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

EXECUTIVE SUMMARY

INRAE welcomes the ambition of the EC to deliver a Biotech Act II unlocking the full transformative potential of biotechnology. INRAE insists that the Biotech Act II **should strengthen the research-innovation continuum**, thus contributing to overcome the three main barriers hindering the EU biotech & biomanufacturing industry: limited market uptake, unpredictable investment, fragmented single market and regulation for bio-based products.

Need for a comprehensive Biotech Act – the cross-cutting nature of biotechnology and the **whole range of application areas** (including food and feed, materials, self-sustained technology, chemicals, fertilisers & plant protection products as well as environmental services) should be covered under Biotech Act II. Each area requires specific attention to ensure that public policies are relevant to stimulate market development and achieve EU strategic goals while taking into account biosafety, equity of access, and preservation of biodiversity. The Biotech Act II should also **ensure the sustainable use of biomass** and anticipate possible conflicts of biomass uses between different sectors**.**

Placing R&D and the research-innovation continuum at the heart of Biotech Act II - maintaining a strong focus on bioeconomy-related research in future EU funding programmes – in addition to recognising the role of Research Performing Organisations (RPOs) as cornerstones to the success of Europe's biotech sector, the EC should recognise and support the crucial role of Research Infrastructures and hybrid entities such as preindustrial demonstrators that bridge gaps between low and high TRLs and mobilise public-private partnerships to nurture the early stages of innovation pipelines. Finally, synergies in funding with national research programmes should be further exploited.

Supporting risk/benefit analysis with solid scientific evidence to accelerate the uptake of biotech products - Biotech Act II should include regulatory sandboxes within domains such as novel foods to ensure that the EU's competitiveness on research excellence is also translated into on-the-ground applications. However, an appropriate legal framework should strictly regulate their implementation to prevent any abuse and ensure end-user safety. This requires strong support to provide robust ex-ante risk analysis based on research to mitigate risks.

Fully exploiting the convergence of biotechnology, data, and AI across Europe – EU strategy regarding AI for biotechnology should rely on robust data-and-metadata standards, trusted innovation ecosystems built on FAIR principles, and the generation of high-quality data needed to train algorithms, laying the groundwork for future biotechnology and biomanufacturing.

As a major European RPO, INRAE (French National Research Institute for Agriculture, Food and Environment) is deeply committed to contributing to the EU leadership on biotechnology, and has recently delivered a policy brief on the matter following an event on February 4th in Brussels. INRAE is convinced of the potential of biotechnology to drive the transition towards a sustainable, low-carbon bio-based economy, contributing to a more competitive and resilient Europe where food security, decarbonised production systems, and a geopolitically balanced supply chain are the norm. We believe that the success of the Biotech Act II will depend not only on ambitious policy objectives, but also on robust scientific evidence, (cutting-edge) technological developments, stakeholder alignment, and practical implementation pathways.

Need for a cross-sectoral & comprehensive Biotech Act II

The forthcoming Biotech Act II must reflect the cross-sectoral nature of biotechnology and the whole range of application areas, each one requiring specific attention to ensure that public policies are adequate to stimulate research and innovation towards market development while taking into account biosafety, equity of access, and preservation of biodiversity. **This is the reason why the forthcoming Biotech Act II must explicitly integrate all (circular) bioeconomy-related sectors in its scope.**

- In the **food** domain, biotechnology is a source of healthier, safer and more sustainable foods. One key application of biotechnology is food fermentation, which 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 utilisation of raw materials, and produce better-quality products. Precision fermentation can also 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 plays 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.

Furthermore, as **biotechnology is deeply connected to biomass** (availability and conversion processes), the Biotech Act II must ensure the sustainable use of biomass and anticipate possible conflicts of biomass uses between different sectors. This calls for:

- Supporting **basic and applied research in providing promising new microorganisms able to broaden the spectrum of natural resources potentially available for use.**
- **Improving data quality and availability to better forecast biomass dynamics to establish a harmonised EU-wide cascading hierarchy for biomass use** and to improve traceability and harmonised metrics.

Overall, the development of biotechnology solutions must also 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.

