EUROPEAN CHEMICALS AGENCY

Helsinki, 28 November 2017

Addressee: [redacted]

Decision number: CCH-D-2114379324-45-01/F
Substance name: BENZYL SALICYLATE
EC number: 204-262-9
CAS number: 118-58-1
Registration number: [redacted]
Submission number: [redacted]
Submission date: 09.03.2016
Registered tonnage band: 100-1000T

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the REACH Regulation), ECHA requests you to submit information on:

1. **Composition of the substance (Annex VI, Section 2.3.):**
   - complete compositional information where the compositional information for the substance is completed up to 100 %;
2. ***In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method: OECD TG 473) or in vitro micronucleus study (Annex VIII, Section 8.4.2, test method: OECD TG 487)* with the registered substance;**
3. ***In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)* with the registered substance provided that the study requested under 2 has negative result;**
4. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) in rats with the registered substance;**
5. **Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: OECD 421 or 422) in rats, oral route with the registered substance;**
6. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rat or rabbit), oral route with the registered substance;**
7. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for human health: revise the exposure assessment for *the uses for which RCRs are above 1* and revise the risk characterisation accordingly;**
8. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for human health:**
   - revise worker contributing scenarios (WCSs) describing activities where aerosol formation is likely to occur using a model that is suitable to assess the exposure during such activities and revise the risk characterisation accordingly;
9. **Exposure assessment (Annex I, Section 5.1.1.) for human health:**
   - provide documentation for the recommended personal protective equipment, i.e. skin protection (i.e. hand and body protection) and respiratory protection;
   - specify the type of glove material, thickness and breakthrough times;
   - specify the filter type/class for the respiratory protective equipment;
   - specify the type and quality of protective clothing.

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI to the REACH Regulation. To ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation.

You have to submit the requested information in an updated registration dossier by **4 June 2020.** You also have to update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and advice and further observations are provided in Appendix 3.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Authorised[1] by Kevin Pollard, Head of Unit, Evaluation E1

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

ECHA
EUROPEAN CHEMICALS AGENCY

Appendix 1: Reasons

IDENTIFICATION OF THE SUBSTANCE

In accordance with Article 10(a)(ii) of the REACH Regulation, the technical dossier must contain information on the identity of the substance as specified in Annex VI, Section 2 to the REACH Regulation. In accordance with Annex VI, Section 2 the information provided has to be sufficient to enable the identification of the registered substance.

1. Composition of the substance (Annex VI, Section 2.3.)

Annex VI, Section 2.3. of the REACH Regulation requires that each registration dossier contains sufficient information for establishing the composition of the registered substance and therefore its identity. In that respect, according to chapter 4.2 of the "Guidance for identification and naming of substances under REACH and CLP" (Version: 2.1, May 2017) – referred to as the "SID Guidance" hereinafter, for well-defined substances the following applies:

1. Each main constituent (i.e. the constituent present at ≥ 80 % for mono-constituent substance or each constituent present at ≥ 10 % and < 80 % for multi-constituent substance) shall be identified and reported individually;
2. Each impurity present at ≥ 1 % or relevant for the classification and/or PBT assessment of the registered substance shall be identified and reported individually;
3. The main constituent and the impurities shall be reported with their typical, minimum and maximum concentration levels;
4. The compositional information should be completed up to 100 %.

The composition reported in IUCLID section 1.2 includes "[redacted]" as the main constituent with a typical concentration of [redacted] % (w/w) and a concentration range reported as > [redacted] % (w/w) and ≤ [redacted] % (w/w). No other constituents have been reported in IUCLID section 1.2.

Taking into consideration the reported minimum concentration value "[redacted] % (w/w)" and the fact that no other constituents have been reported in IUCLID section 1.2, it appears that [redacted] % (w/w) of the substance has not been accounted for.

You have indicated in your comments on the draft decision that the registered substance is a monoconstituent and the GCMS data clearly indicates this. You have agreed to update the dossier.

Consequently, you are requested to provide a complete compositional information where the compositional information for the substance adds up to 100%.

The information shall be included in section 1.2 of IUCLID.

TOXICOLOGICAL INFORMATION

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.
Your registration dossier contains for several endpoints adaptation arguments in form of a grouping and read-across approach under Annex XI, Section 1.5. of the REACH Regulation.

ECHA has considered first the scientific and regulatory validity of your read-across approach in general before assessing the individual endpoints.

Grouping of substances and read-across approach

You have sought to adapt the information requirements by applying a read-across approach in accordance with Annex XI, Section 1.5.

Annex XI, Section 1.5. requires a structural similarity among the substances within a group or category such that relevant properties of a substance within the group can be predicted from the data on reference substance(s) within the group by interpolation.

The following analysis presents your justification for the proposed grouping approach and read-across hypothesis, together with ECHA's analysis for the endpoints sub-chronic toxicity (Annex IX, Section 8.6.2.), screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.) and pre-natal developmental toxicity (Annex IX, Section 8.7.2.). Your read-across and category approach for the endpoint *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.) is addressed under the respective section.

Description of your grouping and read-across approach

You propose read-across from the substance cyclohexyl salicylate (EC No. 400-410-3) (hereafter the 'source substance') for each of the above-mentioned information requirements. You conclude that the source substance can be used to close data-gaps in the health hazard assessment of the registered substance benzyl salicylate (EC No. 204-262-9) (hereafter the 'target substance') as you consider that the read-across approach is scientifically acceptable with high confidence based on your examination of the adequacy and scientific robustness of the provided read-across justifications and corresponding information using assessment elements (AE) of the ECHA Read-across assessment framework (RAAF).

