SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Hexyl salicylate

EC No 228-408-6

CAS No 6259-76-3

Evaluating Member State(s): The Netherlands

Dated: 17 July 2018

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Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2012

Before concluding the substance evaluation a Decision to request further information was issued on: 25 February 2014

Further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

DISCLAIMER

This document has been prepared by the evaluating Member State as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating Member State nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work. The Community rolling action plan (CoRAP) of substances subject to evaluation, is updated and published annually on the ECHA web site[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the registrant(s) concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the final outcome of the Substance Evaluation carried out by the evaluating Member State. The document consists of two parts i.e. A) the conclusion and B) the evaluation report. In the conclusion part A, the evaluating Member State considers how the information on the substance can be used for the purposes of regulatory risk management such as identification of substances of very high concern (SVHC), restriction and/or classification and labelling. In the evaluation report part B the document provides explanation how the evaluating Member State assessed and drew the conclusions from the information available.

With this Conclusion document the substance evaluation process is finished and the Commission, the Registrant(s) of the substance and the Competent Authorities of the other Member States are informed of the considerations of the evaluating Member State. In case the evaluating Member State proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes. Further analyses may need to be performed which may change the proposed regulatory measures in this document. Since this document only reflects the views of the evaluating Member State, it does not preclude other Member States or the European Commission from initiating regulatory risk management measures which they deem appropriate.

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

Contents

Part A. Conclusion

1. CONCERN(S) SUBJECT TO EVALUATION

Hexyl salicylate was originally selected for substance evaluation in order to clarify concerns about:

- Suspected CMR
- Consumer use
- High (aggregated) tonnage
- High RCR
- Wide dispersive use.

During the evaluation also other concerns were identified. The additional concerns were:

- RCRs derived for inhalation and dermal exposure as the underlying information for the DNELs was considered insufficiently reliable regarding:
    - dermal absorption
    - lack of inhalation toxicity information
- exposure assessment for workers and consumers.

More specifically, the concerns comprise the lack of classification for reproduction toxic effects caused by the registered substance, hexyl salicylate. Its main metabolite, salicylic acid, and other analogues are suspected to be reproduction toxic based on the observed reproduction toxic effects in animal studies, but presently no harmonized classification for the registered substance, main metabolite or analogues exists at this moment. Note that ECHA's Risk Assessment Committee (RAC) issued an opinion on salicylic acid that has been adopted in the REACH committee.

Moreover, relatively high values of the risk characterization ratios (RCRs) were derived for a number of worker and consumer exposure scenarios in combination with the complex nature of the technical dossier, including an extensive read across dossier.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

After sending the Decision to the registrant, RAC issued their opinion on a CLH dossier on salycilic acid (RAC 2016), the main metabolite of hexyl salicylate. In the opinion they concluded that a classification for reproduction toxicity category 2 for salicylic acid was justified. The data underlying the opinion were the same as considered during the substance evaluation of hexyl salicylate for that endpoint.

3. CONCLUSION OF SUBSTANCE EVALUATION

The evaluation of the available information on the substance has led the evaluating Member State to the following conclusions, as summarised in the table below.

Table 1

CONCLUSION OF SUBSTANCE EVALUATION	
Conclusions	**Tick box**

Need for follow-up regulatory action at EU level	X
Harmonised Classification and Labelling	X
Identification as SVHC (authorisation)	
Restrictions	
Other EU-wide measures	
No need for regulatory follow-up action at EU level	

In 2012, the substance evaluation led to the Decision of information requests on toxicity, absorption, exposure, and risk management. A 28-day inhalation study was requested to obtain information on inhalation toxicity as the substance is a local acting agent on the skin and is used in spray processes and spray applications. Moreover, a dermal absorption study was requested as the provided information on dermal absorption was unreliable. Together, the newly obtained data have led to the derivation of updated inhalation and dermal DNELs. In parallel, exposure information for numerous exposure scenarios was requested together with risk management information.

As a result, the registrants have updated their dossier and revised the exposure assessment completely, taking the updated DNELs and a IFRA guidance document on exposure assessment into account. The new information and revised exposure assessment clarified previous issues on hazard, exposure and risk management, thereby removing the concerns that were likely due to the use of unreliable toxicological and exposure data in the CSR in combination with the widedispersive use and high tonnages involved.

