Helsinki, 13 July 2016

Addressee: [redacted]

Decision number: CCH-D-2114332783-48-01/F
Substance name: 5-methylhexan-2-one
EC number: 203-737-8
CAS number: 110-12-3
Registration number: [redacted]
Submission number: [redacted]
Submission date: 23.10.2014
Registered tonnage band: > 1000 tonnes/year

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. **Robust study summaries for the two *in vitro* chromosome aberration studies reported in the registration dossier (Article 10 (a)(vii) in conjunction with Annex I, Section 1.1.4.).**

2. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2; test method: EU B.31/OECD TG 414) in a second species (rabbits), inhalation route with the registered substance.**

3. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3; test method: EU B.56./OECD TG 443) in rats, oral or inhalation route with the registered substance; specified as follows:**

    - **Ten weeks premating exposure duration for the parental (P0) generation;**
    - **Dose level setting shall aim to induce some toxicity at the highest dose level;**
    - **Cohort 1A (Reproductive toxicity); and**
    - **Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation.**

4. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for human health: revise exposure estimates for the dermal route without the use of LEV as an exposure modifier and revise the risk characterisation accordingly.**

5. **Exposure assessment and risk characterisation (Article 14(6), Annex I, Section 5.1.1., in conjunction with Annex II, 0.1.2. and 8.2.2.2.(b)(i) and Section 6.) for human health: Hand protection:**
   - specify the type of glove material, thickness and breakthrough times.

6. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment: specify in the Exposure Scenario for industrial use in coatings:**
- **joint efficiency of control measures which has to be achieved in order to ensure identified level of release to air; and**
- **Risk Management Measures (technics/methods with efficiencies of each included) which would ensure necessary level of removal of the substance from emissions to air and revise the risk characterisation accordingly.**

7. **Identification of DNEL(s) and risk characterisation (Annex I, Sections 1.4. and 6.): revise long-term DNEL(s) for dermal route for workers and for inhalation, dermal and oral route for the general population systemic effects using the assessment factors recommended by ECHA Guidance R.8 for DNEL derivation and revise the risk characterisation accordingly *or* provide a detailed justification on how the chosen approach meets the general requirements for DNEL derivation as described in Section 1.4 of Annex I.**

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 of the REACH Regulation. In order 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 an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **21 January 2019**. You shall also 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. 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, shall 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 Ofelia Bercaru, Head of Unit, Evaluation E3

[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.

Appendix 1: Reasons

1. Robust study summaries for the two *in vitro* chromosome aberration studies reported in the registration dossier (Article 10 (a)(vii) in conjunction with Annex I, Section 1.1.4.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH 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. Furthermore, pursuant to Article 10 (a)(vii) in conjunction with Annex I, Section 1.1.4. if there are several studies addressing the same effect, then, having taken into account possible variables (e.g. conduct, adequacy, relevance of test species, quality of results, etc.), normally the study or studies giving rise to the highest concern shall be used to establish the DNELs and a robust study summary shall be prepared for that study or studies and included as part of the technical dossier. Robust summaries will be required of all key data used in the hazard assessment.

ECHA observes that in the registration dossier, section 7.6.1. you have provided results of two *in vitro* mammalian chromosome aberration tests (performed according to OECD TG 473). There are conflicting results from these two studies reported in the dossier. For the study you marked as key study ([redacted]) you concluded that there was no evidence of chromosomal aberrations or polyploidy. For the study by [redacted]) you concluded that chromosomal aberrations were observed in the presence and absence of metabolic activation but only at extremely cytotoxic doses. ECHA considers that the study showing positive findings should be considered as the study giving rise to the highest concern and a robust study summary should be provided for that study. However, you did not provide the robust study summary for either of the tests mentioned above as required by Section 1.4.4. of Annex I of the REACH Regulation and which would be sufficient to confirm your conclusion that the positive results are indeed not relevant because of high cytotoxicity and the negative study should be considered when deriving DNELs.