Your read-across hypothesis and justification is the following: "*This read-across is based on the hypothesis that the target substance and source substance have the same expected mode of action and similar physicochemical properties relevant for the read-across endpoints. The experimental data presented in the paper by Belsito et al, shows that all salicylates undergo hydrolysis which yields salicylic acid and the alcohol of the corresponding alkyl, alkenyl, benzyl, phenyl, phenethyl side chain. This is consistent with information on other alkyl- and alkoxy- benzyl derivatives whereby aromatic esters are hydrolyzed in vivo by carboxylesterases, or esterases, especially the A-esterases.*"

Information provided for the read-across approach

With respect to repeated dose toxicity you have provided a sub-chronic toxicity study (90 days) in rats by the oral route (OECD TG 408; [redacted] 1995, Rel. 2,) performed with the source substance cyclohexyl salicylate (EC No. 400-410-3).

With respect to reproductive toxicity, you have provided a one-generation reproductive toxicity study (OECD TG 415; [redacted] 1995, Rel. 2,) and a pre-natal developmental toxicity study (OECD TG 414; [redacted] 1996, Rel. 2) both performed with the source substance cyclohexyl salicylate (EC No. 400-410-3).

You have also provided a read-across justification document [redacted]

[redacted] [1] attached to the IUCLID section 13.

ECHA analysis of the grouping and read-across approach

With regard to your proposed read-across adaptations for repeated dose toxicity and reproductive toxicity, ECHA has the following observations:

Read-across hypothesis

ECHA understands that your read-across hypothesis is supported by information from the source substance. ECHA further understands that you assume that this source substance and the target substance are metabolised to a common metabolite (salicylic acid) and to the alcohol of the corresponding side chain. You did not specify which alcohols are to be expected for the source and the target substances. However, based on Table 2 of your justification document [1] ECHA understands that it would be benzyl alcohol for the target substance and cyclohexanol for the source substance.

Structural similarity

In your read-across justification document [1] you state that "*The source substance has a >50% structural similarity with benzyl salicylate*". Furthermore, you indicate that "*Both substances are salicylic acid esters and the structural differences are not expected to influence the in vivo interaction of either the target or source substances.*"

In your comments on the draft decision according to Article 50(1) of the REACH Regulation you further state the target and source substance structural differences. You also state that "*data are available on the 2 primary metabolites (benzyl alcohol and salicylic acid) which support the lack of concern and allow to fulfil the endpoints for genotoxicty, repeat dose and developmental and reproductive toxicity. The data on cyclohexyl salicylate provide additional supporting evidence in the RAAF document. This data is available on the ECHA dissemination web site.*"

ECHA acknowledges the assumed main metabolites of the target substance (benzyl alcohol and salicylic acid). However, in absence of further supporting information on the parent structure toxic properties and metabolic behavior of the target substance, ECHA considers that you have not explained or demonstrated why the differences in the target and source substance chemical structures should not influence or lead to underestimating the toxicological properties of the target substance.

ECHA acknowledges the similarity with respect to the salicylic acid group. However, ECHA notes the significant differences between the target and source substances. More specifically, the target substance has an aromatic side chain whereas the source substance has an aliphatic (non-aromatic) cyclohexyl side chain. Such structural difference might result in differences in toxicity of the parent compounds, differences in hydrolysis of the parent compounds and also in differences in the toxicity of metabolites. You did not provide sufficient information to support your claim that the structural differences are not expected to influence the in vivo interaction of either the target or source substances (see below).

Metabolism rate

You explain that "*salicylates undergo hydrolysis which predominantly yields the major metabolite salicylic acid. This is consistent across all the salicylates and therefore the*

relevant experimental data for salicylic acid is also presented in Table 5 for both the acute oral LD50 and one-generation reproductive toxicity tests."

ECHA understands that your read-across hypothesis is supported by metabolism (enzymatic hydrolysis) of the target and the source substances to one common metabolite, salicylic acid and different respective alcohols. However, ECHA notes that you did not provide information on the metabolic rate to support your assumption.

Hence, your claim that "*both parent substances will have the same impact with regard to metabolite production*" is not sufficiently supported and it is not possible to conclude on the impact of the parent substances or the toxicity of the metabolites.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation you state that *"the metabolic rate is not considered to be a critical factor in comparing the toxicity of the target and source substances"* and that "*both target and source substances will be metabolised rapidly in the liver to the corresponding alcohols and salicylic acid."* However, ECHA considers the metabolic rate can have impact on the bioavailability of the parent compounds and thereby affect the toxic potential of the target and source substances which are structurally different.

Toxicological effects

You have provided information on repeated dose toxicity and reproductive toxicity with the source substance to fulfil the standard information requirement for the target substance. However, you did not provide any information on repeated dose toxicity and reproductive toxicity with the target substance, hence no evidence concerning the similarity of toxicological properties of the two substances related to the endpoints in question has been provided.

Furthermore, your hypothesis is arguably supported by formation of the common metabolite salicylic acid and the corresponding different alcohols and potential further metabolites.

