

# EU microbial pest control: A revolution in waiting

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## Abstract

Recent evaluations of the microbial biological control sector indicate that implementing microbial control of pests is still slow in the EU. The top causal factors are the lengthy, expensive, and cumbersome two-stage procedure for approval of biological agents as active substances at the EU level and authorization of formulated products at the national level, limited funding, lack of EU level integrated approaches, and slow implementation of integrated pest management. This article contributes to a better understanding of the factors that limit microbial control of pests in EU agriculture by providing the first evaluation of the evolution of microbial biological control agent (MBCA) EU-level approval combined with that of microbial biological control product (MBCP) national-level authorization, discusses recent trends in research and offers some policy recommendations. By 2020, the EU had caught up with the USA regarding research output, approved MBCAs, and MBCA approval procedures (first stage). Despite improvements from 2014 to 2019, the number of authorized MBCPs (second stage) has progressed slowly and unevenly across the EU. Significant progress is concentrated in countries with more extensive agricultural land and higher research intensity. The EU's focus on promoting more sustainable agriculture by increasing the availability of low-risk pesticides of biological origin as alternatives to conventional chemical pesticides has gained traction in recent years. Nevertheless, more efforts to improve the capacity and expertise of laggard EU Member States to contribute to the approval of MBCA, authorization of MBCP, and stimulating market availability are needed. Furthermore, we recommend introducing more concrete measures to promote the adoption of the microbial control of pests in the National Action Plans for the sustainable use of pesticides.

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**Keywords:** biocontrol; microbial biological control agents; microbial biological control products; integrated pest management; European Union

## 1 INTRODUCTION

Since the beginning of this century, alternative approaches to the intensive use of conventional chemical pesticides have gained political and public support worldwide. The most promising alternatives are organic farming, integrated pest management (IPM), and biocontrol. The latter was hailed as a potential approach that would generate a revolution in pest management and achieve the long-term sustainability of agriculture.<sup>1,2</sup> A recent survey of biocontrol specialists in Europe reveals that the community considers it an integral part of IPM.<sup>3(p16)</sup> Controlling pests using low-risk plant protection products (PPPs) implies using microbial biological control agents (MBCAs) (such as fungi, bacteria, protozoans, viruses, and viroids) and extracts from different organisms or semiochemicals as active ingredients in biological control products (BCP).<sup>4</sup> While MBCA refers to the active 'substance' (which can be either a microorganism or a metabolite from microorganisms) to be used in pest control, they have to be multiplied (for living organisms), extracted or filtrated (for metabolites), and formulated, usually, in liquid or solid forms, as microbial biological control products (MBCPs). Production processes need to ensure the maintenance of efficacy in the field, ease of application, and extended shelf-life. Producing MBCPs using MBCAs is not a straightforward process as laboratory or greenhouse tests and field efficiency can vary dramatically.

Notwithstanding the industry's fast growth in the past decade, a 2016 report<sup>5</sup> evaluated the worldwide biocontrol market (including MBCP and invertebrates) at US\$1.5 billion, only 2% of the chemical pesticide market, and projected to reach US\$3.67 billion by 2022. North America had the highest market share. By 2020, the biocontrol market had increased to 800 million euros in the European Union (EU).<sup>6</sup> Despite the EU's aim to be a leader in this transition, the biocontrol revolution has failed so far to take off.

We build on recent efforts to assess the effectiveness of the EU's peculiar legislative framework, where MBCA approval takes place at EU level while MBCP authorization is dealt with at national level. We focus especially on those studies by Lamichhane *et al.*<sup>3</sup> Balog *et al.*,<sup>7</sup> Matyjaszczyk,<sup>8</sup> Frederiks and Wesseler,<sup>9</sup> Robin and

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Marchand,<sup>10</sup> and Sundh and Eilenberg.<sup>4</sup> Providing the first dynamic country-level analysis of MBCP authorization in the EU Member States (MSs) from 2014 to 2019 and comparative data on research intensity, we found marked improvements under the EU's 2009 regulatory framework. On the one hand, the EU closed the gap with the USA on the number of approved strains and procedures, and research intensity in microbial biocontrol has overtaken that in the USA. On the other hand, as EU MSs are responsible for MBCP authorization, this process remains heterogeneous across the EU. We conclude that despite positive results in MBCA approval, national-level MBCP authorization is uneven. Unlike most recommendations in the recent literature that prioritize the need for legislative improvements, we stress a need to prioritize the capacity and expertise of laggard EU MSs to speed up MBCP authorization. Also, we recommend changing the incentives for researchers, companies, and farmers, especially through the National Action Plans (NAPs) on the sustainable use of pesticides and promoting IPM not just to accelerate MBCP development and authorization, but to also increase product availability and thus the market penetration of MBCP.

The article is structured as follows. First, we comparatively analyze the evolution of the legislative framework that regulates MBCA approval and MBCP authorization, and review the literature on the factors that explain the suboptimal outcomes in the EU. Second, in Materials and Methods, we present the data sources and methodology. Third, we present and discuss comparative data on the cumulative MBCA approval procedures and the number of approved strains between 2001 and 2019 in the EU, the USA, Canada, New Zealand, and Australia. Fourth, we compare the country-level situation of MBCP authorization in the EU in 2014 and 2019, discuss the trends, and present comparative data on the evolution of research in microbial biocontrol. We also correlate country-level authorization data with research intensity evolution and the percentage of agricultural area. In conclusion, we discuss the recommendations that stem from our findings on improving the usage of MBCPs in pest control and how they differ from the recommendations from other recent articles.

While using invertebrate biological control agents (IBCs) is loosely regulated,<sup>11(p4)</sup> usage of microorganisms in pest control is codified into details in most developed countries, especially the EU.<sup>7</sup> Across the globe, the rules on MBCAs are fused within the framework used for conventional chemical pesticides, a situation that explains the two-stage procedure of active agent approval and formulated products authorization in the EU. The EU's first attempt to regulate the sector, Directive 91/414/EEC,<sup>12</sup> has proved to be a sensible obstacle. It has imposed complex procedures comparable to those required for chemical pesticides on an industry for which risks, costs, and potential commercial benefits are significantly smaller.

