EUROPEAN CHEMICALS AGENCY

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DECISION ON SUBSTANCE EVALUATION PURSUANT TO ARTICLE 46(1) OF REGULATION (EC) NO 1907/2006

For hydroquinone, CAS No 123-31-9 (EC No 204-617-8)

Addressees: Registrant(s)[1] of hydroquinone (Registrant(s))

This decision is addressed to all Registrant(s) of the above substance with active registrations on the date on which the draft for the decision was first sent, with the exception of the cases listed in the following paragraph. A list of all the relevant registration numbers subject to this decision is provided as an annex to this decision.

Registrant(s) meeting the following criteria are *not* addressees of this decision:
i) Registrant(s) who registered the above substance exclusively as an on-site isolated intermediate under strictly controlled conditions and ii) Registrant(s) who have ceased manufacture/import of the above substance in accordance with Article 50(3)of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation) before the decision is adopted by ECHA.

Based on an evaluation by National Institute of Health (Instituto Superiore di Sanità) on the behalf of the Italian Ministry of Health as the Competent Authority of Italy (evaluating MSCA), the European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 52 of the REACH Regulation.

This decision does not take into account any updates of the registrations of the concerned Registrant(s) after 2 May 2013.

This decision does not imply that the information provided by the Registrant(s) in the registrations is in compliance with the REACH requirements. The decision neither prevents ECHA from initiating compliance checks on the dossiers of the Registrant(s) at a later stage, nor does it prevent a new substance evaluation process once the present substance evaluation has been completed.

I. Procedure

Pursuant to Article 45(4) of the REACH Regulation the Competent Authority of Italy has initiated substance evaluation for hydroquinone, CAS No 123-31-9 (EC No204-617-8) based on registrations dossiers submitted by the addressees (Registrant(s)) and prepared the present decision in accordance with Article 46(1) of the REACH Regulation.

On the basis of an opinion of the ECHA Member State Committee and due to initial grounds for concern relating to: human health/CMR; Exposure/Wide dispersive use, consumer use, high aggregated tonnage; Risk characterisation ratios close to 1 (human health), hydroquinone was included in the Community rolling action plan (CoRAP) for substance

[1] The term Registrant(s) is used throughout the decision, irrespective of the number of registrants addressed by the decision.

evaluation pursuant to Article 44(2) of the REACH Regulation to be evaluated in 2012. The CoRAP was published on the ECHA website on 29 February 2012. The Competent Authority of Italy was appointed to carry out the evaluation.

In the course of the evaluation, the evaluating MSCA noted additional concerns regarding: acute and sub chronic inhalation exposure for workers during manufacturing and batching processing; a risk characterisation ratio close to 1 (environment) and potential long term effects on aquatic compartment (environment).

The evaluating MSCA considered that further information was required to clarify the above mentioned concerns. Therefore, it prepared a draft decision pursuant to Article 46(1) of the REACH Regulation to request further information. It submitted the draft decision to ECHA on 28 February 2013.

On 4 April 2013 ECHA sent the draft decision to the Registrant(s) and invited them pursuant to Article 50(1) of the REACH Regulation to provide comments within 30 days of the receipt of the draft decision.

By 6 May 2013 ECHA received comments from Registrant(s) of which it informed the evaluating MSCA without delay.

The evaluating MSCA considered the Registrants' comments received and did amend Section III of the draft decision.

In accordance with Article 52(1) of the REACH Regulation, on 31 October 2013 the evaluating MSCA notified the Competent Authorities of the other Member States and ECHA of its draft decision and invited them pursuant to Articles 52(2) and 51(2) of the REACH Regulation to submit proposals to amend the draft decision within 30 days.

Subsequently, five Competent Authorities of the Member States and ECHA submitted proposals for amendment to the draft decision.

On 05 December 2013 ECHA notified the Registrant(s) of the proposals for amendment to the draft decision and invited them pursuant to Articles 52(2) and 51(5) of the REACH Regulation to provide comments on those proposals for amendment within 30 days of the receipt of the notification.

The evaluating MSCA reviewed the proposals for amendment received and amended Sections II and III of the draft decision.

On 16 December 2013 ECHA referred the draft decision to the Member State Committee.

On 6 January 2014 in accordance to Article 51(5), the Registrant(s) provided comments on the proposal(s) for amendment. The Member State Committee took the comments of the Registrant(s) on the proposal(s) for amendment into account.