The suspicion of hexyl salicylate being a CMR was confirmed upon the substance evaluation and supported by the RAC opinion on salicylic acid, the main metabolite of hexyl salicylate. Therefore a follow-up harmonised classification and labelling process is concluded by the evaluating Member State Competent Authority (eMSCA).

4. FOLLOW-UP AT EU LEVEL

4.1. Need for follow-up regulatory action at EU level

4.1.1. Harmonised Classification and Labelling

The initial dossier and present registration dossier contained sufficient information on the reproduction toxicity of hexyl salicylate (hence no information request was issued for this endpoint). In view of the eMSCA, the registration dossier contains information on the main metabolite of hexyl salicylate, salicylic acid, that would prompt a classification Repr. 1B. However, in 2016 RAC has issued an opinion on salicylic acid proposing a harmonised classification for the endpoint reproductive toxicity, Repr. 2; H361d. RAC stated the following: “Taking into account the available data, including pharmacokinetics, in vitro tests with ASA and salicylic acid, developmental studies in animals (positive findings in rat and monkey studies and a negative rabbit study), human epidemiology and medical experience, the RAC considered classification of salicylic acid as Repr. 2; H361d (Suspected of damaging the unborn child) to be justified”. Although it is the registrants responsibility to consider the consequence of the classification of salicylic acid, a

harmonised classification for reproduction toxicity is proposed, that should follow the RAC opinion and thus read: Repr. 2; H361d (Suspected of damaging the unborn child).

The harmonised classification could be extended including a group of salicylates, as the read across by the Registrants, indicate a common mechanism, where salicylic acid is the main metabolite of the salicylate group. Hexyl salicylate is rapidly and almost completely metabolized to salicylic acid via all routes of exposure (based on toxicokinetics data in the Registration dossier, a supporting read across document in IUCLID, and following the results from the requested in vitro dermal absorption study). At this moment, no notifications of classification and labelling of hexyl salicylate are made for reproductive toxicity, while the substance is wide dispersively used.

Following the opinion of RAC for salicylic acid, the classification and labelling proposal for hexyl salicylate should read: Repr. 2; H361d (Suspected of damaging the unborn child).

4.1.2. Identification as a substance of very high concern, SVHC (first step towards authorisation)

N/A

4.1.3. Restriction

N/A

4.1.4. Other EU-wide regulatory risk management measures

N/A

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

5.1. No need for regulatory follow-up at EU level

N/A

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS (IF NECESSARY)

A proposal for harmonised classification and labelling for the endpoint reproductive toxicity is to be prepared including a group of salicylates, that metabolise rapidly to salicylic acid. First, this group needs to be established starting with, but not restricting to, the read across information obtained in the Registration dossier.

Indication of a tentative plan is not a formal commitment by the evaluating Member State. A commitment to prepare a REACH Annex XV dossier (SVHC, restrictions) and/or CLP Annex VI dossier is made via the Registry of Intentions (see Table 2).

Based on the resources and priorities, a proposal for harmonised classification is not intended by the Netherlands at short notice. Therefore, submission of a proposal by Member States, or self-classification by the Registrant, is strongly encouraged.

Table 2

FOLLOW-UP		
Follow-up action	**Date for intention**	**Actor**
Proposal for a harmonised classification according to artice 37(1), CLP regulation.	To be determined	To be determined

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

Hexyl salicylate was originally selected for substance evaluation in order to clarify concerns about:

- Suspected CMR
- Consumer use
- High (aggregated) tonnage
- High RCR
- Wide dispersive use.

During the evaluation also other concerns were identified. The additional concerns were:

- RCRs derived for inhalation and dermal exposure as the underlying information for the DNELs was considered insufficiently reliable regarding:
    - dermal absorption
    - lack of inhalation toxicity information
- exposure assessment for workers and consumers.

More specifically, the concerns comprise the lack of classification for reproductive toxic effects caused by the registered substance, hexyl salicylate. Its main metabolite, salicylic acid, and other analogues are suspected to be reproductive toxicants based on the observed reproductive toxic effects in animal studies, but presently no harmonised classification for the registered substance, main metabolite or analogues exists at this moment. Note that RAC drafted an opinion on salicylic acid that has been adopted in the REACH committee.