Since 2009, with the adoption of the 'pesticide package', the EU has become more active in promoting environmentally friendly agriculture by increasing standards for approving chemical pesticides and their use, and promoting IPM and biocontrol solutions. The pesticide package consists of four legal acts dealing with various aspects of this process. Regulation (EC) No 1107/2009<sup>13</sup> regulated the placing of PPPs and required the EU MS National Action Program for the sustainable use of pesticides (NAP) to improve by 2014 the application of IPM, which would become the compulsory crop protection approach. While Regulation (EC) No 1185/2009<sup>14</sup> updated the collection and dissemination of statistics on pesticides, Directive 2009/127/EC<sup>15</sup> updated requirements on machinery for pesticide application. Directive

2009/128/EC<sup>16</sup> (also called the Sustainable Use Directive or SUD) established a framework to achieve sustainable pesticide use, adoption of IPM, and low-risk approaches to chemical pesticides.

Even with Regulation (EC) No 1107/2009, approval of MBCAs at the EU level and MBCP authorization at the national level remains a two-stage procedure. The approval stage has three phases. In the first phase, a Rapporteur Member State (RMS) performs an assessment lasting 1 year, with the possibility of a 6-month extension (RMS phase). This first phase requires verification of the dossier, evaluation, and distribution of the Draft Assessment Report to other MSs. The second phase involves assessing risk management by the European Food Safety Authority (EFSA) (within 8 months). In the last phase, the European Commission Directorate-General for Health and Food Safety (DG SANTE) puts the procedure to a qualified majority vote in the Standing Committee on Plants, Animals, Food and Feed (PAFF Committee), publishing the dossier that updates the 'list of approved active substances' (within 6–12 months). The authorization is valid for 10 years for normal substances and 15 years for low-risk substances. Active substances may be defined as low risk if it 'may be expected that plant protection products containing that substance will pose only a low risk to human and animal health and the environment' (Article 22).<sup>13</sup> Furthermore, Regulation (EC) No 1107/2009 introduced detailed stipulations on the procedures and deadlines of Zonal evaluations (Articles 33–39) and the process of mutual recognition and authorization (Articles 40–42) of MBCPs, which, if properly implemented, would speed up and increase the predictability of the procedures. Article 40 stipulates that the holder of an authorization granted in one EU MS could ask for mutual recognition if the product is used in comparable agricultural practices in EU MSs from the same zone, other agricultural zones (with some limitations), and all the zones for MBCPs used in greenhouses, for post-harvest treatment, treatment of empty rooms and containers used for storing plants or plant products, or for seed treatment (Article 40.1.c).

In 2011 EFSA published guidance on submitting scientific peer-reviewed open literature for substance approval,<sup>17</sup> and in 2013, two Regulations<sup>18,19</sup> updating data requirements for MBCA approval and MBCP authorization were published. Analyzing Annex Parts A and B of Regulation (EU) No 283/2013,<sup>18</sup> which set out the data requirements for active substances under Regulation (EC) No 1107/2009, reveals a less burdensome procedure for low-risk substances. While the dossier for approval of chemical substances has 207 subsections, the low-risk substances dossier has only 74. The starkest differences come in the sections regarding data on Residues (27 as opposed to five subsections), Fate and behavior in the environment (44 as opposed to five subsections), and Ecotoxicological studies (53 as opposed to 11 subsections). Overall, the data requirements for the dossier are significantly lower and quite distinct, and many requirements are waived.

Nevertheless, these data requirements and principles of uniform evaluation are judged to have limited relevance, containing some requirements impossible to assess, according to Sundh and Eilenberg.<sup>4</sup> While authors stress the limited potential risks on environmental and human health posed by MBCPs when compared with chemical pesticides,<sup>20–22</sup> their efficiency averages 40–50% compared to 80% for chemical pesticides.<sup>10(p956)</sup> Even so, the price for approving an MBCA (one or several strains) as an 'active substance' and MBCP authorization was close to 1 million euros in 2014,<sup>8(p1206)</sup> costs evaluated as too high for the potential market size and host specificity of most MCBAAs.

The MBCP authorization stage is organized in three climatic evaluation zones (Northern, Central, and Southern). A Zonal Rapporteur Member State (ZRMS) assesses the product's efficiency (both for authorization and reauthorization) valid for all MSs from the zone unless an MS's specific circumstances allow it to refuse authorization (over 12 months with a possible extra 6 months if further data is required).<sup>9(pp88–89)</sup> Currently, the EU legislation categorizes MBCPs as either PPPs or biocides.<sup>4(p1271)</sup> Analyzing Annex Parts A and B of Regulation (EU) No 284/2013<sup>19</sup> shows that while the dossier for approval of chemical substances has 150 subsections, the low-risk substances dossier has only 82. The starkest differences come in the sections regarding data on Fate and behavior in the environment (22 as opposed to one subsection) and Toxicological studies (21 as opposed to 12 subsections). Although no EU-level guidelines on environmental risk assessment exist, countries with developed evaluation capacities, such as the Netherlands, have created detailed manuals for the process of authorization of MBCPs.<sup>23</sup> Risk assessment concerns potential unwanted multiplication and infections, and the production of toxic metabolites that could affect nontarget organisms.<sup>23(p21)</sup> Evaluating the risks of an MBCP on the environment considers its mode of action, survival, dispersal, ecological niche, how the microorganisms function in its indigenous environment, and studies on its toxicity, pathogenicity, or infectivity.

