EUROPEAN CHEMICALS AGENCY

Helsinki, 1 September 2016

Addressee: [redacted]

Decision number: CCH-D-2114340417-53-01/F
Substance name: 2-Butyne-1,4-diol
EC number: 203-788-6
CAS number: 110-65-6
Registration number: [redacted]
Submission number: [redacted]
Submission date: 14.04.2015

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. **Identification of PNEC and risk characterisation (Annex I, Section 0.5., 3.3.1. and 6.): revise PNECs for freshwater, marine water and microorganisms in sewage treatment plants by using the PNECs derived in EU RAR *or* provide a detailed justification for not using the PNECs derived in EU RAR, and perform the risk characterisation accordingly;**

2. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for water (fresh and marine), sediment (fresh and marine), soil and microorganisms in sewage treatment plant, and perform the risk characterisation accordingly;**

3. **Identification of DNEL(s) and risk characterisation (Annex I, Section 1.4. and 6.): revise long-term DNEL(s) for workers inhalation and dermal route systemic effects using the assessment factors recommended by ECHA and revise the risk characterisation accordingly *or* provide a detailed justification for not using the recommendations of the ECHA Guidance R.8. for DNEL derivation;**

4. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for human health: provide information on the input parameters and modifiers used as well as justifications for selecting those parameters and modifiers; use the exposure models within their domain of reliable application; and use the maximum pre-defined gloves efficiency values or justify why in this specific case using higher efficiency values is considered appropriate;**

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 Annex I, Section 6.) for workers via dermal route: provide documentation for the recommended personal protective equipment, i.e. hand protection: specify the type of glove material, thickness and breakthrough time.**

You are required to submit the requested information in an updated registration dossier by **8 June 2017. You shall also update the chemical safety report, where relevant.**

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/web/guest/regulations/appeals.

Authorised[2] by Claudio Carlon, Head of Unit, Evaluation E2

[2] 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. Identification of PNEC and risk characterisation (Annex I, Section 3.3.1. 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 3.1.5. of the REACH Regulation requires that the study giving rise to the highest concern shall be used and a robust study summary shall be prepared for that study or studies and included in the technical dossier. In addition, Annex I, Section 3.1.5. requires that if a study giving rise to the highest concern is not used, then this shall be fully justified. Annex I, Section 0.5 further specifies that *"Available information from assessments carried out under other international and national programmes shall be included. Where available and appropriate, an assessment carried out under Community legislation (e.g. risk assessments completed under Regulation (EEC) No 793/93) shall be taken into account in the development of, and reflected in, the chemical safety report. Deviations from such assessments shall be justified."*

ECHA notes firstly that when deriving the PNECs (Predicted No-Effect Concentration) for freshwater and marine water you use as starting point a NOEC (no observed effect concentration) from a long-term study on aquatic invertebrates (*Daphnia*). ECHA notes further that you assigned a Klimisch reliability score 2 for this study and claimed that there is "*not enough information to determine whether the study deviates from the guideline.*" ECHA notes that there is not sufficient information reported on test conditions (including information on test concentrations) and details of results allowing an independent assessment of the study validity and realibility. Thus, ECHA agrees that the robust study summary of that study does not allow to conclude that the reliability of this study would be adequate for PNEC derivation.

ECHA notes secondly that there is an European Risk Assessment Report (EU RAR 2005) according Council Regulation (EEC) No 793/93 publicly available for the registered substance. In that report the PNEC aquatic has been derived using a LC50 from a short-term study on tadpoles of frogs. You have included a robust study summary of that study in your registration dossier. ECHA notes that the PNECs based on that study would provide a higher protection against the hazard to the freshwater and marine water than the PNECs derived by you. You have not provided a justification for this deviation from the EU RAR assessment nor for using for PNEC derivation a study for which the consistency with the test guideline and overall reliability could not be established.

In the comments to the draft decision according to Article 50(1) you indicated your willingness to attach the EU RAR report in your registration dossier. You also pointed out that the EU RAR did not conclude that further aquatic studies would be needed, while you had also included in your dossier the long-term *Daphnia* study. More specifically you indicated firstly that the long-term toxicity study with *Daphnia magna* was not available at the time the EU RAR has been generated.

You indicated secondly that an assessment factor (AF) of 50 would apply for the derivation of PNEC for freshwater according to ECHA guidance on IR&CSA, Chapter R10 (ECHA, May 2008) as there are 2 long-term studies and the LC50 of the most sensitive short-term study (frog tadpoles) is not lower than the lowest NOEC or EC10 of the long-term studies. You indicated thirdly that the long-term toxicity testing was performed according to principles of OECD Guideline 211 and is considered of the same reliability as the study with tadpole larvae.