After discussion in the Member State Committee meeting on 3-7 February 2014, a unanimous agreement of the Member State Committee on the draft decision as modified at the meeting was reached on 7 February 2014. ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Information required

Pursuant to Article 46(1) of the REACH Regulation the Registrant(s) shall submit the following information using the indicated test methods/instructions and the registered substance (hydroquinone) subject to the present decision:

1. Transgenic Rodent Somatic and Germ Cell Gene Mutation Assay (TGR) in rats,oral administration (gavage) during 28 consecutive days (test method: OECD 488). The TGR somatic assay shall be conducted in kidney, stomach, bone marrow, liver and germ cells.
   or
   In vivo alkaline comet assay, according to the method set out in the "SCIENTIFIC REPORT OF EFSA, Minimum Criteria for the acceptance of in vivo alkaline Comet Assay Reports"[1] in rats, oral administration (gavage) on stomach or duodenum, liver, kidney and gonadal cells;

2. Sub-chronic toxicity study (90-day) in rats, inhalation route (test method: B.29/OECD 413) unless the Registrant(s) demonstrate that testing is not feasible due to the explosiveness of the dust in testing preparation;

3. Long-term toxicity testing on fish (test method: OECD 210 (Fish Early-Life Stage Toxicity Test)) taking into account the OECD Guidance document on aquatic toxicity testing of difficult substances and mixtures[2];

4. Effects on soil micro-organism (test method: C.21/OECD 216);

5. Long-term toxicity testing on soil invertebrates and plants (invertebrates: test method: OECD 220 or OECD 232; plants: test method: OECD 208 or ISO 22030);

6. Environmental exposure assessment and the risk characterization for all the identified professional uses;

7. Justification for the non-default use of some values (dilution factor river; effluent discharge of STP; regional releases);

8. Exposure assessment to agricultural soil;

9. Transparent quantitative exposure assessment for all relevant exposures including development of respective exposure scenarios;

10. Justification of the route to route extrapolation from oral route to dermal/inhalation routes in consideration of the fact that the available carcinogenicity and genotoxicity studies are performed via oral route.

Pursuant to Article 46(2) of the REACH Regulation, the Registrant(s) shall submit to ECHA by 23 February 2016 if under the information required under point 1 above the comet assay is performed or by 23 May 2017 in case the transgenic rodent assay is conducted an update of the registration dossiers containing the information required by this decision. The Registrant(s) shall inform ECHA by 21 August 2014 which of the two assays will be performed.

[1] "SCIENTIFIC REPORT OF EFSA, Minimum Criteria for the acceptance of in vivo alkaline Comet Assay Reports" (LINK: http://www.efsa.europa.eu/en/efsajournal/doc/2977.pdf).
[2] OECD SERIES ON TESTING AND ASSESSMENT, Number 23- Guidance document on aquatic toxicity testing of difficult substances and mixtures, Dec. 2000.

At any time, the Registrant(s) shall take into account that there may be an obligation to make every effort to agree on sharing of information and costs with other Registrant(s).

III. Statement of reasons

Based on the evaluation of all relevant information submitted on hydroquinone and other relevant and available information, ECHA concludes that further information is required in order to enable the evaluating MSCA to complete the evaluation of whether the substance constitutes a risk to human health or the environment.

1. TGR assay (OECD 488) or *in vivo* alkaline comet assay in rats by oral route

Hydroquinone was negative in bacterial tests, while mutagenicity was reported in several *in vitro* studies on mammalian cells (McGregor 1988; Galloway 1987; Reddy 1989). *In vivo* genotoxicity in bone marrow and in germ cells was reported after i.p. administration (Ciranni 1988; Adler 1990; Ciranni and Adler 1991). Hydroquinone transplacentally induced micronuclei in the liver of mouse foetuses after oral administration (gavage) of the dams with 80 mg/kg bw (Ciranni 1988a). The same treatment schedule in male mice produced a weak but significant induction of micronuclei in bone marrow (Ciranni 1988b). On the other hand, the administration in the diet of 0.8% HQ / Kg feed (estimated to correspond to 1152 mg/kg bw) gave negative results (O'Donoghue 1999). Hydroquinone did not induce lethal dominant mutation when administered by gavage but this test, rather obsolete and commonly considered of low sensitivity, is not sufficient to exclude an *in vivo* genotoxic potential of hydroquinone in germ cells. It was claimed in the last comments produced by the Registrant(s) on 6 January 2014 that the micronuclei observed in the two Ciranni's studies are due to body temperature increase and therefore are irrelevant to risk assessment, but this assumption is merely hypothetical. In fact the discrepancy in the results of some of the above-mentioned in vivo studies remains unexplained and do not allow to draw a conclusion on the potential systemic genotoxicity of the substance after oral exposure.