More specifically ECHA notes that from the information provided in the dossier on the study with positive result, it is not clear, if the substance induced chromosomal aberrations or polyploidy, which of the results is obtained with or without metabolic activation, and what is the level of the positive result. The key uncertainty for this study is the level of cytotoxicity observed at the concentration inducing chromosomal aberration. In the key study with negative result, the absence of significant increase in cells with chromosomal aberrations, polyploidy or endoreduplication cannot be validated, because concentrations inducing a higher level of cytotoxicity should have been tested, or the reason for not testing higher should be explained. You noted in the dossier that "*reductions of 17%, 18%, 47%, and 18% were observed in the mitotic indices of the cultures treated with 380, 675, 900, and 1200 µg/mL, respectively*". ECHA notes that OECD TG 473 indicates that the top dose should induce a cytotoxicity of app. 50%, i.e. a 50% decrease in the mitotic index compared to the control. Thus, ECHA concludes that in order to interpret results of these studies and verify conclusions made by you, more data/explanations for both these studies are necessary in the registration dossier.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information: Robust study summaries for the two *in vitro* chromosome aberration studies reported in the registration dossier.

2. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in the second species

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

Pre-natal developmental toxicity studies on two species are part of the standard information requirements for a substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

The technical dossier contains information on a pre-natal developmental toxicity study in rats by the inhalation route using the registered substance as test material.

However, there is no information provided for a pre-natal developmental toxicity study in a second species.

You have sought to adapt this information requirement. You provided the following justification for the adaptation: "*For reproductive toxicity tests under Sections 8.7 of Annexes IX and X of the REACh Regulation (Regulation), Column 2 provides that studies do not need to be conducted if the substance is of low toxicological activity (i.e., no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure.*

For pre-natal developmental toxicity studies under Section 8.7.2 in Annex IX, the Regulation requires a study (OECD 414) in one species using the most appropriate route of administration having regard to the likely route of human exposure. For substances manufactured or imported in quantities of 100 tonnes or more (Annex IX) or 1000 tonnes or more (Annex X), Column 2 requires the registrant to make a decision on the need to perform another pre-natal developmental study on a second species based upon the results of the first study and all other relevant data.

Following a careful review of the prenatal developmental toxicity study in the first species and all other relevant data for methyl iso-amyl ketone in accordance with the specific rules set forth in Column 2, the Lead Registrant has determined that performing another pre-natal developmental study in a second species is not warranted.

Based on these results, the LR concludes that there is no data suggesting that developmental toxicity is a concern and that a pre-natal developmental toxicity study using a second species is not warranted. Thus, the LR will not perform another OECD 414 study in a second species under Annex X.

Furthermore, this decision to not conduct additional animal testing is consistent with the objective of Article 25 which stresses that animal testing under the Regulation shall be undertaken only as a last resort and that it is necessary to take measures to limit duplication of other tests. The decision to not conduct an additional OECD 414 study is well justified by the existing data, including the existing OECD 414 study, and to resort to additional testing would be adverse to the objectives of Article 25."

However, ECHA notes firstly that the registered substance shows toxicity (e.g. classification as Acute Tox 4), the toxicokinetic information provided indicates systemic availability both after inhalation and dermal exposure and there is also human exposure as indicated by the exposure estimation performed by you (see section 4 of this Appendix). Therefor your adaptation mentioned in the first paragraph above does not meet the specific rules for adaptation of Annex X, Section 8.7., column 2. ECHA notes secondly that your statement "*Column 2 requires the registrant to make a decision on the need to perform another pre-natal developmental study on a second species based upon the results of the first study and all other relevant data*" applies for standard information requirement at Annex IX. However a pre-natal developmental toxicity studies on two species are part of the standard information requirements for a substance registered for 1000 tonnes or more per year. ECHA notes thirdly that none of the other column 2 adaptations of Annex X section 8.7.2 (based on known mutagenicity or carcinogenicity or classifcation for reproductive toxicity) applies. Finally, ECHA notes that legislator has already taken provisions of Article 25 into account when standard information requirements were set. There are currently no validated alternative (non-animal) methods to assess pre-natal developmental toxicity.