ECHA acknowledges that the long-term toxicity study with *Daphnia* has not been available during the preparation of EU RAR. Furthermore, ECHA agrees that the lowest observed LC50 of 15.5 mg/l for aquatic organisms is for tadpole larvae as well as that the NOEC for algae is recognised as a long-term value (in combination with long-term NOEC value for aquatic invertebrates and/or fish) for the risk assessment purposes. However, as noted above, ECHA observes that there is not sufficient information reported in the registration dossier on conditions and results of the long-term toxicity test with *Daphnia*, including information on test concentrations used and fulfilment of validity criteria listed in test guideline OECD 211 (as apparent from your summary and conclusions in IUCLID) which would allow an independent assessment of the study validity and reliability. ECHA presumes that reliability and relevance of the toxicity study with tadpole larvae was assessed during EU risk assessment. Having regard to the above consideration of your comments and the original reasoning above, ECHA considers that the reliability of the long-term study on *Daphnia* has not been demonstrated and that only reliable studies should be used for the derivation of PNECs for freshwater/marine water and detailed justification should be provided for not using the PNECs derived in the EU RAR.

ECHA notes thirdly that in the registration dossier you report a PNEC for microorganisms in sewage treatment plants (STP) which differs from the one used for the risk assessment in the above mentioned EU RAR. You have not provided a justification for this deviation from the EU RAR assessment.

In the comments to the draft decision according to Article 50(1) you indicated that acute to chronic toxicity ratio indicated for the *Pseudomonas putida* should be applied for predicting long-term toxicity of the substance to *Tetrahymena pyriformis.* Furthermore, you indicated that there are results of another study with *Tetrahymena pyriformis* available which indicate lower toxicity of the substance to this species. Finally, you note that only the test with *Pseudomonas putida* is performed according to a valid guideline.

ECHA notes that there is no justification provided why the acute to chronic ratio which was observed for the *Pseudomonas putida* would be also applicable for predicting long-term toxicity of the substance to *Tetrahymena pyriformis*. Furthermore, Annex I, section 3.1.5. of REACH Regulation notes that "*where there is more than one study addressing the same effect, then the study or studies giving rise to the highest concern shall be used to draw a conclusion and a robust study summary shall be prepared for that study or studies and included as part of the technical dossier. [...] If the study or studies giving rise to the highest concern are not used, then this shall be fully justified and included as part of the technical dossier*".

ECHA observes that there is no justification available in the registration dossier or your comments on why the study with *Tetrahymena pyriformis* that gives rise to the highest concern and was used in EU RAR for the derivation of PNEC for STP shall not be used for the derivation of PNEC for STP for REACH risk assessment purposes. ECHA presumes that reliability and relevance of the toxicity study with *Tetrahymena pyriformis* was assessed during EU risk assessment. Furthermore, ECHA notes that according to ECHA's Guidance on IR&CSA, Chapter R10 (Table R.10-6) (ECHA, May 2008) the studies with *Tetrahymena sp.* can be used for the derivation of PNEC for STP (microorganisms). Thus, ECHA considers this study as relevant and reliable for the REACH risk assessment purposes.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit in the chemical safety report either the following information: Revised PNECs for freshwater, marine water and microorganisms in sewage treatment plants by using the PNECs derived in EU RAR and using reliable studies giving rise to the highest concern and assess the related risks *or* a detailed justification for not using the the PNECs derived in the EU RAR.

2. Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environmental targets

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 5 of the REACH Regulation requires the Registrant to generate exposure scenarios and exposure estimations for the registered substance. 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 shall 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 exposure scenario in the Section 5 have been implemented. In addition, the overall environmental risk caused by the substance shall be reviewed by integrating the results for the overall releases, emissions and losses from all sources to all environmental compartments.

ECHA's Guidance on information requirements and chemical safety assessment, Part B: Hazard Assessment, Section B.8.4. (pages 47 to 48) (version 2.1, December 2011) states that "if no adverse effects have been observed in studies at the highest recommended concentration/doses tested, this would normally indicate that no hazard has been identified and no DNEL or PNEC can be derived and hence exposure assessment for that route of exposure, type of effect or protection target would not be needed".

In the CSR provided by you the exposure assessment for the environment is missing. You claim that no exposure assessment is necessary for the environment by stating that *"As a result of the hazard assessment carried out in accordance to article 14.3, the registrant concludes that the substance does not meet the criteria for classification as dangerous for the environment, therefore the amounts released to the environment were not estimated".*

ECHA notes that you have classified the substance as Acute Tox 3 (oral), Acute Tox 3 (dermal), Acute Tox 3 (inhalation), Skin Corr 1B, Eye damage 1, Skin Sens 1, STOT RE 2 and thus, fulfilling the criteria set out in Article 14(4) of the REACH Regulation to require an exposure assessment and a risk characterisation in the chemical safety assessment.

