European Biostimulants Industry Council
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EBIC POSITION PAPER

How can the European Union Encourage Innovation in Microbial Biostimulants?

EXECUTIVE SUMMARY

- Microbial biostimulants contribute to the development of the bioeconomy. But bio-innovations like these still face many structural challenges from a regulatory framework designed in the Golden Age of Chemistry. EU regulations need to be modernized to meet the needs the bioeconomy. This entails designing appropriate measures to ensure precise characterisation of bio-based components like microorganisms, fostering innovation and ensuring fair competition and equitable market access for all companies.
- Research into beneficial uses of microorganisms is increasing at an exponential rate as new technologies make it faster, easier, more affordable and more accurate to screen and select microorganisms and to understand the added value of microbial consortia. Regulations need to be future-proofed to keep pace with the accelerating pace of product development. Historically, positive lists have done a poor job of keeping up with highly innovative sectors.
- Crtitical differences between chemistry-based products and biology-based products mean that fit-for-purpose measures need to be developed to provide similar incentives to innovate. Evaluating product safety and effectiveness also needs to be adapted to the particularities of products containing microorganisms, especially microorganisms that are common in the environment.
- Sufficient information about products should be provided to authorities and the public to allow for informed decision-making and to ensure safety, health and environmental protection. This should be done in such a way that it does not become a barrier to innovation.

I. INTRODUCTION

Microbial biostimulants contribute to the development of the bioeconomy. But bio-innovations like these still face many structural obstacles from a regulatory framework designed in the Golden Age of Chemistry. EU regulations need to be modernised to meet the needs the bioeconomy.

While the policies and institutions designed for the chemistry-based economy may be ill-adapted to biology-based innovations, many objectives are shared:

- Ensuring that precise characterisation of bio-based components (like microorganisms) as the basis for the evaluation of safety, quality, effectiveness, efficiency;
- Fostering innovation;
- Ensuring fair competition and equitable market access for all companies.

EBIC has written a separate position paper about characterisation of products containing agricultural microorganisms entitled “Precise characterisation of component strains is an essential step for placing safe and effective microbial biostimulants on the market”. This paper you are reading now focuses on how to foster innovation and ensure fair competition for companies producing microbial biostimulants.

II. REGULATIONS NEED TO BE FUTURE-PROOFED TO COPE WITH BREAKTHROUGHS IN MICROORGANISM-BASED INNOVATION

In recent years, there has been growing interest in the potential of microorganisms to help achieve greater sustainability in many sectors of the economy. Agriculture has been no exception. After decades of viewing soil fertility as the result of physical and chemical characteristics of the soil, scientists, farmers and agricultural inputs producers are placing ever greater emphasis on the biological aspects of soil fertility. In addition, researchers have discovered that the functioning and well-being of plants is significantly influenced by the microbiomes around and within those plants. This is similar to discoveries made regarding the human microbiome. Furthermore, there is a growing appreciation that microorganisms bring the most benefits when the right team is working together. Researchers are rapidly improving their understanding of the synergistic effects of naturally occurring consortia, which is inspiring the development of more complex microbial biostimulants than in the past. Regulatory provisions should be well designed so that biostimulants containing microbial consortia do not face burdensome evaluation requirements.

Although exciting breakthroughs are happening at a breath-taking pace, there is general consensus that very few microorganisms have been identified and studied extensively relatively to the large number that exists. Society’s still modest knowledge of microorganisms has, until recently, focused almost exclusively on the most troublesome human, animal and plant pathogens that it want to combat. Beneficial microorganisms have come into the spotlight much more recently. To date, a handful of fairly well-known microorganisms are used in agriculture, but their number and variety are expected to increase rapidly in coming years as technologies and techniques for screening and selection are improved.

Under these conditions, it is a challenge to develop a robust and forward-looking regulatory framework for microorganisms.

III. HOW DOES THE BIOECONOMY DIFFER FROM THE CHEMISTRY-BASED ECONOMY, AND WHY DOES THIS MATTER FOR APPROPRIATE REGULATION?

> ⊙ *Fundamental Principle: Chemical regulation has set the standard for ensuring the safety of many products, particularly those used in the food chain. However, there are significant differences between chemistry-based and biology-based products, and those differences have profound implications for designing effective regulations for the bioeconomy.*

- In its early days the chemical industry faced far less regulation than today. Regulation of chemicals largely arose in response to negative impacts. Regulation of beneficial microorganisms, on the other hand, is being developed in a pre-emptive manner. As a result, there has been a tendency to try to adapt regulatory measures designed for chemical products to biology-based products, rather than creating bespoke, fit-for-purpose measures.