The EU's urgency to develop alternatives to pest control based on chemical pesticides was further strengthened by the European Parliament's Resolution of 15 February 2017 on low-risk biological origin pesticides [2016/2903(RSP)]. It called on EU MSs to 'accelerate the evaluation, authorization, registration, and monitoring of the use of low-risk plant protection products of biological origin while maintaining risk assessment at a high level' and to stimulate approval and cooperation at the level of EU MSs.<sup>24</sup>

Unfortunately, the EU's 2020 'Farm to Fork' strategy<sup>25</sup> goals stress the limited progress achieved toward the goals of the pesticide package, especially in expanding the availability and usage of MBCPs. A series of recent evaluations has proposed various explanations for the persisting gap between the EU and the USA and other countries. Frederiks and Wesseler<sup>9</sup> revealed that while the average period for strain approval and product authorization in the EU decreased from 1845 days under Directive 91/414/EEC to 1369 days under Regulation (EC) 1107/2009, it is still much longer than the average 781 days in the USA. While the EU-level phases accelerated (second and third phases), the EU-RMS phase lagged and became the main procedural obstacle in accelerating MBCA approval. Sundh and Eilenberg explain the lengthy MBCA approval, saying that the knowledge, expertise, and scientific concepts have not been applied in the safety assessment used during the approval process, offering no legal predictability, proportionality, or nondiscrimination.<sup>4</sup> Furthermore, the MBCP authorization averaged 629 days, exceeding the procedural deadlines in four out of five cases.

Lamichhane *et al.*<sup>3</sup> identified limited funding and a lack of projects integrating biocontrol products with other measures as the most critical factors hindering the development of biological pest control. Balog *et al.* showed that by 2017 only 68 biopesticide-active substances were approved and commercially available in the EU, compared with 400 in the USA and 1000 in India.<sup>7(p2204)</sup> This was because of the complexity of the regulations: 14 laws in the EU vs four in the USA and two in China. Furthermore, the mutual recognition of MBCP exceeds procedural deadlines by years, and the division of EU MS into climatic zones generates unnecessary and expensive procedures, usually required for chemical pesticides.<sup>7(p2207)</sup>

Some authors stress that the interpretation of the guidelines for the authorization of MBCPs has varied among countries. Inadequate understanding of the procedure among MS-level authorities and small and medium-sized enterprises, the lack of attractiveness of investment for venture capital, and the number of required product authorization procedures slowed development, considering its vast potential.<sup>11(p9)</sup> Matyjaszczyk also shows that the legislation and costs of authorization of MBCP as biostimulants vary among EU MSs. Denmark and the Czech Republic have a simple procedure with a fee of around 200 euros. In Belgium, Germany, and Poland, costs are under 10 000 euros (with a procedure taking under a year), whereas in Hungary, Italy, and France, costs increase to 20 000–30 000 euros, and the procedure lasts over a year.<sup>8(p1205)</sup>

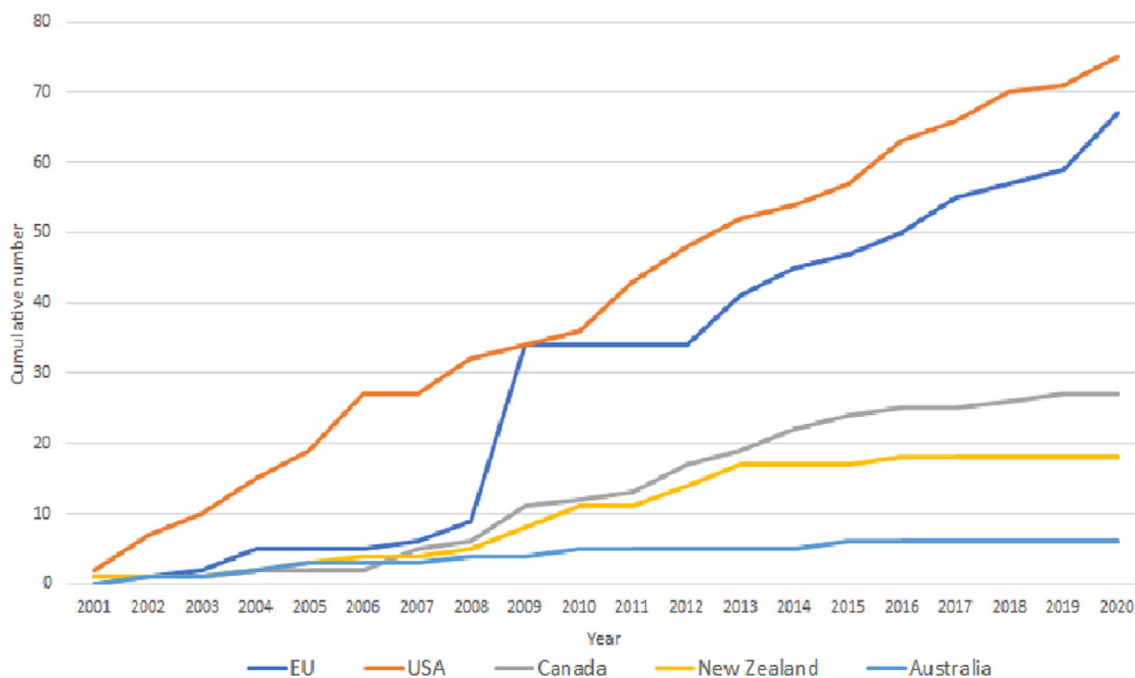
Strasser and Kirchmair assert that faster market penetration of MBCPs is limited given that they are mainly produced by small enterprises that cannot afford the investment in registering niche products with a limited market and high specificity.<sup>22</sup> Even with the reduced requirements for MBCP, the 'cost of registration (tests, toxicity experiments, field trials, development, and fees) in comparison with the market size targeted by a biocontrol substance' are high.<sup>10</sup> However, according to Kvakkestad *et al.*,<sup>26</sup> the market size explanation has a limited explanatory capacity. They compare MBCP authorization in Norway with that in Sweden and Denmark, and argue that, despite similar requirements, the smaller market size in Norway could not explain the longer procedures. Rather, the authorities' restrictive approach to mitigating environmental and human health risks caused the delays.

## 2 MATERIALS AND METHODS

For this article, we have updated and extended the first systematization of approved MBCAs for Australia (AUS), Canada (CA), the European Union (EU), Japan (J), New Zealand (NZ), and the United States of America (USA) (by van Lenternen *et al.*<sup>27</sup>). We have updated the overview of approved active substances in the EU and USA within the period 2000–2017 (by Frederiks and Wesseler, Appendices A and B<sup>9(pp100–103)</sup>) up to 31 August 2019. We have verified all the entries (strains) from the EU Pesticides Database,<sup>28</sup> the US Environmental Protection Agency Pesticide Chemical Search,<sup>29</sup> Canada's Pesticides Database,<sup>30</sup> and New Zealand's Agricultural Compounds and Veterinary Medicines (ACVM).<sup>31</sup> Furthermore, for compiling the EU MS-level authorized MBCPs, we have built on the systematization for 2014 realized by Matyjaszczyk<sup>8(p1204)</sup> and used the EU Pesticides Database.

