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 procedure of the PT 18 biocidal product Konservan P 40 containing permethrin

ECHA/BPC/284/2021

Adopted

17 June 2021

Opinion of the Biocidal Products Committee

On questions on unresolved objections during the mutual recognition procedure of the PT 18 biocidal product Konservan P 40 containing permethrin

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 questions concerning unresolved objections during the mutual recognition procedure of the product “Konservan P 40”.

This document presents the opinion adopted by the BPC.

Process for the adoption of the opinion

ECHA received a request from the Commission on 4 March 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-39 meeting of 15–18 June 2021. Following the adoption of the opinion at BPC-39, the opinion was amended according to the outcome of the discussion.

Adoption of the opinion

Rapporteur: European Chemicals Agency (ECHA)

The BPC opinion was adopted on 17 June 2021.

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 (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 4 March 2021, ECHA received a request for a BPC opinion from the Commission to address two questions relative to unresolved objection during the mutual recognition of the product "Konservan P 40". The biocidal product KONSERVAN P 40 is a permethrin-based PT18 biocidal product to be used by industrial users for vector protection finishes of textiles against mosquitoes and ticks and for wool protection against clothes moths and carpet beetles.

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 product:

1. Dermal absorption is one of the routes of human exposure to biocides. It is acknowledged that biocidal products may contain non-active substances that could affect dermal absorption, for example by altering the skin barrier or by enlarging the skin-area that the product covers. Therefore biocidal products containing the same active substance might have different dermal penetration values.
2. It should be noted that the human exposure to the active substance in the wool/textile treated with the biocidal product depends directly on the combined values of the migration rate of permethrin from the treated article to skin and dermal absorption of permethrin. Therefore both parameters need to be addressed by ECHA. Taking this into account, the following questions have to be addressed by the ECHA opinion:
    - Considering the realistic worst case scenarios for the relevant paths of human exposure for professional users and the general public, ECHA is requested to estimate the migration rate value of permethrin that should be used in performing the risk assessment for the different uses envisaged of the articles treated with the biocidal product 'Konservan P 40' .
    - Considering the realistic worst case scenarios for the relevant paths of human exposure for professional users and the general public, ECHA is requested to estimate the dermal absorption value of permethin that should be used in performing the risk assessment for the different uses envisaged of the articles treated with the biocidal product 'Konservan P 40'. In responding to this question ECHA should consider the relevance of the values applied for dermal absorption by other evaluating authorities in the authorisation of products EULAN SPA 01 (evaluated by the United Kngdom) and NONAX 2008-EU (evaluated by Belgium) and the assessment report for the approval of the active substance.
    - ECHA is requested to determine whether the combination of both values established by ECHA, dermal absorption and the migration rate of permethrin, leads to the conclusion that the biocidal product 'Konservan P 40' has no unacceptable effects on the health of humans, taking into account the different uses envisaged and the relevant paths for human exposure for prosessional use and the general public and considering the proposed normal use of the biocidal product, together with realistic worst-case scenarios for each relevant path of exposure and thus, whether the conditons of Article 19(1)(b)(iii) are met.

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

(a) The Summary of Products Caracteristics (SPC) and the Product Asssesment Report (PAR) of the biocidal product 'Konservan P 40'.

(b) The values for dermal absortion of permethrin and the migration rate established in the assessment report for the active substance permethrin.

(c) The updated BfR Opinion No. 041/2012, 6 July 2012[1].

(d) The Guidance on Dermal Absorption EFSA Panel on Plant Protection Products and their Residues (PPR)[2].

(e) The product assessement reports of the biocidal products containg permethrin as an active substance, i.e. EULAN SPA 01, evaluated by the United Kingdom and NONAX 2008-EU, evaluated by Belgium and in particular the combination of both values, dermal absorption and migration rate of permethrin that have been used during the evaluation of those products.

(f) The available relevant scientific data on migration rates from similar treated articles to skin and dermal absorption, in particular for the active substance permethrin.

2. Background

The referral of the disagreement on the evaluation of the product "Konservan P 40" was submitted on 1 August 2019 by the icMS to the Coordination Group (CG), in accordance with Article 35(2) of the BPR. The referral was discussed during the CG-37 meeting and a teleconference on 26 September 2019. During the discussions, most points of disagreement were resolved, with the exception of one point related to a migration rate value from textile and wool to skin to be used in the human health exposure assessment that remained unresolved even in subsequent correspondence following the teleconference.

Migration rate of 1 % was used in the permethrin Competent Authority Report (CAR), while the refMS FR used refined value of 0.1% based on a BfR opinion[3]. In the absence of product specific data, the refMS used for dermal absorption 75% default value. The exposure assessment was acceptable for the uses in clothing and wool carpet. Due to disagreement by BE CA on the migration rate, the refMS revised the human health exposure assessment using 1% migration rate combined with 3% dermal absorption set in the CAR of permethrin. This combination leads to acceptable exposure, whereas the combination of worst case values 1% migration rate and 75% dermal absorption does not.

During the teleconference, additional supporting information provided by the applicant was discussed and MSs indicated that the revised human health exposure assessment with the migration (1%) and dermal absorption (3%) values might be accepted.

During the final discussion of the referral following the teleconference, 2 MSs (BE and DE) disagreed with the proposed revised PAR. After this, the PAR was revised by the refCA to the final version of October 2019, where 0.1% migration rate and 75% dermal absorption are used.

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[1] https://www.bfr.bund.de/cm/349/introduction-to-the-problems-surrounding-garment-textiles.pdf
[2] https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides_ppp_app-proc_guide_tox_dermal-absorp-2012.pdf
[3] Introduction to the problems surrounding garment textiles (bund.de)

3. Answers to the questions from the Commission

The opinion of the BPC has considered the following:

1. The opinion request by the Commission, and in particular the elements:
   a) The Summary of Products Characteristics (SPC) and the PAR of the biocidal product 'Konservan P 40' (final version, Oct. 2019).
   b) The request to assess both uses of Konservan P 40: Use 1 in fabrics for clothing and Use 2 in non washable wool for carpets/rugs.
   c) The values for dermal absortion of permethrin and the migration rate established in the CAR for the active substance permethrin.
   d) The updated BfR Opinion No. 041/2012, 6 July 2012[4].
   e) The Guidance on Dermal Absorption EFSA Panel on PPR[5].
   f) The product assessement reports of the biocidal products containg permethrin as an active substance, i.e. EULAN SPA 01, evaluated by the United Kingdom and NONAX 2008-EU, evaluated by Belgium and in particular the combination of both values, dermal absorption and migration rate of permethrin that have been used during the evaluation of those products.
   g) The available relevant scientific data on migration rates from treated articles to skin and dermal absorption, in particular for the active substance permethrin.
2. The statement submitted by the refMS FR to COM in accordance with Article 36(1) of the BPR in October 2019.
3. The ECHA screening via R4BP33 of permethrin containing PT8 and PT18 products evaluated under national and union authorisation.
4. The ECHA literature search on dermal absorption and migration rate of permethrin.
5. The outcome of TOX WG discussions on Union authorisation of other permethrin containing PT18 products with open points on migration rate (WGI2020 discussion for product Insecticide Textile Contact) and dermal absorption (WGI2021 discussion for product BC-GK024706-40).
6. The TOX WG discussion at WGI2021 on the art.38 request by Commission that took place on 17 March 2021.
7. The information provided by the applicant after WGI2021 listed in Annex I.
8. The conclusions of the e-consulation launched in May 2021 for the members of the Human Health WG and the applicant[6].

In the absence of dermal absorption study for Konservan P 40 and migration rate study of permethrin from the articles (cloths, carpets) treated with the product, the assessment of these two parameters has to use either default values or estimations and assumptions based on WoE approach.

The questions on the migration rate and the dermal absorption will be addressed by presenting the different options available for their assessment and by assessing the scientific reliability and uncertainty for each option.

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[4] https://www.bfr.bund.de/cm/349/introduction-to-the-problems-surrounding-garment-textiles.pdf
[5] https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides_ppp_app-proc_guide_tox_dermal-absorp-2012.pdf
[6] Link to e-consultation: https://webgate.ec.europa.eu/s-circabc/w/browse/4e2ac0b0-4fae-46f2-9130-4d9b96d95434

Question 1: Migration rate

Considering the realistic worst case scenarios for the relevant paths of human exposure for professional users and the general public, ECHA is requested to estimate the migration rate value of permethrin that should be used in performing the risk assessment for the different uses envisaged of the articles treated with the biocidal product 'Konservan P 40'.

A screening of permethrin containing PT18 products via R4BP3 and a literature search was conducted by SECR to detect all available options on migration rates. The options found vary between 0.1-20% (See Table 1).

The default values of 20% (for cotton and knitwear according to Biocides HH Exposure Methodology), 9% (for dried fluid residues in carpets from Biocides HH Exposure Methodology) and 0.1% migration rate (from BfR opi.041/2021) are proposed not to be used since none of these values is specific for permethrin migration from clothing or wool carpets (See Table 2).

The values specific for permethrin migration (Table 2) found are:

- 0.5% [measured as portion of radiolabelled permethrin in cotton, cotton/nylon fabrics (Snodgrass 1992)]
- 1% [estimated from internal exposure of soldiers to permethrin impregnated battle uniforms in a biomonitoring study (Appel 2008)]

A comparative assessment of these values is performed in "Comparative Assessment of migration rate values", where it is proposed to use:

- **1% migration rate for clothing** as the most appropriate value to provide a reasonable and reliable estimate of the migration of permethrin from treated cloths. This value covers for the limitations of the Snodgrass 1992 study and the uncertainty on the 0.5% measured migration rate. The value is also supported by the 1% migration rate estimated from Appel 2008.
- **0.5 % migration rate for wool carpets** as the most appropriate value to provide a reasonable and reliable estimate of permethrin migration from treated wool carpets, for the following reasons:
    - 0,5% was measured in the Snodgrass study for clothing fabrics under continuous exposure for 7 days.
    - the worst-case conditions of exposure from woollen carpets is a child playing on carpet touching the surface of carpet with sweated hands.
    - the conditions used in Snodgrass study overestimate the conditions of exposure from carpets.
    - this overestimation balances the weaknesses of the study and therefore for the estimation of migration from woollen carpets, the measured migration rate of 0.5% can be considered.
    - the default migration rate values (20% for cotton and knitwear; 9% for carpets), show that much lower migration rate is expected from carpets than from clothing fabrics.

The detailed SECR assessment is included in Q1 Migration rate Assessment, where revisions based on the comments of the members of the Human Health WG and the applicant at the e-consultation launched in May 2021 have also been included.

