Biocidal Products Committee (BPC)

Opinion on a request according to Article 38 of Regulation (EU) No 528/2012 on

on unresolved objections during the mutual recognition of two ethyl butylacetylaminopropionate (IR 3535) containing insect repellents

ECHA/BPC/318/2022

Adopted

2 March 2022

Opinion of the Biocidal Products Committee

On the questions of unresolved objection during the mutual recognition of two ethyl butylacetylaminopropionate (IR 3535) containing insect repellents

In accordance with Article 38 of Regulation (EU) No 528/2012 of the European Parliament and of the Council 22 May 2012 concerning the making available on the market and use of biocidal products, the Biocidal Products Committee (BPC) has adopted this opinion on a question concerning unresolved objections during the mutual recognition of two ethyl butylacetylaminopropionate (IR 3535) containing insect repellents.

This document presents the opinion adopted by the BPC.

Process for the adoption of the opinion

ECHA received a request from the Commission on 17 December 2021. ECHA acts as the rapporteur in this type of procedures as agreed at BPC-3. The rapporteur presented the draft opinion to the BPC-42 meeting of 2 March 2022. Following the adoption of the opinion at BPC-42, the opinion was amended according to the outcome of the discussion.

Adoption of the opinion

Rapporteur: European Chemicals Agency (ECHA)

The BPC opinion was reached on 2 March 2022.

The BPC opinion was adopted by consensus of the members having the right to vote.

The opinion is published on the ECHA website at: https://echa.europa.eu/bpc-opinions-on-article-38.

Further details of the opinion and background

1. Request for the opinion

Article 38 of Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products (the "BPR") establishes that, if so requested by the Commission, pursuant to Article 36(2) or Article 37(2) of the BPR, the Agency shall issue an opinion within 120 days from the date on which the question was referred to it.

On 17 December 2021, ECHA received a request for a BPC opinion from the Commission to address the questions relative to unresolved objections during the mutual recognition of two ethyl butylacetylaminopropionate (IR 3535) containing insect repellents.

The Commission has requested ECHA to formulate an opinion via the BPC on the following questions in order to decide on accepting the claimed uses against wasps and bees:

1. Regarding the complete protection time (CPT):

(i) Whether a duration of protection must be provided for the assessment of efficacy against wasps and bees of the two products in the context of the claim that was authorised by the reference Member State (rMS), and if so, what would be the minimum duration of protection;

(ii) Whether the simulated-use test performed allows the establishment of a duration of protection.

2. Regarding the simulated-use test performed by the applicant:

(i) Whether the simulated-use test should be performed on a human skin-like surface;

(ii) Whether the performed simulated-use test generated data that can be considered to demonstrate to control wasps and bees by repelling those organisms at the recommended dose for the claim 'repels wasps and bees'.

The Commission further indicated that, when addressing the above-mentioned questions, the following elements should be taken into account by the BPC:

a) The product assessment reports (PAR) of the two biocidal products;

b) The Summary of Product Characteristic (SPC) and PARs of the two products previously authorised with a claim of wasp repellence;

c) Available and applicable guidance from international bodies and other standard methods on tests for repellents;

d) Other available guidance from scientific bodies on tests for wasps repellents.

2. Background

Biocidal products "Mouskito Spray" and "Mouskito Junior Lotion" were authorised by Belgium (rMS) under the National authorisation procedure in accordance with Article 30 of the BPR. Both products are repellents (PT 19) intended to be used to protect human skin from insect bites.

"Moskuito Spray" is a ready-to-use insect repellent (PT19) containing IR3535, i.e., ethyl 3-[N-acetyl-N-butyl] aminopropionate, used to protect humans in areas with moderate climate against mosquitoes (*Aedes aegypti, Culex quinquefasciatus*), flies (*Stomoxys calcitrans*), sandflies (*Phlebotomus duboscqi*) and harvest mites (*Trombicula autumnalis*) bites. Mouskito Spray is also a repellent against bees (*Apis mellifera*) and wasps (*Vespula vulgaris*).

"Mouskito Junior Lotion" is a ready-to-use repellent (PT19) containing IR3535, i.e., ethyl 3-[N-acetyl-N-butyl] aminopropionate, used to protect humans in areas with tropical climatic conditions against mosquito (*Aedes aegypti, Culex quinquefasciatus, Anopheles gambiae*) bites and in areas with temperate climatic conditions against mosquito (*Aedes aegypti, Culex quinquefasciatus*), fly (*Stomoxys calcitrans*) and tick (*Ixodes ricinus*) bites. Mouskito Junior Lotion is also a repellent against bees (*Apis mellifera*) and wasps (*Vespula vulgaris*).