## 3 RESULTS AND DISCUSSION

We start by assuming that by 2019, considering the longer average time of the EU's MBCA approval and MBCP authorization procedure, the effects of Regulation (EC) 1107/2009 could be initially evaluated. Data in Figs 1 and 2 show that, until 2008, the EU was significantly behind the USA in terms of approval procedures and approved MBCA strains. Since some approval procedures include several strains, data on the total number of procedures indicate the EU's administrative capacity. The situation has greatly improved in the EU since 2008, leading to a lower lag with the USA in terms of cumulative approval procedures. As some of the approval procedures have included several related strains,

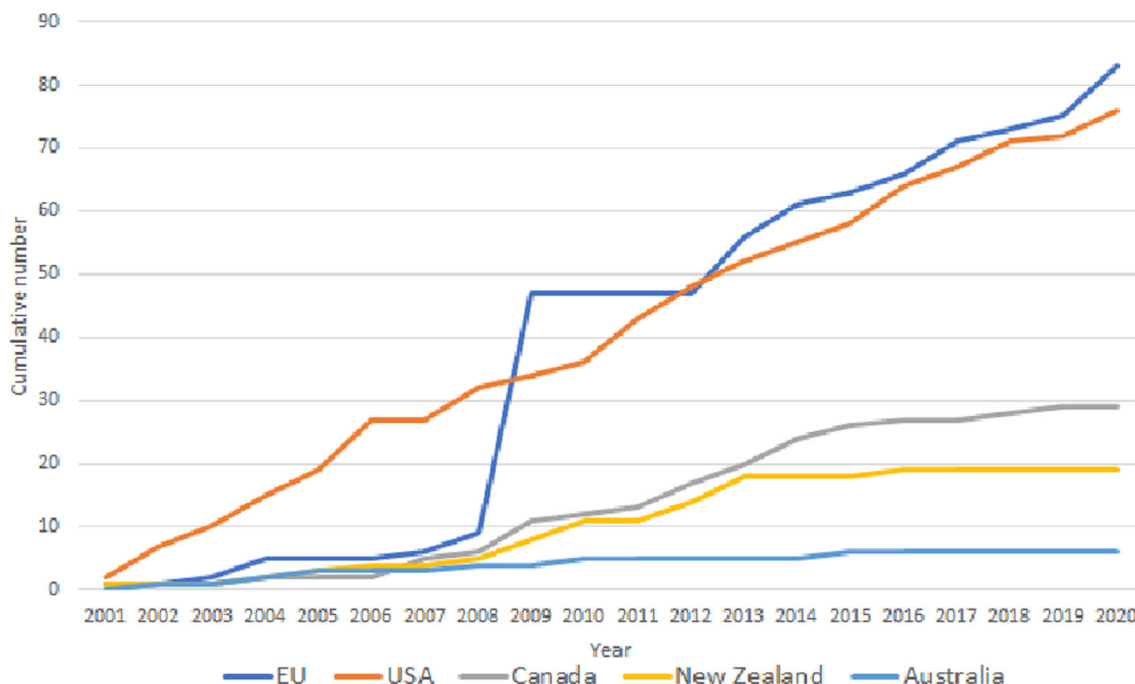


**Figure 1.** The cumulative evolution of microbial biological control agent approval procedures by country/region between 2001 and 2019 (2020 pending approval) in the EU, the USA, Canada, New Zealand, and Australia.

the EU had overtaken the USA regarding the total number of approved MCBA strains by 2008.

Despite considerable improvements in MBCA approval, success in creating the conditions for microbial pest control is also a function of country-level MBCP authorization, the crucial stage ensuring their availability and supporting market penetration. Table 1 shows for each approved MBCA the number of countries with authorized MBCPs in 2014 and 2019. The situation in 2014 was

bleak as approved MBCAs led to an average of only 23% authorized MBCPs, covering only 28% of the agricultural land of EU MSs. By 2019, the situation had improved as MBCP authorization increased to 38%. Very positively, the coverage of EU agricultural land had risen to 50% by 2019. The most widely approved MBCP in 2014 used four *Bacillus thuringiensis* strains (EG 2348, SA-11, SA-12, ssp. *kurstaki* PB 54), species on which most MBCPs are based. Among the strains already available in 2014 and widely



**Figure 2.** The cumulative evolution of approved microbial biological control agent strains by country/region between 2001 and 2019 (2020 pending approval) in the EU, the USA, Canada, New Zealand, and Australia.

**Table 1.** Approved microbial biological control agents in the EU and authorized MBCP in the EU Member States in 2014 and 2019 (based on Tables S1 and S2)