- Unlike novel synthetic chemical molecules, most beneficial microorganisms are common in nature. This means that much empirical knowledge can be derived from observation of microorganisms under naturally occurring conditions, including conclusions about their relative safety or riskiness. While such observation may not fully eliminate the need for laboratory testing, it may reduce the need for testing or change its nature.
- A company that develops a novel synthetic chemical molecule can patent the discovery and benefit from a temporary monopoly on production in order to recoup its costs of development. Newly discovered beneficial microorganisms cannot be patented.[1] As a result, once a microbial strain has been discovered, any company is free to produce it (subject to any applicable regulatory clearances). Therefore measures need to be put in place to ensure that any company wanting to use a microorganism faces similar regulatory costs and administrative requirements in order to ensure fair competition.

[1] However, methods used to identify or evaluate the microorganism as well as aspects of the processed used to ferment the microorganism, encapsulate it and apply it may be subject to patents and other aspects of intellectual property protection.

IV. POSITIVE LISTS ARE NOT THE BEST-SUITED POLICY INSTRUMENT FOR INNOVATIVE SECTORS

> *Fundamental Principle:* ***Positive lists are best suited to sectors where technology is stable and largely standardised. Other approaches better meet the needs of sectors where fostering innovation is an important objective and where a potentially large number of innovations need to be assessed for safety on an ongoing basis.***

For understandable reasons, regulators seek the simplest, most cost effective means to regulate various sectors of the economy while ensuring the best possible balance between fair market access and fostering innovation.

Positive lists[2] of approved products or ingredients are one common method used by regulators. There are many variations on the concept of positive lists. One common variable is how new items are inscribed in the list:

1. Regulators review existing scientific literature and other publicly available sources of data and information to identify candidates for inclusion in a list;
2. Individual companies submit data packages to defend new entries in the list; the new entries can then be used by any economic actor.

The first case has the merit of only using publicly owned information to create what is, in effect, a public good. The drawback of this approach is that it is backward-looking; there is generally a gap of many years between research and development and the publication of a significant body of data in scientific literature. Furthermore, where the products or raw materials studied are not subject to patents, companies may not wish to release data into the public sphere in order to maintain trade secrets.

The second case is better suited in theory to keep up with innovation. However, by transferring private data into the public domain without appropriate compensation, the second case creates a disincentive to innovation. In fact, it actively discourages innovation: since anyone can use the raw material or make the product once listed, there is an incentive for companies to adopt a free rider policy and allow others to innovate in their place. In fact, such an approach taxes innovators and subsidises non-innovative copycats. In effect, it forcibly transforms privately produced data into a public good without provided compensation to the company that has produced the data. This will discourage companies from placing their most innovative products on the European market. Instead, they will prefer markets where fairer rules for competition exist for their innovative products.

In either case, positive lists have generally demonstrated an inability to cope with a fast pace of innovation due to the slow and often politicised process for including new items.

These two cases illustrate the shortcomings of positive lists for innovative sectors. Positive lists are best suited to sectors where technology is stable and largely standardised. Other approaches better meet the needs of sectors where fostering innovation is an important objective and where a potentially large number of innovations need to be assessed for safety on an ongoing basis.

[2] By "positive list", we mean lists that allow any economic actor to use the product(s) or raw material(s) listed. Registries are a special case of positive lists that restrict the access or use to the items registered. Because of this distinction, registries are excluded from our definition of "positive list".

V. DATA PROTECTION ENSURES FAIR CONDITIONS FOR MARKET ACCESS

Discussion around intellectual property and living organisms have often been fraught because of fears related to perceived "patents on life". To be clear, EBIC is not suggesting that the first company to bring a new microbial strain to market should have a monopoly on doing so. Rather, we argue that the conditions for market access should be equitable.

> *Fundamental Principle: Data protection is about ensuring fair market access and fostering innovation, not about acquiring exclusive rights to living organisms.*

For chemical products, this equity is ensured through the REACH provisions on data protection, licensing and compensation. Basically, these ensure that companies investing in producing data to demonstrate the safety of a substance placed on the market are the sole owners of their proprietary data – not the sole companies allowed to place a given substance on the market. REACH also provides provisions for companies to share the costs of data production (through data consortia), to license data to others who want to place the same substance on the market without being part of the same consortium and to share data with downstream users (the compensation for which is built into the cost of the substance.) To reduce the need for animal testing, REACH mandates licensing for data produced through animal testing. REACH does not provide a monopoly right to bring a given substance to market; companies seeking that type of protection must seek patents for their novel molecule(s).

