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Article

Improving the Authorization of Microbial Biological Control Products (MBCP) in the European Union within the EU Green Deal Framework

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Abstract: Developing sustainable agriculture by identifying non-chemical alternative Plant Protection Products (PPP) is a cornerstone in achieving long-sought environmental friendliness. Despite significant legislative and political efforts to promote biocontrol solutions and Integrated Pest Management (IPM), the literature points out the disadvantages posed by European Union's (EU) two-tier system for Microbial Biological Control Agents (MBCA) approval and subsequent Microbial Biological Control Products (MBCP) authorization by each EU Member State (MS). Despite the disadvantages, in a recent article, we showed that the EU had outcompeted the US and other countries in approved MBCA in the last decades; however, MBCP approval at the national level lags. Achieving the EU Green Deal's aim set out in the 'Farm to Fork Strategy' to reduce the use and risk of pesticides by 50% by 2030 is difficult without developing viable alternatives. Why do we not have higher MBCP availability and usage in the EU? Is it the current legislation, its poor application, or some other factors? The current legislative framework stimulated MBCA approval. Thus, we compare MBCA approval and MBCP authorization procedure to evaluate if MBCP authorization is more difficult and thus causes a bottleneck. We find that requirements for MBCP authorization are unnecessarily more complex. We recommend simplifying the MBCP dossier requirements and making them as similar to MBCA as possible to accelerate the MBCP authorization in more EU MS to increase their availability and integration in agronomic crops' pest management plans.

Keywords: biocontrol; plant pests; microbial biological control agents (MBCA); microbial biological control products (MBCP); beneficial microorganisms; European Union

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1. Introduction

As environmental degradation and climate change top our global agenda, agriculture's impact on the environment becomes more and more scrutinized [1–3], and the goal to reduce the environmental and climate footprint of the EU food system has become part of the EU Green Deal [4]. Among the areas that received the most attention is the ever more intensive use of chemical pesticides for pest control, which can persist in the soil decades after application and generate health risks [5]. Integrated Pest Management (IPM) and the employment of biocontrol solutions receive the most public attention and research investment as means to generate sustainable alternatives [6–10]. Also, research on biocontrol solutions has increased significantly in the last three decades [11]. As the European Union (EU) set itself to be a leader in environmental issues and regulatory policies, it upgraded its regulatory framework in 2009 with the 'pesticide package.' One of the four legislative acts, Regulation (EC.) No 1107/2009 [12] codifies the rules for placing pesticides on the market. In 2012 the European Commission proposed a working document through its specialized directorate and developed by the specialized OECD technical

group [13] with some proposed measures on how to proceed with the environmental safety evaluation of microbial biocontrol agents [14]. While the guidelines were not compulsory for the EU MS, they should offer some joint guidance on the decision scheme for evaluating the environmental risk posed by various agents. MBCA are first characterized, with particular attention to non-indigenous ones, then possible modes of action are analyzed, the hosts' range is described, and the tests on their effects on non-target species are designed. The subsequent section details the information on the fate and behavior (soil and aquatic compartment) (Section 3), environmental toxicity (Section 4), refinement options (Section 5), mitigation options (Section 6), and issues to be solved soon (Section 7).

After adopting the 'pesticide package', the legislation covering MBCA approval and MBCP authorization was upgraded with Regulation (EU.) No 546/2011 to set the uniform principles for evaluating and authorizing plant protection products (Annex 2) [15]. Two subsequent Regulations (EU.) No 283/2013 [16] and Regulation (EU.) 284/2013 [17] elaborate on the required dossier for approval of microbial biological control agents (MBCA) and microbial biological control products (MBCP). Despite this regulatory upgrade and the political support for promoting low-risk substances [18], the EU level system remained a two-tier system (EU-level and national level), unlike most other agricultural markets globally. The research on the effects of the EU's regulatory framework on decreasing pesticide use has also accelerated recently [19–21]. A recent evaluation of the extra pressure added by the EU Green Deal on sustainable pest control also shows the importance of incorporating non-chemical alternatives to achieve chemical pesticides decrease in use and risk by 50% by 2030 [22].