Question 2: Dermal absorption

Considering the realistic worst case scenarios for the relevant paths of human exposure for professional users and the general public, ECHA is requested to estimate the dermal absorption value of permethrin that should be used in performing the risk assessment for the different uses envisaged of the articles treated with the biocidal product 'Konservan P 40'. In responding to this question ECHA should consider the relevance of the values applied for dermal absorption by other evaluating authorities in the authorisation of products EULAN SPA 01 (evaluated by the United Kingdom) and NONAX 2008-EU (evaluated by Belgium) and the assessment report for the approval of the active substance.

The Human Health WG in March 2021 did not agree on the dermal absorption value to be used, based on the information available in the CAR of permethrin, the PARs of Konservan P 40, EULAN SPA 01 and NONAX 2008-EU. The majority did not support the 3% value applied in the PAR of Konservan P 40 used in the draft PAR of September 2019.

The applicant supported that the value of 3% is conservative enough for the dry residues of permethrin in fabrics for which the dermal absorption via sweat (aqueous adsorption) is of relevance, whereas the use of default dermal absorption values is overly conservative.

After the Human Health WG discussion, the applicant submitted additional documentation (Annex I), where read-across is proposed from:

- dermal absorption values derived from studies on human volunteers conducted with permethrin in organic solvents;
- in vitro dermal absorption studies conducted with permethrin containing PT8 products.

In order to assess the applicant's arguments, a screening of permethrin containing PT18 products via R4BP3 was conducted by SECR to view all products with similar uses with Konservan P 40 and to report the dermal absorption values used for the scenarios of wearing clothing or of contact with wool carpet (See Table 5). All dermal absorption values found were previously peer reviewed, i.e. commented under mutual recognition of National Authorisations or under Union Authorisations.

Another screening of permethrin containing PT18 and PT8 products was conducted via R4BP3 to collect all dermal absorption studies conducted on permethrin containing products (See Table 6).

The US-EPA evaluation of permethrin dermal absorption used in the assessment of NONAX 2008-EU was also assessed (See "US-EPA assessment of dermal absorption").

The search of permethrin containing PT18 products with similar uses to Konservan P 40 (Table 5) shows that after the finalisation of the permethrin CAR in 2014, the product evaluations have either used or considered the EFSA default values.

It also indicates the absence of product specific data, despite flagging this in the permethrin CAR Doc IIA, 2014: "*At product authorisation a dermal absorption study in vitro on human skin will be required for each formulation type*"; and the note in permethrin PT18 BPC opinion, 2014: "*Further data may be required, in particular regarding the […] dermal absorption of the products and should be provided by applicants at the product authorization stage".* In vitro human skin studies were not available at product authorisation for the large majority of products.

The results of the dermal absorption studies on permethrin containing PT8 and PT18 products (Table 6) show considerable differences in the dermal absorption values of permethrin even for very close or identical concentrations of the active substance. Although for some of the tested products a degree of similarity in their composition is found, it seems that the remaining differences in their ingredients lead to different dermal absorption values (See Annex III[7]). Additionally, differences in the dermal absorption values of water based and solvent based products are identified. The maximum dermal absorption found for a water based product is 12%, whereas for solvent based products with similar permethrin concentration dermal absorption values range from 1.6% up to 28%.

None of the compositions of the tested formulations is comparable to the composition of Konservan P 40.

Similarly, the solutions tested in US-EPA triple-pack approach were not comparable with the composition of Konservan P 40.

Overall and based on the results of the current analysis none of the available dermal absorption tests allow read-across to Konservan P 40.

In the absence of experimental dermal absorption data with Konservan P 40 and since read-across from other formulations is not possible, the use of the dermal absorption default value from EFSA Guidance is proposed.

Formally EFSA (2012) Guidance applies for Konservan P 40 application submitted in 2016. The default value of 75% for dilutions containing ≤ 5% active substance is applicable and used in the final version of PAR Oct. 2019. The EFSA 2012 does not include any default value for dermal absorption of dry residues as it is the case for Konservan P 40 uses in clothing and wool carpets.

The application of EFSA (2017) Guidance for Konservan P 40 would lead to the default value of 70% for EC formulations. Nevertheless, for the dry residues of Konservan P 40 where dermal absorption occurs through sweated skin (worst case) and as the main component of sweat is water, it is justified to consider the default EFSA 2017 value of 50% for water-based products. This value is well above the highest dermal absorption value of 28% measured in the dermal absorption studies conducted with different permethrin PT8 and PT18 products. Therefore, 50% can be considered as representing a conservative and more realistic default dermal absorption.

The use of **50%** dermal absorption value is supported as conservative and more realistic estimate for the dry residues of Konservan P40.

The detailed SECR assessment is included in Q2 Dermal absorption Assessment, where revisions based on the comments of the members of the Human Health WG and the applicant at the e-consultation launched in May 2021 have been also included.

[7] This information in Annex III is considered as confidential information and will be removed from the published opinion.

Question 3: Risk characterisation

ECHA is requested to determine whether the combination of both values established by ECHA, dermal absorption and the migration rate of permethrin, leads to the conclusion that the biocidal product 'Konservan P 40' has no unacceptable effects on the health of humans, taking into account the different uses envisaged and the relevant paths for human exposure for prosessional use and the general public and considering the proposed normal use of the biocidal product, together with realistic worst-case scenarios for each relevant path of exposure and thus, whether the conditons of Article 19(1)(b)(iii) are met.

Risk characterisation for use in clothing and treated carpets

The table below shows the results of the risk assessment when applying the proposed **1%** migration rate of permethrin from treated cloths and **0.5%** from treated wool carpets and using the dermal absorption default value of **50%** from EFSA (2017) Guidance for the dry residues of Konservan P 40. The exposure levels are compared with the $AEL_{medium/long\ term}$ of 0.05 mg/kg bw/day.

Table 7: Risk characterisation of Konservan P 40

Task/ Scenario	Tier	AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
Cutting and sewing textiles (migration rate **1%**)	Tier 1 no PPE	0.05	0.118	237%	No
	Tier 2 PPE: gloves	0.05	0.0233	46%	Yes
wearing treated cloths (migration rate **1%**) adult child 6-11 child 2-5 toddler infant	Tier 1 no PPE	0.05	0.147 0.208 0.230 0.252 0.296	293% 415% 460% 504% 538%	No No No No No
infant playing on treated carpet (migration rate **0.5%**)	Tier 1 no PPE	0.05	0.044	89%	Yes

Based on the exposure model calculations, the exposure to permethrin from clothing treated with Konservan P 40 **is not acceptable.**

The exposure from wool carpets treated with Konservan P 40 **is acceptable.**

The current assessment is based on the default dermal absorption value of 50%, which can be considered to overestimate the risk, although less conservative than the default values of 75% and 70%.

An in vitro human skin dermal absorption study according to OECD TG 428, designed to estimate dermal absorption of dry residues would be needed to establish a more realistic dermal absorption value for Konservan P 40 and to refine the assessment.

Conclusion based on model estimations

Based on model estimations alone, the approval for Konservan P 40 is supported for use in wool carpets but not in clothing.

The assessment considering biomonitoring studies found from the literature review on permethrin uses in clothing and wool carpets follows in the next section.

Assessment based on biomonitoring studies

Apart from the model calculations, biomonitoring studies provide valuable information on human exposure. Such studies are available for permethrin uses in clothing and carpets. The measured systemic human exposure can be compared with the AEL of 0.05 mg/kg bw/day to assess whether there is any health concern.

The BfR Opinion No. 006/2017[8], 25 April 2017 “Sensitization by Permethrin in textiles is unlikely” (in German, English Translation in Appendix 2), summarises the systemic human exposure levels measured in biomonitoring studies with permethrin impregnated clothing and carpets.

For German soldiers (Appel, 2008), an estimate of systemic exposure based on biomonitoring data (measurement of permethrin metabolites in urine) showed an internal body dose of 0.005-0.006 mg/kg bw/d from wearing permethrin-impregnated battle uniforms for median 50 hours per week for 4 weeks.

For U.S. soldiers (Proctor 2014, 2020), the systemic exposure was determined in ambient environmental conditions at 0.0004-0.0084 mg/kg/ bw/day (8 hours of wear for 3 consecutive days) and at 0.0003-0.014 mg/kg bw/d (31 hours of continuous wear) using biomonitoring data. Under conditions of 35°C and 40% relative humidity tested in Proctor 2020, the highest systemic exposure level was 0.010 mg/kg bw/d. The uniforms in Proctor 2014, 2020 studies were were newly purchased and washed once before distributed to soldiers.

For forest workers wearing impregnated pants, Rossbach (2016) determined a mean systemic exposure of 0.0005 mg/kg bw/d.

The application rates of permethrin in the uniforms used in biomonitoring studies comply with the WHO recommendation[9] of 0.125 mg/cm^2 and are comparable with the 0.13 mg/cm^2 application rate of Konservan P 40. The treatment method of the uniforms was by polymer coating which binds solubilized permethrin to the surface of the uniform fabric and provides more standardized concentration of permethrin compared to the immersion method used for Konservan P 40.

[8] https://mobil.bfr.bund.de/cm/343/allergien-sensibilisierung-durch-permethrin-in-textilien-ist-unwahrscheinlich.pdf
[9] Vector control : methods for use by individuals and communities / prepared by Jan A. Rozendaal (who.int)

For indoor exposure to permethrin, one biomoritoring study was found in homes equipped with permethrin-treated wool carpeting (Berger-Preiß, 2002). The study was carried out in 80 homes equipped with woollen wall-to-wall carpets or woven or knotted rugs and it included 145 inhabitants during a 2-year period. Based on the measured permethrin levels in carpet fibers, house dust, and airborne particles, the dermal, oral, and inhalation permethrin intake of young children under 6 years was estimated. This resulted in a total intake of 0.0017 mg/kg bw/d. The study has the following limitations:

- From the 80 households, only from 44 a woollen floor covering sample was taken for analysis. In 39 samples, permethrin was detected in amounts of 1 to 244.9 mg/kg wool (arithmetic mean: 54.6 mg/kg). The application rate of permethrin in Konservaqn P 40 is 0.06 % in the wool, equal to 240 mg permethrin/kg wool. This is in the range of the maximum dose found in Berger-Preiß study, but approximately five times above the arithmetic mean found in the woollen coverings. Hence, the permethrin concentrations in tested in Berger-Preiß 2002 are not representative of the use conditions for Konservan P 40.
- There is also no information to which extent the wool in these households was treated and on the age of these carpets.
- There is no comprehensive information on other permethrin sources.
- The study is focused on inhalation exposure. The role of dermal exposure is examined and discussed only marginally. Only for inhalation exposure, models are included. Hence, any conclusion on dermal exposure of smaller children is questionable.
- The total systemic exposure of 0.0017 mg/kg bw/d from wool carpets was estimated for children under 6 years using model caclulations and a dermal absorption of 2%. The use of a dermal absorption value which cannot be assessed introduces considerable uncertainty.