However, ECHA points out that the list of predicted metabolites that you have provided shows that all the metabolites of the source and target substances, with the exception of salicylic acid, are different. For example, potential metabolites of the target substance are benzyl alcohol, benzaldehyde and benzoic acid, whereas potential metabolites of the source substance are cyclohexanol, cyclohexanone, and cyclohexane diols.

ECHA notes that you referred to information on repeated dose toxicity of salicylic acid and benzyl alcohol and information on reproductive toxicity of benzoic acid and benzaldehyde. However, you did not provide comparative information on the repeated dose toxicity and reproductive toxicity of all main metabolites. ECHA would expect you to provide a robust study summary in IUCLID for information that is most relevant to support the read-across approach. For information supporting the read-across, either detailed information on the results should be provided in the read-across justification document or a summary with appropriate references to publicly available information. Hence, in the absence of such information, the similarities and/or differences in toxicity of the resulting alcohols cannot be assessed nor taken into consideration.

In your comments on the draft decision according to Article 50(1) of the REACH Regulation you state the following

1. *"The read-across hypothesis is supported by profiling information on the target and source substance as per the OECD [Q]SAR Toolbox. Additionally, information on the*

metabolites of the target and source substances strengthens the lack of toxicological classification for genotoxicity and reproductive/developmental toxicity."

2. *"We have already provided substantial information in the RAAF documents which leads to conclude to a low concern for repeat-dose toxicity with benzyl salicylate. In addition, the available experimental data within the REACH dossiers on the metabolites of Benzyl salicylate, salicylic acid (4-Week, NOEL 237 mg/kw bw/day) and benzyl alcohol (13-Week, NOAEL 400 mg/kg bw/day) indicates low toxicity via the oral route. Neither substance is classified for repeat dose toxicity."*
3. *"The close structural substance (source) substance with OECD 421/422 data is cyclohexyl salicylate"*
4. *"In the OECD 414 tests on cyclohexyl salicylate and salicylic acid, the NOAEL for were 360 and 150 mg/kg bw/day respectively. This indicates that salicylates have the magnitude of toxicity in a Pre-natal developmental toxicity study test and no effects on either parent or offspring at >150 mg/kg bw/day. The available experimental data within the REACH dossier on the metabolite benzyl alcohol (OECD 414, LOAEL 750 mg/kg bw/day) also indicates no developmental toxicity via the oral route. Considering the narrow toxicity band for these 2 substances and the high LOAEL for benzyl alcohol, no developmental hazard is associated with the target."*
5. *"In the OECD 415 tests on cyclohexyl salicylate and salicylic acid, the NOAEL for were 180 and 100 mg/kg bw/day respectively. This indicates that salicylates as a group have the same magnitude of toxicity in a reproductive test with no effects on either parent or offspring at >100 mg/kg bw/day. This is also in confirmed by the NOAEL on methyl salicylate in the OECD 415 at 150 mg/k bw/day."*

Furthermore, you propose to update the dossier with supporting robust study summaries as additional argument and in order to fulfil the sub-chronic toxicity information requirement alongside with the updated read-across justification document if ECHA accepts the Registrant's comments to the draft decision.

ECHA notes that the toxicological comparison of the salicylates made by you omits toxicological data for the target substance, which would allow verifying your hypothesis. In addition, low toxicological concern, equal level of toxicity or lack of toxicological classification among given analogue substances does not support the read-across hypothesis by which you intend to predict the toxic properties of the target substance.

Therefore, based on the structural differences of the target (benzyl-side chain) and the source substance (cyclohexyl-side chain), ECHA considers that the read-across adaptations for sub-chronic toxicity and reproductive toxicity are not sufficiently justified. ECHA notes that, for read-across adaptations, it is critical to demonstrate that the structural differences of the target and source substance will not have an impact on the toxicity and that the human health effects can indeed be predicted from the data for the source substance.

Conclusion

ECHA concludes that the Registrant's comments on the draft decision do not provide new information that can be used as a basis to demonstrate that the target substance's toxicological properties can be predicted from data on the source substance. Furthermore, you have not sufficiently explained or demonstrated – as detailed above - why the differences in the target and source substances' chemical structures would not influence the prediction of the toxicological properties of the target substance.

ECHA considers that, in the absence of further supporting information, relevant differences in the toxicological properties of target and source substance and/or their metabolites cannot be ruled out. Based on the above considerations in this section, ECHA also disagrees

with your RAAF assessment element scoring supporting the acceptance of the read-across with high confidence. Therefore, it is not possible to assume/conclude that human health effect of the target substance with respect to sub-chronic toxicity, screening for reproducte/developmental toxicity and pre-natal developmental toxicity can be predicted from the information provided on the source substance. Hence, your read-across adaptation does not comply with the general rules of Annex XI, Section 1.5. of the REACH Regulation.

