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Helsinki, 06 April 2018

Substance name: 2-ethylhexyl trans-4-methoxycinnamate (OMC)
EC number: 629-661-9 (Previously registered as EC 226-775-7)
CAS number: 83834-59-7
Date of latest submission(s) considered[1]: 7/12/2015
Decision/annotation number: Please refer to the REACH-IT message which delivered this communication (in format SEV-D-XXXXXXXXXX-XX-XX/F)
Addressee(s): Registrant(s)[2] of 2-ethylhexyl trans-4-methoxycinnamate (Registrant(s))

DECISION ON SUBSTANCE EVALUATION

Based on Article 46(1) of the REACH Regulation (Regulation (EC) No 1907/2006), you are requested to submit the following information on the registered substance:

1. Either an Amphibian Metamorphosis Assay, test method OECD 231, **or** a Larval Amphibian Growth and Development Assay, test method OECD 241

2. Fish Sexual Development Test, test method OECD 234, using either Japanese Medaka (*Oryzias latipes*) or Zebrafish (*Danio rerio*)

3. Daphnia magna Reproduction Test, test method OECD 211

4. Alga, Growth Inhibition Test, test method OECD 201 **or** Lemna Growth Inhibition Test, test method OECD 221

5. Environmental exposure assessment (as further specified in Appendix 1).

Requirements (3-4) are dependent on the results of requirements (1) and (2). Requirement (5) is dependent on the results of requirements (1-4). The dependencies are explained in Appendix 1 "Reasons".

You shall provide an update of the registration dossier(s) containing the information requests of 1 and 2 by **13 April 2020** from the date of the decision, and the information requests of 3, 4 and 5 (if needed) by **13 July 2021** from the date of the decision, including robust study summaries and, where relevant, an update of the chemical safety report. The full study report(s) have to be submitted for requests 1 and 2. The deadlines take into account the time that you, the Registrant(s), may need to agree on who is to perform any required tests. They have been set to allow for sequential testing.

The reasons of this decision and any further test specifications are set out in Appendix 1. The procedural history is described in Appendix 2. Further information, observations and

[1] This decision is based on the registration dossier(s) at the end of the 12-month evaluation period.

[2] The terms registrant(s), dossier(s) or registration(s) are used throughout the decision, irrespective of the number of registrants addressed by the decision.

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technical guidance as appropriate are provided in Appendix 3. Appendix 4 contains a list of registration numbers for the addressees of this decision. This appendix is confidential and not included in the public version of this decision.

Who performs the testing?

Based on Article 53 of the REACH Regulation, you are requested to inform ECHA who will carry out the studies on behalf of all registrant(s) within 90 days. Instructions on how to do this are provided in Appendix 3.

Appeal

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

Authorised[3] by Leena Ylä-Mononen, Director of Evaluation

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

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Appendix 1: Reasons

Based on the evaluation of all relevant information submitted on the registered substance, 2-ethylhexyl trans-4-methoxycinnamate (OMC), and other relevant available information, ECHA concludes that further information is required to enable the evaluating Member State Competent Authority (MSCA) to complete the evaluation of whether the substance constitutes a hazard or risk to the environment.

The evaluating MSCA will subsequently review the information submitted by you and evaluate if further information should be requested to clarify the concern for environmental risk and endocrine disruption.

1. **Amphibian Metamorphosis Assay (OECD TG 231), or a Larval Amphibian Growth and Development Assay (OECD TG 241)**

The concern(s) identified

The concern is related to the potential for environmental endocrine disruption in non-mammalian (amphibian) species. The endocrine activity of the substance in amphibians should be clarified in order to determine whether it poses a hazard and/or risk to the environment.

Why new information is needed

Information is available from *in vitro* systems and *in vivo* studies on mammalian species which indicates that the registered substance has some limited anti-thyroid activity.