These points show that Berger-Preiß study addresses the exposure conditions several years after application and therefore, is not appropriate to be used for the assessment of the intended use of Konservan P 40 in carpets where the exposure assessment has to be performed under realistic worst case conditions. So, there is no reliable biomonitoring data for the use in wool carpets.

Uncertainty assessment of systemic exposure levels from biomonitoring studies on clothing

The uncertainty in the measurements of systemic exposure to permethrin from biomonitoring studies, and in their applicability to Konservan P 40 is due to the following reasons:

- The volunteers in the biomonitoring studies of Proctor 2014, 2020 and Rossbach (2016) were only males. The Appel 2008 study included female workers but their number is not provided. The average age of tested forestry workers was 44.5 (19 - 61) in Rossbach study, 21.5 (19 - 28) in Proctor 2014, and 18-27 years in Proctor 2020 (average age not provided). In Appel study the age of the volunteers is not indicated; there is only reference to the measurements from two volunteers 21 and 45 years old. Based on the above, it is concluded that the biomonitoring data on clothing were derived mainly from young or middle-age males who were physically active. A lower number of females soldiers and/or army stuff was included who were likely of young age and in good health.

- The uniforms used in biomonitoring studies were treated with polymer coating whereas the treatment of fabrics with Konservan P 40 is done with immersion using binders for the stabilisation of permethrin into the fabric[10].

  To investigate which method stabilises better permethrin into the fabric, information can be derived from efficacy section, page 51 of Konservan PAR, Oct. 2019. The treated fabric provided a complete protection against the bites of ticks at the dose 1236 mg/m², whereas efficacy remained the same after 30 washes at 60°C on sample treated at the dose 493 mg/m². This equals to 60% loss of permethrin. Faudle, 2006 reports for fabric treated with polymer coating method, concentration of permethrin of 550 mg/m2 after 30 washings at 60°C from initial concentration of 1300 mg/cm2 which equals to 58% of permethrin loss. Therefore, it seems that the stabilisation of permethrin into fabric using either method is similar.

- Biomonitoring studies measured the main urinary metabolites of permethrin (cis- and trans-Cl2CA (DCCA) and 3-BPA), whereas small amounts of other urinary metabolites are also formed but were not recorded.

- Additional excretion routes were not considered. The parenteral application of permethrin in humans required for exact determination is not possible because of ethical reasons. In animal experiments, e.g., in rhesus monkeys, certain amounts of cis-permethrin are also excreted in bile via faeces (Sidon, 1988). The authors of Appel 2008 study suggest that inclusion of the missing, non-identified metabolites and faecal excretion could result in approximately 25% higher internal exposure which they added to the calculated internal exposure.

- Urine was collected in the morning in Appel 2008 and Rossbach 2016 studies. The impregnated uniforms had not been worn for several hours in the night before taking the samples. An additional, slightly higher internal exposure could therefore be assumed. This limitation does not apply for urinary sampling after continuous exposure up to 33 hours in Proctor 2014, 2020 studies.

- It has not been fully investigated whether longer-term, routine wear of the treated clothing potentially influences systemic exposure. The exposure levels observed over the deployment period in Appel 2008 were similar after 14 and 28 days of wearing for 16 hours per day (Fig.2). This suggests that systemic exposure appears to stabilize over weeks of wear time.

- The current biomonitoring data cannot cover age-based or health-based differences which are relevant for children, the elderly and individuals in poor health. In the absence of biomonitoring data, it is not possible to conclude on safe use for the general public, and therefore a Risk Mitigation Measure should be applied. Garment treated with Konservan P 40 is intended to be worn by the military, forest workers or by the general public during trekking. In order to exclude exposure of children and to protect the general public, the treated garment should be used to manufacture cloths for military and forestry workers only.

[10] There are two companies who market Konservan P40: Thor SARL and CHT GmbH. Thor SARL is the authorisation holder. Knife coating is another treatment method used only by CHT GmbH who stated that it is not expected that the application method has an impact on the migration rate as the active substance is embedded in the binder matrix which is applied as a complete system (information provided in e-mail communication with the consultant for Konservan P 40).

To account for the uncertainties above, it is proposed:

- To address the main source of uncertainty which is the non coverage of the general population by the biomonitored individuals, by applying the Risk Mitigation Measure for Konservan P 40: Do not use for manufacturing of clothing intended for the general public.
- For the rest of the uncertainties, the maximum individual exposure measured in all biomonitoring studies was considered. Biomonitoring studies on permethrin forestry and army uniforms included almost 400 individuals. The maximum individual systemic exposure measured was **0.014 mg/kg bw/d** (31 hours continuous wear, Proctor 2014).
- An uncertainty factor (UF) of **2.5** is applied to this value to address the remaining uncertainties. This means that 250% increased systemic exposure is considered from the highest individual exposure measured after high exposure conditions. The calculated systemic exposure is 0.014 x 2.5 = **0.035 mg/kg bw/d** which is **70% of the AEL** of 0.05 mg/kg bw/d.

Overall, with the proposed RMM and worst case exposure value combined with conservative UF, the estimated systemic exposure is below the AEL value. This supports the absence of health concern regarding the exposure to permethrin from its use in Konservan P 40 for clothing for professionals in the army and forestry.

Conclusion on risk characterisation based on biomonitoring studies

Biomonitoring data is considered to allow a realistic and more reliable risk assessment than modelling estimations with default values for the risk characterisation of the product Konservan P 40 in treated clothing.

Therefore, **the approval of Konservan P 40 for the use in clothing is supported** based on biomonitoring data with uncertainty analysis and Risk Mitigation Measure: Do not use for manufacturing of clothing intended for the general public.

Overall conclusion

- The use of Konservan P 40 in wool carpets **is acceptable** based on model calculations of exposure. **The conditions of Article 19(1)(b)(iii) are met for this use.**
- Based on model calculation safe use of Konservan P 40 in clothing could not be identified, while the use in clothing **is supported** based on biomonitoring data with uncertainty analysis and Risk Mitigation Measure: Do not use for manufacturing of clothing intended for the general public. **The conditions of Article 19(1)(b)(iii) are met for this use.**

BACKGROUND INFORMATION ON:

- **Q1: Migration rate Assessment**
- **Q2: Dermal absorption Assessment**

Q1 Migration rate Assessment

Background information on the use and measurement of migration rate

Migration rates and transfer coefficients of substances provide a way to estimate indirectly dermal exposure[11]. In order to overcome the limitation of measuring the active substance on the skin, that is often below the detection limit of the analytical method used, the migration (leaching) out of an article is measured instead, as precursor process. The common idea is to determine the rate or the relevant mass percentage of the migration. Migration rate is then used to calculate a dermal exposure estimate. Generally, this approach needs to be used with caution, as this simplification assumes that dermal exposure is linearly dependent on time and/or environmental concentration.

The current dosage methods of insecticides like permethrin in impregnated fabrics do not enable measurement of the concentration of effective active ingredient present (i.e. bioavailable) on the surface of the fabric. All current methods are based on total insecticide extraction measured by weight (mass concentration), resulting in overestimation of dermal exposure related to the use of treated fabric (Dieval, 2017).

Migration rate can be measured directly by:

- models of sweat-mediated transfer of chemicals from clothing (Dusan 2019). Often, the extracted fraction is assumed to be entirely transferred to the skin. Such an approach is likely to overestimate exposures, since only a fraction of the sweat will return to the skin from clothing.
- dermal exposure studies in human subjects wearing dosimeter clothing. This method is considered the more accurate and reliable. No such study is available for permethrin.

Migration rate can be measured indirectly by:

- assessment of dermal exposure in experimental animals exposed to swatches of fabric impregnated with radio-labeled permethrin. Dermal exposure is measured as the radiolabel in excreta plus that recovered from the skin and bindings (Snodgrass 1992).
- human biomonitoring studies of urinary permethrin metabolites measuring internal exposure (Appel, 2008).

Migration rate of permethrin from clothing and wool carpets treated with Konservan P 40

The migration rate of permethrin is influenced by the following factors:

- Treatment method used (e.g. spray treatment, immersion baths (textile manufacturing and home users), polymer coating of fibers, integration into synthetic fibers during the spinning process, micro- and nano-encapsulation);
- use of binders to fix permethrin in the treated fabric;
- Type of fabric (wool, cotton, nylon, blend);
- Washable, non-washable fabric;
- Test formulation;
- Application rate (mg of a.s./cm^2 of fabric).

[11] IPCS, WHO guidance on Dermal Exposure: https://www.who.int/ipcs/publications/ehc/ehc_242.pdf?ua=1

Other factors that may alter the rate of migration are climate (temperature, humidity), sweating and the effects of laundering. Biomonitoring findings suggest that wearing permethrin-treated clothing in hot conditions and high humidity results in higher internal dose of permethrin than under ambient conditions (Proctor, 2020), which indicates higher dermal exposure and/or migration rate of permethrin from the treated clothing. Repeated washing of the impregnated textile seems to have little effect on the relative migration rate, and only resulted in a decrease in permethrin content (Snodgrass, 1992).

The decision on the best option for the migration rate of permethrin would depend on how sufficiently, specifically and reliably the selected option would cover the above factors for the treated articles of Konservan P 40.

The available options on migration rates as found by the screening of permethrin products and the literature search are presented in Table1.

Table 1: migration rates used in permethrin products and calculated in open literature studies

No	Product	Permethrin Content	Type^	Binder	Treatment method	Application rate mg/cm^2	Exposure Scenario	Migration rate	Migration rate Derivation
1.	Nonax 2008-EU	15.35%	CS	Nonax-3009-A + Nonax 3001-A	immersion	0.16	clothing	**20%**	**default value** for cotton and knitwear according to Biocides Human Health Exposure Methodology 2015.
2.	Insecticide Textile Contact	0.86%	EW	No	spraying	5.0	clothing	**20%**	
3.	EULAN SPA 01	10%	EC	No	immersion	0.0625	contact with wool carpet	**1%**	**considered in CAR** 2014, with representative product EULAN SPA 01 with only **use in wool carpets.**
4.	KONSERVAN P 40	40%	EC	- Added in textiles for clothing - Not added in wool for carpets	- Immersion - knife-coating	0.13 (fabrics) 0.06% w/w (carpets)	• clothing • contact with wool carpet	**0.1%**	**default value in BfR Opinion** No. 041/2012, 2012.