Overall, taking into account the experimental results reported both *in vitro* and *in vivo*, at present a role of genotoxicity in the etiology of the tumors observed in the experimental studies and an *in vivo* genotoxic potential of the substance in germ cells cannot be excluded. Therefore, the claim of the Registrant(s) that a new study would not necessarily allow to clarify further the mutagenic potential of the substance because the available results are equivocal is not sufficiently substantiated.

Therefore, additional *in vivo* investigation is needed in order to clarify the concern for genotoxicity. In the absence of the requested study, it is not possible to exclude interactions of hydroquinone with the genetic materials of germ cells neither a contribution of DNA damage to the carcinogenesis process, therefore, only on the basis of the current data set, the substance should be considered as a potential germ cell mutagen and as a potential genotoxic carcinogen.

A TGR assay conducted in rats by oral route on kidney, stomach, bone marrow, liver and germ cells will allow to address both the potential genotoxicity on somatic and germ cells and the mechanism of action relevant to carcinogenicity. The choice of the rat as target species is motivated by the observed carcinogenicity in this species. Furthermore, the request of data on five organs is motivated by the need of information on the target organ in rat for carcinogenesis (kidney), on the site of contact after oral administration (stomach), on a distal site (bone marrow), on rapidly and slowly proliferating tissues (bone marrow and liver) and on germ cells to clarify the concern for germ cell mutagenicity.

It is to be noted that, while this requirement is fully compliant with the OECD guideline 488, the TGR assay is a rather complex procedure and at present a few laboratories have the accreditation to carry out this test. Moreover, at present this test is particularly developed in the mouse and less in the rat, the latter being the most appropriate target species in this specific case. More explicitly, based on information available to ECHA and in line with the comments made by the Registrant(s), the test laboratory validation of the assay in the rat and the relevant tissues for the case at hand may not become available within a reasonable time. It is therefore uncertain whether the assay will be technically available to the Registrant(s). The respective costs of a TGR assay in the rat are not predictable either and cannot be compared to possible alternative test protocols. On that basis it may be that only requesting this study is not appropriate to achieve the objective of substance evaluation for hydroquinone, i.e. to clarify the *in vivo* genotoxic potential. Therefore, an in vivo comet assay in rats as specified below could be an alternative to verify the *in vivo* genotoxic potential of the substance.

The *in vivo* alkaline comet assay shall be conducted in rats by oral administration (gavage) on first site of contact tissues (stomach or duodenum), liver, kidney and gonadal cells. This assay will allow to address both the mechanism of action relevant to carcinogenicity and the genotoxicity on somatic and potentially on germ cells.

The detection of DNA damage in gonadal cells by the comet assay, independently from the cell type, should be considered a demonstration that the gonadal barrier is passed by the test substance and/or its metabolites in a genotoxically active form and, therefore, that there is a potential concern related to the ability to interact with the genetic material of the germ cells.

ECHA acknowledges the comment made by the Registrant(s) that "*the in vivo comet assay cannot address properly the potential heritable DNA damage on germ cells*" however, as explained above, ECHA is of the opinion that the comet assay can detect genotoxic effect in gonadal cells and, therefore, the potential ability of the substance to interact with the genetic material of the germ cells.

Although an OECD guideline on *in vivo* comet assay is still at the stage of draft (its publication is foreseen in 2014) several internationally agreed protocols that meet the criteria of Article 13(3) of the REACH Regulation are currently available. Furthermore, the European Food Safety Authority (EFSA, 2012) and ECHA (as indicated in the 31st Meeting of the ECHA Member State Committee) have recognized earlier these protocols. ECHA considers the *in vivo* comet assay in gonadal cells an adequate genotoxicity test for clarifying this concern for potential germ cell effects.

The test shall follow the EFSA guidance indicating the minimum criteria for the acceptance of *in vivo* alkaline comet assay (EFSA, 2012).

With regards to the deadlines provided to submit either of the required studies, ECHA considers that 21 months from the date of decision are sufficient to conduct the *in vivo* alkaline comet assay as initially foreseen. Due to the foreseeable difficulties in conducting the transgenic rodent assay as indicated by the Registrant(s), ECHA considers that this is accounted for by a deadline of 36 months from the date of decision.