Recognizing the need to accelerate MBCP authorization, on 8 February 2022, the EU MS "endorsed four implementing Regulations that amend the current rules applicable to microorganisms. The new rules reflect the latest scientific developments and are based on the specific biological properties of microorganisms. The current amendments will facilitate the approval of microorganisms for use as active substances in plant protection products and the authorization of products containing them. The purpose is that farmers across the European Union have better access to biological alternatives to chemical pesticides and can protect their crops in a more sustainable manner" [23]. While we agree with the stated aims of the future legislative modifications, we stress that a successful modification depends on the reason why the current legislative framework allowed for accelerating MBCA approval but less for MBCP authorization. We study if the legislative requirements per se cause MBCP authorization delays or if they are instead caused by the inappropriate application of the legislative framework by EU Member States (MS). We review the main arguments in the literature, comparatively analyze the requirements for approval and authorization dossiers for MBCA and MBCP and draw conclusions about the required modifications.

2. Analysis

The recent literature identifies this two-tier system and its imperfections as the main barrier to the faster deployment of large-scale microbial-based solutions for agricultural pest control. The results of the REBECA project, published in 2010 [24], proposed solutions to "accelerate the regulation process for BCAs (Biological Control Agents) and make it more cost-effective without compromising the level of safety for human health and the environment". The recommendation from this action on regulating bacterial and fungal biocontrol agents stresses the discouraging effect the long-lasting and costly procedure has on companies. Other significant problems are the "lack of validated risk assessment methods for microbial, knowledge gaps on the natural distribution of the biocontrol microorganisms and natural exposure of humans and other non-target organisms, and missing definitions allowing the identification of low-risk products" [25]. Moreover, the authors propose wavering many of the obsolete data requirements relevant to chemical pesticides to limit these problems. Current literature indicates that most preconceptions about the potential risks, safety, and environmental toxicity are unwarranted given the limited potential problems in comparison with chemical pesticides [26–30], and they can increase food safety [31].

Balog et al.'s [32] 2016 analysis argues that the EU is behind the US (68 MBCA with 400 in the US), India (1000), Brazil, and China in MBCA approval due to the higher complexity of EU regulation (4 laws in the US compared with 14 in the EU), a situation that leads to low availability of MBCP. A 2018 comparison by Frederiks and Wesseler [33] between the US and EU regulatory frameworks brings data to show that the average time for MBCA authorization and MBCP approval improved from 1845 days under Directive 91/414/EEC [34] to just 1369 days under the new Regulation (EC) 1107/2009 [12]. The authors conclude that as this period is still almost double the time it takes to go through the same process in the USA, the EU is at a significant disadvantage, especially since the main delays appear in the MBCP EU MS authorization stage. Unlike the EU, the US uses a single agency (US Environmental Protection Agency—FDA) and a single dossier to evaluate MBCA and MBCP. After the initial authorization, each USA state can apply its local regulations. In the pre-submission phase, potential applicants are invited to preparatory meetings to speed up the evaluation process to agree on the data requirements and possible data waivers. After the submission, the process has to be completed 16 months after submitting the complete dossier. Additionally, the regulatory procedures in Canada are conducted by one agency (Pest Management Regulatory Agency—PMRA) and take place within 12 months [35]. Villaverde et al. stress the difficulties in motivating manufacturers to produce biopesticides given the difficulties in approval and authorization [36].

Some other authors [37] voice that MBCA approval delays are caused by the fact that although the EU's regulatory processes have solid scientific foundations, the most appropriate scientific concepts, knowledge, and expertise have not been applied in the safety assessment of microorganisms and biological control. They recommend a stronger rooting of MBCA approval and MBCP authorization in fundamental microbiological sciences. Additionally, although the MBCP stage is organized in three climatic zones, and a *Zonal Rapporteur Member State (ZRMS)* assesses an MBCP, the mutual recognition of authorization at the EU MS has significant procedural delays. As costs for the entire process are high, at up to EUR 1 million [38], efficiency is limited to 50% [39], and the overall penetration of MBCP is much more limited than desired [40].

A recent chapter by Guijarro et al. [41] describes the factors that created momentum for MBCP use and the need to modify the current approach to MBCA being treated "as potentially risky organisms that are not only able to produce toxic substances, but are also potentially dangerous because they can multiply, spread, and perhaps genetically adapt", an approach that has not been proven realistically.