Microorganism <sup>†</sup>	Type <sup>1</sup> (pp45–51) of organism	Target(s)	1st EU approval	MBCP authorized in EU countries in 2014	MBCP authorized in EU countries in 2019	Difference 2019–2014 authorized MBCPs	2014% of coverage of EU arable land	2019% of coverage of EU arable land	2014–2019% change of coverage of EU arable land
<i>Isaria fumosorosea</i> Appka 97 (formerly <i>Paeclomyces fumosoroseus</i> )	Fungus	Soft bodied insects	2001	3	7	4	20	34	14
<i>Coniothyrium minitans</i> CON/M/91–08	Fungus	<i>Sclerotinia</i> spp.	2003	15	17	2	78	64	–14
<i>Ampelomyces quisqualis</i> AQ10	Fungus	Powdery mildew	2004	11	12	1	59	49	–10
<i>Glodiadium catenulatum</i> J1446	Fungus	Foliar fungal diseases	2004	8	11	3	30	60	30
<i>Pseudomonas chlororaphis</i> MA342	Bacterium	Seed-borne pathogens on barley and oats	2004	13	13	0	64	63	–1
<i>Bacillus subtilis</i> QST 713	Bacterium	Fungal foliar diseases	2007	5	22	17	31	81	51
<i>Bacillus thuringiensis</i> ssp. <i>tenebrionis</i> NB 176	Bacterium	Beetles	2008	8	7	–1	64	57	–7
<i>Lecanicillium muscarium</i> (formerly <i>Verticillium lecanii</i> ) Ve6	Fungus	Whitefly, thrips	2008	3	6	3	26	39	13
<i>Paeclomyces lilacinus</i> 251	Fungus	Root knot nematodes	2008	2	3	1	10	18	8
<i>Bacillus thuringiensis</i> EG 2348	Bacterium	Lepidopteran caterpillars	2009	21	23	2	89	94	5
<i>Bacillus thuringiensis</i> SA-11	Bacterium	Lepidopteran caterpillars	2009	21	22	1	89	91	2
<i>Bacillus thuringiensis</i> SA-12	Bacterium	Lepidopteran caterpillars	2009	20	22	2	89	91	2
<i>Bacillus thuringiensis</i> ssp. <i>aizawai</i> ABTS-1857	Bacterium	Lepidopteran caterpillars	2009	11	17	6	46	76	30
<i>Bacillus thuringiensis</i> ssp. <i>aizawai</i> GC-91	Bacterium	Lepidopteran caterpillars	2009	17	17	0	0	76	76
<i>Bacillus thuringiensis</i> ssp. <i>israeliensis</i> (serotype H-14) AM65-52	Bacterium	Mosquitoes	2009	2	6	4	18	33	15
<i>Bacillus thuringiensis</i> ssp. <i>kurstaki</i>	Bacterium	Lepidopteran caterpillars	2009	24	24	0	0	96	96

**Table 1.** Continued

Microorganism <sup>s</sup>	Type <sup>1</sup> of organism	Target(s)	1st EU approval	MBCP authorized in EU countries in 2014	MBCP authorized in EU countries in 2019	Difference 2019–2014 authorized MBCPs	2014% of coverage of EU arable land	2019% of coverage of EU arable land	2014–2019% change of coverage of EU arable land
<i>Bacillus thuringiensis</i> ssp. <i>kurstaki</i> ABTS 351 (US - <i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> , strain ABTS-351, fermentation solids, spores, and insecticidal toxins_	Bacterium	Lepidopteran caterpillars	2009	21	24	3	89	96	7
<i>Bacillus thuringiensis</i> ssp. <i>Kurstaki</i> PB 54	Bacterium	Lepidopteran caterpillars	2009	21	24	3	89	96	7
<i>Beauveria bassiana</i> ATCC 74040	Fungus	Spidermites, whitefly, thrips, aphids	2009	7	16	9	33	67	34
<i>Beauveria bassiana</i> GHA	Fungus	Whitefly, thrips, aphids	2009	7	16	9	33	67	34
<i>Cydia pomonella</i> GV (Mexican strain)	Virus	Codling moth	2009	18	22	4	50	96	45
<i>Helicoverpa armigera</i> NPV	Virus	<i>Helicoverpa</i> ssp.	2009	2	5	3	9	38	30
<i>Metarhizium anisopliae</i> var. <i>anisopliae</i> BIPESCO 5/F52	Fungus	Black vine weevil, thrips	2009	6	14	8	33	71	39
<i>Phlebiopsis gigantea</i> (14 strains)	Fungus	Root rot ( <i>Heterobasidion annosum</i> ) in conifers	2009	4	5	1	26	37	10
<i>Pythium oligandrum</i> M1	Fungus	Fungal diseases in cereals and oil seed rape	2009	2	10	8	3	71	67
<i>Streptomyces griseoviridis</i> K61	Bacterium	Fungal soil diseases in vegetables, ornamentals	2009	7	11	4	28	52	24
<i>Trichoderma asperellum</i> (formerly <i>T. harzianum</i> ) ICC012	Fungus	Fungal soil diseases in vegetables, ornamentals	2009	2	6	4	18	49	31
<i>Trichoderma asperellum</i> (formerly <i>T. viride</i> ) T25	Fungus	Fungal soil diseases in vegetables, ornamentals	2009	2	6	4	18	49	31

Table 1. Continued

Microorganism <sup>§</sup>	Type <sup>1</sup> of organism (pp45–51)	Target(s)	1st EU approval	MBCP authorized in EU countries in 2014	MBCP authorized in EU countries in 2019	Difference 2019–2014 authorized MBCPs	2014% of coverage of EU arable land	2019% of coverage of EU arable land	2014–2019% change of coverage of EU arable land
<i>Trichoderma asperellum</i> (formerly <i>T. harzianum</i> ) TV1	Fungus	Fungal soil diseases in vegetables, ornamentals	2009	2	6	4	18	49	31
<i>Trichoderma atroviride</i> (formerly <i>T. harzianum</i> ) IMI 206040	Fungus	Fungal soil diseases in vegetables, ornamentals	2009	1	3	2	6	11	4
<i>Trichoderma atroviride</i> (formerly <i>T. harzianum</i> ) T11	Fungus	Fungal soil diseases in vegetables, ornamentals	2009	1	3	2	6	11	4
<i>Trichoderma gamsii</i> (formerly <i>T. viride</i> ) ICC080	Fungus	Fungal soil diseases in vegetables, ornamentals	2009	1	7	6	6	49	43
<i>Trichoderma harzianum</i> KRL-AG2 (syn. T22)	Fungus	Fungal soil diseases in vegetables, ornamentals	2009	3	15	12	4	67	63
<i>Trichoderma harzianum</i> ITEM 908	Fungus	Soil-borne diseases	2009	3	15	12	4	67	63
<i>Verticillium albo-atrum</i> (formerly <i>V. dahliae</i> ) WCS850	Fungus	Dutch elm disease	2009	0	3	3	0	9	9
<i>Adoxophyes orana</i> GV V-0001	Virus	Summer fruit tortrix	2013	0	7	7	0	44	44
<i>Bacillus firmus</i> I-1582/Bacillus firmus I-201582, two strains	Bacterium	Nematodes	2013	3	8	5	25	43	19
<i>Candida oleophila</i> O	Yeast	Post-harvest fungicide	2013	2	7	5	23	49	26
<i>Isaria fumosorosea</i> Fe 9901	Fungus	Soft bodied insects	2013	1	3	2	6	19	12
<i>Spodoptera littoralis</i> NPV	Virus	<i>Spodoptera littoralis</i> (cotton leaf worm)	2013	1	4	3	6	36	30
<i>Trichoderma asperellum</i> T34	Fungus	Fungal soil diseases in vegetables, ornamentals	2013	0	9	9	0	62	62