In an *in vitro* thyroid receptor transactivation study by Hofmann *et al.*(2009), HepG2 cells (hepatoma derived liver cell line) were stably transfected with a T3 (triiodothyronine) responsive plasmid with a luciferase reporter. OMC tested positive at a concentration of 1 μM (effects 1.5x over vehicle control). In contrast, the endogenous ligand, T3 gave a much more marked positive response at 0.1 nM (122x over vehicle control) using the same assay system. It is concluded that OMC has some limited transactivational capacity *in vitro* at the T3 receptor, but it is significantly less potent than T3.

The information from OECD Conceptual Framework (CF) Level 3 mammalian *in vivo* testing (Schmutzler *et al.*, 2004 and Klammer *et al.*, 2007) also points towards some perturbations of enzymes and hormones relevant to the hypothalamic-pituitary-thyroid (HPT) axis of the endocrine system, but in ovarectomised animals only. In the study by Schmutzler *et al.* (2004), where rats were exposed at 270 and 1450 mg OMC/kg/day in a soya-free diet for 12 weeks, serum thyroid hormone (T4 - thyroxine) levels were decreased at the low dose only and Type 1-deiodinase (DI) activity was decreased at both dose levels. No consistent changes in T3 levels were observed at any dose suggesting that the decrease in Type 1 DI activity was insufficient to impact circulating T3 levels. OMC had no reported effects on TPO (thyroid peroxidase) activity. It is also noted that there was no consistent change in T4 or TSH (thyroid stimulating hormone) and reverse T3 (rT3) was not measured. There is no information available to indicate when blood samples were taken for hormone measurements, making it difficult to determine whether there was any influence of circadian rhythms on the thyroid hormone changes.

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In the study by Klammer *et al.* (2007), where rats were dosed at 10, 33, 100, 333 and 1000 mg OMC/kg/day for 5-days, serum TSH was statistically significantly decreased at 333 and 1000 mg/kg/day, T3 levels were significantly lowered to 63% of control at 1000 mg/kg/day and T4 was statistically significantly decreased by 75% and 59% at 333 and 1000 mg/kg/day. TSH receptor protein increased in the thyroid by 144% at the top dose - and in the liver, Type 1 deiodinase was statistically significant decrease by 38% and 46% at 333 mg/and 1000 mg/kg/day compared to controls. Inconsistent or no effects were observed on these parameters when exposed to the positive control E2. No effect was found on type 2 DI activity and there was also no effect of E2 in this assay. Hypothalamic TRH mRNA (messenger RNA) levels were unaffected. In agreement with Schmutzer *et al.* (2004), OMC did inhibit hepatic type 1 DI activity. However, it would normally be expected that inhibition of hepatic type 1 DI activity would cause decreased T3 levels, and elevated TSH levels as the pituitary responds to the decrease in T3. It is unclear why TSH levels were decreased in this study, although the TRH (thyroid releasing hormone) mRNA data suggest the hypothalamic signal is not perturbed. Also, the TPO data from the studies by Klammer (2007) and Schmutzer *et al.* (2004) appear to exclude inhibition of TPO activity.

Although the precise mode of action is unclear, it can be concluded from the *in vivo* mechanistic studies that OMC can perturb the rat HPT axis. This is consistent with the T4 data from a further developmental neurotoxicity study in rats (Axelstad *et al.*, 2011). However, no adverse effects have been observed in the available mammalian *in vivo* studies on OMC, which can be plausibly linked to a thyroid disrupting mode of action. Currently, the need for further investigations for thyroid disruption in mammals is uncertain due to the lack of clear thyroid related behavioural effects in the developmental neurotoxicity study (Axelstad *et al.*, 2011), the lack of agreement about which other endpoints are regarded as adverse and the lack of standardised methods to investigate such endpoints.