No	Product	Permethrin Content	Type^	Binder	Treatment method	Application rate mg/cm^2	Exposure Scenario	Migration rate	Migration rate Derivation
5.	Pounce 3.2 EC (Snodgrass, 1992)*	38.40%	EC	No	immersion	0.125	clothing	**0.5 % ** **	**measured mean daily migration for permethrin** as portion of the available ^{14}C radiolabelled impregnant appearing in excreta (absorbed) plus that recovered from the skin and bindings (unabsorbed). Max migration was **0.65 %** for sweated cotton fabric in subtropical environment.
6.	Danish EPA survey, 2014 on residues of biocidal active substances. in clothing	NA	NA	NA	NA	NA	Woolen clothing	**NA**	**Migration was measured in artificial sweat** where it was not possible to analyse directly the concentration of permethrin; thus no reliable estimate of migration rate can be calculated from the study.
7.	Not known (Appel, 2008)*	--	--	Polymer	Coating of fabric with permethrin containing polymer	0.13	clothing	**1 %**	**calculated for permethrin** from measured internal dose 5 µg/kg bw/d [dermal absorption of 2%, dose reaching the skin 5/0.02= 250 µg/kg bw/d,

No	Product	Permethrin Content	Type^	Binder	Treatment method	Application rate mg/cm^2	Exposure Scenario	Migration rate	Migration rate Derivation
									standard bw 75 kg, area covered by the uniform 1.5 m2 (US-EPA, 1989), exposure level 1.2 µg permethrin/cm^{2}skin /day, 130 µg permethrin/cm^2 content of tested uniforms].

***:** Summary of the studies is included in Annex II.

****:** rounded value from 0.49%.

^: CS: capsule suspension; EW: emulsion, oil in water; EC: emulsifiable concentrate

NA: not available or not applicable

The migration rates vary from 20% to 0.1%. In order to decide which of the available values is the most appropriate for the uses of Konservan P 40 in clothing and wool carpets, assessment of the shortcomings and advantanges of each value is needed. In addition, all the experimental or biomonitoring data are based on migration from clothing and not from wool carpets, whereas the default value of 0.1% (BfR Opinion) seems to be based on experimental data in artificial sweat as presented in Table 2. The default transfer coefficient of 9% for dried fluid residues in carpets from Biocides Human Health Exposure Methodology is also added as an option.

Table 2: Assessment of migration rate options

Migration rate	Applicability	Pros	Cons	Conclusion
20 % **(default biocides HH exposure methodology)**	fabrics for clothing	• Used in Nonax 2008 EU and BC-JR023293-31 PARs. • Agreed by the members in WGI2020_7-2 for product Insecticide Textile Contact "*in the absence of clear justification for any other leachable fraction / transfer coefficient value*".	• Low specificity. • Low confidence.	More specific values available.
9 % **(default biocides HH exposure methodology)**	Carpet	• Default value for dried fluid residues in carpets from Biocides HH Exposure Methodology	• Based on study[12] with fogger treatment. Not applicable for Konservan P 40.	Not to be used.
1 %	- Fabrics for clothing - wool carpet	• Calculated from human biomonitoring study Appel 2008. • Specific for permethrin • Specific for army battle uniforms • Measured in humans (soldiers) • Same application rate with Konservan P 40 (0.13 mg/cm^2) • Can be used also for wool carpets as conservative estimate • Used in CAR, 2014, as reasonable worst case estimate for wool carpets.	• Calculated based on estimation of 2% dermal absorption taken from California EPA assessment, 1994. Reliability of this value cannot be assessed. • Different treatment method with Konservan P 40. • Study conducted in order to measure the internal exposure, not the migration rate.	Can be used as option for the migration rate.

[12] J. Ross, 1990, Measuring potential dermal transfer of surface pesticide residue generated from indoor fogger use: An interim report; Chemosphere Volume 20, Issues 3–4, 1990, Pages 349-360.

Migration rate	Applicability	Pros	Cons	Conclusion
0.5%	- Fabrics for clothing - wool carpet	• Study Snodgrass 1992 specifically designed to quantitate permethrin migration rate from treated military fabrics under conditions simulating actual wear. • Specific for permethrin. • Almost same application rate and application method with Konservan P 40. • Similar concentration of permethrin and same formulation type (EC) in product Konservan P 40 and Pounce 3.2. • Two types of textiles tested (cotton, mixed cotton/nylon). • Other factors tested (sweating, laundering). • Can be used also for wool carpets as conservative estimate. • Conservative value in terms that it is measured for continuous 24 hrs daily exposure to cloth swatch attached on the skin. • Used by US-EPA for permethrin migration from treated clothing.	• Conducted in rabbits. • 40/60 cis/trans permethrin tested, whereas 25/75 cis/trans permethrin contained in Konservan P 40. • Possible accumulation of lipophilic permethrin to tissues not measured.	Highly specific for permethrin and for measurement of migration rate. To be used as option for the migration rate.
0.1% **(default BfR opi.041/2021)**	- Fabrics for clothing - wool carpet	• Default value for Hydrophobic textile auxiliary in BfR Opinion No. 041/2012, based on publication Krätke, 2004 • Used in final PAR Konservan P 40.	• Krätke 2004, reports that the value of 0.1% was "*Based on experimental data from hydrophobic substances, which are only slightly soluble in sweat; in the case of appropriate investigations, a possible migration was almost always below the detection limit*". • Not clear how this value was estimated. • High uncertainty • Low specificity of the value for permethrin impregnated clothing and wool carpets.	More specific values available.

Comparative assessment of migration rate values

For the comparative assessment of migration rate values, the default values are assessed first and the experimental values follow.

20% migration rate: default value, proposed not to be used since more specific values for the migration of Konservan P 40 in dry residues are available.

9% migration rate: default value determined from data on fogger application, not applicable for Konservan P 40.

0.1% migration rate: default value from BfR opinion 041/2012, proposed not to be used since there is high uncertainty about the scientific data and studies from which derived. The data and studies are not available and no independent scientific assessment can be performed to assess the reliability of this value and how it was derived.

0.5% migration rate: was measured in Snodgrass 1992 for cotton and cotton/nylon fabrics.

1% migration rate: was used in CAR as reasonable worst case estimate for wool carpets and measured for clothing in Appel 2008.

As the type of fabric influences the migration rate, and the uses of Konservan are on cotton, cotton/synthetic fabric for clothing and wool carpets, the assessment of migration rate is performed separately for the 1st use in clothing and the 2nd use in carpets.

Migration rate for clothing

Two options are available, 0.5% from Snodgrass 1992 and 1% from Appel 2008.

The 0.5% migration rate from Snodgrass study is considered the most specific value for Konservan P 40: it has been measured for a similar product in terms of formulation type and permethrin concentration and with similar application rate and treatment method with Konservan P 40. In addition, the objective of the study was to measure the migration rate, whereas in Appel study the objective was to measure the internal exposure of volunteers.

The migration rate Snodgrass 1992 was calculated as the amount of radiolabel detected in excreta plus the amount recovered from skin and bindings. Any amount in exhaled air or any systemic permethrin binding to macromolecules or bioaccumulation in tissues as amount in carcass was not measured, which may lead to underestimation of exposure. In addition, no permethrin metabolite was detected in feces in Snodgrass study. There is no explanation about this by the authors, but it could be due to limitations in the analytical method used.

To overcome these problems, the migrated amount can also be estimated from the difference of the applied amount and the amount that remained on the test fabric and the bindings. For this calculation, it is appropriate to normalise the numbers on 100 % recovery. Using this approach, the migration rate is 0.52%. Comparing this value to the migration rate of 0.49% derived by Snodgrass 1992 and rounded to 0.5%, it is clear that the impact of the amount in the carcass, feces and exhaled air is minimal.

On the other hand, the continuous exposure to cloth swatches attached on the skin of rabbits for the 7 days of study duration in Snodgrass 1992 leads to overestimation of exposure. In addition, in Snodgrass 1992 no binder was used to stabilise permethrin into the cloth, whereas in Konservan P 40 application in fabrics, permethrin is embedded in a binder matrix which is applied as a complete system to the fabric. This is also likely to lead to overestimation of migration in Snodgrass 1992.

In Appel 2008, the migration rate was calculated from the amount reaching the skin as internal exposure assuming 2% dermal absorption. The use of the dermal absorption value which cannot be assessed introduces considerable uncertainty in the estimation of the migration rate. Only urinary metabolites were measured in Appel study. It was estimated that non-identified metabolites and faecal excretion could result in approximately 25% higher internal exposure, which was added to the calculated internal exposure.

In Snodgrass study, the product used for cloth treatment contained cis:trans-permethrin 40:60. Considering that 50% of cis isomer and 80% of trans isomer are excreted in urine, the migration rate 0.5% from Snodgrass study might underestimate the migration rate of permethrin in Konservan P 40 which contains cis:trans-permethrin 25:75. Other studies (NAP, 1994) show greater retention of the cis isomer in body tissues and especially in fat.

In addition, the Snodgrass study was performed in rabbits and although physical transfer of permethrin from cloth to skin should be similar in humans and rabbits, the migration rate was measured as the percentage of ^{14}C recovered from excreta and deposits on skin surface. Therefore, the metabolism and the dermal absorption in rabbits were factors that impacted the calculation of the migration rate. In general the rabbit skin is more absorptive than human skin, therefore the dermal absorption and the amount of radiolabel in excreta is expected to be higher in rabbits than in humans. On the other hand, differences in metabolism between humans and rabbits may exist and their impact on migration rate cannot be assessed.

Overall, although being the most specific study, the Snodgrass study has limitations that may increase the uncertainty on the migration rate measured. To cover for this uncertainty, an increase from 0.5% to **1%** migration rate is considered reasonable and conservative enough to estimate the migration rate from treated cloths. The 1% migration rate estimated from Appel 2008 can be considered as supportive of this value.

Migration rate for wool carpet

Two options are available, **0.5%** from Snodgrass 1992 and **1%** from CAR, 2014.

The 1% migration rate from CAR, was considered as worst case estimate for the migration of permethrin from wool carpets. It is not supported by experimental data.

The 0.5% was measured in the Snodgrass study for clothing fabrics under continuous exposure for 7 days, whereas, the worst-case conditions of exposure from woollen carpets is a child playing on carpet touching the surface of carpet with sweated hands. Therefore, the conditions used in Snodgrass study overestimate the conditions of exposure from carpets. This overestimation balances the weaknesses of the study and consequently for the estimation of migration from woollen carpets, the measured migration rate of 0.5% can be considered.