**Table 1.** Continued

Microorganism <sup>s</sup>	Type <sup>1</sup> (pp45-51) of organism	Target(s)	1st EU approval	MBCP authorized in EU countries in 2014	MBCP authorized in EU countries in 2019	Difference 2019–2014 authorized MBCPs	2014% of coverage of EU arable land	2019% of coverage of EU arable land	2014–2019% change of coverage of EU arable land
<i>Trichoderma atroviride</i> I-1237	Fungus	Wound pathogens and fungal soil diseases	2013	0	5	5	0	40	40
<i>Aureobasidium pullulans</i> DSM 14940 and DSM 14941, two strains	Yeast	Bacterial and fungal flower and foliar diseases	2014	10	11	1	44	63	19
<i>Bacillus amyloliquefaciens</i> ssp. <i>plantarum</i> (syn. <i>Bacillus subtilis</i> var. <i>subtilis</i> var. <i>amyloliquefaciens</i> ) D747	Bacterium	Seedling fungal pathogens	2014	0	8	8	0	45	45
<i>Bacillus pumilus</i> QST 2808	Bacterium	Fungal foliar diseases	2014	0	0	0			0
<i>Pseudomonas</i> sp. DSMZ 13134	Bacterium	<i>Rhizoctonia solani</i> in potato	2014	2	19	17	3	85	82
Pepino mosaic virus CH2 isolate 1906	Virus	Pepino mosaic virus	2015		15			78	
<i>Streptomyces lydicus</i> WYEC 108	Bacterium	Soil-borne and foliar diseases	2015		0			0	
<i>Bacillus amyloliquefaciens</i> (formerly <i>B. subtilis</i> ) MBI 600	Bacterium	Seed treatment, soil-borne diseases	2016		10			56	
<i>Saccharomyces cerevisiae</i> LAS02	Yeast	Fungal diseases in fruits	2016		0			0	
<i>Trichoderma atroviride</i> SC1	Fungus	Wound pathogens	2016		12			63	
<i>Bacillus subtilis</i> var. <i>amyloliquefaciens</i> FZB24	Bacterium	Fungal foliar diseases	2017		0			0	
<i>Beauveria bassiana</i> 147	Fungus	Red palm weevil, soft bodied insects	2017		1			17	
<i>Beauveria bassiana</i> NPP111B005	Fungus	Banana weevil, red palm weevil	2017		2			21	
Pepino Mosaic Virus isolate VC 1	Virus	Pepino mosaic virus	2017		1			6	
Pepino Mosaic Virus isolate VX 1	Virus	Pepino mosaic virus	2017		1			6	
<b>Average (%)</b>				<b>23</b>	<b>38</b>		<b>28</b>	<b>50</b>	

**Table 2.** Authorized microbial biological control products (MBCPs) as a percentage of approved microbial biological control agents (MBCAs) in EU Member States in 2014 and 2019 (based on Tables S1 and S2) arranged by evolution 2014–2019

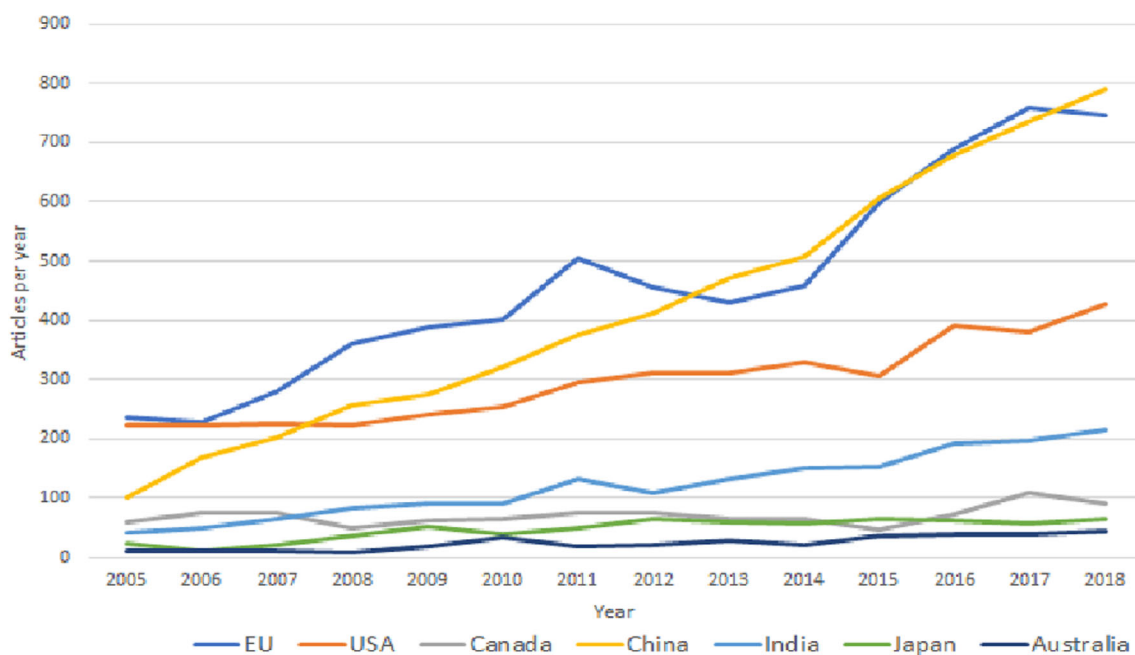
	% evolution between 2014 and 2019	Authorized MBCP in 2014	% of approved MBCA in 2014	Authorized MBCP in 2019	% of approved MBCA in 2019
<i>Average/country</i>	<b>+15</b>		<b>23</b>		<b>38</b>
Spain	45	14	33	41	77
Poland	38	9	21	31	58
Portugal	33	10	23	30	57
Netherlands	30	13	30	32	60
France	30	22	51	43	81
UK	29	16	37	35	66
Greece	26	14	33	31	58
Ireland	26	2	5	16	30
Germany	24	9	21	24	45
Sweden	20	10	23	23	43
Croatia	19	0	0	10	19
Denmark	18	10	23	22	42
Belgium	18	16	37	29	55
Austria	17	12	28	24	45
Luxemburg	13	8	19	17	32
Cyprus	10	11	26	19	36
Hungary	9	10	23	17	32
Bulgaria	9	2	5	7	13
Slovenia	5	10	23	15	28
Czech Republic	4	7	16	11	21
Lithuania	4	7	16	11	21
Italy	4	29	67	38	72
Latvia	3	1	2	3	6
Romania	3	6	14	9	17
Estonia	3	2	5	4	8
Slovakia	2	12	28	16	30
Finland	0	4	9	5	9
Malta	−14	6	14	0	0