However, amphibians are sensitive to thyroid hormone perturbation and it is not possible to conclude from the limited ecotoxicological information available that adverse effects in amphibian species would not occur. A study is therefore required to determine whether the observed mechanistic interactions could lead to adverse effects on amphibian (sub)populations at relevant environmental concentrations. Based on the results of a limit or range-finding test, it may be possible to conduct an Amphibian Metamorphosis Assay (OECD TG 231) as an initial screening step at Level 3 in the OECD CF. However, if effects in this are anticipated (or indicated), it would be more appropriate to conduct a Larval Amphibian Growth and Development Assay (OECD TG 241) at Level 4 in the OECD CF. The decision on the final choice concerning which of the above mentioned two test(s) to conduct in order to fully address this concern rests with you as the Registrants. The results may provide further information on thyroid disruption which could be used in conjunction with the current database and any new scientific or test method developments to evaluate whether additional testing may be necessary.

What is the possible regulatory outcome

Possible regulatory outcomes are that further information may be required to address the potential environmental hazard or risk, or that the registered substance may, or may not, be considered to be an environmental endocrine disruptor according to the current World Health Organisation/International Programme on Chemical Safety working definition (WHO/IPCS, 2002). This may trigger its consideration as a possible substance of very high concern (SVHC) under REACH Article 57(f) along with further subsequent regulatory risk management activity.

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Considerations on the test method and testing strategy

The test is required to be conducted on the registered substance according to either OECD Test Guideline 231 (Amphibian Metamorphosis Assay) or OECD Test Guideline 241 (Larval Amphibian Growth and Development Assay). It should investigate potential endocrine-mediated effects resulting from exposure to the test substance according to recommendations in the test guideline. The test should identify whether the registered substance can interfere with the normal function of the HPT axis during the metamorphosis of amphibian tadpoles or on their growth and development, normally from the species *Xenopus laevis*. The study should be conducted up to the limit of solubility of the registered substance in the test medium and close attention should be paid to the analysis and presentation of actual measured concentrations of the substance. Reference should be made to OECD Guidance document (No. 23) on aquatic toxicity testing of difficult substances and mixtures. Based on pre- or range-finding tests, it may be possible to conduct this as a limit test, but if any potential ED-related effects are seen, then it would be desirable to determine a no observed effect concentration (NOEC) value for these effects.

The full study report should be submitted to allow consideration of the raw data and their statistical analysis. If it is first decided to conduct a screening study at Level 3 in the OECD CF, i.e. an Amphibian Metamorphosis Assay (AMA), OECD TG 231, then, depending on the results from this and other studies requested in this decision, further testing according to Level 4 in the OECD CF may be required at a later stage (i.e. the Larval Amphibian Growth and Development Assay (LAGDA), OECD TG 241). Alternatively the LAGDA test may be conducted in the first instance.

Consideration of alternative approaches

No other approaches have been presented in the registration dossier regarding effects of OMC on the HPT endocrine axis of fish or amphibians, but ECHA has assessed whether alternative approaches could be used to address the concern expressed in this Decision. ECHA considers that there are sufficient reliable *in vitro* and *in vivo* mammalian data already at Levels 2 and 3 in the OECD CF to indicate a plausible endocrine mode of action of OMC on thyroid hormones or pathways. Therefore non-mammalian *in vitro* testing just focussed on determining this mode of action is not justified as the concern would remain.

It may also be possible for the test to be conducted on the structural analogue substance, isopentyl p-methoxycinnamate (IPMC) (CAS no. 71617-10-2), for which Substance Evaluation on similar issues has also been undertaken. However, a scientifically reasoned case justifying read-across of results from a study on IPMC to the registered substance would be necessary (according to ECHA's Read Across Assessment Framework, 2015 or later version). This would need to present evidence to allow conclusions to be drawn about relative potencies and bioavailability of the two substances in aquatic test systems.

Consideration of your comments on the draft decision and PfAs

In your comments you agreed to perform the AMA test and made several suggestions for the test design. Firstly you suggested to determine the water solubility of the substance under relevant test conditions. ECHA agrees that this would be useful to ensure the study can be performed at or up to the limit of solubility. ECHA highlights that the measurements should be made without the addition of test organisms.

