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COMMISSION IMPLEMENTING REGULATION (EU) 2025/2068

of 15 October 2025

renewing the approval of the active substance milbemectin in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council, and amending Commission Implementing Regulation (EU) No 540/2011

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC ([1]), and in particular Article 20(1) thereof,

Whereas:

(1) Commission Directive 2005/58/EC ([2]) included milbemectin as an active substance in Annex I to Council Directive 91/414/EEC ([3]).

(2) Active substances included in Annex I to Directive 91/414/EEC are deemed to have been approved under Regulation (EC) No 1107/2009 and are listed in Part A of the Annex to Commission Implementing Regulation (EU) No 540/2011 ([4]).

(3) The approval of the active substance milbemectin, as set out in Part A of the Annex to Implementing Regulation (EU) No 540/2011, expires on 31 May 2026.

(4) An application for the renewal of the approval of the active substance milbemectin was submitted to Germany, the rapporteur Member State, and the Netherlands, the co-rapporteur Member State, in accordance with Article 1 of Commission Implementing Regulation (EU) No 844/2012 ([5]) within the time period provided for in that Article.

(5) The applicant submitted the supplementary dossier required to the rapporteur Member State, the co-rapporteur Member State, the Commission and the European Food Safety Authority ('the Authority') in accordance with Article 6 of Implementing Regulation (EU) No 844/2012. The application was found to be admissible by the rapporteur Member State.

(6) The rapporteur Member State prepared a draft renewal assessment report in consultation with the co-rapporteur Member State and submitted it to the Authority and the Commission on 29 June 2017.

(7) The Authority made the supplementary summary dossier available to the public. The Authority also circulated the draft renewal assessment report to the applicant and to the Member States for comments and launched a public consultation on it. The Authority forwarded the comments received to the Commission.

([1]) OJ L 309, 24.11.2009, p. 1, ELI: http://data.europa.eu/eli/reg/2009/1107/oj.
([2]) Commission Directive 2005/58/EC of 21 September 2005 amending Council Directive 91/414/EEC to include bifenazate and milbemectin as active substances (OJ L 246, 22.9.2005, p. 17, ELI: http://data.europa.eu/eli/dir/2005/58/oj).
([3]) Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market (OJ L 230, 19.8.1991, p. 1, ELI: http://data.europa.eu/eli/dir/1991/414/oj).
([4]) Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances (OJ L 153, 11.6.2011, p. 1, ELI: http://data.europa.eu/eli/reg_impl/2011/540/oj).
([5]) Commission Implementing Regulation (EU) No 844/2012 of 18 September 2012 setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market (OJ L 252, 19.9.2012, p. 26, ELI: http://data.europa.eu/eli/reg_impl/2012/844/oj).

(8) In June 2019, the Authority requested additional information from the applicant on the endocrine disrupting properties of milbemectin pursuant to Article 13(3a), first subparagraph, of Implementing Regulation (EU) No 844/2012. The applicant submitted information to the Authority to assess whether the scientific criteria for the determination of endocrine disrupting properties set out in point 3.6.5 and point 3.8.2 of Annex II to Regulation (EC) No 1107/2009 were met.

(9) In May 2023, the rapporteur Member State made an updated draft renewal assesment report available to the Authority, the Member States and the Commission. In its updated draft renewal assessment report, the rapporteur Member State considered the additional information regarding the criteria to identify endocrine disrupting properties and concluded that milbemectin does not meet the endocrine disrupting criteria for humans nor for non-target organisms.

(10) On 5 July 2023, the Authority communicated to the Commission its conclusion ([6]) indicating that, taking into account the approval criteria set out in Annex II to Regulation (EC) No 1107/2009, plant protection products containing milbemectin can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009.

(11) The Commission presented a renewal report to the Standing Committee on Plants, Animals, Food and Feed on 11 March 2025 and a draft of this Regulation on 9 July 2025.