With regard to the selection and evaluation of beneficial microorganisms, policy measures should ensure a similar level of equitable conditions for market access:

- If another company wants to place the same microorganism on the market, it should have to provide a comparable level of data to justify safety and effectiveness. The second company may produce its own data or negotiate a data-sharing agreement with the original company to have brought the microorganism to market. However, it should never use another company's data without permission and appropriate compensation.
- There may be limited cases where compulsory data-sharing (under license and with compensation) is appropriate, notably with an aim to reducing animal testing.
- Companies should be prepared to share all appropriate data with public authorities so they can fulfill their regulatory obligations. However, other economic actors should not be able to make use of these data without appropriate licensing and compensation. On the other hand, companies should provide sufficient information about composition, instructions for use, effects, etc. to allow for safe and effective use of the products in questions and informed decisions by end users and consumers.

> *Fundamental Principle: Companies are investing heavily to identify the best-performing and safest micro-organisms for use in biostimulants. The micro-organisms identified cannot be patented.*

- In many sectors of the economy, companies are investing heavily to identify micro-organisms that have the most potential to provide beneficial characteristics with the least risk. As noted in another EBIC position "Precise characterisation of component strains is an essential step for placing safe and effective microbial biostimulants on the market",

characterisation of the strain is a critical first step to determine safety and performance characteristics.

- Unlike the world of synthetic chemistry where novel molecules can be patented, the strains of micro-organisms that are identified through research and development are not subject to patent.[3]

[3] Part or all of the processes used to screen, select, cultivate and package viable microorganisms may be eligible to be patented but not the strain itself.

VI. ANNEX – A NON-EXHAUSTIVE LIST OF MICROORGANISM STRAINS, SPECIES AND GENERA FOR WHICH BIOSTIMULANT EFFECTS HAVE BEEN IDENTIFIED[4]

Acetobacter diazotrophicus
Achromobacter piechaudii ARV8
Acinetobacter spp.
Aeromonas spp.
Agrobacterium radiobacter
Alternaria spp.
Azoarcus spp.
Azospirillum brasilense
Azospirillum diazotrophicus
Azospirillum lipoferum
Azotobacter chroococcum
Bacillus atrophaeus
Bacillus edaphicus
Bacillus firmus
Bacillus licheniformis
Bacillus megaterium
Bacillus muciaraglaginous
Bacillus mucilaginous
Bacillus polymyxa
Bacillus pumilus
Bacillus sphaericus
Bacillus spp.
Bacillus subtilis
Bacillus subtilis var. amyloliquefaciens
Beijerinckia spp.
Burkholderia cepacia
Colletotrichum spp.
Comamonas acidovorans
Curvularia spp.
Delftia acidovorans
Erwinia spp.
Flavobacterium spp.
Funneliformis (formerly known as *Glomus*) *mosseae*
Fusarium spp.
Gluconacebacter diazotrophicus
Herbaspirillum seropedicae
Herbaspirillum spp.
Klebsiella pneumoniae
Kluyvera ascorbata
Micrococcus spp.
Neotyphodium spp.
Paenibacillus macerans
Paenibacillus polymyxa
Pantoea agglomerans
Piriformospora indica
Pseudomonas aureofaciens
Pseudomonas chlororaphis
Pseudomonas fluorescens
Pseudomonas mendocina
Pseudomonas putida
Pseudomonas solanacearum
Pseudomonas spp.
Pseudomonas syringae
Serratia entomophila
Staphylococcus kloosii
Streptomyces griseoviridis
Streptomyces spp.
Streptomyces lydicus
Trichoderma spp.
Rhizobia spp.
Rhizophagus irregularis (formerly known as *Glomus intraradices)*
Saccharomyces cerevisae

[4] Sources for this list include: Glick, B.R. (2012) "Review Article: Plant Growth-Promoting Bacteria: Mechanisms and Applications." Scientifica (2012) Article ID 963401:1-15. Available online at http://dx.doi.org/10.6064/2012/963401; du Jardin, P. (2015) "Plant biostimulants: Definition, concept, main categories and regulation." Scientia Horticulturae (2015) 196:3–14; Rouphael, Y. P. Franken et al. (2015) "Arbuscular mycorrhizal fungi act as biostimulants in horticultural crops." Scientia Horticulturae (2015) 196:91-108; Calvo, P., L. Nelson, J.W. Kloepper (2014) "Agricultural uses of plant biostimulants". Plant and Soil (October 2014): 383/1:3-41. Available online at http://rd.springer.com/article/10.1007%2Fs11104-014-2131-8.