2. *In vitro* cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

An "*in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study" is a standard information requirement as laid down in Annex VIII, Section 8.4.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation.
Information provided for the read-across approach

You have provided the following study summaries in IUCLID:

1. *in vitro* mammalian chromosome aberration test (OECD test method not indicated) with the source substance methyl salicylate (EC No. 204-317-7)
2. *in vivo* mammalian erythrocyte micronucleus tests (equivalent or similar to OECD TG 474) with the source substance ethyl hexyl salicylate (EC No. 204-263-4)
3. *in vivo* mammalian erythrocyte micronucleus test (according to OECD TG 474) with the source substance cyclohexyl salicylate (EC No. 400-410-3)

You have also provided attached to the IUCLID section 13
1. a read-across (category) justification documents Justification for read-across in the REACH registration of Benzyl Salicylate (EC No. 204-262-9, CAS No. 118-58-1) MUTAGENICITY [2]
2. justification for read-across to support the REACH registration of Benzyl Salicylate (CAS No. 118-58-1; EC No. 204-262-9) for *in vitro* gene mutation study in bacteria and *in vitro* cytogenicity study in mammalian cells (chromosome aberration) with empirical and mechanistic chemical profile of benzyl salicylate and methyl salicylate [3]
3. justification for read-across to support the REACH registration of Benzyl Salicylate (CAS No. 118-58-1; EC No. 204-262-9) for *in vivo* mutagenicity test (micronucleus test) with empirical and mechanistic chemical profile of benzyl salicylate and ethyl hexyl salicylate [4]

Description of your grouping and read-across approach

You indicate that: "*This is a category approach for which the read-across hypothesis is based on different compounds which have the same type of effect(s). [...] The category is based on 11 salicylic substances [...]. All 11 category members have similar profiling alerts for mutagenicity [...] and the structural differences are not expected to influence the degree of DNA interaction and therefore the mutagenicity of either the target or source substances.*"

You provided the following read-across hypothesis and justification: "*This read-across is based on the hypothesis that the target substance and source substances have similar mutagenicity properties as a result of structural similarity, the same expected mode of action and similar physicochemical properties relevant for the read-across mutagenicity endpoints.*"

You conclude that: "*the salicylates as a group are concluded to be without mutagenic/genotoxic potential.*"

In the justification document [2], [3] and [4] you identified three main source substances, methyl salicylate (EC No. 204-317-7), cyclohexyl salicylate (EC No. 400-410-3) and ethyl hexyl salicylate (EC No. 204-263-4) (hereafter the 'source substances). In the justification document [2] you state that cyclohexyl salicylate and ethyl hexyl salicylate "*share structural similarities and also mechanistic action similarities which are both general and endpoint specific*" and that "*the source and target substance have similar human health properties as a result of structural similarity, the same expected mode of action for mutagenicity and similar physicochemical properties.*" In the justification document [3] you state further that target substance and methyl salicylate "*are sufficiently similar such that available toxicological data from the Source Substance can be used to address the following endpoints in the REACH registration dossier for the Target Substance. In vitro gene mutation study in bacteria - Ames test. In vitro cytogenicity study in mammalian cells (chromosome aberration).*" In the justification document [4] you state that target substance and ethyl hexyl salicylate "*are sufficiently similar such that available toxicological data from the Source Substance can be used to address the following endpoints in the REACH registration dossier for the Target Substance. In vivo mutagenicity test: micronucleus test.*"

ECHA's analysis of the grouping and read-across approach

Category definition

ECHA observes that especially for "Mutagenicity" you are supporting your read-across approach with information from a category. However, you did not define the applicability domain of your category and you did not describe inclusion and exclusion criteria. Furthermore, ECHA notes that the listed 10 potential source salicylic acid compounds contain wide range of saturated, unsaturated, branched and unbranched side chains which indicate major structural differences. Such structural differences would require solid justification.

Furthermore, ECHA notes that the target substance is the only salicylic acid category member among the selected analogue substances having an aromatic side chain. Hence, such substance can be considered as "outlier" of the category. Therefore, in the absence of a category definition with appropriate inclusion and exclusion criteria and demonstrating that the respective functional groups not common to all the category members do not affect the anticipated toxicity, the target and source substances cannot be considered as appropriate members of your category.

Read-across/category hypothesis

With respect to structural similarities and structural differences you mention that "*The 10 source category members have > 50% structural similarities with the target benzyl salicylate. This high degree of structural similarity increases the confidence along with the profiling as discussed, that this category will react in a similar manner in both an in vitro and in vivo test system.*"

However, ECHA notes a quantified structural similarity by itself is not sufficient basis for read-across adaptation and that the remaining structural dissimilarities between the source and target substances suggest different properties with regard to mutagenicity, as explained below in context with predicted DNA binding. Therefore, ECHA considers that the structural similarities between target substance and the 10 source substances of the category described as > 50% do not add confidence in your read-across adaptations for mutagenicity endpoints.

Furthermore, according to the predicted metabolite(s) provided for benzyl salicylate, cyclohexyl salicylate, and ethyl hexyl salicylate, the target substance leads to unique metabolic products (i.e. benzoic acid, benzyl alcohol and benzaldehyde). ECHA also notes that, despite of the identified breakdown products, the metabolic rates remain unknown.

You also explain that "*The target benzyl salicylate has a profile alert for "potential" DNA binding via the OECD profiler. This is not observed for the 2 main source substances or the 9 other salicylates that make up the category. Therefore, based on the negative BlueScreen and bacterial reverse mutation data, it would appear that this mechanism is not accurate. In addition, the target benzyl salicylate has no alerts via the OASIS DNA profiler and this is the same as for the rest of the category members (11 members). Considering that 8 category members have negative BlueScreen data and 7 have negative bacterial reverse mutation data, it has been shown that the bacterial mutation endpoint has been covered for all 11 category members and been shown not to be an issue for salicylates.*"

ECHA acknowledges that the target and source substances do not have OASIS DNA profiler alert. However, ECHA notes that OECD QSAR toolbox profiler suggests DNA binding after metabolic activation for the target substance but not for the source substances.