Therefore, pursuant to Article 46(1) of the REACH Regulation, the Registrant(s) are required to carry out either of the following studies using the registered substance subject to this decision:

a TGR assay in rats (OECD 488) treated via oral administration (gavage) in kidney, stomach, bone marrow, liver and on germ cells;
or
an *in vivo* alkaline comet assay (EFSA, 2012) in rats treated via oral administration (gavage) on first site of contact tissues (stomach or duodenum), liver, kidney and gonadal cells.

2. Sub-Chronic inhalation toxicity study (90-day)

The technical dossier does not contain a study on sub-chronic inhalation toxicity. The approach used by the Registrant(s) for the derivation of the no effect levels (DNEL) long-term–inhalation, local effects is considered not appropriate. Indeed this derivation is carried out in consideration of the significant reduction of chronic eye effects in the workers since the first years of production due to the installation of measures to reduce worker exposure. The DNEL calculated with this approach is established by the Registrant(s) in a concentration of 1 mg/m^3. However this approach is not supported by any scientific information. Hence it is necessary to provide toxicological information in order to derive a reliable DNEL to characterise the risk of local effects. This information is needed to establish whether the suspected concern (risk characterization ratio close to 1 for several exposure scenarios) may be realised or not. Without the requested information it will not be possible to verify whether there remains an uncontrolled risk with the substance that should be subject to further risk management measures.

In relation to Annex XI, 1. of the REACH Regulation, ECHA notes that the registration dossier does not contain any classification for sub-chronic inhalation toxicity. The information provided in the justification for waiving is not adequate for the purpose of classification and labelling and/or risk assessment and the sub chronic toxicity of hydroquinone should be investigated due to concerns regarding sub chronic exposure for workers during manufacturing and batching processing.

Furthermore, the derivation of a DNEL based on the sub-chronic toxicity study would allow also to address the short term effects.

In response to ECHA's draft decision, some different epidemiological data was submitted by the Registrant(s). The evaluation of these studies performed by the evaluating MSCA has highlighted several methodological and descriptive flaws that do not allow to consider the studies as suitable for addressing this end-point. On the other hand it has to be noted that another epidemiological study, not submitted by the Registrant(s) but available in literature, showed the possibility of respiratory effects related to long term inhalation exposure.

This study by Chodat and Colleagues, published by the British Journal of Industrial Medicine (Br J Ind Med. 1988 Jun;45(6):376-80. Allergy and occupational exposure to hydroquinone and to methionine), reported a statistically significantly higher prevalence of respiratory symptoms in a group of 33 employees exposed to hydroquinone, trimethyl-hydroquinone, and retinenehydroquinone as compared to 55 non exposed workers of the same chemical plant. The level of immunoglobulin G in hydroquinone exposed subjects (m ± SD = 12-5 g/l ± 2 6) was significantly higher than in the control group (10-6 g/l ± 2-4; p < 0 002), suggesting that exposure to hydroquinone and its derivatives induce ventilatory impairment, perhaps by an immunological mechanism.

ECHA points out that in the latest comments made by the Registrant(s) on 6 January 2014 the Registrant(s) refer also to a proposal for amendment made by one competent authority of a Member State that is related to the Acute Inhalation Toxicity study endpoint instead of

the Sub-Chronic inhalation toxicity study. ECHA considers this comment related to Sub-Chronic Inhalation Toxicity study out of the scope of the Proposal for Amendments.

The Registrant(s) pointed out in the last commenting phase that hydroquinone is intentionally made as large particles that are not respirable. However, it is important to highlight that the intent of ECHA, with the request of the sub-chronic inhalation toxicity study, is to investigate on the possible local effects of the substance on the upper respiratory tract. For this reason the concern is related to the inhalable fraction of the substance and not only to the respirable one.

In the same comments, the Registrant(s) stated that hydroquinone has no functional groups indicating explosive properties (as reported in the section 4.14 of the IUCLID dossier). Whereas the absence of such groups appears to meet the specific rules of adaptation as indicated in Annex VII – 7.11. of the REACH Regulation and consequently to omit the information for explosive properties, the Registrant(s) indicated that there is a risk for a dust explosion which would prevent the performance of an inhalation toxicity study due to the potential explosiveness of the atmosphere to be generated for the purpose of testing. The Registrant(s) in particular report that:

> *"In-house process safety studies have reported a high risk of dust explosiveness when the product is milled to a smaller size. In tests performed under conditions similar to the Norm DIN EN 13821, where the product is milled and sieved to achieve a particle size < 63 µm (samples with D50 at 15 to 20 µm and D90 < 44 µm equivalent diameter), the normalized Minimum Ignition Energy (MIE) is lowered significantly (MIE <10 mJ, and for the smaller average sizes, MIE was ca. 1-3 mJ) compared to the products as manufactured (most commonly flakes or needle forms), and thus the free-falling powder presents a higher susceptibility to static charges (Kst > 300 bar.m/s, ST3 rating)".*

ECHA points out that currently there is no actual evidence for such a potential provided by the Registrant(s) in the registration dossiers.