In addition, the default migration rate values (20% for cotton and knitwear; 9% for carpets), show that much lower migration rate is expected from carpets than from clothing fabrics.

Overall, **0.5%** is considered a reasonable and conservative enough value for the migration rate of permethrin from wool carpets.

Conclusion on migration rate

Use in clothing: **1%** is considered as the most appropriate value to provide a reasonable and reliable estimate of the migration of permethrin from treated cloths.

Use in wool carpets: **0.5%** is considered the most appropriate value to provide specific and reliable estimate of permethrin migration from treated wool carpets.

Q2 Dermal absorption Assessment

Background information on the dermal absorption assessment of Konservan P 40

For the uses in clothing and wool carpets, the absorption of the dried residue on skin is relevant. In the absence of specific dermal absorption data for the biocidal product, FR eCA used a default dermal absorption for dried residues of 75% for risk assessment of Konservan P 40 (See final PAR, Oct.2019).

As indicated by the eCA in the PAR, the bridging with the dermal absorption value (3%) set in the CAR of permethrin was not considered acceptable since it is based on a study carried out with the active substance alone, not considering the impact of the different formulants present in the product. The eCA argument applies also for the human volunteer dermal absorption studies conducted with permethrin in organic solvents (listed in Annex I), and proposed for read across by the applicant.

Moreover, KONSERVAN P 40 is classified skin sens 1 – H317 due to its content of permethrin which is not the case for the tested formulations in the dermal absorption studies above. Therefore, in accordance with the applicable dermal absorption guidance (EFSA Journal 2012; 10(4):2665), the default value of 75% has been used to perform the risk assessment for the exposure scenarios of wearing treated garment (adults, children) and infant crawling on treated carpet.

US-EPA assessment of dermal absorption

The US-EPA assessment is based on the triple pack approach using the rat and human *in vitro* dermal absorption data with the rat *in vivo* dermal absorption data and is included in Appendix 1. The results are summarised below.

Table 3: US-EPA evaluation; Permethrin Dermal Absorption Using the Triple Pack Approach

	Dermal absorption (% of application)		
	Permethrin (µg/cm^2)		
	2.25	20	200
Human/ *in vitro*	1.3	2.7	2.1
Rat/ *in vitro*	20	18	24
Rat/ *in vivo* (1 day)	22	22	28
Rat/ *in vivo* (5 day)	38	38	30
Estimated Human/ *in vivo* (1 day)	**1.4**	**3.3**	**2.5**
Estimated Human/ *in vivo* (5 day)	**2.5**	**5.7**	**2.7**

In the Evaluations listed in Table 4, US-EPA has set the dermal absorption of permethrin either at 3.3% or 5.7% for all uses and scenarios assessed. US-EPA used in 2009 assessment the most conservative value of 5.7% estimated at 120 hours after administration, whereas in the more recent evaluations from 2017 and 2020, the value of 3.3% is used by considering the *in vivo* dermal absorption in rats at 10 hours after administration.

Table 4: Dermal absorption values used by US-EPA (Source www.regulations.gov)

Year	Document Title	Dermal absorption value	Dermal Absorption assessment and conclusion quoted from US-EPA's documents
2009	Permethrin: 6th revision of the HED chapter of RED document.	**5.7 %**	*The estimated in vivo human dermal absorption factors ranged from 1.4% to 5.7%. Based on the rat in vivo study, the increase in absorption at 120 hours indicated that radiolabel (permethrin) remaining in the skin after washing at 24 hours was bioavailable. Also, the in vivo or in vitro absorption of permethrin was relatively consistent at all three doses. Therefore, 5.7% is the selected dermal absorption factor for use in permethrin exposure and risk assessments. It should be noted that 5.7% was the highest estimated human in vivo dermal absorption using the parallelogram approach for permethrin and thus, the revised cancer risk assessments using this dermal absorption factor should be considered conservative in nature.*
2017	Permethrin. Occupational and Residential Exposure Assessment for Registration Review	**3.3 %**	*Data are available to allow for use of the triple pack approach, including an in vivo rat dermal penetration study and an in vitro dermal absorption study using both rat and human skin. The in vivo dermal penetration study in rats indicated a dermal absorption factor of 21.7%, at 10 hours after administration. The comparative in vitro dermal penetration study using human and rat skin showed that 18% of an applied dose was absorbed through rat skin and 2.3% through human skin, which indicates that in vitro rat skin is 6.6 times more permeable than in vitro human skin. Therefore, a dermal absorption factor of 21.7/ 6.6 = 3.3% is considered appropriate for cancer risk assessment.*
2020	Permethrin: Human Health Risk Assessment for New Use on "Fruit, Small, Vine Climbing, Except Fuzzy Kiwifruit, Subgroup 13-07F"; Multiple Crop Group Conversions/Expansions; and the Establishment of a Tolerance without a U.S. Registration for Tea, AND the Revised Draft Risk Assessment (DRA) for Registration Review.	**3.3 %**	*The permethrin PK profile is similar to the general PK profile of other pyrethroids, i.e., rapid absorption and clearance and extensive metabolism. Data are available to allow for use of the triple pack approach, including an in vivo rat dermal penetration study and an in vitro dermal absorption study using both rat and human skin. The in vivo dermal penetration study in rats indicated a dermal absorption factor of 21.7%, at 10 hours after administration. The comparative in vitro dermal penetration study using human and rat skin showed that 18% of an applied dose was absorbed through rat skin and 2.3% through human skin, which indicates that in vitro rat skin is 6.6 times more permeable than in vitro human skin. Therefore, a dermal absorption factor of 21.7/6.6 = 3.3% is considered appropriate for risk assessment.*

Notably, in the most recent assessment of 2020, no dermal exposure assessment is

performed with the justification that "*No effects observed in the dermal toxicity study, and low dermal absorption based on dermal penetration studies. Using the oral data with the dermal penetration factor would lead to a Point of Departure near the limit dose*". The assessment includes a wide variety of uses and exposure scenarios, for which dermal exposure assessments are missing (See Table 6.1.1 on page 33, "Residential handler exposure an drisk estimated for permethrin" and Section 6.2, page 36, "Residential Post-Application Exposure and Risk Estimates").

Conclusion on US-EPA dermal absorption values

All tested permethrin solutions in US-EPA triple pack approach were prepared in ethanol and are not comparable to Konservan P 40 composition. Further, much higher dermal absorption values than 2.7% have been measured for permethrin products in *in vitro* human skin dermal absorption studies (see Table 6 below), and therefore the value used by US-EPA is not considered a reliable estimate for the purpose of this opinion. Therefore, the use of the US-EPA values for addressing the dermal absorption of the dried residue of Konservan P 40 is not supported.

Dermal absorption values from other permethrin products under BPR

A search was performed in R4BP3 in order to find permethrin PT18 products with similar uses to Konservan P 40 and to report the dermal absorption values used for the scenarios of wearing clothing or contact with wool carpet. The dermal absorption values are listed in Table 5. All values were peer reviewed, i.e. commented under mutual recognition of National Authorisations or under Union Authorisations.

Table 5: Dermal absorption values of Permethrin PT18 products with uses similar to Konservan P 40

No	Product (authorisation)	Permethrin Content	Type #	C&L (HH)	Application rate mg/cm²	Exposure Scenario	Dermal absorption	Dermal absorption Derivation and impact on exposure assessment
1.	Nonax 2008-EU (NA-APP)	15.35 %	CS	**Skin Sens. 1**	0.16	clothing	**5.7%**	**US-EPA most conservative triple pack value**. Exposure **<u>is unacceptable even with 75% dermal absorption</u>** as calculated by FR who disagreed on 5.7% due to high uncertainty, but agreed to close the point.
2.	EULAN SPA 01(NA-APP)	10%	EC	Eye Irrit. 2	0.0625	contact with wool carpet	**3%**	**CAR 2014 value**, with representative product EULAN SPA 01.
3.	KONSERVAN P 40 (NA-APP)	40%	EC	**Skin Sens 1** Acute oral tox. Cat 4	0.13	• clothing • contact with wool carpet	**75%**	**Default value, EFSA 2012** During CG-37 discussion and referral of Konservan P 40, FR eCA proposed 3% dermal absorption combined with 1% migration rate. DE and BE disagreed supporting 75% dermal absorption and 1% migration rate, **leading to unacceptable exposure.**

No	Product (authorisation)	Permethrin Content	Type #	C&L (HH)	Application rate mg/cm²	Exposure Scenario	Dermal absorption	Dermal absorption Derivation and impact on exposure assessment
4.	Insecticide Textile Contact (UA-APP)	0.86 %	EW	Null	5.0	clothing	**50 % ***	**Default value, EFSA 2017. Leads to unacceptable exposure assessment (negative BPC opinion)**. BE eCA proposed originally 5.7%, not accepted by WG members.
5.	BC-GK024706-40^ (UA-APP)	0.9%	net	Null	0.027	Sleeping under permethrin impregnated bednet, 1/3 of body surface in contact with net	**3 % ****	**CAR 2014 value, <u>assessment is acceptable even with 50 % default</u>** EFSA 2017 value, as calculated in NL comments. Read-across to the CAR data was agreed since: - the tested solution in the CAR study was considered worst case with respect to the bednet in terms of active substance concentration and co-formulants. - BC-GK024706-40 is not classified as skin sensitiser.

***** agreed at the AHFU of WGI2020; ****** agreed at WGI2021; **^**: PAR not publicly available; **NA-APP**: national authorisation; **UA-APP**: union authorisation; **#**: CS: capsule suspension; EW: emulsion, oil in water; EC: emulsifiable concentrate.

Table 5 shows that after the finalisation of the permethrin CAR in 2014, the product evaluations have either used or considered the EFSA default values, and authorisation has been granted only to products with acceptable exposure assessment with the use of default values.

It also indicates the absence of product specific data despite flagging this in the permethrin CAR Doc IIA, 2014: "*At* product *authorisation a dermal absorption study in vitro on human skin will be required for each formulation type*"; and the note in permethrin PT18 BPC opinion, 2014: "*Further data may be required, in particular regarding the […] dermal absorption of the products and should be provided by applicants at the product authorization stage".* In vitro human skin studies were not available at product authorisation for the large majority of products.

Considering the proposal of 1% and 0.5% of migration rates in the present opinion, which leads to non acceptable exposure scenarios if combined with 75% dermal absorption, a screening in R4BP3 of all permethrin PT8 and PT18 products was performed in order to identify the products tested for dermal absorption and to investigate whether read-across and refinement of Konservan P 40 dermal absorption would be possible. The results are presented in Table 6. All products have been tested in the in vitro human skin dermal absorption test according to OECD TG 428.