ECHA also notes that in Table 5 of your read-across justification document [2] you are referring to information from BlueScreen tests as supporting information to your read-across adaptations. However, you did not provide study summaries of these tests in IUCLID. You state that BlueScreen test "specificity" is currently 96% and "sensitivity" 87% and that "*available fragrance industry data comparing BlueScreen data to the available experimental data for genetox testing indicates that the "specificity" is 90%.*" Furthermore, since this is not a test method approved by OECD, it would be necessary to provide more detailed information on this test. For example, clarification on the study principle and more detail on its ability to detect gene mutations and/or cytogenicity is required. Please note that ECHA expects you to provide robust study summary/summaries in IUCLID for information that is addressing either a standard information requirement and/or that is most relevant to support your read-across approach.

Therefore, ECHA considers that the absence of genotoxic effects for the target substance, for which an alert for DNA binding after metabolic activation exists, cannot be predicted from an absence of effects in studies with the selected source substances, for which no such profiler alerts exists.

You conclude that the three main source substances mentioned above can be used to close data-gaps in the health hazard assessment of the registered substance as you consider the read-across approach is scientifically acceptable with high confidence based on your examination of the adequacy and scientific robustness of the provided read-across justifications and corresponding information using assessment elements (AE) of the ECHA Read-across assessment framework (RAAF).

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you state that "*the REACH dossiers on the metabolites of the target and source substances (salicylic acid, benzyl alcohol and cyclohexanol) are available for consultation on the ECHA website following registration*" and that "*there is no indication of mutagenicity concern for these substances in the absence and presence of S9-mix*."

You also include in your comments QSAR toolbox reports
1. "Prediction of chromosome aberration for benzyl salicylate" (*in vitro* mammalian chromosome aberration test),
2. "Prediction of chromosome aberration for benzyl salicylate" (*in vivo* micronucleus assay), and
3. "Prediction of chromosome aberration for benzyl salicylate" (*in vivo* micronucleus test in bone marrow)

which you state, "*confirms that the target substance does not cause chromosome aberrations in mammalian cells".* However, the data matrix has not been provided and no further references or study reports are made available. In addition, the read-across substances included in the report are mostly different from the substances listed in the read-across justification document [2].

You note that "*from the category it can clearly be seen that these structural differences including the aromatic side on benzyl salicylate, do not result in differences to the following:*
- *Toxicity of the parent compounds.*
- *Differences in enzymatic hydrolysis of the parent compounds.*
- *Potential toxicity due to metabolite formation.*
- *Overall mutagenicity/genotoxicity*"

ECHA acknowledges the supporting documentation provided in the comments but notes that robust study summary/summaries for information that is addressing either a standard information requirement and/or that is most relevant to support your read-across approach have not been provided and therefore an independent evaluation of the read-across supporting documentation is not possible.

As explained above, ECHA considers that, in the absence of further supporting information, differences in target and source substance toxicological properties cannot be ruled out but are rather expected and therefore disagrees with your RAAF AE scoring supporting the acceptance of the read-across with high confidence. ECHA considers that it is not possible to assume/conclude if human health effect of the target substance with respect to mutagenicity can be predicted from the information provided on the source substance.

ECHA considers that to clarify the concern for potential genotoxicity of the registered substance, it is necessary to provide experimental information on *in vitro* cytogenicity in mammalian cells with the registered substance.

Conclusion on your read-across approach

For the reasons as set out above, and taking into account all of your arguments, ECHA considers that this grouping and read-across approach does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. of the REACH Regulation. Therefore, this adaptation cannot be accepted and there is a data gap for the endpoints covered by this read-across approach.

Consequently there is an information gap and it is necessary to provide information for this endpoint.
ECHA considers that the *in vitro* mammalian chromosome aberration test (test method OECD TG 473) and the *in vitro* mammalian cell micronucleus test (OECD TG 487) are appropriate to address the standard information requirement of Annex VIII, Section 8.4.2. of the REACH Regulation.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: *In vitro* mammalian chromosome aberration test (test method: OECD TG 473) or *in vitro* mammalian cell micronucleus study (test method: OECD TG 487).

3. *In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

An "*In vitro* gene mutation study in mammalian cells" is an information requirement as laid down in Annex VIII, Section 8.4.3. of the REACH Regulation, "if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2." is obtained.

ECHA notes that negative results have been obtained from the gene mutation study on bacteria (Annex VII, Section 8.4.1., the information requirement of Annex VIII, Section 8.4.2. has been adapted using invalid read-across adaptation (see below) and the registration dossier does not contain a valid study record for this information requirement. Therefore, adequate information *on in vitro* gene mutation in mammalian cells needs to be present in the technical dossier for the registered substance to meet this information requirement provided that the study requested under 2 has negative result.

You have sought to adapt this information requirement according to Annex VIII, Section 8.4.3. You provided the following justification for the adaptation:

"According to Regulation (EC) No. 1907/2006, Annex VIII, section 8.4.3, an in vitro gene mutation study in mammalian cells is not required if negative results are obtained in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. Since adequate data from reliable in vivo mammalian gene mutation tests are available, testing for this endpoint is not required."

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex VIII, Section 8.4.3., because an *in vitro* gene mutation study in mammalian cells is required if *negative* results are obtained in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. Furthermore, as explained above, your read-across adaptation for *in vitro* cytogenicity in mammalian cells or *in vitro* micronucleus study (Annex VIII, Section 8.4.2.) based on *in vitro* and *in vivo* information from source substances is rejected.