The products are reported to work by the following mode of action: *"The exact biochemical mode of action is not known, but it is assumed to be an olfactory-based effect as insects avoid entering regions with IR3535 vapours"*.

The referral of the disagreement on the evaluation of the product "Mouskito Junior Lotion" was submitted on 19 June 2019 and the referral of the disagreement of the product "Moskuito Spray" was submitted on 11 July 2019 by the initiating concerned Member State (icMS) France to the Coordination Group (CG) in accordance with Article 35(2) of the BPR. During the discussions at the CG, most points of disagreement were resolved, with the exception of one point, related to the efficacy of the products against wasps and bees. The rMS considered that the efficacy against wasps and bees is demonstrated in the field trials provided by the applicant. However, the icMS contested that the efficacy has been demonstrated and the CPT was determined. As the CG did not reach a consensus agreement, the rMS referred the unresolved objection to the Commission in accordance with Article 36(1) of the BPR.

The following issues were identified:

- the design of the field trials did not allow a determination of the CPT;
- the icMSs questioned whether the efficacy of the product was established, since the product was not applied on a human skin-like surface.

3. Answers to the questions from the Commission

The opinion of the BPC has considered the background information provided by the Commission in the opinion request, the PARs of the products in question and the conclusion reached during the meeting of the Efficacy Working Group (EFF WG) that took place on 20 January 2022.

Regarding the CPT:

Question 1: *Whether a duration of protection must be provided for the assessment of efficacy against wasps and bees of the two products in the context of the claim that was authorised by the reference Member State, and if so, what would be the minimum duration of protection?*

Efficacy data relevant to the actual conditions of use are needed to substantiate the claim. Wasps and bees can sting to attack and in defence when provoked, and their painful stings constitute a real hazard to humans. Stings from wasps and bees can cause severe systemic allergic reactions and occasionally fatal anaphylaxis and emotional distress. According to Bilò

and Bonifazi (2009) prevalence of sensitisation to insect venom is estimated at between 9.3% and 28.7% in adults and the incidence of insect sting mortality ranges from 0.03 to 0.48 fatalities per 1000000 inhabitants per year[1]. Therefore wasps' and bees' stings are a real concern to vulnerable individuals. Thus, the protection time is a very important parameter, especially for products used against dangerous insects and having claims like *"Repellent - to protect human skin from insect bites"*.

The claimed duration of protection should be determined with appropriate efficacy data and stated in the SPC and on the label as relevant information for the users. The minimum protection time is not set in the Guidance on the Biocidal Products Regulation, Volume II Efficacy - Assessment and Evaluation, Parts B+C (efficacy guidance) for wasps or other target organisms and it is not considered relevant, since the claimed duration of protection must be aligned with the tested one.

Question 2: *Whether the simulated-use test performed allows the establishment of a duration of protection?*

In the current efficacy guidance, the pass criteria for repellents against wasps in simulated-use tests or field trials are not set, and there are no efficacy norms and criteria for repellents against bees. Efficacy criteria set in the guidance against mosquitoes may stand for wasps and bees, as flying insects with potential hazards to humans, hence, the duration of protection against wasps and bees could be estimated on the basis of complete protection time (CPT), i.e. ~100% protection, in simulated-use tests. CPT is defined as the time between the repellent application and the time of two or more bites on the treated skin, or the first confirmed bite (a bite followed by another within 30 min.). However, using human volunteers is questionable for products intended to be used as topical repellents against dangerous insects like wasps and bees due to ethical reasons.

In the field trial conducted by the applicant, the repellent effectiveness of the biocidal product was investigated using traps, i.e. plastic bottles, filled with sugar solution and detergent to catch the target organisms. The surfaces of the traps were treated with the test product twice a day or remained untreated.

The trap with an attractant as a test subject for repellency against bees and wasps in a field trial, instead of humans, could be acceptable considering that:

i. the repelled insects do not even come into contact with the attractive source,

ii. the fact that bees and wasps sting only if disturbed which is difficult to simulate particularly with humans, and

iii. ethical issues raised by exposure of humans to inevitable and painful bee and wasp stings.