Moreover, relatively high values of the risk characterization ratios (RCRs) were derived for a number of worker and consumer exposure scenarios in combination with the complex nature of the technical dossier, including an extensive read across dossier.

During the evaluation in 2012, additional concerns were identified related to RCRs derived for inhalation and dermal exposure as the underlying information for the DNELs was considered insufficiently reliable. Moreover, many gaps and omissions were identified in the exposure assessment for workers and consumers.

Table 3 describes briefly the outcome of the substance evaluation based on the information provided in January 2017 following the Decision on hexyl salicylate in 2014 (see Section 7.2 for the procedure).

Table 3

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Reproductive toxicity	Sufficient information available to move forward to a harmonised classification proposal. In view of the recent RAC opinion (RAC 2016) for salicyclic acid main metabolite for hexyl salicylate) Repr. 2 is proposed.
RCRs close to 1 (concern in initial dossier in 2012)	Sufficient information available to assess the RCRs. REGs recalculated DNELs and RCRs based on new provided information. At this moment no concerns were identified by the eMSCA for both workers and consumers.

7.2. Procedure

The decision-making procedure is described in the Decision on hexyl salicylate dated 25 February 2014 (ECHA 2014).

In 2014 the registrant lodged an appeal against the decision which was dismissed by the ECHA Board of Appeal in 2015. The information requested was ruled to be provided by January 2017.

Briefly, information requests in the Decision were to provide a 28-d inhalation study, an in vitro dermal absorption study, information and measurements on worker and consumer exposure, information on RMMs, and to update the CSR and registration dossier accordingly.

Since January 2017 the updated registration dossier has been evaluated by the eMSCA. The registrants provided a 28-d inhalation study, even though this study did not meet all the OECD requirements, and the in vitro dermal absorption study. The eMSCA considers that registrants did not fully meet the information requests regarding the exposure assessment of workers and consumers and RMMs. Nevertheless, the eMSCA has evaluated the data provided and could conclude on the concerns specified under Section 7.1.

7.3. Identity of the substance

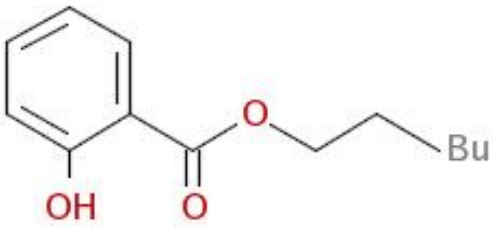
Table 4

SUBSTANCE IDENTITY	
Public name:	Hexyl salicylate
EC number:	228-408-6
CAS number:	6259-76-3

Index number in Annex VI of the CLP Regulation:	-
Molecular formula:	C13H18O3
Molecular weight range:	222.2802
Synonyms:	n-hexyl salicylate Benzoic acid, 2-hydroxy-, hexyl ester Hexyl o-hydroxybenzoate

Type of substance X Mono-constituent ☐ Multi-constituent ☐ UVCB

Structural formula:



7.4. Physico-chemical properties

Table 5

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	Hexyl salicylate is described as a colourless liquid.
Melting/freezing point	The freezing point of the test material has been determined to be 269 ± 0.5 K.
Boiling point	The boiling point of the test material has been determined to be 571 ± 0.5 K at 100.62 kPa.
Vapour pressure	The vapour pressure of hexyl salicylate was determined to be 7.7 x 10^-5 kPa at 23 °C.
Water solubility	The solubility of hexyl salicylate was determined to be 2 mg/l at 23 °C.
Partition coefficient n-octanol/water (Log Kow)	The partition coefficicient n-octanol/water found for hexyl salicylate was: log Pow = 5.5
Flammability	A flash point of 151 ºC was recorded for Hexyl Salicylate, as Hexyl salicylate it is not a gas oil, diesel, light heating oil with flash point up to 75°C or a halogenated substance, mixture containing halogenated, volatile or non volatile flammable substance, it should not be subject to hazard class 'flammable liquid'.