The applicant submitted also a proposal for read across and refinement based on *in vitro* dermal absorption studies (Webbley, 2015) testing Preventol Products, which are presented in Table 6. The applicant supported that "*Since the rate of absorption is generally inversely*

related to the *concentration of the active substance, the available in-vitro data on Permethrin derived from various formulation (Webbley 2015a,b) overestimate dermal absorption of formulation containing higher content of Permethrin. A read-across is considered justified. Therefore a dermal absorption value of 3 % for water based products and 10 % for solvent based products as a conservative realistic worst-case assumption should be considered for the product. In focus of the risk assessment is the exposure occurring during handling and wearing of impregnated textiles containing the BP Konservan® P 40. Only the Permethrin content which is extractable via sweat (aqueous adsorption) is of relevance. A dermal absorption rate of 3 % as a conservative realistic worst-case approach is therefore applicable*".

Table 6: Permethrin products tested for dermal absorption

Product	Product Type	Active substances	Formulation Type tested	% permethrin tested	Dermal Absorption	study reference, EFSA GD
Indorex Spray	PT18	Permethrin,pyriproxyfen	AL Solvent based	**0.018**	**28%**	[OECD 428, Raynaud, 2016] EFSA 2012
Indorex pumpspray	PT18	Permethrin,pyriproxyfen	AL Water based	**0.091**	**12%**	[OECD 428, Raynaud, 2016] EFSA 2012
Indorex fogger	PT18	Permethrin,pyriproxyfen	AD Solvent based	**0.12**	**16%**	[OECD 428, Raynaud, 2016] EFSA 2012
BC-HT023609-18^	PT08	Permethrin	ME	**0.25**	**17%**	[OECD 428, Brufau Donés, 2016] EFSA 2012
BC-KD023607-51^	PT08	Permethrin, IPBC,Propiconazole	AL Water based	**0.25**	**2%**	[OECD 428, Brufau Donés, 2016] EFSA 2012
Preventol Pimer TIP	PT08	Permethrin Tebuconazole IPBC	Solvent based	**0.06**	**10.42%**	[OECD 428; Webbley, 2015] EFSA 2012
Preventol Aqua Primer PIP	PT08	Permethrin Propiconazole IPBC	Water based	**0.1**	**2.62%**	[OECD 428; Webbley, 2015] EFSA 2012

Product	Product Type	Active substances	Formulation Type tested	% permethrin tested	Dermal Absorption	study reference, EFSA GD
Preventol Aqua Primer PIP Termites	PT08	Permethrin Propiconazole IPBC	Water based	**0.4**	**1.60%**	[OECD 428; Webbley, 2015] EFSA 2012
TX201 TRAITEMENT MEUBLES PARQUETS	PT08	Permethrin	AL Solvent based	**0.7**	**28%**	[OECD 428, Bernal J. 2015] EFSA 2012
V33 TRAITEMENT POUTRES ET CHARPENTES	PT08	Permethrin	AL Water based	**0.6**	**4%**	[OECD 428, Bernal J. 2015] EFSA 2012

AL: any other liquid or Ready to use microemulsion; **ME**: Micro-emulsion; **AD**: Aerosol dispenser; **^**: PARs not publicly available yet, products approved.

The results show considerable differences in the dermal absorption values of permethrin even for very close or identical concentrations of the active substance. Although for some of the tested products a degree of similarity in their composition is found, it seems that the remaining differences in their ingredients lead to different dermal absorption values (See Annex III). Additionally, differences in the dermal absorption values of water based and solvent based products are identified. A water based product (Indorex Pump Spray) shows a dermal absorption of 12%, whereas for solvent based products with similar permethrin concentration dermal absorption values range from 1.6% up to 28%. None of the compositions of the tested formulations is comparable to Konservan P 40.

Overall and based on the results of the current analysis none of the dermal absorption tests presented allows read across to Konservan P 40.

Conclusion on dermal absorption

In the absence of experimental dermal absorption data with Konservan P 40 and since read across from other formulations is not possible, the use of the dermal absorption default value from EFSA Guidance is proposed. This approach is consistent with PAR evaluations after finalisation of permethrin CAR, 2014.

Formally EFSA (2012) Guidance applies for Konservan P 40 application submitted in 2016. The default value of 75% for dilutions containing ≤ 5% active substance is applicable and used in the final version of PAR Oct. 2019. The EFSA 2012 does not include any default value for dermal absorption of dry residues as it is the case for Konservan P 40 uses in clothing and wool carpets.

The application of EFSA (2017) Guidance for Konservan P 40 would lead to the default values of 70% for EC formulations. Nevertheless, for the dry residues of the product where dermal absorption occurs through sweated skin (worst case) and as the main component of sweat is water, it is justified to consider the default EFSA 2017 value of **50%** for water-based products. This value is well above the highest dermal absorption value of 28% measured in a considerable number of dermal absorption studies conducted with different permethrin products. Therefore, 50% can be considered as representing a conservative and more realistic

default dermal absorption.

The use of **50 %** dermal absorption value is supported as conservative and more realistic estimate for the dry residues of Konservan P 40.

Annex I

List of information provided by the applicant after WGI2021:

1. BfR Opinion No. 006/2017, 25. April 2017 (in German): https://mobil.bfr.bund.de/cm/343/allergien-sensibilisierung-durch-permethrin-in-textilien-ist-unwahrscheinlich.pdf ;

2. BfR Opinion No. 006/2017, 25. April 2017 (translated): Allergies: sensitization by Permethrin in textiles is unlikely.

3. Allsup et all, 1986, Clinical study “The perculaneous absoprton of Topically applied 14C-Permethrin in normal volunteers”.

4. Bartelt and Hubbell, 1987, Clinical study “Perculaneous absoprton of Topically applied 14C-Permethrin in volunteers”. [Original study report of the CAR 2014 dermal absorption study, Section A6.2, Annex Point IIA6.2(2) Percutaneous absorption (in vivo test - human)]

5. Konservan® P 40 - Dermal absorption of Permethrin, Thor GmbH Konservan® P 40, 26.09.2019. [Applicant’s position paper]

6. Table of three permethrin PT8 products owned by Lanxess Deutschland GmbH and tested in vitro for dermal absorption.

7. Webbley 2015, Addendum to Final Report, [14C]-Permethrin: In Vitro Dermal Penetration Study for product Preventol Primer TIP. [Calculation of the potentially absorbed dose for the purposes of derivation of a dermal absorption value]

Annex II

References

Snodgrass et al, 1992, PERMETHRIN TRANSFER FROM TREATED CLOTH TO THE SKIN SURFACE: POTENTIAL FOR EXPOSURE IN HUMANS, Journal of Toxicology and Environmental Health, 35:91-105, 1992.

To quantitate leaching from treated clothing, swatches of fabric impregnated with 14C-labeled permethrin were applied to the backs of rabbits for 1 wk. The swatches were continuously held in place by tape for 7 days. Permethrin migration was quantitated by measuring the fate of the 14C label. Conditions that could affect leaching and/or absorption were also evaluated, ie the presence of sweat, different fabric types (cotton, cotton/nylon) and the effects of pre-laundering. Results showed that fabric treated with permethrin at a rate of 0.125 mg/cm2 lost the substance to the skin surface at an average rate of **0.49%/d**. This was calculated from the exposures in rabbits at the end of the 7-d, where about 3.2% of the available permethrin had reached the skin (2% having been recovered from excreta, ie absorbed, plus 1.2% remaining on the skin surface). Pre-laundering the treated fabric had little effect on migration rate, nor did the other variables tested. Repeated washing resulted in a decrease in permethrin content. After ten washing cycles, the content had dropped to 45-60% of the initial value, depending on the textile fiber (cotton, cotton-nylon blend). Extrapolated to the product lifetime with up to 50 washing cycles, the time-weighted mean value for the impregnation was 26% of the initial value (NAP, 1994).

Internal exposure to humans from wearing permethrin-treated (0.125 mg/cm2) military clothing was predicted to be 0.68 µg/kg bw/d considering 2% dermal absorption in humans (Taplin and Meinking, 1987).

Appel et al, 2008, Risk assessment of Bundeswehr (German Federal Armed Forces) permethrin-impregnated battle dress uniforms (BDU), Int. J. Hyg. Environ. Health 211 (2008) 88–104.

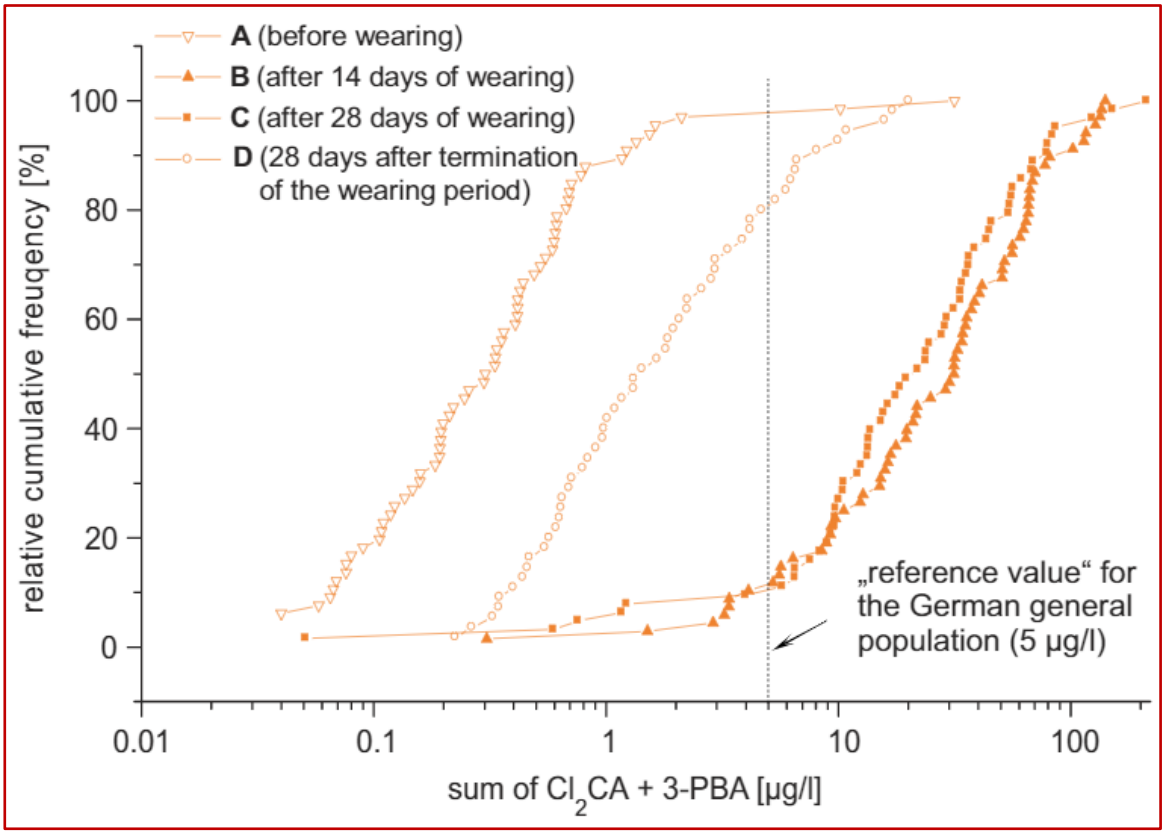
The paper estimates the extent of dermal permethrin uptake by soldiers (above 600 test persons from two studies) wearing impregnated uniforms by determining urine metabolites of permethrin. The excretion levels of the subject with the maximum amount of metabolites correspond to an internal exposure of around 5–6 µg/kg bw/d, considering that biomonitoring could not take all urine metabolites and other elimination routes into account. The authors note that in Snodgrass study, the exposure was considerably lower at 0.68 µg/kg bw/d. However, in that case fabric was impregnated by means of dipping, whereas the value of 5–6 µg/kg bw/d, is estimated from the available experiments on human biomonitoring for the treatment method used here (coating of the fabric with a permethrin containing polymer).