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You also proposed to conduct the study as a limit test at the limit of water solubility under relevant test conditions. If adverse effects occur, you would then conduct a full study. The option for this test design was already offered in the draft decision and it is in principle reasonable and in the interests of animal welfare. If you do use this approach you will need to ensure that there are no statistically significant effects to allow a conclusion of "no effects" from the limit test, and provide justification for the statistical approach used. You will also need to ensure that the test is not performed at concentrations causing lethality.

You noted that the test is designed to provide a NOEC, rather than ECx, and the Decision has been amended accordingly.

Finally, you suggested sharing the draft study protocol and relevant pre-test results with the evaluating MSCA for approval of the protocol. The evaluating MSCA is ready to comment on the draft study protocol, although it will not be in a position to provide "approval" as the final responsibility for the test and assessment lies with you as the Registrants.

Two Member State Competent Authorities (MSCAs) made proposals for amendment (PfAs) on this request, and in response this Decision has been amended to offer a choice of whether you conduct either the AMA (OECD TG 231) or LAGDA (OECD TG 241) test. However, your suggestions for designing and conducting the test can equally be applied whichever test guideline is chosen.

In your subsequent comments on the PfAs made by MSCAs, you disagreed with the suggestion from one MSCA that 'there is a high likeliness for adverse effects in amphibians' so requiring the performance of a LAGDA instead of an AMA test. You have indicated that you still consider it appropriate to first conduct the AMA test along with some initial screening and range-finding studies to determine any acute toxicological threshold. If there was a postive outcome in the AMA test it is likely that you would, in any case, need to further address this concern using a LAGDA study.

Additionally one MSCA proposed revisions to the text relating to the summary of the mammalian data used to justify this request. Taking your comments on this PfA into account, the suggested text on the uncertainties in the current mammalian database has been revised.

In the draft decision sent to MSCAs for commenting a single deadline of 33 months was given for the submission of all 5 information requirements. A PfA suggested splitting the deadline, giving 18 months to complete this study and the Fish Sexual Development Test (FSDT) OECD 234; the remaining tests (requests 3, 4 and 5), if needed, should be submitted by the later deadline (33 months). In your comments on the draft decision you did not question the original deadline of 33 months, but in your comments on the PfA you indicated that 18 months for the endocrine disruption testing would be insufficient and requested an additional 6 months on both deadlines. Specifically you cited the need for extensive preliminary testing due to the poor water solubility and high log Kow of the substance, together with your proposal for a non-GLP Fish Early Life Stage test (FELS OECD 210 limit test) and acute amphibian testing for range-finding purposes. While ECHA considers the original test time scale would allow for preliminary testing, the need for the FELS could result in more time being required than normal for the FSDT. Therefore the test deadlines were increased by 6 months as specified in the Decision.

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Conclusion

Therefore, based on the substance evaluation and in accordance with Article 46(1) of the REACH Regulation, ECHA concludes that you are required to carry out the following study using the registered substance subject to this Decision:

A study conducted according to either an Amphibian Metamorphosis Assay, OECD Test Guideline 231, **or** a Larval Amphibian Growth and Development Assay, OECD Test Guideline 241.

2. Fish Sexual Development Test OECD 234

The concern(s) identified

The concern is related to the potential for environmental endocrine disruption in non-mammalian (fish) species. The endocrine activity of the substance in fish should be clarified in order to determine whether it poses a hazard and/or risk to the environment.