Explosive properties	Hexyl salicylate does not contain any groups associated with explosivity. Explosive properties are associated with the presence of certain chemical groups in a molecule which can react to produce very rapid increases in temperature or pressure. When there are no chemical groups associated with explosive properties present in the molecule then a substance or mixture shall not be classified as explosive.
Oxidising properties	Considering the structural environment of oxygen in the molecule and the oxygen balance of Hexyl salicylate (CAS: 6259-76-3), it can be concluded, beyond reasonable doubt, that Hexyl salicylate (CAS: 6259-76-3) is unlikely to be an oxidizer and will be incapable of reacting exothermically with combustible materials. It need not be tested experimentally for oxidizing properties
Granulometry	The study does not need to be conducted if the substance is marketed or used in a non solid or non granular form. Hexyl salicylate is a liquid at room temperature.
Stability in organic solvents and identity of relevant degradation products	The stability of substance is not considered critical.
Dissociation constant	Hexyl salicylate does not contain an ionizable functionality. Due to chemical structure no disassociation is to be expected.
Viscosity	Viscosity of Hexyl salicylate was carried out using a Brookfield Viscometer. The viscosity of Hexyl salicylate was determined to be 10 cps at 25 °C equivalent to 10 mPa s at 25°C.

7.5. Manufacture and uses

7.5.1. Quantities

Table 6

AGGREGATED TONNAGE (PER YEAR)				
☐ 1 – 10 t	☐ 10 – 100 t	☐ 100 – 1000 t	☒ 1000- 10,000 t	☐ 10,000-50,000 t
☐ 50,000 – 100,000 t	☐ 100,000 – 500,000 t	☐ 500,000 – 1000,000 t	☐ > 1000,000 t	☐ Confidential

7.5.2. Overview of uses

Table 7

USES Use(s)	
Uses as intermediate	
Formulation	Formulation of fragrance products, compounding
Uses at industrial sites	Industrial use of washing and cleaning products, fragrance products
Uses by professional workers	Professional use of washing and cleaning products, fragrance products, polishes and wax blends, cosmetics.
Consumer Uses	Use of fragranced products, cosmetics, polishes and wax blends, biocides, cleaning agents and detergents, air care products
Article service life	Scented clothes, scented paper articles, scented CD, other scented articles, e.g. candles.

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

Not applicable

7.6.2. Self-classification

Self-classification by the registrants in the joint registration dossier:

Aquatic Chronic 1; H410: Very toxic to aquatic life with long lasting effects.
Skin Sens 1B; 1H317: May cause an allergic skin reaction.

Number of Aggregated Notifications: 21
Other mentioned classifications:
Aquatic Acute 1; H400
Eye Irrit. 2; H319
Skin Irrit. 2; H315
STOT SE 3; H335 (May cause respiratory irritation).

In 2012, hexyl salicylate was also self-classified as Skin Irrit. 2; H315 by the registrants, but apparently this was removed in their latest update of the registration dossier.

7.7. Environmental fate properties

Not applicable

7.8. Environmental hazard assessment

Not applicable

7.9. Human Health hazard assessment

7.9.1. Toxicokinetics

Please refer to the Decision on hexyl salicylate dated 24 February 2014. In the initial registration dossier information on dermal absorption was provided (Jimbo (1983) and Watkinson et al. (1992)), which was considered not reliable to conclude on dermal absorption. Therefore an in vitro dermal absorption study was requested in a substance evaluation decision.

In January 2017, the registration dossier was updated with the results of the newly performed dermal absorption study, that was performed according to OECD test guideline 428. In this study, account was taken for differences in concentrations on the skin and metabolite formation in the skin. Three different conditions of dermal absorption were tested in the study.The highest reported dermal absorption that could be derived from this study was taken forward in the CSR. A dermal absorption of 7.8% was derived from this study.

The previously used dermal absorption was approximately a factor 1000 lower. It further shows that the data from Jimbo (1983) and Watkinson et al. (1992), which in fact used that data from Jimbo (1983) cannot be considered reliable for any salicylate in general, and for hexyl salicylate in particular.

As a result of the newly derived dermal absorption value, the dermal DNEL was adjusted accordingly. The dermal absorption value is used to derive the dermal DNEL by route to route extrapolation from an oral study.