In your comment(s) on the draft decision according to Article 50(1) of the REACH Regulation you state that "*the REACH dossiers on the metabolites of the target and source substances (salicylic acid, benzyl alcohol and cyclohexanol) are available for consultation on the ECHA website following registration*" and that "*there is no indication of an increase in the in vitro mammalian gene mutation for these substances in the absence and presence of S9-mix.*"

You also include in your comments a QSAR toolbox report "*Prediction of Gene mutation for benzoic acid, 2-hydroxy-, pentyl ester*" which, you state, "*confirms that the target substance does not cause gene mutations in mammalian cells*". However, the data matrix has not been provided and no further references or study reports are made available. In addition, the read-across substances included in the report are mostly different from the substances listed in read-across justification document [2].

ECHA acknowledges the supporting documentation provided in the comments but notes that robust study summary/summaries for information that is addressing either a standard information requirement and/or that is most relevant to support your read-across approach have not been provided and therefore an independent evaluation of the read-across supporting documentation is not possible. In addition, as explained above in Appendix 1, sections 2 and 3 of this decision, your read-across adaptations of the mutagenicity information requirements is rejected.

Therefore, your adaptation of the information requirement for *in vitro* mammalian gene mutation test is also rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA considers that the *in vitro* mammalian cell gene mutation tests using the *Hprt* and *xprt* genes (OECD TG 476) and the *in vitro* mammalian cell gene mutation tests using the thymidine kinase gene (OECD TG 490) are appropriate to address the standard information requirement of Annex VIII, Section 8.4.3.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: *In vitro* mammalian cell gene mutation test (test method: OECD TG 476 *or* OECD TG 490) provided that the study requested under 2 has negative result.

4. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

A "sub-chronic toxicity study (90 day)" is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.
You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a Repeated Dose 90-Day Oral Toxicity in Rodents (OECD TG 408) with the source or analogue substance cyclohexyl salicylate (EC No. 400-410-3). You provided comment(s) on the draft decision according to Article 50(1) of the REACH Regulation which have been acknowledged and discussed above in Appendix 1, section 'Grouping of substances and read-across approach' of this decision.

Furthermore, as explained above in Appendix 1, section 'Grouping of substances and read-across approach' of this decision, your adaptation of the information requirement is

rejected.

Hence, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration. More specifically, the substance is a liquid of very low vapour pressure and the reported concentrations applied in uses with industrial / professional spray applications are low (<[redacted]%). Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

According to the test method EU B.26./OECD TG 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Repeated dose 90-day oral toxicity study (test method: EU B.26./OECD TG 408) in rats.

5. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Screening for reproductive/developmental toxicity" (test method OECD TG 421 or 422) is a standard information requirement as laid down in Annex VIII, Section 8.7.1. of the REACH Regulation if there is no evidence from available information on structurally related substances, from (Q)SAR estimates or from *in vitro* methods that the substance may be a developmental toxicant. No such evidence is presented in the dossier. Therefore, adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.
You have not provided any study record of a screening for reproductive/developmental toxicity in the dossier that would meet the information requirement of Annex VIII, Section 8.7.1.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a one-generation reproduction toxicity study (OECD TG 415) with the analogue or source substance cyclohexyl salicylate (EC No. 400-410-3). You provided comment(s) on the draft decision according to Article 50(1) of the REACH Regulation which have been acknowledged and discussed above in Appendix 1, section 'Grouping of substances and read-across approach' of this decision.

Furthermore, as explained above in Appendix 1, section 'Grouping of substances and read-across approach' of this decision, your adaptation of the information requirement is rejected.

Hence, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test methods OECD TG 421/422, the test is designed for use with rats. On the basis of this default assumption ECHA considers testing should be performed with rats.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Reproductive/developmental toxicity screening test (test method: OECD TG 421) *or* Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (test method: OECD TG 422) in rats by the oral route.

Notes for your consideration

For the selection of the appropriate test, please consult ECHA *Guidance on information requirements and chemical safety assessment*, Chapter R.7a, section R.7.5 and 7.6 (version 6.0, July 2017). You should also carefully consider the order of testing especially the requested screening (OECD TG 421/422) and the developmental toxicity studies (OECD TG 414) to ensure unnecessary animal testing is avoided, paying particular attention to ECHA's end point specific guidance document[2].

6. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

A "pre-natal developmental toxicity study" (test method EU B.31./OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a prenatal developmental toxicity study (OECD TG 414) with the analogue or source substance cyclohexyl salicylate (EC No. 400-410-3). You provided comment(s) on the draft decision according to Article 50(1) of the REACH Regulation which have been acknowledged and discussed above in Appendix 1, section 'Grouping of substances and read-across approach' of this decision.

Furthermore, as explained above in Appendix 1, section 'Grouping of substances and read-across approach' of this decision, your adaptation of the information requirement is

[2] ECHA Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7a: Endpoint specific guidance Version 5.0, December 2016, p 461-2 (https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf).

rejected.

Hence, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test method EU B.31./OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default assumption ECHA considers testing should be performed with rats or rabbits as a first species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a first species (rat or rabbit) by the oral route.

7. Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for human health

In accordance with Articles 10(b) and 14(1) of the REACH Regulation, the registration must contain a chemical safety report (CSR) which documents the chemical safety assessment (CSA) conducted in accordance with Article 14(2) to (7) and with Annex I to the REACH Regulation.