In addition, based on this data and using a dermal absorption rate of 2% (NAP, 1994), the permethrin dose reaching the skin was estimated to be 250 µg/kg bw/d. Considering a standard body weight of 75 kgr and the area covered by the uniform of 1.5 m3, an exposure level of about 1.25 mg permethrin/cm2 skin per day can be calculated. Based on this daily dermal exposure and the content of the tested uniforms of 0.13 mg permethrin/cm^2, a release of around 1% permethrin per wearing event can be derived.

In a subsequent study from the same group[13], the authors note that "*Although this is about twice the release rate previously found in animal experiments with fabric impregnated by immersion of 0.49%/d (Snodgrass, 1992; NAP, 1994), internal exposure found in our study group seems to be explicable by dermal uptake*".

[13] Uptake of permethrin from impregnated clothing, B. Rossbach, Toxicology Letters 192 (2010) 50–55.

Figure 1: Relative cumulative frequencies for the metabolite excretion in wearers of impregnated uniforms at different dates of sampling



Proctor et al, 2014; Permethrin exposure from fabric-treated military uniforms under difference wear-time scenarios. J Exp Sci Environ Epidemiol. 2014;24:572–8.

The objective of the project was to ascertain whether urinary biomarkers of permethrin exposure are detected after wearing post-tailored, fabric-treated military uniforms under two different wear-time exposure scenarios. Study A occurred over 3.5 days and involved six participants wearing treated uniforms continuously for 30–32 h. Urine collection occurred at scheduled time points before, during, and after wearing the uniform. Study B, conducted over 19 days, included 11 participants wearing treated uniforms for 3 consecutive days, 8 h each day (with urine collection before, during, and after wear). Urinary biomarkers of permethrin (3-phenoxybenzoic acid (3PBA), cis- 2,2-(dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid (cDCCA), trans- 2,2- (dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid (tDCCA)) were detected during and after wear. Biomarker detection generally occurred over the 10- to 12-h period after putting on the uniform and subsided 24 h following uniform removal (in both Study A and B scenarios). Those wearing permethrin-treated uniforms under the longer wear-time scenario (Study A) excreted significantly higher cumulative mean levels compared with those in Study B (3.29 times higher for 3PBA and 2.23 times higher for the sum of c/tDCCA (Pr0.001)). Findings suggest that wearing permethrin-treated clothing does increase absorbed, internal dose levels of permethrin above population levels and is significantly related to wear-time duration.

Proctor et al, 2020; Permethrin exposure from wearing fabric-treated military uniforms in high heat conditions under varying wear-time scenarios, Journal of Exposure Science & Environmental Epidemiology, volume 30, pages 525–536(2020)

This study examined the effect of high-temperature conditions and uniform wear time durations (expeditionary, 33 h continuous wear; garrison, 3 days, 8 h/day wear) on permethrin exposure, assessed by urinary permethrin biomarkers, from wearing post-tailored, factory-treated military uniforms. Four group study sessions took place over separate 11-day periods, involving 33 male Soldiers. Group 1 (n = 10) and Group 2 (n = 8) participants wore a study-issued permethrin-treated Army uniform under high heat environment (35 °C, 40% relative humidity (rh)) and expeditionary and garrison wear-time conditions, respectively. For comparison, Group 3 (n = 7) and Group 4 (n = 8) participants wore study-issued permethrin-treated uniforms in cooler ambient conditions under operational and garrison wear-time conditions, respectively. Urinary biomarkers of permethrin (3-phenoxybenzoic acid, and the sum of *cis*- and *trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid) were significantly higher under high temperature compared to ambient conditions, regardless of wear-time situations (Group 1 vs. Group 3; Group 2 vs. Group 4; $p < 0.001$, for both). Under high-temperature conditions, expeditionary (continuous) compared to garrison wear-time resulted in significantly ($p < 0.001$) higher urinary biomarker concentrations (Group 1 vs. Group 2). Differences related to wear-time under the ambient conditions (Group 3 vs. Group 4) were not statistically significant. Findings suggest that wearing permethrin-treated clothing in heat conditions results in higher internal dose of permethrin above that observed under ambient conditions. Detailed results are provided below:

Estimated daily dose at approximate peak excretion (12 h post heat/wear time)

Group No	Daily dose estimate (µg/kg/day) geometric mean (range)
Group 1 (n = 9)a	6.88 (3.31–10.01)
Group 2 (n = 8)	2.60 (0.02–8.49)
Group 3 (n = 6)a	3.33 (2.62–4.43)
Group 4 (n = 8)	2.81 (0.99–4.97)

Groups 1 and 3 (operational/expeditionary: 33 h continuous uniform wear)
Group 1: in simulated hot environment (35 °C, 40% rh)
Group 3: in comparison, ambient environment (average conditions 3 °C, 80% rh)
Groups 2 and 4 (garrison: 3 day, 8 h/day uniform wear)
Group 2: in simulated hot environment (35 °C, 40% rh)
Group 4: in comparison, ambient environment (average conditions 13 °C, 60% rh)
[a] One sample excluded because creatinine value was outside accepted range

Rossbach et al, 2016; Biomonitoring and evaluation of permethrin uptake in forestry workers using permethrin-treated tick-proof pants, Journal of Exposure Science and Environmental Epidemiology (2016) 26, 95–103

A randomized case–control trial was conducted to analyze uptake of the insecticide/arcaricide permethrin in wearers of permethrin-impregnated and non-impregnated pants in German forestry. Eighty-two male workers were each equipped for a 16-week period with permethrin-treated (test group) or with non-treated work pants (control group). Pants with or without lining to protect againstcuts, obtained from two different distributors, were worn in each group. Urinary permethrin metabolite levels were measured byGC-MS/MS before, during and after wearing of the pants. Permethrin uptake was calculated using additional questionnaire data. In the control group, metabolite levels in the range of environmental background exposure (median: ~ 0.5µg/l) were measured. Subjects wearing impregnated pants showed consistently significantly higher exposure levels even before the first use of the pants with a maximum after 1 week of wearing the pants (median: ~ 12.5µg/l). Significant differences in internal exposure were found depending on which of the distributors the pants came from. Metabolite levels decreased probably due to permethrin losses associated with laundering the pants. Calculated permethrin uptake is below the value corresponding to the WHO-proposed acceptable daily intake. Based on these data, a marginally increased cancer risk compared with the general population cannot be excluded when wearing impregnated pants over a working-lifetime period.

Danish EPA, 2014; Survey and health and environmental assessments of biocidal active substances in clothing; Survey of chemical substances in consumer products, No.128, 2014

The overall objectives of this study have been i) to survey the use and occurrence of biocidal active substances applied to protect textiles (clothing) against pests and microbial degradation during transport from manufacturer to consumer,and ii) to assess the possible risks to consumers and the environment from such use, focusing on clothes imported from countries outside the EU.

The study encompassed the following main components: Survey of the use of biocides in clothes, chemical analyses and laboratory tests (migration and wash tests), consumer health risk assessment and environmental risk assessment.

Based on the outcome of the survey,a programme for chemical analysis and testing of clothes samples was established and conducted. It was ascertained that biocidal products were most likely to have been applied to clothes made of natural fibres such as cotton (primarily), wool or silk. As the highest risk of exposure of consumers to biocides in clothes was considered to occur through skin contact, products involving direct skin contact during use (underwear, shirts, t-shirts, trousers, pyjamas and scarves) were prioritized in the selection of samples. Initially, the samples were screened by GC-MS for a wide range of substances to identify possible residues of relevant chemicals.

A total of 34 samples were analysed chemically, of which the majority was made of cotton; however, samples of clothes made of wool and silk were also included. In cases that positive identification of biocides occurred, the samples were tested for biocide migration to artificial sweat and release to wash water during textile washing. Only two biocidal active substances were identified in the samples:formaldehyde (bactericide) and permethrin (insecticide).

The permethrin occurrences were at concentrations of 367-407 mg/kg clothes. Both samples containing permethrin also contained fomaldehyde. Permethrin was detected in clothes made only of wool. In the migration tests, permethrin occurred in the artificial sweat in amounts

corresponding to 1.94 mg/kg. In the wash tests, the release of permethrin (only one test) was 30% (111 mg/kg).

Based on the measured concentrations in the clothes and the migration to sweat, the daily external dermal dose associated with the use of a child's undershirt for 24 hours was calculated to a maximum of 0.14 mg/kg bw/day. For permethrin the DNEL was calculated at 0.14 mg/kg bw/day, based on a NOAEL of 5 mg/kg bw/day established in an oral test with dogs where damage to the adrenal glands was observed. The risk characterisation ratio was thus 0.25 without correction for dermal absorption and 0.014 with correction,assuming 100 % uptake following oral administration. This indicates that the content of permethrin measured in the clothes alone would not pose a risk to children or adults.

Dieval et al, 2017; An improved extraction method for surface dosage of insecticides on treated textile fabrics, Malar J (2017) 16:14

Background: Tens of millions of people live in mosquito-infested regions and controlling mosquito-borne diseases is one of the major interventions aimed at alleviating poverty worldwide. The use of insecticide-treated textiles is one of the most widespread control measures. This includes bed nets, battle clothing or, more generally, textiles use for clothing. These textiles are generally treated with permethrin as active ingredient, which is dosed after extraction of the active molecule present throughout the fabric (measured in mg permethrin/g of fabric) and does not take the effective concentration on the textile surfaces into account. The objective of this study was to propose an improved dosage method that enables measurement of the bioavailable or effective part of active ingredients on the surface of textile treated with insecticides.

