ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 21 July 2017

Addressee: [redacted]

Decision number: CCH-D-2114363910-50-01/F
Substance name: 1,1'-(methylenedi-p-phenylene)bismaleimide
EC number: 237-163-4
CAS number: 13676-54-5
Registration number: [redacted]
Submission number: [redacted]
Submission date: 18.01.2016

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. **In vivo mammalian alkaline comet assay (Annex VIII, Section 8.4, column 2; test method: OECD TG 489) in rats, oral route, on the following tissues: liver, glandular stomach and duodenum with the registered substance;**

2. **Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1., column 2; test method: Daphnia magna reproduction test, EU C.20/OECD TG 211) with the registered substance;**

3. **Long-term toxicity testing on fish (Annex VIII, Section 9.1.3., column 2; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) with the registered substance;**

4. **Exposure assessment and risk characterisation (Annex I, Section 5.1.1. and 6.) for workers: provide documentation for the recommended personal protective equipment, i.e. hand protection and respiratory protection;**
   - specify the type of glove material, thickness and breakthrough times;
   - specify the filter type/class for the respiratory protective equipment;
   - specify the type and quality of protective clothing;

5. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for human health: revise a qualitative exposure assessment demonstrating the likelihood that effects are avoided for mutagenicity, acute toxicity (inhalation) and skin sensitisation for relevant exposure scenarios and detail the operational conditions and risk management measures and revise the risk characterisation accordingly.**

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 **30 July 2018 . 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 Kevin Pollard, Head of Unit, Evaluation E1

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

Appendix 1: Reasons

1. **In vivo mammalian alkaline comet assay (Annex IX, Section 8.4, column 2)In vivo mammalian alkaline comet assay (Annex VIII, Section 8.4, column 2)In vivo mammalian alkaline comet assay (Annex VIII, Section 8.4, column 2)**

Pursuant to Articles 10(a)(vi), 12(1)(c) and 13(4) of the REACH Regulation, a technical dossier registered at 10 to 100 tonnes10 to 100 tonnes per year shall contain as a minimum the information specified in Annexes VII to VIII Annexes VII to VIII of the REACH Regulation.

"Mutagenicity" is an information requirement as laid down in Annex VIII, Section 8.4. of the REACH Regulation. Column 2 of Annex VIII, Section 8.4. provides that "Appropriate in vivo mutagenicity studies shall be considered in case of a positive result in any of the genotoxicity studies in Annex VII or VIII."

The technical dossier contains an *in vitro* study (*In vitro* Mammalian Chromosome Aberration Test) performed according to OECD Guideline 473 with the registered substance that shows positive results. You concluded that the test substance showed evidence of clastogenic activities in this *in vitro* mammalian cell system under the test conditions employed. The positive result indicates that the substance is inducing chromosomal aberrations under the conditions of the test.

An appropriate *in vivo* genotoxicity study to follow up the concern on chromosomal aberrations is not provided for the registered substance. Consequently there is a need to address the possible concern and it is necessary to provide additional information already at the present tonnage level for the substance in question (10 to 100 tonnes per annum).

According to the ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017)Chapter R.7a, section R.7.7.6.3, the mammalian erythrocyte micronucleus test ("MN test", OECD TG 474), the mammalian bone marrow chromosomal aberration test ("CA test", OECD TG 475) or the *in vivo* mammalian alkaline comet assay ("comet assay", OECD TG 489) are suitable to follow up positive *in vitro* result on chromosomal aberrations if the test substance or its metabolite(s) will reach the target tissue. However, on basis of the information provided in the dossier, it is highly uncertain whether the test substance or its metabolites will reach the target tissue. Due to this, the MN and CA tests might not be appropriate tests. Therefore, ECHA considers the *in vivo* comet assay to be the most appropriate for the substance subject to the decision as also tissues at the site of contact can be investigated.

In your comments according to Article 50(1) of the REACH Regulation, you stated that "*we accept this request for information.*"

According to the test method OECD TG 489, the test shall be performed in rats. Having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s), performance of the test by the oral route is appropriate.