The eMSCA concluded that the concern of possible underestimation of hexyl salicylate's dermal systemic toxicity and consequently the risk is now removed.

7.9.2. Acute toxicity and Corrosion/Irritation

See remark in section 7.9.4

7.9.3. Sensitisation

See remark in section 7.9.4

7.9.4. Repeated dose toxicity

Please refer to the Decision on hexyl salicylate dated 24 February 2014. In the initial registration dossier, no inhalation toxicity study was available while there was a concern for possible local effects in the airways in view of irritant and sensitizing properties of hexyl salicylate to the skin. In view of the local toxicity of hexyl salicylate, a 28-d study by inhalation was considered sufficient to cover the gap in the risk assessment for hexyl salicylate as no inhalation study was available to cover the concern for possible local effects in the airways. As for systemic toxicity, a sub-chronic study was already available via the oral route. Hence, a 28-d inhalation toxicity test was requested according to OECD test guideline 412.

In January 2017, the registration dossier was updated with the results of the newly performed 28-d inhalation study, that was performed according to OECD test guideline 412.

The registrants provided a 28-d inhalation study with hexyl salicylate and included some information on a rangefinder study to determine the concentrations. The eMSCA notes that the study did not fulfil all requirements as set out in OECD testing guidelines. The OECD test guidelines provide useful instructions for the dose selection of repeated dose

systemic toxicity studies, e.g. that the highest dose should "induce toxic effects but not death or severe suffering" and that the aim is to observe a dose-response. Justifications must be provided in cases such doses cannot be achieved for whatever reason. In the highest concentration group no clear signs of toxicity were observed, nor justifications are given why higher concentrations could not be tested. The rangefinder study did not show clear signs of toxicity (similar highest concentration) and therefore it would have been expected that higher concentrations were tested. Moreover, it is noted that this study cannot be used for classification and labelling purposes as the highest concentration is below classification cut-offs, so it is inconclusive due to dose selection. The study does provide information on the presence or lack of effects that can be used for risk assessment purposes with caution. It does not provide adequate information on possible severe effects at higher doses, which could have been an argument for additional safety actions.

The registrants indicated that even at the top dose no treatment related effects occurred and therefore the NOAEC in this study was set at the top dose. The eMSCA is of the opinion that in the top dose treatment related effects, even though not statistically significant and showing only mild effects, can be considered relevant. Moreover, the rangefinder study showed similar effects at the same dose (based upon which the top dose was selected). Therefore, the eMSCA finds that the NOAEC is subject to uncertainty and has evaluated the DNEL and subsequently derived RCRs bearing in mind that uncertainty.

It is noted that the 28-d inhalation study resulted in approximately a factor two higher inhalation DNEL than initially was derived by the registrants based on route-to-route extrapolation from an oral study in 2012. In 2012, the inhalation DNEL was based on nephrotoxicity in the rat after oral exposure to isoamyl salicylate.

The use of the inhalation toxicity study to derive a point of departure for risk assessment for local toxicity and/or specific inhalation toxicity was considered appropriate for the following reasons:

- Relevant route of exposure applied in the study

- Possible local effects in the airways are taken into account, and

  The inhalation study also includes general toxicity effects such as the observed nephrotoxicity.

Therefore, it is concluded that the concern of a possible underestimation of inhalation related (local or specific) hazard is removed from a risk assessment perspective.

However, it is noted that the 28-day study does not include reproductive toxicity endpoints. Hence, the newly derived inhalation DNEL of 0.4 mg/m^3 (see Table 8) does not cover for reproductive toxicity. To cover for possible reproductive toxicity effects via inhalation exposure the overall NOAEL for reproductive toxicity should be used as point of departure (factor 1.5 higher than the overall NOAEL of 50 mg/kg bw/d taken by the registrant; see Table 8) and apply route-to-route extrapolation. Or, conservatively, the previous inhalation DNEL can be used (0.219 mg/m^3). It is further noted that when evaluating the inhalation study and subsequent derivation of the DNEL and RCRs, as described above, there is no concern for reproductive toxic effects.