Additionally, ECHA notes that effects were observed in some environmental toxicity studies. In particular, e.g. in the short-term aquatic toxicity studies an EC50 of 26.8 mg/L was observed in *Daphnia* and an EC50 of 15.5 mg/L in tadpoles of *Xenopus laevis*. Furthermore, the above mentioned EU RAR indicates that effects were observed on microorganisms needed for the proper functioning of a STP (*Tetrahymena pyriformis* EC50 = 1,343 mg/l). Consequently ECHA concludes that hazards have been identified necessitating an exposure assessment and risk characterisation for the following environmental compartments: water (fresh and marine), sediment (fresh and marine), soil and microorganisms in sewage treatment plant.

In the comments to the draft decision according to Article 50(1) you indicated your disagreement with the obligation to perform an exposure assessment and risk charaterisation for environment. You justified it firstly by the fact that the EU RAR concluded that "*There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already. Conclusion (ii) is reached for the environment because the risk assessment shows that no risks are expected for all environmental compartments regarded.*" Secondly you stated that the scope of the exposure assessment defined in Section 5 of Annex I REACH, "shall cover any exposures that may relate to the hazards identified in Sections 1 to 4 implying only hazards identified in the referred hazard assessment, with the term "hazards identified" to be understood as "classified in the relevant hazard class / hazard category" as defined in the CLP Regulation (cf. Fischer, StoffR 4/2010 "The Scope of Exposure Assessment within the Chemical Safety Assessment under REACH").

You specified further that the term "hazard" without referring to a classification hazard is not separately defined in the REACH Regulation. In this context, there is no justification for ECHA's reference to the OECD definition of "hazard identification" and, by extension, "adverse effect", as present in the Guidance on information requirements and chemical safety assessment, Part B: Hazard assessment (ECHA, version 2.1, December 2011). Neither Article 14 nor Annex I of the REACH Regulation support applicability of the OECD definition of "hazard identification" or "adverse effects" for either the hazard assessment or the exposure assessment under REACH.

You also stated that Article 3 of the CLP Regulation stipulates that a substance is regarded as hazardous, if it fulfils the classification criteria relating to physical hazards, health hazards or environmental hazards, laid down in Parts 2 to 5 of Annex I CLP. Concerning the term "hazards identified", Sections 1-4 of Annex I REACH do not contain any thresholds or criteria which lead to a qualification as "hazards identified" below the classification level. In the case of two hypothetical substances X and Y, where X is only hazardous for humans and Y is non-hazardous for both human and environment, this approach of ECHA would lead to inconsistency in evaluation. Supposing that neither substances fulfil the criteria for being regarded as PBT or vPvB, no human or environmental exposure assessment is required for substance Y, but with this approach a complete exposure assessment, including the environment is expected for substance X. However, similar to substance Y, substance X has no hazard classification for environmental exposure. This difference in treatment of comparable situations is not reasonable.

You also referred to the pending Board of Appeal case on this topic (A-015-2014).

As regards your comment on the EU RAR conclusions ECHA notes that the REACH, general provisions for the Chemical Safety Assessment (CSA) and preparing CSRs are set out in REACH Annex I. As already addressed above these provisions require that the CSA shall take into account the information generated through an assessment carried out under EU legislation (e.g. RARs completed under ESR). These assessments need to be reflected in the CSR, and deviations need to be justified. However, in accordance with REACH Annex I, additional and new elements need to be included in the CSR that were not included in the RARs. These include, among others, generation of exposure scenarios that are then used in exposure assessment and risk characterisation.

With regard to your comments challenging the request for exposure assessment for not being consistent in the understanding of the term 'hazard' in the provisions of the REACH and CLP Regulation, ECHA points out the following.

Generally, two of the main purposes of both the REACH and CLP Regulation are to ensure a high level of protection of human health and the environment (Article 1(1) of the REACH and CLP Regulation respectively). The additional steps in a chemical safety assessment of exposure assessment and risk characterisation serve this objective as they allow estimating and characterising any risk to mankind or the environment. Your formal arguments that this shall be done only for CLP-classified hazards ignore this overall context.