According to the test method (OECD TG 489), the test shall be performed by analysing tissues from liver as primary site of xenobiotic metabolism, glandular stomach and duodenum as sites of direct contact.Following a Member State Competent Authority (MSCA) proposal for amendment (PfA), ECHA notes there are several expected or possible variables

between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the substance, and probable different local absorption rates of the substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to sample both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.

In your comments on the MSCA PfA, you acknowledge that there is residual uncertainty about the genotoxicity endpoint and accept the requirement to conduct the *in vivo* comet assay. However, reagrding sampling of tissues, following internal discussion it is the conclusion of your toxicology experts that there is no significant benefit to assessing cells from both the stomach and duodenum / jejunum as suggested in PfA. You would request that the final decision should make clear that only one of these tissues is required to satisfy the information requirement. In additon, you agree that cells from the liver are required to assess the genotoxic effect following metabolism of the substance.

ECHA notes you have not provided any scientific justification to prove that you condiser that there is no significant benefit to assessing cells from both the stomach and duodenum / jejunum. 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.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: *In vivo* mammalian alkaline comet assay (test method: OECD TG 489) in rats, oral route, on the following tissues: liver, glandular stomach and duodenum.

Notes for your consideration

You are reminded that according to Annex IX, Section 8.4., column 2 of the REACH Regulation, if positive results from an *in vivo* somatic cell study are available, "the potential for germ cell mutagenicity should be considered on the basis of all available data, including toxicokinetic evidence. If no clear conclusions about germ cell mutagenicity can be made, additional investigations shall be considered".

You may consider examining gonadal cells in addition to the other aforementioned tissues, as it would optimise the use of animals. ECHA notes that a positive result in whole gonads is not necessarily reflective of germ cell damage since gonads contain a mixture of somatic and germ cells. However, such positive result would indicate that the substance and/or its metabolite(s) have reached the gonads and caused genotoxic effects. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

2. Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1., Column 2)

Pursuant to Articles 10(a)(vi), 12(1)(c) and 13(4) of the REACH Regulation, a technical dossier registered at 10 to 100 tonnes per year shall contain as a minimum the information specified in Annexes VII to VIII of the REACH Regulation.

"Short-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex VII, Section 9.1.1. of the REACH Regulation. Furthermore, pursuant

to Annex VII, Section 9.1.1, Column 2 the long-term aquatic toxicity study on *Daphnia* (Annex IX, Section 9.1.5.) shall be considered if the substance is poorly water soluble. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement. The choice of the appropriate test(s) will depend on the results of the chemical safety assessment.

ECHA considers that substances poorly soluble in water require a longer time to be significantly taken up by the test organisms and so steady state conditions are likely not to be reached within the duration of a short-term toxicity test. For this reason, short-term tests may not give a true measure of toxicity for such substances and toxicity may actually not even occur at the water solubility limit of the substance if the test duration is too short. Still, long-term toxicity cannot be excluded and needs to be investigated already at the tonnage band currently applicable for the substance subject to the present decision.

ECHA observes that there is no information on long-term *Daphnia* toxicity reported in the registration dossier. ECHA acknowledges that there is short-term toxicity study with *Daphnia* (aquatic invertebrate) reported in the dossier where no toxicity was observed at the water solubility limit of the substance. However, ECHA notes that the substance is poorly water soluble (WS<1mg/l), but not highly insoluble in water. Thus, ECHA considers that short-term toxicity test with aquatic invertebrates is not sufficient for the substance as the lack of toxicity at the short-term test cannot exclude long-term toxicity.

Moreover, ECHA notes that the information on aquatic invertebrates toxicity is necessarly needed for the proper Chemical Safety Assessment of the substance. As noted in the Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7b (version 4.0, June 2017) standard information on aquatic toxicity (on aquatic invertebrates, fish and aquatic plants) is necessary to enable the environmental hazard assessment, i.e. for use in classification and labelling and derivation of the PNECwater (Predicted No Effect Concentration for water), and for determination of the toxicity (T) criterion in the PBT assessment.