Placing R&D and the research-innovation continuum at the heart of Biotech Act II

To remain a global leader in biotechnology, the EU must act with consistency and ambition across the whole research and innovation continuum.

a. **This requires supporting scientific excellence as the foundation of innovation, while accelerating the translation of knowledge into impactful bio-based solutions**. In concrete terms, the EU needs to ensure adequate funding across the entire spectrum of research, from basic research to innovation in biotechnology related to the bioeconomy.

Sustained research efforts are necessary to fill numerous key knowledge and technology gaps that are currently hampering the growth of biotechnology. Feedstock variability, process intensification, energy and water efficiency are among the outstanding challenges that must be solved for biomanufacturing to reach its full potential. A continuous and iterative dialogue between scientists, innovators, policy makers and public & private investors, as well as consumers, should be envisioned in Biotech Act II. One example is the INRAE-coordinated BIOLEAD project, a CSA which will deliver an action-oriented roadmap providing evidence-based recommendations for the rapid adoption and scale-up of bio-based solutions.

This argues in favour of RPOs playing a central role in Biotech Act II. As hubs for research and innovation, they are essential for creating knowledge on biotechnologies, training the next generation of biotech professionals, supporting start-ups and SMEs, and providing access to research infrastructures that enable scaling-up and de-risking of new technologies. Their contribution to unbiased research and public engagement is also vital for building trust and ensuring responsible innovation.

b. **The key role played by research infrastructure and pre-demonstrators in supporting SMEs' prototyping processes and risk mitigation strategies should be acknowledged.**

Scaling biotechnology requires understanding of the research-development-innovation-industrialisation continuum. This calls for improving access to Research and Technology infrastructures and investment/funding.

The EC should recognise and support the crucial role of hybrid entities such as preindustrial demonstrators, as well as research infrastructures (RIs), 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 at various scales.

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, the French Government has been launching and financing this type of hybrid entities (Ferments du Futur, Toulouse White Biotechnology, MetaGenoPolis) which have greatly contributed to the translation of research into innovation by supporting SMEs and start-ups. EU authorities should as well increase their investment in those hybrid entities.

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

c. **Finally, synergies in funding with national research programmes should be further exploited**. For example the French National programme B-BEST (*Bioproductions : biomass, biotechnologies and sustainable technologies for chemicals and fuels*) (65 M€, 2023-2030) supports early-stage research to drive innovation in the bio-based sector, strengthening France's competitive industrial base while funding large interdisciplinary projects. The outcomes could be further scaled-up / tested at EU level to maximise the impact.

This calls for the EU to put various kind of resources (regulatory framework, facilitating tools, etc.) into the coordination of 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 with massive public investments in research on societal challenges. In addition, to improve countries and regions capacity to uptake biobased solutions, **we recommend moving from networking toward structured European collaboration, encouraging co-investment and long-term partnerships, and for Member States to support flagship collaborations between scientific and technical institutions.**

Support risk/benefit analysis with solid scientific evidence to accelerate the uptake of bioproducts

In the food sector, a benefit-risk analysis that includes the assessment of the environmental impacts of new food ingredients, for example obtained using precision fermentation, compared to conventional food ingredients, should be performed.

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.

A **regulatory sandbox** is an interesting regulatory innovation of its own. If used smartly, it can benefit both consumers and the economy. **Biotech Act II should therefore include regulatory sandboxes within domains such as novel foods to ensure that EU's** competitiveness on research excellence is also translated into on the ground applications. 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 pandemic management, demonstrate the need for the utmost precaution. It would be preferable for the EU to provide the necessary resources to produce a robust ex-ante risk analysis through research 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.

Seizing opportunities offered by Artificial Intelligence (AI) to fully exploit the convergence of biotechnology, data and AI across Europe

Data and AI are core enablers of biotechnology innovation. However, multiscale dynamic bioprocesses generate data sparsity. Combined with a lack of standards, this leads to low-quality, poorly interoperable datasets. 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. The following actions are therefore needed:

- **Recognising data infrastructures as strategic assets, equivalent to research infrastructures**
- **Developing a roadmap for a FAIR European Biotech & Biomanufacturing Data Space**
- **Supporting interdisciplinary initiatives, building a business case for federated data approaches**
- **Supporting standardisation across research and industry**
- **Ensure that Europe is a standards setter rather than a standards follower**