ensure that they have adequate financial means. Transnational access (TNA) programmes constitute a tried-and-tested framework to achieve this. Therefore, RIs must be given the resources to operate TNA on an ongoing basis.

Skills and competences. There is a need for continued investment in building and upgrading skills and (novel) competences, including initial training and long-life learning. Initiatives supported by the European Skills Agenda may help in supporting the Biotech Act.

Mobility. Programmes that allow researchers to move between countries (such as those funded by the MSCA programme) foster research capacity and therefore improve the creativity, efficiency and quality of research (check E-MUSE project). They should be promoted in support to the implementation of the Biotech Act (as well as other strategies).

Talents attraction. The EU should finance research programmes able to attract talents worldwide, especially in this competitive field of biotechnology where Asian and American fellows are fast-evolving.

6. Seizing opportunities offered by Artificial Intelligence

Artificial intelligence (AI) has immense potential in biotechnology, from drug discovery and development to personalised advice in medicine or agricultural practices. But AI integration is often hampered by technical complexities, a **lack of standardised datasets for training algorithms**, **or difficulty in accessing data**. By fostering initiatives and policies that make AI accessible, foster collaboration and promote open science and FAIR principles, the Biotech Act should accelerate transformative advances in biotechnology across Europe.

INRAE is leading the European project BIOINDUSTRY 4.0 which focuses on the development of AI solutions for biotechnology. These include the development of data standards and a pipeline to produce high quality data and metadata for use by AI. Moreover, the project is developing digital twins connecting which will ultimately serve to automatize bioprocesses and control/command loops. Early findings suggest that **it is necessary to pursue work on data and metadata standards, ensuring that Europe is a standards setter rather than a standards follower**. In this regard, there is strong

competition from the USA. Moreover, the project reveals the need to develop secure data sharing frameworks. These are required to federate data from different sources, thus ensuring that sufficient volumes of good quality data are available to train algorithms.

One option to further develop AI for biomanufacturing considering the European context is to rely on an **EU-wide network of interconnected innovation ecosystems**, with all ecosystems operating according to a common set of standards to ensure interoperability. To set up such a network it will be necessary to develop and deploy suitable data mutualisation frameworks (e.g. federated AI learning; sovereign clouds) and suitable governance schemes. Moreover, as a strategic priority for the European Union, it appears both logical and vital to **develop a biotechnology and biomanufacturing dataspace. European guidelines and good practices** to deal with data could help to ensure the storage of those data, the quality of data generated, the property of those data, security, etc. The Biotech act should integrate key technologies such as AI/ML (machine learning) according to open science principles.

7. Raising public awareness and understanding of innovations in biotechnology

Innovations linked to life sciences can positively contribute to the development of healthier, safer and more sustainable products and practices in the agri-food sector among others. However, despite various benefits, innovations may generate some reluctance among parts of the population. Several factors explain this reluctance, such as distrust of new technologies or cultural habits; misinformation, cognitive biases or past mistakes. Biotechnology is a particularly sensitive field with violent public opinion reactions and fear/distrust in technologies such as genetically modified or genome edited organisms, cloning, gene therapies or the use of human embryos. This is not new but it is acutely enhanced in the current era of fake news and distrust in science. In addition, biotechnology raises **complex ethical issues and potential risks** which should not be overlooked in the Biotech Act.

It is essential that **citizens have a better understanding of the work of scientists**. This may apply to all scientific sectors, not only biotechnology although the need is particularly acute when addressing activities concerning life and life sciences. Bringing research and innovation closer to citizens brings benefits for both society and the research institutions themselves, as it promotes citizens being better informed and science more highly valued. It is important to help the public **understand the issues at stake** because these are complex subjects that are difficult for non-scientists to grasp. To improve the acceptability of biotechnology, it is necessary to better understand consumer / civil society concerns and reactions regarding these novelties and to highlight some possibilities allowing compensation for this reluctance, including though education and dissemination of knowledge. The European Commission could therefore consider deploying a scientific dissemination programme coordinated at EU level, capitalising on existing tools and actions such as those implemented in some Horizon Europe projects (open and participatory science activities, living labs, etc.). Dissemination of scientific information through social media (SoMe) can promote connectivity within the scientific community, overcome barriers to access to sources, increase debate, and reveal layperson perspectives and preferences. The general principles guiding dissemination of professional information via SoMe must remain in line with the general principles of ethics, deontology, and scientific validity that guide science.