ECHA is of the opinion that it is necessary to provide data and a report of the experiment performed in order to demonstrate that an ST3 rating should be assigned. In this case, the registration dossiers should be updated with the relevant information.

Subject to reliable and verifiable documentation of a ST3-rating, no sub-chronic inhalation toxicity study for hydroquinone shall be provided based on the explosivity of its dust.

Therefore, if the requested documentation to substantiate the explosiveness properties does not demonstrate that the substance can be related to the concern of the explosiveness of the dust, pursuant to Article 46(1) of the REACH Regulation, the Registrant(s) are required to perform a Sub-chronic toxicity study (90-day) in rats, inhalation route (test method: B.29/OECD 413).

3. Long-term toxicity testing on fish

The Registrants' justification for data waiving for long-term toxicity testing on fish is based on the results of the acute toxicity showing that fish is not more sensitive than invertebrates or algae. In that case, according to the integrated testing strategy, if based on the results of the long-term Daphnia study and an applied assessment factor of 50 no risks are indicated, no long-term fish testing may need to be conducted. However, a study of fish acute toxicity

(DeGraeve et al., 1980)[3] proves that fish is substantially (by a factor of 10) more sensitive than invertebrates or algae. The study is considered reliable as it was used to classify hydroquinone in the harmonised system as Aquatic Acute 1, with an M-factor of 10. The available chronic toxicity testing on invertebrates, provided by the Registrant(s), raise an additional environmental concern due to the long-term effects of hydroquinone on the aquatic compartment. A further investigation of the chronic effects on fish, the most sensitive taxonomic group, is required in order to clarify the ecotoxicological profile of the substance.

Moreover, based on the results for chronic toxicity to aquatic organisms, the Registrant(s) are required to refine the predicted no effect concentrations (PNECs) applying assessment factors in accordance with ECHA's Guidance, Chapter R.10. In the comments of the Registrant(s) on the initial Draft Decision they consented to the requests stating that *"the chronic fish toxicity study will be performed which will enable the refinement of the PNEC value for soil based on equilibrium method, and the soil exposure assessment is improved"*. ECHA agrees with the Registrant(s) that the long-term toxicity testing on fish will be used to refine PNEC value of the aquatic compartment, as well as the PNEC soil through application of equilibrium partitioning method (EPM). The Registrant(s) should consider the Integrated Testing Strategy (ITS) as recommended in Section R.7.11.6., Chapter R.7c of the ECHA Guidance on Information requirements and Chemical Safety Assessment (version 1.1., November 2012), and determine the need for further testing on terrestrial organisms ("Chronic or long-term toxicity tests on plants and/or soil invertebrates can be used to derive a PNECsoil").

Therefore, information on long-term toxicity testing on fish is required in order to enable the evaluating MSCA to assess the ecotoxicological profile of the substance and to refine the PNECs. The requested information is needed to verify whether there remains an uncontrolled risk to the environment that should be subjected to further risk management measures.

One competent authority of a Member State proposed to conduct pre-test experiments to determine whether the Fish Early-Life-Stage (FELS) study should be carried out using either a pre-oxidised test solution or the parent substance. Moreover, the Member State proposed to include an analysis of the known oxidised degradant p-benzoquinone in the test. The Registrant(s) agreed with these proposals. ECHA highlights that one of the formed oxidation products is p-benzoquinone. It is classified in the harmonised system as very toxic to aquatic life (Aquatic Acute 1, M-F 10), and therefore it has the same acute toxicity of the registered substance. However, because of the known rapid degradation of hydroquinone into p-benzoquinone in aqueous solution, the Registrant(s) shall take into account the indications provided in the OECD guidance document on aquatic toxicity testing of difficult substances and mixtures to determine the suitable exposure conditions in the assay. This may include a need to analyse for the degradant p-benzoquinone. As the experimental conditions can influence the results of the toxicity test on fish, a detailed report of the test design with a justification of the most appropriate way to express the results shall be provided by the Registrant(s).