In our recent article [8], we analyzed Annex Part A and B from both Regulations and compared the requirements for approving MBCA vs. synthetic pesticides substances and authorizing MBCP vs. products based on synthetic pesticides. We showed that the dossiers required for MBCA approval and MBCP authorization have significantly fewer sections and subsections. Requirements are sensibly lower regarding data requirements for Residues, Fate, and behavior in the environment and Ecotoxicological studies. We concluded that despite its multiple inefficiencies, the current EU legislative framework on MBCA approval has allowed it to overtake the US in terms of MBCA strains, but that the main hurdle comes from the fact that most approved strains result in MBCP being submitted for authorization in just a few states. While Sundh and Eilengerg [37], following the recommendation by the International Biocontrol Manufacturers Association [42], advocated for a unique authorization body based on the expertise of the EU MS with the highest experience, we voiced the need to adopt a strategy that would diffuse as much as possible the expertise on authorizing MBCP, a fundamental step in the wide adoption of biocontrol solutions and IPM.

3. Materials and Methods

In this article, we take on the claim that the EU's two-tier approval and authorization system is the main culprit of the EU's slower progress in implementing biocontrol solutions by evaluating the differences between requirements in the MBCA approval with the

requirements for MBCP authorization. In other words, while we agree that the two-tier system adds some unwanted complexity, we aim to analyze to what extent the dossiers required for MBCA approval are similar to those for MBCP authorization and, thus, do not add high extra costs for the second stage. To perform this analysis, we compared Part B of Annexes two of Regulation 283/2013 and Regulation 284/2013, Annexes dealing with MBCA approval on MBCP (the term used in the Regulation is PPP) authorization.

4. Results and Discussion

4.1. Comparative Analysis of Sections

We start by discussing the commonalities between the two Annexes. First, the general structure of the dossier is relatively similar to the number of sections and their general characteristics (Table 1). The MBCP dossier required in Part B of the Annex of Regulation 284/2013 has only two extra sections: *Data on application* and *Efficacy data*, both referring to peculiar aspects of how the MBCP is formulated. Additionally, the total number of subsections is relatively the same in most sections, especially in the *Effects on human health* section. This section has 21 subsections in the MBCA dossiers and 12 for the MBCP dossier.

Table 1. Comparison of the sections and number of sections required for completing the dossier for MBCA authorization in Regulation 283/2013 and MBCP approval in Regulation 284/2013.

283/2013		**284/2013**	
MBCA	**Part B**	**Part B**	
Number of Subsections	**Name of the Section**	**Number of Subsections**	**Name of the Section**
7	Identity of the microorganism	6	Identity of the plant protection product
13	Biological properties of the microorganism	21	Physical, chemical, and technical properties of the plant protection product
		9	Data on application
9	Further information on the microorganism	7	Further information on the PPP
2	Analytical methods	2	Analytical methods
		14	Efficacy data
21	Effects on human health	12	Effects on human health
5	Residues in or on treated products, food, and feed	1	Residues in or on treated products, food, and feed
5	Fate and behavior in the environment	1	Fate and behavior in the environment
11	Effects on non-target organisms	6	Effects on non-target organisms
1	Summary and evaluation of the environmental impact	1	Summary and evaluation of the environmental impact
74		**80**	**Number of sub-sections**

As soon as we look closely at the structure of the subsections, sensible differences appear immediately. The first section, the *Identity of the microorganism/PPP,* the MBCP dossier, has some extra sections requiring data on: *1.4. Detailed quantitative and qualitative information on the composition of the preparation 1.5. Physical state and nature of the preparation 1.6. Function—the organisms it is designed to control*. The second section of the MBCA dossier requires data on the microorganism's biological properties, while the MBCP requires data on the physical, chemical, and technical properties of the PPP. The *Further data section* of the two dossiers is totally different between the two dossiers, with only two common sections (measures in case of accident and production for destruction and decontamination).

Instead, the *Analytic methods* are fairly similar among the two dossiers, and the MBCA also refers to the manufactured product.

As discussed in the literature [36,37], the evaluation of the risks posed by MBCP in the EU framework is significantly influenced by the approach to evaluating synthetic PPP and thus requires a wide array of studies that are not appropriate or relevant for the observed risks of applying MBCP. The *Efficacy data* section is unique to the MBCP dossier and requires no less than 12 types of effects. In the introduction of the section, the guidelines are elaborated in a very general form, requiring *sufficient data* to evaluate each of these effects on the specific climatic region where the MBCP is evaluated for authorization. This aspect leads to much latitude on the authority that performs the evaluation. The section requires a complex array of data that must be collected under various conditions to evaluate the overall efficacy of the MBCP.