It is highlighted again that this study cannot be used for classification and labelling purposes and is limited in the use for information exchange in the supply chain that might follow from classification and labelling regulations.

7.9.5. Mutagenicity

Not evaluated.

7.9.6. Carcinogenicity

Not evaluated.

7.9.7. Toxicity to reproduction (adverse effects on sexual function and fertility and developmental toxicity)

The initial dossier and present registration dossier contained sufficient information on the reproductive toxicity of hexyl salicylate (hence no information request was issued for this endpoint).

With respect to the inhalation DNEL, please refer to the section 7.9.4. on repeated dose toxicity.

In view of the eMSCA, the registration dossier contains information on the main metabolite of hexyl salicylate, salicylic acid, that would prompt a classification as Repr. 1B. However, RAC has issued an opinion (March 2016) on salicylic acid proposing a harmonised classification for reproductive toxicity, Repr. 2, H361d. In our view, as hexyl salicylate readily metabolizes to salicylic acid, registrants should self-classify hexyl salicylate based on the classification for salicylic acid, to conform with the CLP regulation, following the RAC opinion on salicylic acid.

Please refer to the RAC (2016) opinion on salicylic acid.

7.9.8. Hazard assessment of physico-chemical properties

Not evaluated.

7.9.9. Selection of the critical DNEL(s)/DMEL(s) and/or qualitative/semi-quantitative descriptors for critical health effects

The eMSCA evaluated the in vitro dermal absorption study and 28-d inhalation toxicity study and how the results were used for updating the dermal and inhalation DNELs.

Table 8

CRITICAL DNELS/DMELS					
Endpoint of concern	**Type of effect**	**Critical study(ies)**	**Corrected dose descriptor(s) (e.g. NOAEL, NOAEC)**	**DNEL/ DMEL**	**Justification/ Remarks by eMSCA**
Repeated dose toxicity - dermal	nephrotoxicity	Drake et al. 1974	50 mg/kg bw/d (oral study), route to route by assuming 100% oral absorption and 7.8% dermal absorption leads to 641 mg/kg bw/d	6.4 mg/kg bw/d (worker) 3.2 mg/kg bw/d (consumer)	There is no data to support the 100% oral absorption. Using this value for route-to-route extrapolation is not worst-case. A factor 2 was taken into consideration when evaluating the dermal RCRs.

Repeated dose toxicity – inhalation	Reduced body weight, reduced food consumption	Confidential report, 2016	249 mg/m^3, corrected dose (duration and respiratory volume) is 125 mg/m^3 for workers and 62 mg/m^3 for consumers	1.7 mg/m^3 (worker) 0.4 mg/m^3 (Consumer)	The reduced body weight and food consumption in males in the top dose (249 mg/m^3) may be regarded as adverse. An additional uncertainty factor of 5 was taken into consideration for both DNELs when evaluating the inhalation RCRs. When taking this factor 5 into consideration it also covers for reproductive toxicity (see explanation in section 7.9.4).

7.9.10. Conclusions of the human health hazard assessment and related classification and labelling

On basis of the provided information the RCR are well below one, meaning no concern for occupational or consumer use.

The eMSCA considers the information sufficient for a proposal for harmonised classification and labelling for hexyl salicylate as Repr. 2; H361d (Suspected of damaging the unborn child), which is based on a RAC (2016) opinion for salicylic acid.

7.10. Assessment of endocrine disrupting (ED) properties

Not evaluated.

7.11. PBT and VPVB assessment

Not evaluated.

7.12. Exposure assessment

A lot of shortcomings were identified in the initial registration dossier on hexyl salicylate. Therefore, the registrants were requested to fill out omissions in the exposure assessments and to perform measurements in case clear data gaps existed. Please refer to the Decision on hexyl salicylate dated 24 February 2014 for details on the requests.