Annex I, Section 5. of the REACH Regulation indicates that the objective of the exposure assessment shall be to make a quantitative or qualitative estimate of the dose/concentration of the substance at which humans are or may be exposed. The exposure assessment shall consider all stages of the life-cycle of the substance resulting from the manufacture and identified uses and shall cover any exposures that may relate to the identified hazards.

Annex I, Section 6 of the REACH Regulation requires the Registrant to characterise the risk for each exposure scenario and to consider the human population (exposed as workers, consumer or indirectly via the environment and if relevant a combination thereof) and the environmental spheres for which exposure to the substance is known or reasonable foreseeable, under the assumption that the risk management measures described under the respective exposure scenario in Section 5 of the same Annex have been implemented. Risk characterisation consists of e.g. a comparison of the exposure of each human population known to be or likely to be exposed with the appropriate DNEL. For any exposure scenario, the risk to humans and to the environment can be considered to be adequately controlled, throughout the lifecycle of the substance that results from manufacture and/or identified uses, if the exposure level estimates in Section 6.2 do not exceed the appropriate DNEL. For those human effects and those environmental spheres for which it was not possible to determine a DNEL, a qualitative assessment of the likelihood that effects are avoided when implementing the exposure scenario shall be carried out.

According to Article 14(4), the CSR must include an exposure assessment and risk characterisation in the chemical safety assessment if the substance fulfils the criteria for any

of the listed hazard classes or categories set out in Annex I to Regulation (EC) No 1272/2008 or is assessed to be a PBT or vPvB. You have classified the registered substance as eye irritation class 2, skin sensitisation 1B and aquatic chronic 3, thus for hazards, which are listed in Article 14(4).

Following REACH Regulation Annex 1, Section 6.4 and ECHA's *Guidance on information requirements and chemical safety assessment* (Version 3.0, May 2016) Part E: Risk Characterisation, the risk to humans can be considered to be adequately controlled, if the exposure level estimates do not exceed the appropriate DNEL (derived no effect level) and consequently the calculated RCR (risk characterisation ratio) is below 1, respectively.

ECHA notes that you have identified unsafe uses in the exposure assessment and risk characterisation. More specifically, you have presented RCRs above 1 for several exposure scenarios in professional end-use of fragranced end-products in the CSR. The highest RCRs you present are as high as [redacted] for the combined routes and phases for the use in general purpose cleaner, spray and wipe (CS-13) application, and in surface disinfectants, spray and rinse (CS-26) application. Even though the RCRs are above 1, you have not provided any explanation how the uses may be still be recognised as being safe. In the CSR, you have noted that *"for a number of scenarios, the RCR calculated for combined phases is greater than 1 indicating a potential risk. In these cases, the exposure predicted with higher tier tools (ConsExpo for dermal exposure, ART too for inhalation exposure) should be taken into account."* However, you have not demonstrated that the use of those tools would lead to an acceptable lower risk characterisation, *i.e.* by specifying the conditions of safe use.

In your comments on the draft decision, you have agreed to provide updated DNELs and exposure scenarios.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to revise the exposure assessment and risk characterisation (Annex I, Sections 5. and 6.): revise the exposure assessment for the uses for which RCRs are above 1 and revise the risk characterisation accordingly.

8. Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for human health

In accordance with Articles 10(b) and 14(1) of the REACH Regulation, the registration must contain a chemical safety report (CSR) which documents the chemical safety assessment (CSA) conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

As explained under section 7 above, you have classified the substance for certain hazards, which triggers the obligation to include an exposure assessment and risk characterisation in the chemical safety assessment in the CSR according to Article 14(4) of the REACH Regulation.

Article 14(6) as well as Annex I, Section 0.1., 5.1.1., 5.2.4., 5.2.5. and 6.2. of the REACH Regulation require registrants to identify, estimate the exposure and apply appropriate measures to adequately control the risks identified in a CSR. The exposure shall be estimated by using representative exposure data or appropriate models and risks shall be characterized in the CSR under the assumption that relevant risk management measures have been implemented.

ECHA notes that in your CSR you have many worker contributing scenarios (WCS) in exposure scenarios 3 and 4, where you describe industrial and professional spraying activities, i.e. PROC 7 and PROC 11 respectively, and roller application or brushing (PROC 10). In all these tasks aerosol formation is likely to occur. You have used the exposure tool, ECETOC TRA version 3, to estimate the exposure levels.

However, ECHA notes that ECETOC TRA version 3 does not address aerosol exposure; it only predicts vapour phase exposure for liquid substances and is not appropriate to evaluate exposure to spray aerosol. In this context, the inhalation exposure of the registered substance, which has a low vapour pressure (vp 0.0104 Pa at 25°C), may be underestimated and the estimated worker exposures may be associated with a higher level of uncertainity. ECHA also notes that there are a number of WCS where the RCRs are only slightly below 1. For example, the combined RCRs are [redacted] and [redacted] in the WCS-8 and 9, respectively, in exposure scenario 3 and [redacted] and [redacted] in the WCS-2 and 8, respectively, in exposure scenario 4. However, if the aerosol formation had been taken into account in the exposure estimation, the use might be concluded as being unsafe (an RCR>1). Therefore you are requested to use a different model that is more suitable for low volatility substances to assess the exposure during spraying, roller application or brushing activities, e.g. Stoffenmanager or ART model.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to revise the exposure assessment and risk characterisation (Annex I, Sections 5. and 6.): revise worker contributing scenarios (WCSs) describing activities where aerosol formation is likely to occur using a model that is suitable to assess the exposure during such activities and revise the risk characterisation accordingly.