(12) The Commission invited the applicant to submit its comments on the conclusion of the Authority and, in accordance with Article 14(1), third subparagraph, of Implementing Regulation (EU) No 844/2012, on the renewal report. The applicant submitted its comments, which have been carefully examined and taken into due consideration.

(13) It has been established with respect to one or more representative uses of at least one plant protection product containing the active substance milbemectin that the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009 are satisfied.

(14) It is therefore appropriate to renew the approval of milbemectin. In accordance with Article 14(1) of Regulation (EC) No 1107/2009, read in conjunction with Article 6 thereof, and in the light of current scientific and technical knowledge and the outcome of the risk assessment, it is, however, necessary to provide for certain conditions, in particular, to reduce drift to terrestrial and aquatic areas outside the treated field, where appropriate.

(15) In addition, in order to increase the confidence in the conclusion that any possible aneugenicity and phototoxicity potential of milbemectin does not pose a concern for human health, the applicant should provide information to confirm the absence of aneugenic potential of milbemectin and an in vitro phototoxicity study with milbemectin as confirmatory information.

(16) Furthermore, given that new scientific and technical knowledge on comparative metabolism has been developed during the evaluation process which was not available at the time of the submission of the supplementary dossier for milbemectin, notably a Scientific Opinion ([7]) on testing and interpretation of comparative *in vitro* metabolism studies published by EFSA in 2021, the applicant should provide an *in vitro* comparative metabolism study with milbemectin as confirmatory information.

([6]) *EFSA Journal* 2023;21 (7):8126 Available online: www.efsa.europa.eu.

([7]) EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), Hernandez-Jerez AF, Adriaanse P, Aldrich A, Berny P, Coja T, Duquesne S, Focks A, Marinovich M, Millet M, Pelkonen O, Pieper S, Tiktak A, Topping CJ, Widenfalk A, Wilks M, Wolterink G, Gundert-Remy U, Louisse J, Rudaz S, Testai E, Lostia A, Dorne J-L and Parra Morte JM, 2021. Scientific Opinion of the Scientific Panel on Plant Protection Products and their Residues (PPR Panel) on testing and interpretation of comparative in vitro metabolism studies. *EFSA Journal* 2021;19(12):6970, 61 pp. https://efsa.onlinelibrary.wiley.com/doi/full/10.2903/j.efsa.2021.6970.

(17) Finally, to increase the confidence in the conclusion that risk mitigation measures will be protective for all aquatic organisms outside of the field and given that the scientific and technical knowledge on conducting the aquatic risk assessment has evolved since the time the supplementary dossier for milbemectin were submitted, the applicant should provide an updated risk assessment for the aquatic sediment organisms as confirmatory information.

(18) It is therefore appropriate to renew the approval of milbemectin subject to the conditions set out in the Annex to this Regulation. Implementing Regulation (EU) No 540/2011 should be amended accordingly.

(19) Commission Implementing Regulation (EU) 2025/99 ([8]) extended the approval period of milbemectin to 31 May 2026 in order to allow the renewal process to be completed before the expiry of the approval period of that active substance. However, given that a decision on renewal has been taken ahead of that extended expiry date, this Regulation should apply earlier than that date.

(20) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Plants, Animals, Food and Feed,

HAS ADOPTED THIS REGULATION:

Article 1

Renewal of the approval of the active substance

The approval of the active substance milbemectin, as specified in Annex I to this Regulation, is renewed, subject to the conditions laid down in that Annex.

Article 2

Amendments to Implementing Regulation (EU) No 540/2011

The Annex to Implementing Regulation (EU) No 540/2011 is amended in accordance with Annex II to this Regulation.