In response to a Member State Competent Authority (MSCA) proposal for amendment (PfA) to insert the legal reference to request information on long-term toxicity testing on aquatic invertebrates you indicate that the registered substance has been shown to be hydrolytically unstable (a hydrolytic half-life of less than 12 hours under all pH conditions) and therefore unlikely to persist in the aquatic environment and has a low potential for bioaccumulation in the aquatic environment (low octanol-water partition coefficient (log Pow = 1.5) and therefore long-term aquatic toxicity testing is considered unnecessary. In addition, in your comments to the MSCA PfA, you outline your testing approach that *Daphnia* reproduction study should be conducted in the first instance, and the requirement whether to conduct the long-term fish toxicity study or not should be reviewed with reference to the results of the *Daphnia* reproduction test. You consider that your approach could potentially avoid unnecessary testing in a vertebrate species and would therefore be preferable on grounds of animal welfare.

ECHA notes that according to *Guidance on information requirements and chemical safety assessment*, Chapter R.7b (version 4.0, June 2017) "*OECD recommends testing parent compound for Disappearance Time 50 (DT50 >3) days, breakdown products for DT50 <1h and case-by-case basis for anything in between. A flow-through test is recommended for substances with a DT50 of 4 h as 50% of the nominal parent substance concentration can be maintained with 6 volume renewals per day. ECETOC (2003) and the TGD recommend to test parent substance with a DT50 as low as 12 h, as based on maximum half life allowing*

80% maintenance of parent compound in flow-through system and >1% in short term test. However, this should be considered on a case-by-case basis depending on the technical feasibility of performing such a study." ECHA notes that a flow-through test design is possible for the OECD TG 211. Thus, ECHA considers that the testing of the registered substance is technically feasible and relevant for CSA.

You indicate that the substance has a low octanol-water partition coefficient (log Pow = 1.5). ECHA notes the registered substance also is considered poorly soluble in water. From these values, ECHA notes the correlation between water solubility and octanol-water partition coefficient values for this registered substance appears low i.e. low water solubility and low octanol-water partition coefficient. However, there is no provided justification on this aspect. ECHA consideres that you could investigate this correlation prior to conducting long-term aquatic toxicity studies.

As per the notes for consideration by the registrant in the long-term fish toxicity study, according to ECHA *Guidance on information requirements and chemical safety assessment*, Chapter R.7b (version 4.0, June 2017) (Section R.7.8.5., including Figure R.7.8-4), if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially more sensitive, long-term studies may be required on both. As noted above, ECHA considers that short-term toxicity test with aquatic invertebrates is not sufficient for the substance as the lack of toxicity at the short-term test cannot exclude long-term toxicity. The same is valid for the fish toxicity, i.e. there is no information available to conclude on sensitivity of fish and aquatic invertabrates to the substance.

If you decide to adapt the testing requested according to the specific rules outlined in Annexes VI to X and/or according to general rules contained in Annex XI of the REACH Regulation, to ensure compliance with this standard 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.

ECHA notes that guidance on how degradation/transformation products should be considered for various standard information requirements is given in different sections of ECHA's Guidance on Information Requirements and Chemical Safety assessment (for e.g. Chapter R.7b, version 4.0, June 2017; Chapter R.11, version 3.0, June 2017).

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.

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: *Daphnia magna* reproduction test (test method: EU C.20./OECD TG 211).

Notes for your consideration

Please see notes for your consideration under section 3 below.

3. Long-term toxicity testing on fish (Annex VIII, Section 9.1.3., Column 2)

Pursuant to Articles 10(a)(vi), 12(1)(c) and 13(4) of the REACH Regulation, a technical dossier registered at 10 to 100 tonnes10 to 100 tonnes per year shall contain as a minimum the information specified in Annexes VII to VIII of the REACH Regulation.