Methods: The proposed method relies on mechanical extraction of active molecules on the surface of the textile in direct contact with either the skin or with the targeted arthropod.Results: The results showed that the amount of permethrin measured using the current method is about 200 times higher than the effective surface concentration of the insecticide. In addition, the type of weave or knit influences the effective concentrations of permethrin on the surface of the textile. With the current dosage method, the variation in the concentration of permethrin depending on the type of weave is maximum 8%, whereas with the proposed method, it varies by about 50%. These results were confirmed by bioassays, in which the type of weave significantly affected ($p < 10-3$) the 100% knockdown time of Anopheles gambiae.

The accurate calculation of the amount of active ingre-dient present only on the surface of the fabric is an important aspect that should be taken into account in risk assessment. To be even more accurate and to system-atically obtain a satisfactory level of bioefficacy (which depends on the bioavailability of the active ingredient), this part of the insecticide should not be determined based on mass concentration (mg/m2 or g/kg) but on the effective surface concentration of the insecticide. According to the WHO criteria, the maximum permethrin concentration authorized for textile treatment is 1300 mg/m2, which is the concentration also used by militaries. Based on the results of the tests, and mass concentration (mg/m2 or g/kg), all the treated fabrics tested in this study should be considered as potentially toxic and their sale prohibited. However according to the improved method of measuring the surface concen-tration of insecticide, in reality, none of these fabrics are cytotoxic to humans.

Conclusions: The bioefficacy of insecticide treatments of fabrics is directly correlated with the effective concentration of insecticide on the textile surface, which can be quantified using the method proposed. This improved method could be used to redefine the limits of actual concentrations of active substance after assessment of the bioefficacy of the treatment and

the risk to human health. Further, it enables assessments of the kinetics of insecticide migration in the case of long-lasting insecticide treatment.

Krätke et al, 2004; Migration methods and models for estimating possible exposure to textile adjuvants and dyes from clothing textiles during normal use. Bundesgesundheitsbl - Gesundheitsforsch -Gesundheitsschutz 2004 · 47:810–813.

English translation provided by the applicant:

Migration under application conditions

The release of substances from textiles changes over the course of the period of use. In several studies, the migration of color substances determined experimentally under simulated conditions of use [3, 4, 5, 6].

In studies by the DWI and the Ecological and Toxicological Association of Dyes (ETAD), the textiles were washed several times in a standardized manner, and the elution of dyes was measured after the different wash cycles. 28 (DWI) and 50 (ETAD) washing / wearing cycles were recorded.

The Textiles Working Group was able to derive 3 essential results from these investigations:

1. The migration values vary considerably, depending on the type of fiber, the dye used, the amount applied, the depth of the shade, the extraction agent and the aftertreatment.

2. Despite the large differences, exposure can be estimated using standard methods, whereby a distinction can be made between textile dyes and textile auxiliaries.

3. The migration rate after 28 simulated washing / wearing cycles is less than 10% of the value measured for the first migration

Very little data on migration are available for textile auxiliaries.

A distinction must be made between auxiliaries that are added to the textile liquor during manufacture, but which should not remain on the textile, and finishing agents that are intended to be attached to the textile.

The first group includes very hydrophilic substances, such as B. Surfactants. These are practically completely removed during the manufacturing process or at the latest when washing textiles, so that only a low migration rate of possible residues can be assumed here. Less hydrophilic substances with a certain color fiber affinity is also used. A migration rate of 1.9% was determined experimentally for one component of a water repellent.

The second group includes the hydrophobic substances, which are only slightly soluble in sweat; in the case of appropriate investigations, a possible migration was almost always below the detection limit. For leveling agents, rates of 0.1–0.2% for the first migration were measured.

Berger-Preiss et al, 2002; Indoor pyrethroid exposure in homes with woollen textile floor coverings, Int. J. Hyg. Environ. Health 205, 459 ± 472

In order to investigate human's exposure to permethrin from treated woollen textile floor coverings and possible adverse health effects, a study was carried out in 80 private homes in Hannover (Germany) equipped with woollen textile floor coverings (wool wall-to-wall carpets or woven or knotted rugs). For indoor monitoring, permethrin was determined both in house dust and on suspended particles. While permethrin concentrations in house dust (<2 mm) were high (arithmetic mean: 53.7 mg/kg, 90th percentile 129.1 mg/kg), the permethrin concentrations in the air (suspended particles) were very low (arithmetic mean 2.8 ng/m^3, 90th percentile 5.8 ng/m^3, first sampling). Additional experiments demonstrate that permethrin on suspended particles result from carpet fiber abrasion (and not from an evaporation/re-condensation process). The internal exposure of the 145 inhabitants participating in the study was determined by biological monitoring (permethrin metabolites in urine). In a first sampling period almost 14% of the samples showed concentrations of the metabolite DCCA and almost 23% of the metabolite 3-PBA above the limit of detection(0.2 mg/l). A model was developed which allows the calculation of the metabolite concentration in urine due to inhalative uptake of permethrin. Even for the worst case situation, the calculated metabolite concentrations were ca. 30 times lower than the experimental results. The observed concentrations of metabolites are comparable to those of the background concentrations of the general population in Germany, suggesting that they must origin from other sources than woollen textile floor coverings. The indoor and biological monitoring data as well as the evaluation of the reported symptoms give no indication of an adverse health effect due to carpet treatment by permethrin.

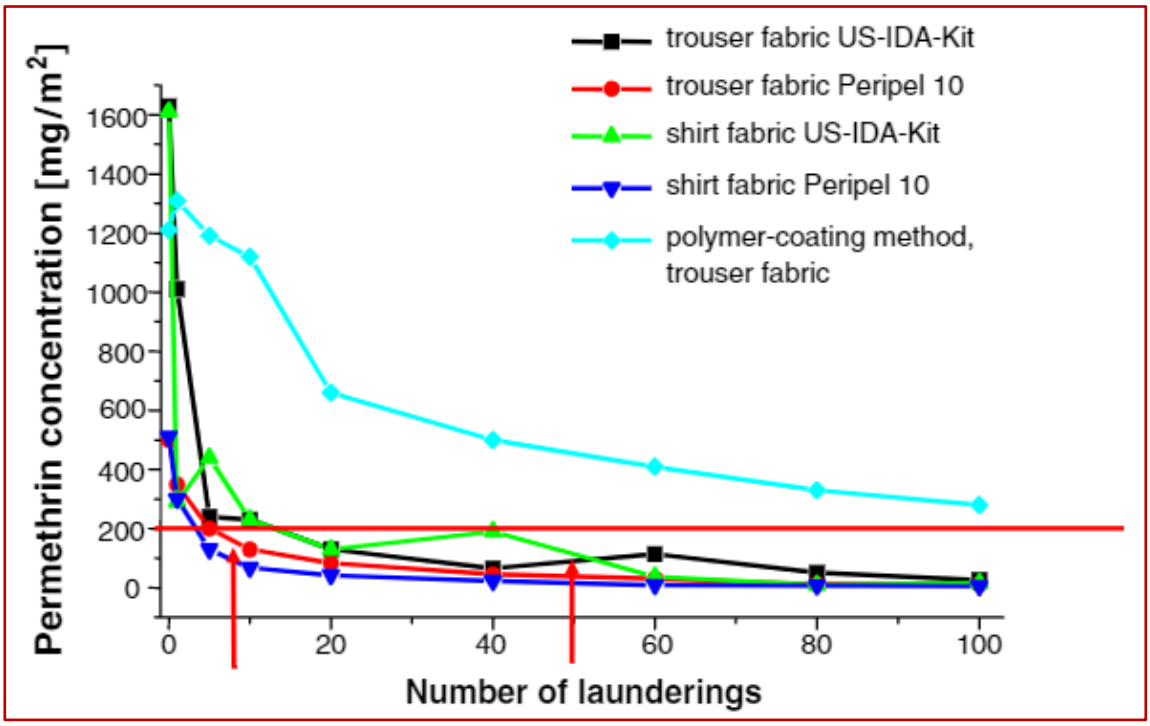
California EPA, 1994; Medical Toxicology and Worker Health and Safety Branches Department of Pesticide Regulation, PERMETHRIN (PERMANONE TICK REPELLENT) RISK CHARACTERIZATION DOCUMENT (REVISED).

NAP 1994, Health Effects of Permethrin Impregnated Army Battle-Dress Uniforms, Subcommittee to Review Permethrin Toxicity from Military Uniforms, Committee on Toxicology Board on Environmental Studies and Toxicology Commission on Life Sciences, National Research Council, NATIONAL ACADEMY PRESS Washington, D.C.1994

Dusan et al, 2019, Clothing-Mediated Exposures to Chemicals and particles, Journal Environmental science & technology, 53(10)

Faulde et al, 2006; A new clothing impregnation method for personal protection against ticksand biting insects, International Journal of Medical Microbiology 296 (2006) S1, 225–229

Figure 2: Residual amount of permethrin in fabric measured after up to 100 launderings.



Annex III

Comparison of permethrin products with similar compositions.

Table 8: Preventol Products

Preventol Aqua Primer PIP termite		**Preventol Aqua Primer PIP**		**Preventol Primer**	
IPBC	0.30	IPBC	0.30	IPBC	0.50
Propiconazol	0.9	Propiconazol	0.9	Tebuconazole	0.2
Permethrin	**0.40**	**Permethrin**	**0.1**	**Permethrin**	**0.06**
PU-alkyd resin	5.0	PU-alkyd resin	5.00	alkyd resin	6.00
Polar solvent	4.30	Polar solvent	4.00	Polar solvent	4.76
Siccative	0.45	Siccative	0.45	Siccative	0.25
auxiliaries	0.30	auxiliaries	0.30	auxiliaries	0.54
In-can preservative	0.25	In-can preservative	0.25	**Aliphatic hydrocarbons**	Add 100
Water	Add 100	**Water**	Add 100	--	--
Dermal absorption	**1.60%**		**2.62%**		**10.42%**

Table 9: Indorex Products

Ingredients	**Indorex Spray**	**Indorex fogger**
Permethrin	**0.017%**	**0.11%**
Pyriproxyfen	0.0063%	0.08%
Surfactant	0.05%	0.0655%
Solvent A	95.3%	72.5%
Solvent B	--	20%
Propellant	4.5%	7.2%
Defoamer	0.1%	--
Dermal absorption	**28%**	**16%**

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