Therefore, your adaptation of the information requirement cannot be accepted. Thus, 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 for Annex X, Section 8.7.2. and it is necessary to provide information for this endpoint.

The test in the first species was carried out by using a rodent species (rats). According to the test method EU B.31/OECD TG 414, the rabbit is the preferred non-rodent species. On the basis of this default consideration, ECHA considers that the test should be performed with rabbits as a second species.

ECHA notes that the pre-natal developmental toxicity study on the first species was performed via inhalation. ECHA has initially requested testing by the oral route due to default considerations as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, July 2015) R.7a, chapter R.7.6.2.3.2. In the comments to the draft decision you indicated that in view of the use of the registered substance as a solvent inhalation is the most relevant route of human exposure and the toxicological database of the substance consists of inhalation studies. Therefore testing should be performed by the inhalation route. ECHA notes that since the substance to be tested is a liquid of medium volatility and irritating only at high concentrations, testing by inhalation is also an appropriate route for identification of potential reproductive hazards and can be regarded as the most appropriate route of administration for the registered substance. For those reasons, ECHA concludes that testing should be performed by the inhalation 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 second species (rabbits) by the inhalation route.

3. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

The basic test design of an extended one-generation reproductive toxicity study (Cohorts 1A and 1B, without extension of Cohort 1B to include a F2 generation, and without Cohorts 2A, 2B and 3) is a standard information requirement as laid down in Column 1 of Section 8.7.3., Annex X of the REACH Regulation. If the conditions described in Column 2 of Annex X are met, the study design needs to be expanded to include the extension of Cohort 1B, Cohorts 2A/2B, and/or Cohort 3.

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 an extended one-generation reproductive toxicity study in the dossier that would meet the information requirement of Annex X, Section 8.7.3.

In section 7.8.1. of the IUCLID dossier, you have provided a waiver including weight-of-evidence (WoE) according to Annex XI, 1.2. However, ECHA notes that this adaptation does not meet the general rule for adaptation according to Annex XI; Section 1.2. because of the following insufficiencies:

Your weight-of-evidence is based on the assumption that the registered substance has a low potential for inducing reproductive toxicity. In this respect and as a preliminary remark, ECHA emphasises that an assumption of "low potential" per se is not sufficient to waive this standard information requirement at Annex X because it does not fulfil an adaptation according to column 2 of Annex X, Section 8.7.3 (see considerations for a similar adaptation in section 2 of this Appendix). In particular, the use of weight of evidence approach to omit this test requires that absence of dangerous properties with respect to fertility and postnatal development should be demonstrated by using several independet sources of information which are sufficient to support this notion (see Annex XI, Section 1.2).

In your WoE justification, you have provided the following studies: an OECD 421 inhalation reproductive/developmental screening study, an OECD 414 inhalation pre-natal developmental toxicity study and an OECD 413 repeat dose inhalation toxicity test with a histological and gross morphological examination of male and female reproductive organs.

An evaluation of the information provided within the WoE justification for the case as presented in the registration dossier indicates the following:
For male and female fertility, including sperm parameters, an absence of effects is noted. However, the available study results (OECD TG 421) have lower statistical power. No information on oestrus cyclicity is provided; there is no immediate indication for concern because fertility was not impaired. Based on the available information (OECD TG 421, OECD TG 413) from organ weight changes, there is no indication of an endocrine disrupting mode of action. However, information on potential effects on relevant hormone levels is not available so far. The results from the OECD TG 421 measure growth and survival only until post natal day 4, but not until sexual maturation and until adulthood. No malformations were observed in the OECD TG 414 performed. However, sexual marturation of the F1 generation was not investigated. Furthermore, there is no information on histopathological evaluation of reproductive organs in adult F1 animals.