Both the REACH and CLP Regulation distinguish between the terms 'hazard', 'hazardous' and 'hazard classes'. The legislator would have used the term 'hazard classes' only if that was his intention for Annex I, Section 5 to the REACH Regulation. This becomes clear from the distinct references used in Article 3 of the CLP Regulation, Article 14(4) and Annex I, Sections 0.6.3. and 5. to the REACH Regulation. Under REACH, a hazard is identified by the results generated from the tests used to fulfil the information requirements set out in Annexes VII to XI. Pursuant to Article 13(3) of the REACH Regulation tests define endpoints/effects to be observed and reported for identification of (no)effect levels/concentrations as well as a limit dose and therefore, if a hazard is identified it is when an adverse effect is observed below that limit dose.

The REACH and CLP Regulations can be interpreted in a coherent and consistent way without reducing unnecessarily their respective scopes. The chemical safety assessment/report is regulated by law in order to assess and document that any risks arising from a substance are adequately controlled during manufacture and use. The burden of safe use lies with operators. ECHA therefore considers the additional steps of exposure assessment and risk characterisation for any identified hazard irrespective of classification as a measure in line with the precautionary principle that is underpinning the REACH Regulation (Article 1(3)) and which you seem to ignore.

Pursuant to Annex I, Section 3.0.2. of the REACH Regulation five environmental spheres shall be assessed for hazards. Annex I, Sections 5 and 6 require an exposure assessment and risk characterisation for the "*environmental spheres for which exposure to the substance is known or reasonably foreseeable*". Following your argumentation, the environmental exposure assessment and risk characterisation would only be possible for the aquatic environmental sphere since the results for a number of standard data requirements for the other environmental spheres (e.g. information on soil/sediment toxicity,) do not lead to the classification of substances as hazardous, as no hazard classes or classification criteria exist. It cannot be correct that a large part of standard data requirements set out in the REACH Annexes would become irrelevant. Instead, the legislator has a clear intention to use the standard information required in Annexes VII to X of the REACH Regulation for the hazard assessment without prejudice of classification needs.

For reasons of proportionality, the requirement of a chemical safety assessment is limited to those substances meeting the criteria for classification of any hazard class/category set out in Article 14(4) of the REACH Regulation/Annex I CLP Regulation. In that regard the request by ECHA to understand exposure and risk of the substance subject to the present decision is not exceeding of what is appropriate and necessary to attain the objectives of the legislation. The identified hazard in this case has been demonstrated by mortality of Daphnia, frog tadpoles and bacteria necessary to the proper functioning of sewage treatment plants as outlined above. At the same time, as ECHA is not requiring exposure assessment and risk characterisation on all environmental spheres, but in relation to those where a hazard has been indentified, it does not exceed what is necessary to address the concern.

ECHA respects the principle of equal treatment as it requires for any substance meeting the criteria for classification in any of the hazard classes/categories an exposure assessment and risk characterisation.

Finally, ECHA has issued guidance on when exposure assessment and risk characterisation are expected (Guidance on information requirements and chemical safety assessment Part B: Hazard assessment; Version: 2.1; December 2011).

In conclusion, ECHA considers that your arguments cannot lead to omit the required data that is needed in order to comply with the REACH Regulation.

Finally ECHA notes that there is no ruling by the Board of Appeal yet concerning the appeal mentioned by you (at the time of adoption of this decision at MSC-48, 6-9 June and 14-15 June 2016).

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation of the REACH Regulation, you are requested to generate an exposure assessment and risk characterisation for water (fresh and marine), sediment (fresh and marine), soil and microorganisms in sewage treatment plant and perform the risk characterisation accordingly.

3. 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, 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 inhalation and dermal route for workers 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. 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 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 full justification for the DNELs derived for workers 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.

In the comments to the draft decision according to Article 50(1) you indicated firstly that the long-term DNELs for workers inhalation and dermal route systemic effects used in the assessment base on ECETOC's Guidance on Assessment Factors how to derive a DNEL (Technical Report, 2010) because, the assessment factors for intra- and inter-species differences proposed there apply more a scientific approach and not standard default procedures as in the case of ECHA's document. You indicated further that this approach has been proven by analysis of a wide range of scientific literature conducted by ECETOC. In your opinion this makes the ECETOC's proposal for AFs more realistic and not overly conservative. In order to support this position you referred to the value of occupational exposure limit (OEL) for 2-Butyne-1,4-diol proposed by SCOEL (The Scientific Committee on Occupational Exposure Limits) in March 2011 and that in line with ECHA Guidance R8., Appendix R.8-13, available occupational exposure limits (OELs) can be taken into account in deriving DNELs. The indicative 8-h OEL value for inhalation exposure to 2-Butyne-1,4-diol amounts to 0.5 mg/m3. In comparison, the DNEL value for long-term inhalation exposure for workers indicated by ISP Marl in the CSR amounts to 0.02 mg/m3, i.e. it is more than one order of magnitude lower than the value recommended by SCOEL. Therefore, you concluded that the above mentioned gives enough evidence to support the fact that DNEL values derived using ECETOC assessment factors are sufficiently protective.

