Biocidal Products Committee (BPC)

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

Questions on unresolved objections during the mutual recognition of two IR3535 containing insect repellents

ECHA/BPC/179/2017

Adopted

12 December 2017

Opinion of the Biocidal Products Committee

On the questions on unresolved objections during the mutual recognition of two IR3535 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 number of questions concerning unresolved objections during the mutual recognition of two IR3535 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 7 September 2017**.** ECHA acts as the rapporteur in this type of procedures as agreed at BPC-3. The rapporteur presented the draft opinion to the BPC-23 meeting of 12 December 2017. Following the adoption of the opinion at BPC-23, the opinion was amended according to the outcome of the discussion.

Adoption of the opinion

Rapporteur: ECHA

The BPC opinion was reached on 12 December 2017.

The BPC opinion was adopted by simple majority of the members present having the right to vote. The opinion and the minority positions including their grounds are published on the ECHA webpage at:

https://echa.europa.eu/regulations/biocidal-products-regulation/approval-of-active-substances/bpc-opinions-on-other-requests-under-the-biocidal-products-regulation.

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), the Agency shall issue an opinion within 120 days from the date on which the in question was referred to it.

On 7 September 2017, ECHA received a request for a BPC opinion from the Commission to address several questions relative to unresolved objections during the mutual recognition of two IR3535 containing insect repellents.

The UK contested that the application rate of the product used in the exposure assessment against mosquitoes and ticks is lower than the application rate used in the efficacy studies. As the Coordination Group (CG) did not reach a consensus agreement on the acceptability of such discrepancy, Belgium, as reference Member State (refMS), referred on 18 July 2017 the unresolved objections to the Commission in accordance with Article 36(1) of the BPR.

The refMS considers that the approach followed in the assessment of the products is consistent with the approach followed for the approval of the active substance, where the discrepancy between the dose proven efficacious in efficacy tests and the dose used for the exposure assessment was accepted.

The Commission has requested ECHA to formulate an opinion via the BPC on the following questions in order to decide on the authorisation of the two products:

(a) Taking into account the information and guidance[1] available at the time of the submission of the applications for product authorisation, are the conclusions reached by the refMS regarding the conditions in Article 19(1)(b)(i) and (iii) valid?

(b) Regarding the approach followed by the refMS (i.e. accepting the above-mentioned discrepancy):

  (i) Does reliance on such approach give rise to serious concern (e.g. biocidal products do not meet the criteria of Art 19(1)(b)(i) and (iii))?

  (ii) Should the approach in new guidance (i.e. Recommendation 11 of *HEAdhoc*) be followed in order to conclude whether the conditions in Article 19(1)(b)(i) and (iii) are met for these two products?

(c) Regarding efficacy tests other than the arm-in-cage test (i.e. at a lower, realistic dose rate), which are the currently available, standardised protocols for both laboratory and field trial tests?

The Commission further indicated that, when addressing the above-mentioned questions, the BPC should take into account the possible regulatory consequences of the BPC opinion on similar PT 19 products, as discussed in the 23rd meeting of the Coordination Group (CG-23). In particular, where accepting the above-mentioned discrepancy would lead to the conclusions that the conditions in Article 19(1)(b) are not met, pursuant to Article 48(1)(a) of the BPR Member States would have to cancel or amend some existing authorisations for which that discrepancy was deemed to be acceptable.

[1]See the relevant cut-off dates in document CA-July12-Doc.6.2.d-Final, available at https://circabc.europa.eu/w/browse/03bce60b-cf04-49aa-8172-e9c6a75205a7

2. Background

The referral of the disagreement on the evaluation of the products “Insect Repellent Pump Spray IR3535 20%” and “Insect Repellent Aerosol IR3535 30%” was submitted on 14th February 2017 by the concerned MS (cMS) UK to the Coordination Group (CG) in accordance with Article 35(2) of the BPR. The referral was discussed in two teleconferences on 5th April and 2nd May 2017 and during the CG-22 and CG-23 meetings. During the discussions, most points of disagreement were resolved, with the exception of one point related to the discrepancy between the value used for the application rate in the exposure assessment and the one used in the efficacy studies.

The application rate used in the exposure assessment was lower than the one used in the efficacy studies. The refMS considered that the dose-rate used in the efficacy tests was not realistic and, following the approach used in the evaluation of the active substance IR3535, a lower rate was established to be used for the exposure assessment.