In the test, the number of trapped target organisms was counted at 24 h intervals. The percentage of repellence was presented as an overall percentage of reduction of trapping 10 days after first treatment, by comparing the number of insects caught in the untreated and in the treated traps. Determination of the CPT against wasps and bees would require to measure the time elapsed until the first (confirmed) insect caught in the treated traps. As the

[1] M. B. Bilò and F. Bonifazi. 2009. The natural history and epidemiology of insect venom allergy: clinical implications. Clinical & Experimental Allergy, 39: 1467–1476

product was reapplied after 8 h, the data do not allow the establishment of the duration of complete protection.

Question 3: Regarding the simulated-use test performed by the applicant: *Whether the simulated-use test should be performed on a human skin-like surface?*

According to the efficacy guidance: *"The data provided in support of the intended claims must be sufficient to cover the use patterns and it should demonstrate the efficacy of the product based on the submitted label claim"* and "*The tests should be designed to mimic the practical use situation. The study results should provide a clear picture of the efficacy of the product".*

The tests performed by the applicant, in fact, are field trials conducted in orchards. The efficacy data provided were generated using a field trial based on plastic traps containing sugar solution. However, the surface of plastic bottles (non-porous material) used as traps is significantly different from any material simulating the properties of human skin, especially in terms of absorbance and odour, which may affect the efficacy of the repellent.

The test design should mimic the practical in-use situation as much as possible, e.g. it would be preferable to use an absorbent human skin-like surface/texture like animal skin, or any artificial porous material modified in a way to simulate human skin.

For products with a repellent effect against wasps and bees no agreed protocols or guidelines are available, nevertheless, as stated in the efficacy guidance, the applicant may use other methods, where the studies are scientifically robust, well reported and provide a clear answer to the question. Some examples of test designs can be found from literature.[2] In case of doubts about whether the efficacy data are sufficient to cover the claimed use, the Efficacy Working Group can be consulted via an e-consultation, and in addition, in case of non-conclusive feedback, a discussion may take place at the WG meeting to decide about a suitable test design.

Question 4: Regarding the simulated-use test performed by the applicant: *Whether the performed simulated-use test generated data that can be considered to demonstrate to control wasps and bees by repelling those organisms at the recommended dose for the claim 'repels wasps and bees'?*

The submitted data from the field trials are in principle valid, could demonstrate the efficacy of products intended to be used as spatial or surface repellents and could substantiate a claim "repels wasps and bees". However, the provided test is not relevant for the intended use, i.e. topical repellents against wasps and bees. The products in question are to be applied on human skin and thus used to protect individuals against insect bites/stings. The generated data should be relevant to this intended use. Here, the treated surface (plastic) of the traps in the performed test set-up does not sufficiently mimic the practical use situation.

4. Overall conclusion

A topical insect repellent having a claim against wasps and bees is expected to protect the user against stings by insects. As stings by the wasps and bees can be dangerous to vulnerable people due to allergic reactions towards the venom, it is necessary to demonstrate

[2] Boevé, J-L *et al.* 2016. Field Method for Testing Repellency of an Icaridin-Containing Skin Lotion against Vespid Wasps. Insects, 7(2):22

Boevé, J-L *et al.* 2014. Screening of Repellents against Vespid Wasps. Insects, 5: 272-286

the efficacy and the duration of the protection of such product. The duration of protection has to be clearly stated in the SPC and on the label.

There is no agreed efficacy test protocol or criteria for topical repellents against wasps and bees available. It is the applicant's responsibility to provide efficacy data from studies designed to mimic the practical use situation to substantiate the label claim. The eCA/refMS and the Efficacy Working Group can be consulted to decide whether the proposed test protocol is suitable to substantiate the claimed use.

In principle, the efficacy data from the study provided by the applicant are valid, but they are not appropriate to substantiate the claimed use. The treated material (plastic) that was used in the test set-up does not sufficiently mimic the human skin in order to support the use as topical repellent on human skin against wasps and bees. The trap with an attractant as a test subject for repellents against bees and wasps in a simulated-use test or a field trial, instead of humans, could be an acceptable test set-up considering that the repelled insects do not even come into contact with the attractive source, bees and wasps sting only if disturbed which is difficult to simulate, and ethical issues raised by exposure of humans to inevitable and painful bee and wasp stings.

Information regarding the time elapsed until the first (confirmed) insect caught in the treated traps is not provided in the test to allow the establishment of the duration of complete protection time against wasps and bees, and the test design cannot be considered suitable to demonstrate efficacy for the claimed use.

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