authorized in MBCPs at the EU MS level were two other *Bacillus thuringiensis* (ssp. *kurstaki* and ssp. *aizawai* GC-91), *Pseudomonas* sp. DSMZ 13134, *Pythium oligandrum* M1, and two strains of *Trichoderma harzianum* (KRL-AG2 and ITEM 908). Encouragingly, all MBCAs increased their authorization percentage in MBCPs with just three exceptions, indicating the limited failures to produce marketable MBCPs. However, there have been few authorized MBCPs based on MBCA approved since 2014. Only *Pseudomonas* sp. DSMZ 13134 (19 countries) and *Pepino mosaic virus* CH2 isolate 1906 (15 countries) were present in MBCPs authorized in more than half of the EU MSs.

The country-level situation of authorized MBCPs in the EU in 2014 and 2019 (Table 2) shows considerable variations. In 2014, the countries with the most authorized MBCPs were Italy (67%), France (51%), the UK (37%), and Belgium (37%). By 2019, the authorization rate in France had increased to 81%, followed by Spain (77%), Italy (72%), and the UK (66%). Countries with the most significant progress between 2014 and 2019 were Spain (45% increase) and Poland (38% increase), both with significant agricultural sectors. Not unexpectedly, both in 2014 and 2019, all the post-communist EU MSs except Poland had the lowest number of approved strains and the lowest improvement rate between 2014 and 2019. Malta is the only country that had fewer

authorized MBCPs in 2019 than in 2014, possibly caused by the elimination of some MBCPs whose MBCA approval had expired.

To verify whether the authorization of MBCPs is indeed more prevalent in countries with more agricultural land, we have correlated the percentage of each EU MS approved MCBP (of the total available MCBAs) in 2014, 2019 and the change from 2014 to 2019, with the percentage of the country's agricultural land of the entire EU arable land. We used two-tailed Pierson bivariate correlations [\*\*indicates a correlation significant at >0.01 level (two-tailed); \*indicates a correlation significant at >0.05 level (two-tailed)]. The percentage of arable land a country has of the total of EU arable land is positively correlated with MBCP authorization both in 2014 (0.44\*\*) and in 2019 (0.557\*\*) (full data in Table S3).<sup>32</sup> Furthermore, this positive correlation holds even for the progress between 2014 and 2019 in the percentage of authorized MBCPs. As the correlations use data on the entire population of interest, all the EU MSs, the analysis indicates a consistent association between larger agricultural sectors and more authorized MBCPs. It is worth stressing that correlation is not causation and that the exact causal mechanism remains to be tested using multivariate analysis and, if it holds, to be investigated with qualitative techniques. Given that companies are the main actors in MBCP authorization, choosing the MS to which to submit a dossier, an



**Figure 3.** Evolution of articles per year on research in microbial biological control agents indexed in Clarivate Analytics Web of Science by country/region between 2005 and 2018 in the EU, the USA, Canada, China, India, Japan, and Australia.

in-depth investigation should evaluate their structure of incentives.

One of the key factors that influences the evolution of MBCA approval and MBCP authorization is the level of investment in research programs, which is reflected in research output. While interest in funding relevant biological control research programs has improved, it is still evaluated at only 1% of research investment in chemical pesticides.<sup>1(pp15–20)</sup> The biocontrol community survey by Lamichhane *et al.*<sup>3</sup> identified the limited funding for biocontrol research as one of the main hindrances to the development of biocontrol in Europe. To comparatively assess the EU's position on the global stage, we extracted the number of articles in the field of microbial biocontrol in each EU MS in each year from 2005 to 2018 (the latest year available), using Clarivate Analytics Web of Science (WoS) (all subcollections), a precise database, allowing complex search syntaxes to discriminate research relevant to MBCA. While analyzing all biopesticide research published in WoS, Balog *et al.*<sup>7(pp2208)</sup> assessed that the EU was behind the USA, China, and India. Instead, our research, focusing on microbial biocontrol research (Fig. 3), revealed that the EU is, along with China, a global leader in the number of research articles and that the total number of articles has constantly increased up to and including 2018.

In a further step, we have tested the correlation between country-level MBCP authorization and country-level research in the field of microbial biocontrol. The number of research articles on microbial biocontrol (published by 2014) correlates with product approval in 2014 at 0.70\*\* and in 2019 at 0.78\*\*. Also, the change in approved strains in EU MSs is positively correlated (0.47\*\*) with the research articles on microbial biocontrol, indicating that countries more prone to fund research in MBCAs also improved access to MBCPs between 2014 and 2019. Although this data does not test the direct link between research on specific MBCAs and authorization of MBCPs at the country level, it indicates that research efforts are not randomly distributed across

EU MSs but correlated with country-level MBCP authorization. While the exact mechanisms remain to be investigated, data show that most research efforts are concentrated in a limited number of EU MSs, a factor that contributes to the fragmentation of efforts identified by Lamichhane *et al.*<sup>3</sup>

## 4 CONCLUSION

This article contributes to the literature, explaining the factors that hinder a faster development of the EU microbial pest control sector and identifying measures to ameliorate this process. Instead of concentrating on the limitations of the MBCA approval process, we have focused on understanding how MBCA approval translates into country-level MBCP authorization and how this process correlates with the importance of agriculture and the degree of research intensity in microbial biocontrol.