As a general principle, the application rate proven efficacious should be considered for the exposure assessment, and, according to Article 19(2) of the BPR, the realistic worst case conditions under which the biocidal product may be used shall be taken into account in the evaluation.

In the standard PT19 efficacy tests against mosquitoes, the dose rate is often overestimated, as it is generally recognised in the case of the arm in cage test. In these tests, a high mosquito biting pressure is needed in order to have significant statistical data. This high biting pressure results in the need of a product application rate higher than that expected to be used under normal circumstances.

The two products evaluated included claims against mosquitoes and ticks. Two laboratory efficacy tests supported the use against ticks and an arm in cage test and a field study supported the use against mosquitoes. In all these studies, the refMS considered that the application rate used was unrealistic.

In particular, in the case of the field study for mosquitoes[2],

(1) the area where the field trial was conducted was one with an extreme high biting pressure; and

(2) the test subjects, aware of the high biting pressure, were instructed to spray the product onto their exposed limbs, without further distribution by hand, resulting in an applied dose higher than one would achieve when considering the actual use of these products.

Considering these two aspects, the refMS, based on expert judgement, concluded that these application rates were unrealistic for the claimed use, and performed the human exposure assessment with a lower application rate than that proven efficacious in the efficacy studies, in line with the approach followed in the CAR for IR3535.

During the final discussion of the referral in CG-23, 18 out of 24 MSs participating in the meeting supported the view of the refMS. The CG members who did not agree with the position of the refMS were of the opinion that a discrepancy in the application rate used in the exposure assessment and that used in the efficacy tests was not acceptable. Furthermore, it was mentioned that a field test should be regarded as realistic. In the case of ticks, several MSs commented that the arm in cage test could be performed using a realistic application rate.

[2] With reference to the PAR, the field test was conducted in 2 different habitats known for supporting high densities of mosquitoes (including aggressive Aedes mosquitoes): native flowering shrubs were distributed in the grassland, in which thousands of mosquitoes were nectar feeding and sheltering. The picnic area is surrounded by forest and flooded marshland.

3. Answers to the questions from the Commission

The opinion of the BPC has considered the background material provided by the Commission in the opinion request, as well as the PAR of the products, the final minutes of CG-23[3] and the conclusions reached during the Efficacy Working Group meeting that took place on September 2017 (EFF WG-IV-2017).[4]

Question (a): ***Taking into account the information and guidance available at the time of the submission of the applications for product authorisation, are the conclusions reached by the refMS regarding the conditions in Article 19(1)(b)(i) and (iii) valid?***

The conditions referred to in Article 19(1)(b)(i) and (iii) for the authorisation of a biocidal product establish that:

(i) the biocidal product is sufficiently effective;

(iii) the biocidal product has no immediate or delayed unacceptable effects itself, or as a result of its residues, on the health of humans, including that of vulnerable groups, or animals, directly or through drinking water, food, feed, air, or through other indirect effects;

The applications for the products "Insect Repellent Pump Spray IR3535 20%" and "Insect Repellent Aerosol IR3535 30%" were submitted on 16 December 2014. Considering the two year cut-off date for applicability of guidance, the applicable efficacy guidance at the time of submission was the document CA-Dec-12-Doc.6.2.a-Final[5]: 'Product Type 18 – insecticides, acaricides and products to control other arthropods and Product Type 19 – repellents and attractants (only concerning arthropods)' (referred to in this document as TNsG-EFF).

In line with the legal text of the BPR[6], the TNsG-EFF mentions that, for assessing efficacy, "*Assessment will be made mainly in relation to the claims for the effectiveness of the product made on the product label. This assessment will take into account the pest(s) to be controlled, indoor or outdoor use, the method(s) of application, application rates and use patterns of the product, maximum storage period of the product, together with any other specific claims made for the product.*" Further, the TNsG-EFF states that "*the test methods applied and the test conditions should be clearly and fully described and must address the efficacy claim that appears on the product label*."

The Competent Authority Report (CAR) of the active substance states that "*Full/robust efficacy studies for all claimed target organisms for IR3535®-based formulations are required at the Product Authorisation Stage.*"

The particularities of these two applications related to the assessment of efficacy were discussed during the EFF WG-meeting (EFF WG-IV-2017). The EFF WG agreed that, in line with the applicable guidance at the moment of submission of the applications, the claimed

[3] Referral document submitted to the Commission by the refMS on the "Referral of unresolved objections to the Commission according to Article 36 of BPR."