ECHA notes that the provided evidence with limited statistical power suggest the absence of severe effects on fertility in parental (P0) animals, but is not sufficient to assume or conclude on the presence or absence on effects on the offspring (F1) with regard to growth and maturation, sexual maturation including histopathology on reproductive organs or less prominent effects on fertility in parental animals. Therefore, the WoE waiver is not sufficient to conclude/assume that the substance has or has no effects on fertility and development and sexual maturation of the F1 generation, and your adaptation of the information requirement cannot be accepted.

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.

Thus, an extended one-generation reproductive toxicity study according to column 1 of 8.7.3., Annex X is required. The following refers to the specifications of this required study in accordance with column 2 of Section 8.7.3., Annex X.

Premating exposure duration and dose-level setting

To ensure that the study design adequately addresses the fertility endpoint, the duration of the premating exposure period and the selection of the highest dose level are key aspects to be considered. According to ECHA Guidance (Chapter R.7a: Endpoint specific guidance, R.7.6, Version 4.0 – July 2015), the starting point for deciding on the length of premating exposure period should be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

ECHA considers that ten weeks premating exposure duration is required in this case, because there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA Guidance.

The highest dose level shall aim to induce some toxicity to allow comparison of effect levels and effects of reproductive toxicity with those of systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels.

It is recommended that results from a range-finding study (or range finding studies) for the extended one-generation reproductive toxicity study are reported with the main study. This will support the justifications of the dose level selections and interpretation of the results.

Species and route selection

According to the test methods EU B.56/ OECD TG 443, the rat is the preferred species. ECHA considers this default parameter appropriate and testing should be performed in rats.

ECHA has initially requested testing by the oral route due to default considerations as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, July 2015) R.7a, chapter R.7.6.2.3.2. In the comments to the draft decision you indicated that testing should be performed by the inhalation route (see section 2 of this Appendix above). ECHA notes that since the substance to be tested is a liquid of medium volatility and irritating only at high concentrations, testing by inhalation is also an appropriate route for identification of potential reproductive hazards and can be regarded as the most appropriate route of administration for the registered substance.

However, since the test method is new and mainly intended for administration of the test material by the oral route, there might be practical reasons for not testing by the inhalation route. In case testing by inhalation cannot be performed, the oral route should be used. Therefore, ECHA provides the option that the extended one-generation reproductive toxicity study should be performed either by the oral or by the inhalation route.

Outcome

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit an extended one-generation reproductive toxicity study (test method EU B.56./ OECD TG 443), in rats, oral or inhalation route, according to the following study-design specifications:

- Ten weeks premating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce some toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation.

Notes for your consideration

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3 if new information becomes available after this decision is issued to justify such an inclusion. Inclusion is justified if the new information shows triggers which are described in Column 2 of Section 8.7.3., Annex X and further elaborated in ECHA Guidance. You may also expand the study to address a concern identified during the conduct of the extended one-generation reproduction toxicity study and also due to other scientific reasons in order to avoid a conduct of a new study. The justification for the expansion must be documented. The study design must be justified in the dossier and, thus, the existence/non-existence of the conditions/triggers must be documented.

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

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

Pursuant to sections 0.6.2 and 0.6.3 of Annex I of the REACH Regulation the chemical safety assessment (CSA) performed by a Registrant shall include an exposure assessment according to section 5 of Annex I. Annex I, section 5.2.4 of the REACH Regulation, requires the Registrant to perform an estimation of the exposure levels for all human populations (workers, consumer and humans liable to exposure via the environment) for which exposure to the substance is known or reasonably foreseeable. Each relevant route of exposure (inhalation, oral, dermal and combined through all relevant routes and sources of exposure) shall be addressed. In addition, Annex I, section 5.2.5 of the REACH Regulation indicates that appropriate models can be used for the estimation of exposure levels.

ECHA notes that you have used ECETOC TRA version 2 to estimate exposure for a variety of worker exposure scenarios. More precisely you have used the local exhaust ventilation (LEV) exposure modifier even when inappropriate such as for estimating dermal exposure.