"Short-term toxicity testing on fish" is a standard information requirement as laid down in Annex VIII, Section 9.1.3. of the REACH Regulation. Furthermore, pursuant to Annex VIII, Section 9.1.3, Column 2 the long-term aquatic toxicity study on fish (Annex IX, Section 9.1.6.) shall be considered if the substance is poorly water soluble. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement. The choice of the appropriate test(s) will depend on the results of the chemical safety assessment.

ECHA considers that substances poorly soluble in water require longer time to be significantly taken up by the test organisms and so steady state conditions are likely not to be reached within the duration of a short-term toxicity test. For this reason, short-term tests may not give a true measure of toxicity for such substances and toxicity may actually not even occur at the water solubility limit of the substance if the test duration is too short. Still, long-term toxicity cannot be excluded and needs to be investigated already at the tonnage band currently applicable for the substance subject to the present decision.

ECHA observes that there is no information on long-term fish toxicity is reported in the registration dossier. ECHA acknowledges that there is short-term toxicity study with fish reported in the dossier where no toxicity was observed at the water solubility limit of the substance. However, ECHA notes that the substance is poorly water soluble (WS<1mg/l), but not highly insoluble in water. Thus, ECHA considers that short-term toxicity test with fish is not sufficient for the substance as the lack of toxicity at the short-term test cannot exclude long-term toxicity.

Moreover, ECHA notes that the information on fish toxicity is necessarly needed for the proper Chemical Safety Assessment of the substance. As noted in the Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7b (version 4.0, June 2017)standard information on aquatic toxicity (on aquatic invertebrates, fish and aquatic plants) is necessary to enable the environmental hazard assessment, i.e. for use in classification and labelling and derivation of the PNECwater (Predicted No Effect Concentration for water), and for determination of the toxicity (T) criterion in the PBT assessment.

In response to a MSCA PfA to insert a legal reference to request information on long-term toxicity testing on fish you indicate that the registered substance has been shown to be hydrolytically unstable (a hydrolytic half-life of less than 12 hours under all pH conditions) and therefore unlikely to persist in the aquatic environment and has a low potential for bioaccumulation) in the aquatic environment (low octanol-water partition coefficient (log Pow = 1.5) and therefore long-term aquatic toxicity testing is considered unnecessary. In addition in your comments to the MSCA PfA, you outline your testing approach that *Daphnia* reproduction study should be conducted in the first instance, and the requirement whether to conduct the long-term fish toxicity study or not should be reviewed with reference to the results of the *Daphnia* reproduction test. You consider that your approach could potentially avoid unnecessary testing in a vertebrate species and would therefore be preferable on grounds of animal welfare.

ECHA notes that according to *Guidance on information requirements and chemical safety assessment*, Chapter R.7b (version 4.0, June 2017)"*OECD recommends testing parent compound for Disappearance Time 50 (DT50 >3) days, breakdown products for DT50 <1h and case-by-case basis for anything in between. A flow-through test is recommended for substances with a DT50 of 4 h as 50% of the nominal parent substance concentration can be maintained with 6 volume renewals per day. ECETOC (2003) and the TGD recommend to*

test parent substance with a DT50 as low as 12 h, as based on maximum half life allowing 80% maintenance of parent compound in flow-through system and >1% in short term test. However, this should be considered on a case-by-case basis depending on the technical feasibility of performing such a study." ECHA notes that a flow-through test design is possible for the OECD TG 211. Thus, ECHA considers that the testing of the registered substance is technically feasible and relevant for CSA.

You indicate that the substance has a low octanol-water partition coefficient (log Pow = 1.5). ECHA notes the registered substance also is considered poorly soluble in water. From these values, ECHA notes the correlation between water solubility and octanol-water partition coefficient values for this registered substance appears low i.e. low water solubility and low octanol-water partition coefficient. However, there is no provided justification on this aspect. ECHA consideres that you could investigate this correlation prior to conducting long-term aquatic toxicity studies.