9. Exposure assessment (Annex I, Section 5.1.1.) for human health

In accordance with Articles 10(b) and 14(1) of the REACH Regulation, the registration must contain a chemical safety report (CSR) which documents the chemical safety assessment (CSA) conducted in accordance with Article 14(2) to (7) and with Annex I to the REACH Regulation.

Article 14(6) as well as Annex I, 0.1., 5.1.1., 5.2.4. and 6.2. of the REACH Regulation require registrants to identify and apply appropriate measures to adequately control the risks identified in a CSR. The exposure shall be estimated and risks shall be characterized in the CSR under the assumption that relevant risk management measures have been implemented.

According to Annex I, 0.3., 0.5. and 5.1.1. the applied Risk Management Measures (RMM) have to be described in the CSR. The CSR needs to contain sufficient information to allow ECHA to gain assurance that the risks are adequately controlled and that appropriate risk management measures can be prescribed by actors in the supply chain. Accordingly, the supplier is required to describe the relevant RMM in detail in the Safety Data Sheet in order to minimize the exposure for workers handling the registered substance (e.g. the type of gloves to be worn, protection equipment for parts of the body other than the hand or respiratory protection shall be clearly specified based on the hazard of the substance or mixture and potential for contact and with regard to the amount and duration of exposure in accordance with Annex II, section 8.2.2.2.(b)(i), (ii) and 8.2.2.2.(c) respectively). The information provided in the Safety Data Sheet (SDS) shall be consistent with information in the Chemical Safety Report (Annex II, section 0.1.2. of the REACH Regulation).

ECHA notes that specific detailed information on the recommended personal protective equipment is missing both from the CSR and from the information on safe use within the IUCLID dossier. In IUCLID Section 11 you have reported following:
Hand protection: The suitability for a specific workplace should be discussed with the producers of the protective gloves.
Eye protection: Eye wash bottle with pure water. Tightly fitting safety goggles.
Skin and body protection: Impervious clothing. Choose body protection according to the amount and concentration of the dangerous substance at the work place."
In the CSR, you indicated the following for hand protection/protection of the parts of the body other than hand: Workers wear appropriate working suites *in the compounding facility. Workers should wear chemical resistant gloves during activities with high potential for dermal exposure, such as cleaning and maintenance. Depending on the intrinsic hazards of* the substances it may be necessary that workers wear chemical resistant safety goggles.

To ensure the safe use of a substance, Annex I, Section 5.1.1. requires a description of the risk management measures to reduce or avoid direct and indirect exposure of humans.

Gloves are reported in the CSR and IUCLID Section 11 as required personal protective equipment to prevent dermal exposure to the substance. ECHA points out that gloves that are capable of preventing exposure to the skin for a pre-determined duration shall be specified. Typically, this information, as a minimum, has to specify the glove material and, depending on the exposure scenarios, may also need to include the breakthrough time and thickness of the glove material. Gloves need to be manufactured and tested according to CEN standard EN 374:2003 – Gloves giving protection from chemicals and micro-organisms.

Respiratory protection is reported in the CSR and IUCLID Section 11 as required personal protective equipment to prevent inhalation exposure to the substance. ECHA states that typically, this information, as a minimum, has to specify the type/class of filters that are capable of preventing inhalation exposure for a pre-determined duration and delivering the assessment protection factor specified by you.

ECHA further maintains that, where protective clothing is specified as a means to reduce exposure to the registered substance, it has to be capable of providing the required barrier properties. This can only be assured through provision of clothing that has been tested to ensure a minimum performance against splash/spray/jet challenge. The minimum standard for liquid chemicals is "Type 6" protective clothing that meets the standard of EN 13034:2005 – *Chemical protective clothing offering limited protection against liquid chemicals (type 6 and type PB [6] equipment),* typically disposable coveralls. Unspecified workwear that has not been tested according to the appropriate standards for permeation and penetration resistance is not chemical protective clothing, as defined, and is unlikely to provide any demonstrable protection. It may even act as a longer-term source of exposure.

In your comments on the draft decision, you have agreed to update the required information levels of PPE.

Therefore, pursuant to Article 41(1) you are requested to provide documentation for the recommended personal protective equipment, i.e. skin protection (i.e. hand and body protection) and respiratory protection:
- specify the type of glove material, thickness and breakthrough times;
- specify the filter type/class for the respiratory protective equipment;
- specify the type and quality of protective clothing.

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 1 March 2017.

Concerning your comment on the initiation date for the compliance check, ECHA notes that the compliance check initiation date in the decision is not correctly reflecting the initiation of evaluation work of your dossier. This inconsistency is due to an IT-system update during the evaluation and root cause technical by nature. Therefore, the assessment of the dossier and the attached read-across justifications started in practise earlier on 9 November 2016. ECHA considers that full and comprehensive assessment has not been compromised.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

ECHA notified you of the draft decision and invited you to provide comments.

ECHA took into account your comments and did not amend the request(s).

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s).

ECHA referred the draft decision to the Member State Committee.

You did not provide any comments on the proposed amendment(s).

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-56 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This compliance check decision does not prevent ECHA from initiating further compliance checks on the present registration at a later stage.

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.