Additionally, with reference to the dermal route, you indicated that the DNEL value was derived based on NOAEL for oral route, with assumption that 100% of substance will be absorbed via skin contact. In your opinion this is the most conservative approach possible (the worst case scenario) and no additional factors for derivation of DNEL are necessary.

ECHA notes firstly that ECHA guidance R.8 does not encourage to use default assessment factors, it encourages the following hierarchy: first to use substance specific data, if that is not available, to use analogue data and only if that is not available, to use default assessment factors (quote from page 22 of guidance): *Assessment factors are numerical values. They are used to address the differences between the experimental data and the human situation, taking into account the uncertainties in the extrapolation procedure and in the available data set. In principle, all data on a specific substance need to be reviewed thoroughly in order to use, as far as possible, substance-specific information for the establishment of appropriate values for the various assessment factors. When substance-specific information is not available, data on analogues, which act with the same mode of action as the chemical under consideration, should be taken into account. However, when the available data do not allow the derivation of substance-specific or analogue-specific assessment factors, default assessment factors should be applied. Although very often necessary to rely upon, the default assessment factors represent a fall back position rather than the starting point.*

ECHA notes secondly that you have not provided any substance specific information (see below for consideration of your specific comments) or analogue data. ECHA points out that the AFs of ECETOC guidance are not substance specific tailored values, but default values, although different from the above-mentioned ECHA guidance default values that apply when no substance specific or analogue substance data can be used. You do not specify why these ECETOC default values would be more science based than the ones in ECHA guidance. ECHA notes, however, that ECHA guidance includes several pages of scientific references to justify the principles of that guidance, including the selection of assessment factors. ECHA further points out that this guidance has been agreed together with Member States Competent Authorities and other stakeholders in a clearly defined review process to ensure that they correctly ensure safe use against the hazardous properties taking into account the uncertainties arising from the factors listed in Annex I section 1.4. of REACH. The ECETOC guidance has not undergone such a scientific regulatory review process.

ECHA notes, however, that for the inhalation route you refer to an indicative OEL (IOEL) set by SCOEL. ECHA guidance R.8 Appendix R8-13 indeed explains that "*A registrant is allowed to use an IOEL as a DNEL for the same exposure route and duration, unless new scientific information that he has obtained in fulfilling his obligations under REACH does not support the use of the IOEL for this purpose.*" In the current dossier you have, however, neither referred to this approach nor provided a justification why the data set used for setting the IOEL would still apply. ECHA underlines further that if adequately justified such an OEL would only be applicable as a DNEL for the same route (inhalation) and the same population (workers).

As regards the dermal route ECHA notes that you argue that using an assumed absorption of 100% via skin contact would be a conservative worst case scenario not necessitating any additional factors for deriving DNELs. ECHA notes that this assumption is linked to route-to-route absorption (Chapter R.8.4.2 b of ECHA guidance). The assessment factors are, however, meant to address uncertainty from intra- and interspecies variation that deal with the data that are used in such a route-to-route extrapolation (Chapter R.8.4.3 c of ECHA guidance). ECHA agrees that using a 100% assumed absorption via skin contact is indeed an eligible assumption according to ECHA guidance (page 19) and no additional assessment factor is to be applied for the *route-to-route extrapolation exercise* of the DNEL derivation. However the intra- and interspecies AFs are to be applied after the route-to-route extrapolation as specified in the above-mentioned ECHA guidance chapters on route-to-route extrapolation and selection of assessment factors.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to revise long-term DNEL(s) for workers inhalation and dermal route systemic effects using the assessment factors recommended by ECHA and revise the risk characterisation accordingly *or* provide a detailed justification for not using the recommendations of ECHA Guidance R.8 for DNEL derivation.

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 Articles 10(b) and 14(1) of the REACH Regulation the registration shall contain a chemical safety report (CSR) which shall document the chemical safety assessment conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation. In accordance with Article 14(4), the CSR must include an exposure assessment and risk characterisation, due to the substance being classified as hazard class category 1, PBT or vPvB. As already noted in section 2 of this Appendix, the registered substance fulfills this condition that requires an exposure assessment and risk characterisation in the chemical safety assessment.

Article 14(6) as well as Annex I, 0.5., 5.2.4. and 6.2.-6.4. of the REACH Regulation require registrants to identify and apply appropriate measures to adequately control the risk identified in the 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. Annex I, 5.2.5. states that appropriate models can be used for the estimation of exposure levels.