As per the notes for consideration by the registrant in the long-term fish toxicity study, according to ECHA *Guidance on information requirements and chemical safety assessment*, Chapter R.7b (version 4.0, June 2017) (Section R.7.8.5., including Figure R.7.8-4), if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially more sensitive, long-term studies may be required on both. As noted above, ECHA considers that short-term toxicity test with aquatic invertebrates is not sufficient for the substance as the lack of toxicity at the short-term test cannot exclude long-term toxicity. The same is valid for the fish toxicity, i.e. there is no information available to conclude on sensitivity of fish and aquatic invertabrates to the substance.

If you decide to adapt the testing requested according to the specific rules outlined in Annexes VI to X and/or according to general rules contained in Annex XI of the REACH Regulation, to ensure compliance with this standard 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.

ECHA notes that guidance on how degradation/transformation products should be considered for various standard information requirements is given in different sections of ECHA's Guidance on Information Requirements and Chemical Safety assessment (for e.g. Chapter R.7b, version 4.0, June 2017; Chapter R.11, version 3.0, June 2017).

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.

Regarding test method , ECHA considers that the FELS toxicity test according to OECD TG 210 is the most sensitive of the standard fish tests available as it covers several life stages of the fish from the newly fertilised egg, through hatch to early stages of growth and should therefore be used (see ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b, Figure R.7.8-4). The test method OECD TG 210 is also the only suitable test currently available for examining the potential toxic effects of bioaccumulation (ECHA Guidance Chapter R7b, version 4.0, June 2017). For these reasons, ECHA considers the FELS toxicity test using the test method OECD TG 210 as appropriate and suitable.

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: Fish, early-life stage (FELS) toxicity test (test method: OECD TG 210).

Notes for your consideration

According to ECHA *Guidance on information requirements and chemical safety assessment* Chapter R7b (version 4.0, June 2017) (Section R.7.8.5., including Figure R.7.8-4),if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially more sensitive, long-term studies may be required on both.

Due to the low solubility of the substance in water and abiotic degradation OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA Guidance, Chapter R7b, table R. 7.8-3 summarising aquatic toxicity testing of difficult substances should be consulted by the Registrant for choosing the design of the requested long-term ecotoxicity tests and for calculation and expression of the result of this test.

4. Exposure assessment and risk characterisation (Annex I, Section 5.1.1. and 6.) for workers

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 (CSA) conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

Pursuant to Article 14(4) of the REACH Regulation, if the substance is fulfils the criteria for any of the hazard classes listed in that provision or is assessed to be a PBT or vPvB, the CSA shall include exposure assessment (Annex I, Section 5) and risk characterisation (Annex I, Section 6).

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 CSR (Annex II, section 0.1.2. of the REACH Regulation).

In the present case, ECHA notes that you have classified the registered substance as acute toxic (inhalation), category 3; skin sensitiser, category 1A; germ cell mutagenic, category 2,

which are all hazard classes listed in Article 14(4) of the REACH Regulation, which means that an exposure assessment and a risk characterisation are warranted.

ECHA further 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 and respiratory protection: "workers are required to wear Personal Protective Equipment (dermal protection and a respirator)", while in IUCLID Section 11 has reported: "Appropriate respirator which is approved or made according to a standard approved by the relevant national body for health and safety" and "Rubber gloves".

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. Gloves need to be manufactured and tested according to CEN standard EN 374:2003 – Gloves giving protection from chemicals and micro-organisms.

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

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

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

5. 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 (CSA)

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

Further, Annex I, Section 6.5. of the REACH Regulation states that for those human effects [...] for which it was not possible to determine a DNEL [...], a qualitative assessment of the likelihood that effects are avoided when implementing the exposure scenario shall be carried out.

ECHA notes that the registered substance is Identification of degradation products and skin sensitisation 1A. According to ECHA's Guidance on information requirements and chemical safety assessment, Chapter E, section E.3.4, pages 18 to 32, as well as ECHA Guidance R.8. Appendix R. 8-10, for endpoints such as irritation/corrosion, sensitisation, acute toxicity, mutagenicity, where no dose descriptor is available, a more qualitative assessment has to be chosen. This qualitative approach shall define operational conditions (OCs) and risk management measures (RMMs) to prevent exposure and adequately protect against contact with the registered substance.