The *Effects on human health* sections for the MBCA and MBCP dossiers are surprisingly different. They have a different logic of elaboration, specifically since the MBCA dossier requires an evaluation of the "risks for man, directly and/or indirectly associated with the handling and use of plant protection products containing the microorganism, and the risk for manhandling treated products, and the risk for man arising from residual traces of contaminants remaining in food and water" [16]. Regulation 283/2013 requires the studies to be organized in two tiers. The first tier aims to collect basic information for all MBCA, while the second is only for those MBCA where specific negative effects have been observed.

The *Residues in or on treated products, food and feed,* and *Fate and behavior in the environment* section from the MBCP only require the data already provided in the MBCA dossier if the data can be extrapolated from the MBCA evaluation. Also, the *Effects on non-target organisms* sections overlap significantly, requiring similar data on the effects on birds, aquatic organisms, bees, earthworms, and non-target soil microorganisms. Instead, the MBCA Dossier in Regulation 284/2013 requires extra effects on fish, freshwater invertebrates, and algae.

4.2. Results of Compararasion

While there are many similarities between the logic and structure of the two dossiers, the formulations among the two dossiers often appear quite different and are written in a different logic. As long as other regulatory bodies around the world require unique dossiers for MBCA and MBCP, there should not be any major obstacle in reformulating the two Annexes to minimize the differences among the dossiers. The MBCP dossier should differ only in the subsections where extra data on the specificities of the MBCP are essential, and they have not been covered in the initial dossier for MBCA approval. While the MBCA dossier requires data on sensitization, or genotoxicity testing (in vitro, cell culture study), the MBCP dossier requires data on specific types of toxicity (oral, inhalation, percutaneous) and other types of effects (skin and eye irritation) caused by exposure in various agronomic activities. This data is also required in the MBCA dossier to a certain degree. Additionally, given that the dossier of MBCP approval is similarly complex as the MBCA approval and the limited expertise on these issues at the level of many EU MS [32], the complexities introduced by the formulation of the dossier do not help in accelerating the process of MBCP authorization. While some authors advocate moving MBCP authorization to the EU level, either by creating a unique authority or by concentrating MBCP authorization in the EU MS with the highest expertise, we argue that an approach that would simplify and streamline the requirements for MBCA approval and MBCP authorization, in combination with efforts to disseminate knowledge on evaluation at the level of EU MS could provide similar benefits, while also avoiding the contentious issue of centralization.

5. Conclusions

The European Union's 'Farm to Fork Strategy,' part of the EU's Green Deal, set the ambitious goal to decrease both use and risks caused by synthetic pesticides by 50% by

2030. By the beginning of 2022, no significant pesticide usage decrease has been measured, as no systemic alternatives are in place yet. Out of the multiple non-chemical alternatives reviewed by Tataridas et al. [22], such as enhanced cultivation techniques, non-chemical tools, competitive plant material, and new technologies, we consider that microbial control of pests with MBCP has a high potential to offer systemic alternatives, which can be incorporated in the sustainable pest control practices in agronomy.

In this article, we seek to contribute to the debate on the efficiency of the current EU regulatory framework on MBCA approval and MBCP authorization. We aim to understand how we could achieve higher MBCP availability and usage in the EU. Is it the current legislation, its poor application, or some other factors? Should the legislation be changed, or should it be better applied? The same legislation allowed accelerating MBCA approval but failed to ensure similar levels of MBCP authorization at the level of EU MS.

The efforts to provide sustainable and efficient alternatives to the current predominant agricultural practices extensively based on synthetic pesticides would require a paradigmatic shift towards fully employing IPM and making MBCP widely available. The current two-tier EU system is unique among major agricultural regulatory regimes suited for the specific nature of the EU. While maintaining the general features of the system, the changes brought by Regulation No 1107/2009, Regulation 283/2013, and Regulation 284/2013 allowed the EU to accelerate MBCA approval significantly. The limited progress in making MBCP widely used in the EU is caused by the problems in the second authorization stage [32,33,36,37]. Our analysis showed that despite similarities, sensible approaches in the logic of formulation of the sections that require the most burden and costs (*Effects on human health*) could impose high extra costs in the MBCA authorization stage.

While the EU is the only region with a two-tier system, changing the two-tier system for MBCA approval and MBCP authorization would be very difficult. Nevertheless, MBCP authorization could be accelerated and made more appealing to potential investors by minimizing the differences between the dossiers required for MBCA (Regulation 281/2013) and MBCP (Regulation 284/2013) and MBCP authorization. We recommend requiring only the strictly necessary extra studies and information, but otherwise, using the same dossier as for the initial MBCA approval.

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