Therefore, pursuant to Article 46(1) of the REACH Regulation, the Registrant(s) are required to carry out the following study using the registered substance subject to this decision: Long-term toxicity testing on fish, test method OECD 210.

[3] DeGraeve GM Geyer DL, Meyer JS, Bergman HL (1980) Acute and embryo larval toxicity of phenolic compounds to aquatic biota Arch Environ Contam Toxicol 9: 557-568.

4. Effects on soil micro-organisms

The Registrants' justification for data waiving for toxicity to soil organisms states that a direct and indirect exposure to the soil compartment is unlikely. However, the results of the chemical safety assessment (risk characterisation ratios in the range 0.894 – 1.000) indicate the need to investigate further the effects of the substance on terrestrial organisms.

Following a proposal for amendment, the evaluating MSCA agreed with the indication that soil micro-organisms may not be covered by the EPM (equilibrium partitioning method) approach. The PNECaquatic does not take into considerations any toxicity data on micro-organisms and, therefore, the PNECsoil based on EPM approach may not provide sufficient protection for terrestrial micro-organisms.

Therefore, this information is needed to verify whether there remains an uncontrolled risk to the environment that should be subjected to further risk management measures.

Moreover, the Registrant(s) (in the comments on the proposals for amendment to the draft decision) agreed to perform the toxicity study on soil micro-organisms (OECD 216).

Therefore, pursuant to Article 46(1) of the REACH Regulation, the Registrant(s) are required to carry out the following study using the registered substance subject to this decision: Short-term toxicity testing on soil micro-organism, test method: C.21/OECD 216).

5. Long-term toxicity testing on soil invertebrates and plants

The Registrants' justification for waiving the toxicity to soil organisms states that a direct and indirect exposure to the soil compartment is unlikely, however, the results of the chemical safety assessment (risk characterisation ratios in the range 0.894 – 1.000) indicate the need to investigate further the effects of the substance on terrestrial organisms. As indicated at point 4 above, the Registrant(s) should consider the ITS as recommended in Section R.7.11.6., Chapter R.7c of the ECHA Guidance on Information requirements and Chemical Safety Assessment (version 1.1., November 2012), and determine the need for further testing on terrestrial organisms (Long-term toxicity testing on soil organisms).

Based on the results of the toxicity for soil compartment, the Registrant(s) are required to refine the PNEC soil based on the lowest EC_{50}/NOEC values, resulting from information requirement listed under point 4 and 5.

In the risk characterisation, exposure levels are compared to quantitative hazard information and control of a risk for a substance is demonstrated when risk characterisation ratios are below one. In case risks are not controlled, the chemical safety assessment process can be refined. The Registrant(s), at the beginning, can decide one or both of the following options:

- Improve hazard information (information requirement listed under point 4 and 5)
- Improve exposure information (information requirement listed under point 9) and/or consider to introduce sufficient risk management measures (RMMs).

Information on long-term toxicity testing on soil organisms is required in order to enable the evaluating MSCA to assess the ecotoxicological profile of the substance and to refine the PNEC soil. The requested information is needed to verify whether there remains an uncontrolled risk to the environment that should be subjected to further risk management measures.

Pursuant to Article 46(1) of the REACH Regulation, the Registrant(s) are required to carry out the following studies: Long-term toxicity testing on soil organisms: invertebrates, (test method: OECD 220 or OECD 232); plants (test method: OECD 208 or ISO 22030, with at least 3 species tested, one monocotyledonous and two dicotyledonous species from different groups), if following the ITS strategy there is any need for further testing on terrestrial organisms.

6. Environmental exposure assessment and the risk characterization for all the identified professional uses

Exposure scenarios (ES), exposure assessment and risk characterization should address all identified uses. The Registrant(s) have not performed the environmental exposure assessment and the risk characterization for the ES 3b, 5b and 6b (professional use) and they do not provide any appropriate justifications. The evaluating MSCA noted an additional concern for the substance which is related to the risk characterisation ratio close to 1 for environment, therefore the required information are essential to clarify the concern.

Appropriate justification on identified uses is required in order to enable the evaluating MSCA to assess the exposure estimation of the substance. The requested of appropriate justification is needed to verify whether there remains an uncontrolled risk to the environment that should be subjected to further risk management measures. The Registrant(s) consented to the request stating that they agree to revise the Chemical Safety Report (CSR) for environmental exposure for the professional uses.