([8]) Commission Implementing Regulation (EU) 2025/99 of 21 January 2025 amending Implementing Regulation (EU) No 540/2011 as regards the extension of the approval periods of the active substances Aureobasidium pullulans (strains DSM 14940 and DSM 14941), Bacillus amyloliquefaciens subsp. plantarum D747, benalaxyl-M, cyprodinil, dichlorprop-P, formetanate, fosetyl, halosulfuron-methyl, imazamox, milbemectin, phenmedipham, pirimicarb, Pseudomonas sp. strain DSMZ 13134, pyrimethanil, pyriofenone, pyroxsulam, spinosad, sulphur, Trichoderma harzianum Rifai strains T-22 and ITEM 908, Trichoderma asperellum (formerly T. harzianum) strains ICC012, T-25 and TV-1, Trichoderma atroviride (formerly T. harzianum) strain T11, Trichoderma gamsii (formerly T. viride) strain ICC080, triticonazole and ziram (OJ L, 2025/99, 22.1.2025, ELI: http://data.europa.eu/eli/reg_impl/2025/99/oj).

Article 3

Entry into force and date of application

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

It shall apply from 16 November 2025.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 15 October 2025.

For the Commission
The President
Ursula VON DER LEYEN

ANNEX I

Common Name, Identification Numbers	IUPAC Name	Purity (1)	Date of approval	Expiration of approval	Specific provisions
Milbemectin Milbemectin is a mixture of $M.A_3$ and $M.A_4$ CAS No: $M.A_3$: 51596-10-2 $M.A_4$: 51596-11-3 CIPAC No: 660	$M.A_3$: (10E,14E,16E)- (1R,4S,5′S,6R,6′R,8R,13R, 20R,21R,24S)- 21,24-dihydroxy-5′,6′,11,13,22-pentamethyl-(3,7,19-trioxatetracyclo[15.6.1.1^{4,8}.0^{20,24}] pentacosa-10,14,16, 22-tetraene)-6-spiro-2′- (tetrahydropyran)-2-one; $M.A_4$: (10E,14E,16E)- (1R,4S,5′S,6R,6′R,8R,13R, 20R,21R,24S)-6′-ethyl-21,24- dihydroxy-5′,11,13,22-tetramethyl-(3,7,19-trioxatetracyclo[15.6.1.1^{4,8}.0^{20,24}] pentacosa-10,14,16,22-tetraene)-6- spiro-2′-(tetrahydropyran)-2-one	≥ 950 g/kg	16 November 2025	15 November 2040	For the implementation of the uniform principles as referred to in Article 29(6) of Regulation (EC) No 1107/2009, the conclusions of the renewal report on milbemectin, and in particular Appendices I and II thereto, shall be taken into account. In this overall assessment Member States shall pay particular attention to: — the specification of the technical material as commercially manufactured; — the protection of operators and workers ensuring that conditions of use include the application of adequate personal protective equipment; — the protection of bees and pollinators that may be exposed to the active substance by visiting the flowers present in the crop at the time of application; — the protection of aquatic organisms. Conditions of use shall include risk mitigation measures, in particular to reduce drift to terrestrial and aquatic areas outside the treated field, where appropriate.

Common Name, Identification Numbers	IUPAC Name	Purity (1)	Date of approval	Expiration of approval	Specific provisions
					The applicant shall submit confirmatory information as follows: 1. to confirm that the bone marrow was exposed in the available in vivo micronucleus test or to confirm the absence of the aneugenic potential of milbemectin; 2. an in vitro comparative metabolism study with milbemectin (at least in the pivotal species used to characterise milbemectin's toxicity and in comparison with human metabolism); 3. an in vitro phototoxicity study with milbemectin, testing the range of wavelengths (between 290 and 700 nm) where the absorption coefficient is > 10 L x mol^{-1} x cm^{-1}; 4. an updated risk assessment for the aquatic sediment organisms in accordance with the EFSA Guidance document on tiered risk assessment for plant protection products for aquatic organisms in edge of field surface waters. To allow for proper comparison of the sensitivity with other species, this confirmatory information should include a spiked-sediment test (OECD TG 218) and spiked-water test (OECD TG 219) with Chironomidae exposed to milbemectin, where milbemycin A_3/milbemycin A_4 is present in the same ratio than in other ecotoxicology studies. The applicant shall submit to the Commission, the Member States and the Authority the information referred to the points above by 5 November 2027.