ECHA notes that you have conducted a qualitative assessment. In your hazard conclusions, you have identified acute and long-term local effects via inhalation and dermal route. The hazards that are behind these observations are acute toxicity (inhalation) and skin sensitising properties. In your hazard conclusions, you have not included mutagenicity even though you have identified adverse health effect in your hazard assessment and you have classified the substance as germ cell mutagen, category 2. ECHA notes that you need to perform qualitative risk characterisation also for the mutagenicity.

ECHA notes that you have added some recommended RMMs e.g. use of local exhaust ventilation, use of dermal and/or respiratory protection into the conditions of use in the exposure scenarios. ECHA noticed that in some scenarios you have automatic substance metering (ES 1, contributing scenario 5) or closed system (ES1, contributing scenario 6), which are preferred with high hazard substance. However, there are still deficiencies in describing OCs e.g. physical form of the product, concentration of substance in product and duration and frequence of task. In your conclusion on risk characterisation, you have stated as follows: "*Transfer of the neat powder material takes place under controlled conditions; workers receive specific training in the handling of hazardous material prior to conducting these operations, and are required to wear Personal Protective Equipment (dermal protection and a respirator); in addition engineering controls including Local Exhaust Ventilation is employed to prevent the spread of the material away from immediate area in which the operation takes place*" and also "*Occasional brief worker exposure may occur when the equipment is opened for sampling, cleaning, or maintenance, however in these circumstances precautions are taken to prevent significant exposure*".

According to the Guidance on information requirements and chemical safety assessment, Chapter E, table E.3-1, the risk management measures and operational conditions to be considered in the Exposure Scenario for a mutagenic (category 2), skin sensitising (category

1A), and acute toxic substance should be such as to "any measure to eliminate exposure should be considered", "very high level of containment required, except for short term exposures" and "avoid contact with contaminated tools and objects" and PPEs should entails the use of "substance/task appropriate gloves", "skin coverage with appropriate barrier material based on potential for contact with the chemical" and "substance/task appropriate respirator". Indeed, the primary approach to control exposure is to ensure, as far as possible, prevention of dermal contact and risk of exposure via inhalation.

Also it is reminded that the use of PPE in the working environment should be seen as last resort when deciding on control measures and should only be used when all other options have been exhausted.

ECHA notes that the qualitative assessment carried out by you does not specify to a sufficient level of detail which are the RMMs/OCs implemented in the exposure scenarios to prevent and control exposure via dermal contact and inhalation. Especially ES1 contributing scenarios 3 and 4 needs more detailed description of OCs and RMMs. A list of those measures is reported in Guidance Part E, table E.3.1 and the RMMs/OCs shall be aligned to a substance of such hazards (high hazard for dermal and inhalation risk). The 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.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to revise a qualitative exposure assessment demonstrating the likelihood that effects for acute toxicity (inhalation), mutagenicity and skin sensitisation are avoided for all identified uses and to detail the operational conditions and risk management measures and revise the risk characterisation accordingly.

Appendix 2: Procedural history

The compliance check was initiated on 7 October 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.

You were notified that the draft decision does not take into account any updates after the date when the draft decision was notified to you 5 November 2015, based on the registration with submission number [redacted]. In your comments you indicated your intention to change the tonnage band of the Joint Submission from 100-1000 tonnes per year to 10-100 tonnes per year. You updated your registration on 18 January 2016 with submission number [redacted]. In your update the tonnage band was changed from 100-1000 tonnes per year to 10-100 tonnes per year. Exceptionally therefore, and given the specific circumstances of this case, ECHA has taken into account the update of 18 January 2016 in this decision.

ECHA took into account your comments, and the tonnage band downgrade, and amended the requests and the deadline of the decision. The testing proposal included in your dossier update with submission number [redacted] was not admissible, since the endpoint was already addressed in this decision.

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

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

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

ECHA referred the draft decision to the Member State Committee.

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

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-54 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.*

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.