ECHA notes that according to the information provided in the CSR, you have used the ECETOC TRA model and EASE model for estimating exposure via inhalation and dermal route for exposure scenarios 2-4, both with and without the use of exposure modifiers for those models. The industrial and professional uses of the registered substance include Process Categories that refer to spraying applications, roller application or brushing and dipping and pouring applications (PROCs 7-10-11-13) which may potentially give rise to high exposures. ECHA notes that the modified exposure estimates are around 0.01 -0.05 mg/m^3 for exposure via inhalation and 0.00 mg/kg bw/day for dermal exposure while the input parameters and modifiers used are not described. ECHA notes that in the CSR, you have indicated that the estimates are presented in Appendix 1. Nevertheless such an Appendix could not be found in the CSR. In the absence of information on the input parameters, modifiers used and justifications for selecting those parameters and modifiers ECHA concludes that the very low exposure estimates provided for all contributing scenarios of exposure scenarios 2-4 are not adequately justified.

In the comments to the draft decision according to Article 50(1) you indicated that all exposure estimates for scenarios 2-4 were presented in Appendix 1, which by accident was not included in the dossier at the moment of the submission. Therefore, you have attached the Appendix to your comments. The modifiers applied for the exposure estimation are included in your comments and in Appendix 1.

ECHA has the following observations on the modifiers applied:

- 0.375 for duration factor - spray time limited to 3 hours per typical 8-hour shift (basis for DNEL): ECHA observes that the ECETOC TRA model follows a banding approach while the introduction of a reduction factor due to a time limitation, as in the case of this modifier, corresponds to a linear approach, which is not supported by the tool. In order to do so, you would need to use another estimation tool
- 0.05 (even lower values, as low as 0.01 and 0.005 are reported for some exposure scenarios in Appendix 1 of your comments) for LEV (local exhaust ventilation) reduction factor for dermal exposure (low volatile substance in closed system): ECHA notes that a factor of 0.05 corresponds to an exposure reduction of 95 % and underlines that even for inhalation such exposure reduction is difficult to achieve. As reported in ECETOC TRA, Technical Report No. 114, for inhalation exposure when LEV is selected the associated effectiveness will range from 80% to 95% for professional/industrial. Moreover ECHA notes that the LEV will have little effect on dermal exposure due to the low volatility of the substance. According to Guidance R.14 (Version 2.1 – November 2012, page 21), section R.14.4.8, one of the limitations of ECETOC TRA for workers is to underestimate the dermal exposure for some situations with local exhaust ventilation. In order to compensate for the limitations, the effectiveness of the local exhaust ventilation shall be set to zero or any other values below the 90 to 99 % assumed in the model (to reach a conservative estimate). A 95% reduction factor for dermal exposure based on the use of LEV is very ambitious, and you have provided no further justification.
- 0.02 for the use of gloves with intensive controls: ECHA notes that a reduction factor of 0.02 corresponds to an exposure reduction of 98 %. Firstly, ECHA observes that the maximum effectiveness achievable with gloves is 95% for industrial users (as reported in ECETOC TRA, Technical Report No. 114). Secondly ECHA underlines that reduction factors for the use of gloves relates to the level of training provided to workers in wearing them in order to achieve a certain level of protection (which however cannot go beyond 95%).
- 0.01 for 10% solution (consistent with EU Risk Assessment): within the model ECETOC TRA, the recommended exposure modifiers for substances present at a concentration of 10% in a mixture is 0.6, representing an exposure reduction of 40 %, as reported also in ECHA Guidance R.14, R.14.4.8. ECHA underlines that the model shall be used within its domain of applicability and according to the modifiers there included, unless a specific and adequate justification is provided. You have not provided such a justification.
- 0.1 for the "very low" vapour pressure up to 40°C and tendency to remain in processing solutions at temperatures <100°C: ECHA observes that the proposed modifier is not embedded in the model and not justified by you and therefore is not appropriate.
- 0.55 for 55% solution (consistent with EU Risk Assessment): within the model ECETOC TRA, the recommended exposure modifiers for substances present at a concentration of 55% in a mixture is 1, representing an exposure reduction of 0 %, as reported also in ECHA Guidance R.14, R.14.4.8. ECHA underlines that the model shall be used within its domain of applicability and according to the modifiers there included, unless a specific justification, currently not included, can be brought forward.
- 0.03 (which is reported also as low as 0.01 in Appendix 1 of your comments) for an additional factor applied on the basis that product will be classified as a skin irritant, corrosive, or molten and, out of necessity, workers will avoid all but incidental contact: ECHA observes that the proposed modifier is not embedded in the model used and there is no justification provided why these classifications would result in an additional protection factor of 0.03 beyond the factors that are already embedded in the model based on the risk management measures applied.