Despite the inefficiencies identified by Balog *et al.*,<sup>7</sup> Matyjaszczyk,<sup>8</sup> Frederiks and Wesseler,<sup>9</sup> and Sundh and Eilenberg,<sup>4</sup> we show that the EU's legislative framework allowed it to catch up in terms of MBCA approval and even slightly overtake the USA for approved MBCA strains. Also, Robin and Marchand<sup>10</sup> show MBCA approval increased most after Regulation (EC) No. 1107/2009 compared with natural substances, semiochemicals, or chemical pesticides. By providing the first dynamic evaluation of MBCP authorization, we show that the situation is less than satisfactory, although the trend is positive. Most MBCPs are submitted for approval in just a few countries, mostly with larger agricultural areas and higher research intensity. We show that between 2014 and 2019, some visible improvements have been achieved in many EU countries, except for most post-communist new EU MSs (with the notable exception of Poland) and most smaller states. Nevertheless, with a few exceptions, all MBCAs had increased MS-level availability, indicating that companies are able to identify potential profitable national markets.

While improving MBCP availability depends on private companies' investment in the approval process and product development, the differences between EU MSs' interest in promoting microbial pest control affect the market penetration of these products. The lack of commitment from EU MSs is still a major limitational factor in developing the biocontrol industry, as adoption of IPM is still not enforced in the EU. In a recent article<sup>33</sup> evaluating the NAPs required by the SUD Directive of eight EU MSs [Denmark, Germany, the Netherlands, France, the UK (a member of the EU until 31 January 2020), Romania, Hungary, and Poland], we have shown that despite promoting low-risk alternatives as one of the SUD goals, relevant measures are present only in the NAPs of two MSs (Denmark and France). In the rest of the NAPs, the issue was discussed, but no concrete measures, timetable, or indicators to promote the use of low-risk alternatives (mostly MBCPs) were present.

We agree with the recurrent recommendation stemming from the literature that further improvements to the EU's regulatory framework are necessary. However, we stress prioritizing efforts into the national-level MBCA approval and MBCP authorization stage, and changing the structure of incentives for researchers, companies, and farmers to increase their availability. Based on the recommendations of the EU initiative REBECA (Regulation of Biological Control Agents), Balog *et al.* recommend improving the implementation of regulations, accelerating risk assessments of MBCPs, and accelerating MBCA approval.<sup>7</sup> We stress that any modification of the 'pesticide package' would be highly contentious, would require much effort from the EU institutions and MSs, and would shift the focus from what we consider the main priority, given our current findings: improving the application of the current 'pesticide package' at the EU MS level so as to fit within the procedural deadlines during both MBCA approval and MBCP authorization. As only four EU MSs performed the RMS phase, and more than 50% of RMSs exceeded procedural deadlines between 2009 and 2016, Frederiks and Wessler consider the EU MS level to be the main bottleneck. They recommend involving only RMSs with proven capacity and even having RMSs specializing in specific types of evaluation and better exchanges of good practice from the successful RMSs like Belgium, France, and the Netherlands or EFSA. They also stress that the unequal expertise of RMSs also leads to exceeding procedural deadlines in MBCP authorization in 80% of cases.<sup>9</sup> Kvakkestad *et al.*'s explanation for MBCP authorization delays in Norway is less likely to be relevant for poorer countries, with a much lower research intensity and lower institutional capacity.<sup>26</sup> Thus, our analysis also indicates the scientific assessment procedures by EU MSs in both the approval and authorization stages, and not the political decision procedure, to be the cause of limited progress.

Frederiks and Wessler's recommendation indicates an implicit centralization of the approval of MBCAs and authorization of MBCPs, leading to the concentration of MBCP authorization in wealthier countries with larger agricultural areas. Centralization could speed up the authorization of MBCPs in the short term but would prevent adequate dissemination of expertise to the rest of the EU MSs and thus would not guarantee a higher market penetration of MBCPs. However, MBCP authorization is not the last of the major hurdles, as employing MBCPs is much more knowledge-intensive and depends on implementing IPM. We consider that this expertise is fundamental to all EU MSs for the sustainable development of microbial pest control. Market penetration of MBCPs fundamentally depends on making the transition to IPM, which in turn depends

on changing the structure of incentives for farmers and increasing the level of expertise on using more knowledge-intensive crop protection measures.

While the recommendation adopted by the International Biocontrol Manufacturers Association in 2018, explicitly presented by Sundh and Eilenberg,<sup>4(p2177)</sup> regarding a unique centralized procedure involving MSs and a unique biocontrol-specific body was opposed by the European Commission (EC), less radical changes could be feasible.<sup>34</sup> The EC could emphasize upgrading the capacity of EU MS competent authorities (especially in terms of microbiological expertise and risk assessment) and systematization in terms of costs and paperwork. Also, as the mutual recognition process tends to exceed procedural deadlines, more robust procedures should be required, including a tacit mutual recognition. Efforts by the EC<sup>35</sup> to develop guidance for zonal evaluations and mutual recognition are important, but more efforts to enact these requirements are needed.

Given their higher costs, limited availability, effectiveness, and high specificity, MBCPs can substantially increase their market penetration only if IPM becomes the dominant approach to agriculture in the EU. Furthermore, to improve the incentives for companies and researchers, additional efforts to promote low-risk alternatives and IPM in the EU MSs NAPs are crucial, as also stated in a recent report by the European Parliament.<sup>33</sup> As the 'Farm to Fork' strategy<sup>25</sup> is a core component of the 'European Green Deal,' current developments represent an important window of opportunity. Nevertheless, the EC's push for the EU MSs to address more seriously the aims of the SUD<sup>36</sup> can be achieved only with a significant boost to the availability and use of MBCPs.

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## CONFLICT OF INTEREST

We, the authors, declare there is no conflict of interests regarding the publication of this article.

## DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article

## SUPPORTING INFORMATION

Supporting information may be found in the online version of this article.

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