PAR of products "Insect Repellent Pump Spray IR3535 20%" and "Insect Repellent Aerosol IR3535 30%" submitted via the R4BP3 on 17 May 2017 (BC-BL013906-42 and BC-HQ013914-29).

CG-22 and CG-23 minutes: "CG-M-22-2017-Final Confidential" and "CG-M-23-2017-Final Confidential" available at: https://webgate.ec.europa.eu/echa-scircabc/w/browse/0e27efa4-3174-48ee-be0f-d33866cfd7d5

[4] Draft minutes available at: https://webgate.ec.europa.eu/echa-scircabc/w/browse/a9939813-aa24-4830-8f19-218dbc6c1976

[5] Available at https://circabc.europa.eu/w/browse/4e747d83-f60b-450d-8d32-1d55478391aa

[6] See paragraph 51 of Annex VI to the BPR.

use of the product must be supported by sufficient efficacy data, i.e. at the specified application rate.

Claim against mosquitoes:

The EFF WG considered the conditions under which the field study against mosquitoes was performed as realistic.

The efficacy data submitted to support these two applications correspond to a higher application rate than that specified in the use pattern of the products. Therefore, the claimed uses of these products are not supported by efficacy data. This implies that the conditions of Article 19(1)(b)(i) are not met.

It should be noted that with the application rate derived from the efficacy studies for mosquitoes, the risk assessment for human health would conclude that the use of the product "Insect Repellent Aerosol IR3535 30%" leads to an unacceptable risk for all user groups and that a restriction of use to adults and children older than 6 is needed for the product "Insect Repellent Pump Spray IR3535 20%".

Claim against ticks:

The EFF WG agreed that the application rates used in standard arm in cage test for ticks are realistic. Therefore, the application rate derived from the efficacy studies should be used for the exposure assessment.

The efficacy data submitted to support these two products correspond to a higher application rate than that specified in the use pattern. Therefore, the claimed use of these products is not supported by efficacy data. This implies that the conditions of Article 19(1)(b)(i) are not met.

It should be noted that with the application rate derived from the efficacy studies for ticks, the risk assessment for human health would conclude that the use of the product "Insect Repellent Aerosol IR3535 30%" leads to an unacceptable risk for all user groups and that a restriction of use to adults and children older than 6 is needed for the product "Insect Repellent Pump Spray IR3535 20%"

As a conclusion to this question, taking into consideration the guidance applicable at the time of submission of the application of these two products and the claimed use against ticks and mosquitoes, the efficacy data submitted was not sufficient to prove the efficacy of the product at the proposed application rates. The conditions of Article 19(1)(b)(i) are therefore not met.

The conditions in Article 19(1)(b)(iii) are met when considering the application rate as specified in the use of the two products against ticks and mosquitoes. However, considering the application rate derived from the efficacy studies, there is an unacceptable risk for the product "Insect Repellent Aerosol IR3535 30%" for all user groups and a restriction of use to adults and children older than 6 years would be needed for the product "Insect Repellent Pump Spray IR3535 20%". The conditions in Article 19(1)(b)(iii) would not be met at this application rate for the product "Insect Repellent Aerosol IR3535 30%". For the product "Insect Repellent Pump Spray IR3535 20%", the conditions in Article 19(1)(b)(iii) would be met with a restriction of use to adults and children above 6 years.

With reference to the use of the product specified in the PAR, the conclusions reached by the refMS are considered as not valid.

Question (b): ***Regarding the approach followed by the refMS (i.e. accepting the above-mentioned discrepancy):***

1. ***Does reliance on such approach give rise to serious concern (e.g. biocidal products do not meet the criteria of Art 19(1)(b)(i) and (iii))?***
2. ***Should the approach in new guidance (i.e. Recommendation 11 of HEAdhoc) be followed in order to conclude whether the conditions in Article 19(1)(b)(i) and (iii) are met for these two products?***

According to Article 19(1)(b)(i), for the authorisation of a biocidal product, the following must be fulfilled: "….the biocidal product, when used as authorised…is sufficiently effective".

1. During the EFF WG-IV-2017 it was agreed that it is not acceptable to have a discrepancy between the proven efficacious application rate and the application rate used for the exposure assessment. Incomplete efficacy data to support the application rate described in the use pattern of a product implies that the conditions of Article 19(1)(b)(i) are not met.

   There is not a clear definition on how "serious concern" should be interpreted, therefore, it is difficult to conclude whether not meeting the conditions of Article 19(1)(b)(i) or (iii) in these cases can be considered as a "serious concern" impacting the efficient and safe control of the harmful organisms. Even though the efficacy of these products at the application rate claimed is not proven, this does not mean that these products are not efficacious.