Additionally, ECHA notes that in Appendix 1 of your comments, the following modifiers are introduced:

- 0.1 "inhalable" size particles are expected to be < 0.1% by weight: ECHA underlines that modifiers embedded in the ECETOC TRA model are only related to concentration of the substance and there are none connected to the particle size. ECHA concludes that the proposed modifier is not embedded in the model and you have not provided any justification for such a reduction factor.
- 0.1 to account for small quantity handled or handling with a fume hood (PROC15): ECHA notes that this reduction factor is not embedded in the ECETOC TRA model and therefore cannot be accepted since an adequate justification has not been provided.

ECHA concludes that the modifiers presented in your comments and Appendix 1 therein are either incorrect, in comparison to the recommendations contained in ECETOC TRA, Technical Report No. 114 and REACH Guidance R.14, or not adequately justified.

ECHA notes secondly that you have used the ECETOC TRA model for estimating exposure via inhalation and dermal route to the registered substance, which is a solid. Nevertheless, in the description of the exposure scenarios, in the product characteristics, the physical form chosen is liquid with a vapour pressure <0.5 kPa, with the indication that it covers the use of 1,4-butynediol in solution. However, as reported in ECETOC TRA Technical Report no.114, Table 3, this model cannot predict exposure to solids dissolved in liquids. This specifically refers to inhalation exposure predictions and concerns the formation of vapor and liquid/solid phases, i.e. such as aerosols formed during spraying applications. Therefore in this case the requirement to provide an assessment of exposure is likely to be met either through the use of other tools capable of estimating such exposure, as suggested in the ECETOC TRA Technical Report no.114, or through the presentation of workplace measurements as described in the ECHA Guidance on information requirements and chemical safety assessment Chapter R.14, Occupational exposure estimation.

In the comments to the draft decision according to Article 50(1) you indicated that the physico-chemical properties of 2-Butyne-1,4-diol, namely very high water solubility and very low Henry's Law constant, indicate that the substance will not readily volatilise from water and therefore one should not expect formation of vapour and liquid/solid phases. As a consequence, where spraying includes 2-Butyne-1,4-diol in solution, ECETOC TRA can give reliable estimations of the actual exposure. Therefore, you consider the exposure predicted for an aqueous solution of 2-Butyne-1,4-diol as appropriate.

While ECHA acknowledges the high water solubility and low Henry law's constant of the registered substance, it nevertheless observes that, based on the current CSR submission, it is not clear whether the solvent used is water. The exposure prediction for an aqueous solution could be adequate if you provide clear evidence that the solvent used is water. Nevertheless, ECHA notes that aerosol formation is independent from the physical-chemical properties indicated above but is rather related to the task conducted (e.g. spraying applications). For the reasons above, ECHA cannot conclude on the reliability of the estimation in solution.

ECHA notes thirdly that you have used ECETOC TRA to estimate exposure for a variety of worker exposure scenarios using efficiency for gloves of 98% to estimate the exposure via dermal route. However, ECHA notes that according to the guidance for the model used (ECETOC TRA 114) the maximum pre-defined values are 95% for industrial users and 90% for professional users. You have not included in the CSR any case specific justification (e.g. related to the substance or the specific recommended or implemented personal protection measures or based on relevant biomonitoring data) for deviating from the recommended efficiency factor in using ECETOC TRA.

As explained above, the information provided on the dermal exposure estimates for the registered substance in the chemical safety report does not meet the requirements for preparing a chemical safety report as described in Annex I.

Consequently, it is necessary to revise the dermal exposure estimates or to provide a justification explaining why in this specific case using higher efficiency values for gloves (98%) is considered appropriate.

In the comments to the draft decision according to Article 50(1) you indicated that use of gloves of 98% efficiency has been proposed due to the fact that good industrial practice for handling 2-Butyne-1,4-diol under industrial conditions should include wearing protective gloves over a disposable inner glove coupled with specific training. This specific guidance for dermal protection ensures an efficacy of 98% at further reducing these incidental or intermittent exposures. Based on this, you argue that you have sufficiently clarified and defended the use of a higher glove efficacy versus the maximum values specified by ECETOC which are basic and conservative.

ECHA underlines that protection factors assigned to gloves relate to the training received by workers in wearing them and are not connected to the possibility of wearing two pair of gloves. It should be noted that the material is assumed to provide a complete barrier for the specified breakthrough time, however it is the level of training provided to the workers (how they are worn) that dictates the protection factor. Finally, ECHA observes that the maximum effectiveness achievable with gloves is 95% for industrial users (see ECETOC TRA, Technical Report No. 114). For the reasons above, ECHA underlines that an efficiency of 98% for the use of gloves is not acceptable in connection with estimating dermal exposure using ECETOC TRA.