ECHA underlines that the Guidance on information requirements and chemical safety assessment, R.14 version 2.1 (section R.14.4.8, page 21) advises against the use of the LEV modifier for dermal exposure estimation. At page 21 ECHA's R.14 Guidance states, "*The dermal exposure for some situations with local exhaust ventilation is underestimated compared to measured data (e.g. RISKOFDERM project). In the light of knowledge having become available since EASE was published, the LEV effect on dermal exposure assessment may sometimes be overestimated by the model. To be more confident on the dermal exposure prediction under LEV conditions, the assessor could continue with higher tier assessment (e.g. Riskofderm). He could also recalculate the dermal exposure level outside the tool by setting the effectiveness of the local exhaust ventilation regarding dermal exposure to "0" or any other value significantly below the 90 to 99% assumed in the TRA (to reach a conservative estimate).*"

ECHA notes that the calculated exposure estimates are likely to be unrealistically low and therefore the worker exposure assessment for the dermal route needs to be revised. In the CSR, for many exposure scenarios, if the LEV dermal exposure modifier was not taken into consideration, the dermal RCRs would become above 1 therefore not demonstrating safe use.

As explained above, the information provided on the dermal exposure estimates for the registered substance in the chemical safety report does not meet the general provisions for preparing a chemical safety report as described in Annex I. Consequently it is necessary to revise the dermal exposure estimates.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to revise exposure estimates for the dermal route without the use of LEV as an exposure modifier and revise the risk characterisation accordingly.

Notes for your consideration

The revised DNELs requested with this decision shall be taken into account when assessing the related risks (see section 7 of this Appendix below).

Taking into account the need to revise the calculated DNEL(s), you shall ensure that the calculated risk characterisation ratios will still be below 1, in order to demonstrate the safe use of the registered substance

5. Exposure assessment and risk characterisation (Article 14(6), Annex I, Section 5.1.1., in conjunction with Annex II, 0.1.2. and 8.2.2.2.(b)(i) and Section 6.) for human health

Pursuant to Articles 10(b) and 14(1) of the REACH Regulation, the registration shall contain a chemical safety report which shall document the chemical safety assessment conducted in accordance with Article 14(2) to (7) and with Annex I of 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 characterised 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 minimise 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 the CSR, you indicated the following for hand protection: "use suitable [...] gloves", while in IUCLID Section 11 has reported: "For operations where prolonged or repeated skin contact may occur, chemical-resistant gloves should be worn. Contact health and safety professional or manufacturer for specific information."

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. Generally, 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.

Therefore, pursuant to Article 41(1)(c) you are requested to provide documentation for the recommended personal protective equipment, i.e. Hand protection: specify the type of glove material, thickness and breakthrough times.

6. Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment

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

Pursuant to sections 0.6.2 and 0.6.3 of Annex I of the REACH Regulation the chemical safety assessment (CSA) performed by a Registrant shall include an exposure assessment according to section 5 of Annex I. The exposure assessment consists of the generation of exposure scenarios and the exposure estimation. Pursuant to Annex I, section 5.2.1 of the REACH Regulation the exposure estimation entails three elements: emission estimation, assessment of chemical fate and pathways and estimation of exposure levels.

Pursuant to Annex I, section 5.2.2, the emission estimation shall be performed under the assumption that the risk management measures (RMMs) and operational conditions (OCs) described in the exposure scenario (ES) have been implemented. These final RMMs and OCs should be included in the ESs provided in a CSR as described in Section 5.1.1 of Annex I.