   Should it be considered that not meeting the conditions of Article 19(1)(b)(i) results in a serious concern, the authorisation of other PT29 products would need to be reviewed.

2. The recommendation 11 of the HEAdhoc WG gives a recommendation on how to perform the exposure assessment of PT19 products. A realistic application rate should be used to determine the exposure assessment of the product. Within this context, the recommendation provides standard default application rate values for PT19 products that can be used in the absence of application rate data generated by the applicant.

   It should be noted that efficacy data should always be provided regardless of whether the application rate values used in the exposure assessment are the standard default values defined in the Recommendation, or alternative values generated by the applicant. In this respect, the Recommendation 11 does not introduce any new elements regarding efficacy data requirements and will not impact the assessment of whether a product meets the conditions of Article 19(1)(b)(i).

<u>Question (c):</u> ***Regarding efficacy tests other than the arm-in-cage test (i.e. at a lower, realistic dose rate), which are the currently available, standardised protocols for both laboratory and field trial tests?***

For the efficacy evaluation of biocidal products against mosquitoes different types of tests can be used (i.e. laboratory, simulated-use tests and field tests). For the time being there are no precise efficacy tests/standard protocols testing a realistic efficacious dose.[7] Only some modifications of existing tests/protocols are possible. The available arm-in-cage test comprises a worst case scenario and therefore parameters such as mosquito biting pressure and applied dose rate may not reflect those encountered under realistic conditions.

Available efficacy guidelines against mosquitoes are listed in Appendix 17 of the Volume II Efficacy - Assessment and Evaluation (Parts B+C) Version 1.0[8]. Useful information on the principles of test design, criteria for efficacy testing and evaluation of mosquito repellents for human skin can be found in the "Guidelines for efficacy testing of mosquito repellents for human skin" developed by WHO[9].

In the absence of precise harmonised guidance/standards, applicants are expected to conduct efficacy tests (field trials could be considered) that are relevant to their product and support

[7] The DE CA has started an initiative to modify the current test conditions of the arm in cage test to be able to test realistic application dose rates and give information about protection times relevant to field conditions. The results of this study were available by the end of November 2017 and were presented at the PT 19 Workshop in Berlin (30.11.-1.12.) for discussion.

[8] Document accessible on https://echa.europa.eu/guidance-documents/guidance-on-biocides-legislation.

[9] WHO/HTM/NTD/WHOPES/2009.4

a realistic situation. Under these circumstances, standards can be adapted to account for the particularities of the product. This is in line with the requirements mentioned in the TNsG *"If the available guidelines are not suitable, the applicant may use their own methods (intra-company Standard Operating Procedures), on condition however, that the study is scientifically robust, well reported and provides a clear answer to the question. In addition, the test methods applied and the test conditions should be clearly and fully described and must address the efficacy claim that appears on the product label."* This aspect is also mentioned in the WHO guidance[9] to which the TNsG makes reference, where it explains that test conditions such as the number of volunteers participating in the tests should be estimated in order to allow statistical significant results.

It is however acknowledged that the absence of a precise guidance leads to a case-by-case assessment that could give rise to inconsistencies in the assessment of different applications.

4. Overall conclusions and additional remarks

1. The information available in in these two applications against mosquitoes and ticks is not sufficient to demonstrate that the product is sufficiently effective when used as claimed. Unacceptable risks are identified for all user groups when used at the efficacious dose for one of the biocidal products. The conclusions reached by the refMS are considered as not valid.

2. Reliance on the approach followed by the refMS (i.e. accepting the discrepancy) is considered as not satisfying the conditions in Article 19(1)(b).

3. There is no precise agreed guidance at the EU on how to generate efficacy data when using the recommended application rates. In the absence of such guidance, applications can only be assessed on a case-by-case basis, which might lead to inconsistent outcomes for similar products. Agreement on new, harmonised guidance enabling applicants to generate data to demonstrate the efficacy of the product in a predictable manner may take an undefined period of time.

4. The existence of a precedent with other PT19 products where the discrepancy between the application rate used for the exposure assessment and that used in the efficacy studies was accepted may have led to a misunderstanding by applicants regarding the efficacy data requirements for PT19 applications.

Conclusions 1 and 2 above are relevant for other PT 19 on-going applications and PT 19 authorised products for which the assessment was based on the above-mentioned discrepancy.

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