Therefore, pursuant to Article 46(1) and Annex I, sections 5 and 6 of the REACH Regulation, the Registrant(s) are required to perform the environmental exposure assessment and the risk characterization for professional use.

7. Justification for the non-default use of some values (dilution factor river; effluent discharge of STP; regional releases)

The evaluating MSCA noted an additional concern for the substance which is related to the risk characterisation ratio close to 1 for environment, therefore the following information are essential to clarify the concern. The Registrant(s) consented to the request stating that they agree to revise the CSR for environmental exposure for the professional uses.

a. Dilution factor river

Referring to the exposure scenario manufactory, the Registrant(s) do not provide an appropriate scientific justification for the use of the dilution factor river: 7350 (site-specific [redacted]: river [redacted]). The ECHA Guidance Chapter R.16 (pg 62) states that *"for situations with very high dilution factor, the mixing zone of the effluent in surface water may be very long and the overall area that is impacted by the effluent before it is completely mixed can be very substantial. Therefore in case of site specific assessment the dilution factor that is applied for calculation of the local concentration in surface water should not be greater than 1000".*

b. Effluent discharge of STP

Referring to the exposure scenario manufactory, the Registrant(s) do not provide an appropriate scientific justification for the use of the effluent discharge of (sewage treatment

plant (STP): 4.7E+06. The ECHA Guidance Chapter R.16 (pg 54) states that "*if no specific data are known, effluent STP should be based on an average wastewater flow of 200 l per capita per day for a population of 10000 inhabitants*".

c. Regional releases

Referring to the regional exposure, in the CSR ([redacted]) the Registrant(s), in contrast to the default parameterization, reported that no direct release into surface water bypassing the waste water treatment plant (WWTP) was considered. The ECHA Guidance Chapter R.16 (pg 17 and 46) states that "*when calculating the total regional releases, by default, 80% of the wastewater is assumed to be treated in a STP and 20% to go directly to surface water without any treatment*".

Information on the use of non-default values are required in order to enable the evaluating MSCA to assess the exposure estimation of the substance. The requested information is needed to verify whether there remains an uncontrolled risk to the environment that should be subjected to further risk management measures.

Therefore, according to the requirements of Article 46(1) and Annex I, 5.1.1. and 5.2.4. of the REACH Regulation, the Registrant(s) are requested to update the related environmental exposure assessment applying a default value or giving a scientific justification for the non-default use of values, and update the CSR accordingly. The Registrant(s) consented to the requests of the evaluating MSCA.

8. Exposure assessment to agricultural soil

The assumption that the industrial sludge is not used as agricultural fertilizer is a restriction in spreading of sludge and it should be indicated in the CSR as RMM, as mentioned in ECHA Guidance Chapter R.13.

Therefore, according to the requirements of Article 46(1) and Annex I, 5.2.4. of the REACH Regulation, the Registrant(s) are requested to update the CSR, including the assumption in the section containing RMM.

Referring to the calculated predicted effect concentrations (PEC) agric. soil values (around 0.11 µg/Kg wwt), the related risk characterisation ratio values for soil are all around 1, therefore, the Registrant(s) are requested to verify the exposure assessment to agricultural soil.

In risk characterisation, exposure levels are compared to quantitative hazard information, control of risk for a substance is demonstrated when risk characterisation ratios are below one. In case risks are not controlled, the CSA process can be refined. The Registrant(s), at the beginning, can decide one or both of the following options:

- Improve hazard information (information requirement listed under point 4 and 5)
- Improve exposure information (information requirement listed under point 9) and/or consider to introduce sufficient RMMs.

Information on exposure assessment to terrestrial compartment is required in order to enable the evaluating MSCA to assess the environmental exposure of the substance and to refine the PECs. The requested information is needed to verify whether there remains an uncontrolled risk to the environment that should be subjected to further risk management measures.

Therefore, pursuant to Article 46(1) and Annex I, sections 5 and 6 of the REACH Regulation, Registrant(s) are required to perform the environmental exposure assessment and the risk characterization for terrestrial compartment. The Registrant(s) consented to the requests of the evaluating MSCA.

9. Quantitative exposure assessment

The Registrant(s) are requested to perform transparent quantitative exposure assessment for all relevant exposures and to develop exposure scenarios and contributing scenarios accordingly. The exposure scenarios for all groups of population are lacking. There is no transparency in relation to a conclusion like e.g.: "the photo hobbyist is considered as educated person with the necessary awareness to the hazard potential" (CSR Chapter 9.2.2).