Following the update of the registration dossier in January 2017 new exposure information was provided. It is noted that the registrants did not fulfil the requirements as set out in the Decision. No measurements or surveys were performed by the registrants as was requested in the Decision. Instead, the entire exposure assessment was restructured following the IFRA guidance (2012). The IFRA guidance contains preset exposure scenarios and contributing scenarios for workers and consumers within the fragrance branche organisation. The registrants have indicated which of the contributing scenarios are relevant for their uses and consistently referred to the IFRA guidance for

the rationale behind the exposure parameters. As a consequence of this different approach, uses and exposure scenarios have been renamed and different PROCs have been assigned, describing the exposure scenarios. Despite the fact that the requirements of the Decision were not fulfilled, the eMSCA has evaluated the exposure assessment nonetheless. The evaluation was aimed at whether the previous identified uses are still covered and if there is a concern of underestimating exposures.

The revised exposure assessment did not lead to additions or deletions of uses. The revised exposure assessment based on the IFRA guidance is in a way more refined than the initial exposure assessment in a sense that it is sector-specific. There was no generic trend detectable if the exposures were consistently higher or lower than the initial assessment.

Data underlying the exposure assessment are confidential and therefore only the eMSCA's main observations have been provided in the sections below.

7.12.1. Human health

7.12.1.1. Worker

The inhalation exposure of workers has been assessed using ART, while the dermal exposure has been assessed using ECETOC TRA v3 for worker. The worker exposure has been evaluated following the anticipated high exposure tasks based on PROCs, RCRs, and ad random during the evaluation by the eMSCA. By evaluating/re-doing the worker exposure assessments it was noted that occasionally the results deviated where in most of these cases the eMSCA would derive higher exposure estimates. These deviations result from input or calculation errors or to input selections that could not be supported by information in the CSR or IFRA guidance. In those cases, the eMSCA took worst case input parameters to see if that may lead to RCRs close to or higher than 1. However, in all cases even where exposures were added to assess the combined exposure, the resulting RCRs taking into account the additional uncertainty factors specified in section 7.9.9, Table 12, were sufficiently low, i.e. RCRs below 0.2 to very low RCRs.

The newly derived RCRs included the adaptations of the inhalation and dermal DNELs, where the dermal DNEL was lowered significantly. In the initial dossier the RCRs for dermal exposure were very low, whereas now they range up to 0.1, occasionally by recommending wearing dermal protection (gloves). For the reasons above, the eMSCA has no remaining concern for worker exposure.

It should be noted that the registrants failed to comply delivering breakthrough times of gloves recommended to use for hexyl salicylate. Such information can be requested from the gloves manufacturer. The information is requested to ensure that workers are informed about the duration gloves can be worn during shifts and when they need replacement. As gloves are recommended for some exposure scenarios to ensure safe use this information needs to be provided in the IUCLID dossier and shared across the supply chain. Further, it is also a requirement under the OSH Regulation. The eMSCA is of the opinion that this information request should be followed up preferably by the Registrants or otherwise by enforcement authorities. The eMSCA does not see any use in requesting the same information again via the substance evaluation process.

7.12.1.2. Consumer

The exposure assessment of consumers was revised using the AISE react tool (an exposure assessment tool build on the principes of the ECETOC TRA consumer tool) and for spraying the BAMA tool. As for the worker exposure assessment, some deviations were noted when re-doing the assessment using the same tools. In case of spray

applications, the registrants failed to deliver a dermal exposure assessment where dermal exposure is to be anticipated. However, in all cases where the exposure estimates were amended and completed by adding the dermal exposure, the resulting RCRs taking into account the additional factors specified in section 7.9.9, Table 12, were sufficiently low, i.e. RCRs below 0.1.

Therefore, the eMSCA has no remaining concern for consumer exposure.

7.12.2. Environment

Not evaluated.

7.12.3. Combined exposure assessment

Please refer to sections 7.12.1.1 and 7.12.1.2.

7.13. Risk characterisation

Please refer to sections 7.12.1.1 and 7.12.1.2.

7.14. References

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7.15. Abbreviations

ASA	acetylsalicylic acid
CLH	Classification and labelling harmonisation
CLP	Classification, labelling and packaging

CoRAP	Community rolling action plan
CSR	chemical safety report
DN(M)EL	Derived No(Minimal) effect level
ECHA	European Chemicals Agency
eMSCA	evaluation Member State Competent Authority
NOAEC	No observed adverse effect concentration
RAC	Risk Assessment Committee
RCR	risk characterization ratio
REG	registrant
RMM	risk management measure
SVHC	substances of very high concern