(1) Further details on the identity and specification of the active substance are provided in the renewal report.

ELI: http://data.europa.eu/eli/reg_impl/2025/2068/oj

The Annex to Implementing Regulation (EU) No 540/2011 is amended as follows:

(1) in Part A, entry 110 on milbemectin is deleted;

(2) in Part B, the following entry is added:

No	Common Name, Identification Numbers	IUPAC Name	Purity (1)	Date of approval	Expiration of approval	Specific provisions
'176	Milbemectin Milbemectin is a mixture of $M.A_3$ and $M.A_4$ CAS No: $M.A_3$: 51596-10-2 $M.A_4$: 51596-11-3 CIPAC No: 660	$M.A_3$: (10E,14E,16E)- (1R,4S,5′S,6R,6′R,8R,13R, 20R,21R,24S)-21,24-dihydroxy-5′,6′,11,13,22-pentamethyl-(3,7,19-trioxatetracyclo[15.6.1.1^{4,8}.0^{20,24}]pentacosa-10,14,16, 22-tetraene)-6-spiro-2′- (tetrahydropyran)-2-one; $M.A_4$: (10E,14E,16E)- (1R,4S,5′S,6R,6′R,8R,13R, 20R,21R,24S)-6′-ethyl-21,24- dihydroxy-5′,11,13,22-tetramethyl-(3,7,19-trioxatetracyclo[15.6.1.1^{4,8}.0^{20,24}]pentacosa-10,14,16,22-tetraene)-6-spiro-2′-(tetrahydropyran)-2-one	≥ 950 g/kg	16 November 2025	15 November 2040	For the implementation of the uniform principles as referred to in Article 29(6) of Regulation (EC) No 1107/2009, the conclusions of the renewal report on milbemectin, and in particular Appendices I and II thereto, shall be taken into account. In this overall assessment Member States shall pay particular attention to: — the specification of the technical material as commercially manufactured; — the protection of operators and workers ensuring that conditions of use include the application of adequate personal protective equipment; — the protection of bees and pollinators that may be exposed to the active substance by visiting the flowers present in the crop at the time of application; — the protection of aquatic organisms. Conditions of use shall include risk mitigation measures, in particular to reduce drift to terrestrial and aquatic areas outside the treated field, where appropriate.

No	Common Name, Identification Numbers	IUPAC Name	Purity ([1])	Date of approval	Expiration of approval	Specific provisions
						The applicant shall submit confirmatory information as follows: 1. to confirm that the bone marrow was exposed in the available in vivo micronucleus test or to confirm the absence of the aneugenic potential of milbemectin; 2. an in vitro comparative metabolism study with milbemectin (at least in the pivotal species used to characterise milbemectin's toxicity and in comparison with human metabolism); 3. an in vitro phototoxicity study with milbemectin, testing the range of wavelengths (between 290 and 700 nm) where the absorption coefficient is > 10 L x mol^{-1} x cm^{-1}; 4. an updated risk assessment for the aquatic sediment organisms in accordance with the EFSA Guidance document on tiered risk assessment for plant protection products for aquatic organisms in edge of field surface waters. To allow for proper comparison of the sensitivity with other species, this confirmatory information should include a spiked-sediment test (OECD TG 218) and spiked-water test (OECD TG 219) with Chironomidae exposed to milbemectin, where milbemycin A_3/ milbemycin A_4 is present in the same ratio than in other ecotoxicology studies. The applicant shall submit to the Commission, the Member States and the Authority the information referred to the points above by 5 November 2027.

([1]) Further details on the identity and specification of the active substance are provided in the renewal report.'

ELI: http://data.europa.eu/eli/reg_impl/2025/2068/oj