For the exposure scenario ES 3C: Consumer end-use stage Photo chemicals (Hobby use), in the CSR the Registrant(s) carried out only a qualitative exposure estimate while the available information on the determinants allow to perform a quantitative estimate. Although ECHA agrees with the proposed RMMs for this scenario by the Registrant(s) in the CSR, the Registrant(s) should perform a quantitative exposure assessment in the risk characterisation. For this purpose the evaporation model in CONSEXPO v. 4.0 could be used in order to estimate the potential inhalation exposure for consumers due to handling liquid solutions when dipping prints and negatives.

In the comments received on 6 January 2014 the Registrant(s) accepted to update the registration dossier with a quantitative exposure assessment for all relevant exposure scenarios.

Therefore, according to the requirements of Article 46(1) and Annex I, 5.1.1. of the REACH Regulation, the Registrant(s) are requested to update the CSR and the relevant sections of the IUCLID dossiers.

10. Route to route extrapolation

One competent authority of a Member State proposed to request a justification for the route-to-route extrapolation from oral to the other routes (dermal/inhalation) as a first hepatic pass is noted by oral route that does not exist for the other routes, and can impact the bioavailability and thus, toxicity of the substance in the organism. Little information on metabolism in particular for the inhalation route, which is one of the main routes of exposure, is available in the toxicokinetics part. This information is notably relevant for genotoxicity and carcinogenicity endpoints which are performed by oral route and also for the derivation of the DNEL long-term inhalation, systemic effects. Therefore, a justification to extrapolate the results of toxicological endpoints, from oral to inhalation/dermal route should be provided.

In the comment received on 6 January 2014 the Registrant(s) provided a justification which is considered adequate by ECHA but is not available yet in the technical registration dossiers.

Therefore, according to the requirements of Article 46(1) of the REACH Regulation, the Registrant(s) are requested to update the CSR and the relevant sections of the IUCLID dossier.

IV. Adequate identification of the composition of the tested material

The substance identity information submitted in the registration dossiers has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation. In relation to the required tests, the sample of substance used for the new studies shall have a composition that is within the specifications of the substance composition that are given by all Registrant(s). It is the responsibility of all the Registrant(s) to agree on the tested materials to be subjected to the tests subject to this decision and to document the necessary information on composition of the test material. The substance identity information of the registered substance and of the sample tested must enable the evaluating MSCA and ECHA to confirm the relevance of the testing for the substance subject to substance evaluation. Finally, the studies must be shared by the Registrant(s).

V. Avoidance of unnecessary testing by data- and cost- sharing

Avoidance of unnecessary testing and the duplication of tests is a general aim of the REACH Regulation (Article 25). The legal text foresees the sharing of information between Registrant(s). Since several Registrant(s) of the same substance are required to provide the same information, they are obliged to make every effort to reach an agreement for every endpoint as to who is to carry out the test on behalf of the other Registrant(s) and to inform ECHA accordingly within 90 days from the date of this decision under Article 53(1) of the REACH Regulation.

If ECHA is not informed of such agreement within 90 days, it shall designate one of the Registrant(s) to perform the tests on behalf of all of them. If a Registrant(s) performs a test on behalf of other Registrants, they shall share the cost of that study equally and the Registrant(s) performing the test shall provide each of the others concerned with copies of the full study reports.

This information should be submitted to ECHA using the following form stating the decision number above at:

https://comments.echa.europa.eu/comments_cms/SEDraftDecisionComments.aspx

Further advice can be found at http://echa.europa.eu/datasharing_en.asp.

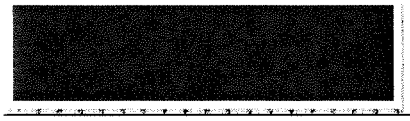
VI. General requirements regarding Good Laboratory Practice

ECHA always reminds Registrant(s) of the requirements of Article 13(4) of the REACH Regulation that ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP). National authorities monitoring GLP maintain lists of test facilities indicating the relevant areas of expertise of each facility.

VII. Information on right to appeal

An appeal may be brought against this decision to the Board of Appeal of ECHA under Articles 52(2) and 51(8) of the REACH Regulation. Such an appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal

procedure can be found on the ECHA's internet page at http://echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.



Jukka Malm
Deputy Executive Director

Annex: List of registration numbers – This annex is confidential and not included in the public version of this decision