Finally ECHA notes that the registered substance has a harmonised classification as Skin Sens 1 and Skin Corr 1B. However, you have not considered local dermal effects in the risk characterisation based on ECETOC TRA and EASE model exposure estimates. Consequently there is a need either for a qualitative assessment for local dermal effects or for demonstrating that the quantitive risk characterisation for systemic effects via dermal route also ensures safe use against local dermal effects through the definition of risk management measures (RMMs) and operational conditions (OCs) that ensure prevention of dermal contact and adequately protect against local effects. *Practical Guide How to undertake a qualitative human health assessment and document it in a chemical safety report* (Practical Guide 15, (version 1, November 2012)) provides further details on how to carry out a qualitative assessment.

In the comments to the draft decision according to Article 50(1), you indicated that, based on the experimental results, it is impossible to indisputably conclude on the skin sensitizing properties of the substance and thereofore you are inclined to state that the risk management measures and occupational conditions ensuring prevention from dermal contact, proposed on the basis of quantitative risk characterization are sufficient, in particular having regard to the very low value of DNEL for long-term dermal exposure. You also stated that the same applies, in your opinion to the classification as skin. corr. 1B. The RMMs and OCs have been already included in the risk characterisation and the efficiency of gloves has been intentionally increased to 98%. Staff training is recommended in all cases and containment and enclosed systems are used as appropriate.

ECHA notes that contrary to your comment on uncertainty of skin sensitizing potential, the registered substance has a harmonized classification as Skin Sens. 1 and Skin Corr. 1B. You adhere to those classifications in the classification and labelling section of your registration. Based on the current classification, you are requested either to perform a qualitative assessment, as explained in REACH Guidance, Part E: Risk Characterisation or to demonstrate safe use against local dermal effects trough the quantitative risk characterisation.

ECHA observes that the risk management measures (RMMs) and operational conditions (OCs) currently recommended in the CSR are not in line with the appropriate RMMs and OCs as listed in Table 3-1 of the Practical Guide 15 for such type of hazards. Moreover, as already reported above, the maximum effectiveness achievable with gloves is 95% for industrial users (see ECETOC TRA, Technical Report No. 114). For the reasons above, ECHA underlines that you shall either conduct a qualitative assessment for local dermal effects or demonstrate that the quantitative risk characterisation also ensures safe use against local dermal effects.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation you are requested to revise exposure estimates for industrial and professional uses by providing information on the input parameters and modifiers used and justifications for selecting those parameters and modifiers, by using the exposure models within their domain of reliable application and by using the maximum pre-defined gloves efficiency values or justifying why in this specific case using higher efficiency values is considered appropriate.

Notes for your consideration

ECHA notes that you have used ECETOC TRA version 2 in the exposure estimation while the latest version available is version 3. You should consider using the most updated version of the prediction model when revising the exposure estimates as described above. Any deviation from default values used within a model or published in the REACH guidance must be adequately justified. The use of alternative values without adequate justification is not-compliant with REACH.

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 have indicated the following for hand protection: depending on the process category either "*Wear chemically resistant gloves (tested to EN374) in combination with specific activity training [PPE17]*"or "*Wear chemically resistant gloves (tested to EN374) in combination with intensive management supervision controls [PPE18]*", and in IUCLID Section 11 no personal protective equipment details for hand protection have been reported.

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 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.

In the comments to the draft decision according to Article 50(1) you indicated you agreement on the fact that the above specifications are currently not included in the guidance on safe use of your registration dossier. You further indicated that such information is typically included in IUCLID Chapter 11 which corresponds to the eSDS and you agree to provide it there in an update. You indicated further that this should be sufficient, since the CSR should not be regarded as a stand-alone document, but also refer to the information in the IUCLID file and, thus, the eSDS.

ECHA notes that the request is to provide the gloves specifications. The reasoning refers to the information in the CSR needing to be consistent with the safety data sheet is merely to explain the link between the registration dossier and the eSDS. ECHA further notes that currently the gloves specifications are mentioned neither in IUCLID section 11 nor in the CSR.

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 time.

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 16 September 2015

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation:

ECHA notified you of the draft decision and invited you to provide comments. ECHA took into account your comments and amended the deadline and did not amend the requests.

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

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

ECHA invited you to comment on the proposed amendments.

ECHA referred the draft decision to the Member State Committee.

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

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-48 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 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.