In accordance with the ECHA *Guidance on information requirements and chemical safety assessment* (Chapter R.16: Environmental Exposure Estimation, Version 2.1 – October 2012, chapter R.16.1.2), release estimation consists of the determination of the local and regional release rates for each use, starting from the appropriate release factors and the tonnage assigned to any identified use. ECHA notes that in the CSR, the exposure assessment is based on the release factors from the ESVOC sector specific environmental release categories (ESVOC SpERCs). In the ES for the Industrial use in coatings you specify that release factor to air is applicable after typical on-site RMMs consistent with EU Solvent Emissions Directive requirements have been implemented. Respective ESVOC SpERC 4.3a.v1, used as a basis to justify release factors to environment for this exposure scenario, indicates that efficiency of air emission controls is 90%. ECHA observes that in the provided ES you have not specified efficiency of control measures which has to be achieved in order to ensure identified level of release to air and you have not specified any RMMs (technics/methods) which would ensure necessary level of removal of the substance from emissions to air.

Therefore, pursuant to Article 41(1)(c) you are requested to specify in the ES for industrial use in coatings: joint efficiency of control measures which has to be achieved in order to ensure identified level of release to air and RMMs (technics/methods with efficiencies of each included) which would ensure necessary level of removal of the substance from emissions to air.

7. Identification of DNEL(s) and risk characterisation (Annex I, Section 1.4. and 6.)

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

Annex I, Section 1.4.1 of the REACH Regulation requires that the following factors shall, among others, be taken into account when deriving DNELs:

a) the uncertainty arising, among other factors, from the variability in the experimental information and from intra- and inter-species variation;
b) the nature and severity of the effect;
c) the sensitivity of the human (sub-)population to which the quantitative and/or qualitative information on exposure applies;
d) and that the DNELs reflect the likely route(s), duration and frequency of exposure.

The ECHA *Guidance on information requirements and chemical safety assessment* Volume 8, Chapter R.8 provides further details and specifically provides default factors which should be applied to derive DNELs in the absence of substance specific information.

The assessment factors (AF) applied by you when deriving long-term DNELs for systemic effects for dermal route for workers and for inhalation, dermal and oral route for the general population are not in line with the default factors listed in the ECHA guidance.

More specifically, the assessment factor for the remaining interspecies differences (factor 2.5) has not been used. Furthermore, the assessment factor for the intraspecies differences for workers has been reduced from 5 to 3 and for the general population from 10 to 5. No substance specific justification has been provided for these deviations from the default values.

As explained above, the information provided on DNELs for the registered substance in the chemical safety report does not meet the general provisions for preparing a chemical safety report as described in Annex I, 1.4.1. Consequently it is necessary to revise the DNELs or to provide a detailed justification.

You are given two options: you shall revise the DNELs for workers and the general population by applying the assessment factors recommended by ECHA that are appropriate in this case. Subsequently, you shall re-assess related risks.

In the alternative, you shall, in accordance with Annex I, 1.4.1, provide a detailed justification for the DNELs derived for workers and the general population provided in the chemical safety report by specifying how the following has been taken into account:

a) the uncertainty arising, among other factors, from the variability in the experimental information and from intra- and inter-species variation;
b) the nature and severity of the effect;
c) the sensitivity of the human (sub-)population to which the quantitative and/or qualitative information on exposure applies;
d) and that the DNELs reflect the likely route(s), duration and frequency of exposure.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to revise long-term DNEL(s) for workers dermal route systemic effects and for the general population inhalation, dermal and oral route systemic effect using the assessment factors of ECHA Guidance R.8 for DNEL derivation and revise the risk characterisation accordingly *or* provide a detailed justification on how the chosen approach meets the general requirements for DNEL derivation as described in Section 1.4 of Annex I.

Notes for your consideration

The results of the studies requested with this decision shall be taken into account when revising the DNELs.

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 July 2015

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

ECHA took into account your comments and amended the requests.

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

ECHA received a proposal for amendment and did not modify the draft decision.

ECHA invited you to comment on the proposed amendment.

ECHA referred the draft decision to the Member State Committee.

Your comments on the proposed amendment were taken into account by the Member State Committee.

The Member State Committee reached a unanimous agreement on the draft decision during its MSC-47 meeting 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 request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In carrying out the test(s) required by the present decision it is important to ensure that the particular sample of substance tested 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. If the registration of the substance covers different grades, the sample used for the new test(s) must be suitable to assess these. Furthermore, there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.