Why new information is needed

Information is available from *in vitro* and *in vivo* studies on mammalian and non-mammalian species which is sufficient to show that the registered substance could interact with the hypothalamic-pituitary-gonadal (HPG) axis of the endocrine system in mammals and fish. This includes studies on fish at Level 3 in the OECD CF for Testing and Assessment of Endocrine Disrupters (OECD, 2012) in particular studies by Christen *et al.* (2011), Inui *et al.* (2003) and Zucchi (2011). In the study by Christen *et al.* (2011), adult male and female fathead minnow (*Pimephales promelas*) were exposed to mean measured concentrations of 5.4, 37.5, 245 and 394 µg OMC/L for 14 days. There was statistically significant down-regulation of the oestrogen receptor gene (ERα) at 394 µg/L OMC, the androgen receptor (AR) at 37.5, 244.5 and 394 µg/L OMC and 3β-hydroxysteroiddehydrogenase (3β-HSD) at 244.5 and 394 µg/L OMC in the liver of female fish (all by more than 1.5x compared with controls). This indicated potential anti-oestrogenic and anti-androgenic activity following exposure to OMC. Activity of 3β-HSD was also down-regulated in the liver of male fish, indicating some oestrogenic activity. Changes in gene expression were organ specific as there was no significant effect on ERα, AR or 3β-HSD in the brain or ovary of female fish and there was no effect of ERα or AR in male fish (any organ). Plasma vitellogenin (VTG) levels were significantly increased in male fish exposed at 244.5 µg OMC/L but this was not dose-dependent as no significant effects were seen at the highest test concentration. There was no significant effect of OMC on gonadosomatic index (GSI) or on the number or score of nuptial tubercles, but there were significant effects reported on the histology of male and female fish gonads at the highest test concentration of 394 µg/L OMC, these effects were interpreted by the authors as consistent with an oestrogenic or anti-androgenic effect.

In the study by Inui *et al.* (2003), the potential oestrogenic effects of OMC on adult male Japanese Medaka (*Oryzias latipes*) were investigated. The fish were exposed to nominal concentrations of 0.034, 0.34, 3.4 and 34 mM OMC for seven days, but maintenance of these concentrations was not analytically verified. There were indications that plasma VTG levels were slightly elevated in a dose-dependent manner, but no level of statistical significance was given. There were, however, significant effects reported in a dose-dependent manner at all concentrations on mRNA expression of oestrogen mediated genes for VTG and also in choriogenin (CHG) proteins and for the oestrogen receptor (ERα). These effects could be consistent with positive autoregulation of this receptor following exposure to oestrogenic compounds.

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In the study by Zucchi *et al.* (2011), adult male zebrafish (*Danio rerio*) were exposed to median measured concentrations of 2.2 and 840 µg/L OMC for 14 days. OMC caused slight but statistically significant up- and down-regulation of key genes associated with hormonal pathways with some evidence for oestrogenic activity (ERα in the whole body; ERβ in the whole body and liver; VTG-1 in the liver) and anti-androgenic activity in the liver and whole body of fish. Conversely, there was down-regulation of VTG-1 in all other tissues except the liver. The authors concluded that OMC weakly affects genes involved in hormone pathways, but they also reflected that it is difficult to link the results of this study to a specific mode of action. OMC may act through several mechanisms/modes of action involved in the sex hormonal pathways, and this may explain the varied changes in gene expression observed. However, owing to the varied and inconsistent gene expression levels found in the whole body and specific tissue analysis, the results of this study are not conclusive in determining a potential for apical, population-relevant endocrine disrupting (ED) effects in fish.

Considered altogether, the above information points towards alterations in gene expression of various (anti-) oestrogenic and androgenic pathways and in VTG levels in fish consistent with some evidence of endocrine activity. This is sufficient to lead to a concern. However, the information is also inconclusive due to inconsistencies in whether effects were up- or down-regulated, whether they were all statistically significant and uncertainties over the exposure concentrations in the studies. All were non-standard guideline, public domain studies and many effects were observed above the reported limit of solubility of the registered substance (0.22-0.75 mg/L). Not all of the data were supported by clear and direct measurement of relevant physiological endpoints. A further reliable (Klimisch 2) Level 3 study on fish by Kunz *et al.* (2006) did not show in any VTG induction in fathead minnow following a 14-day exposure to OMC.

Although the precise mode of action is unclear, it can be concluded from the *in vitro* and *in vivo* studies that OMC can perturb the rat HPG axis. The substance may affect several mechanisms/modes of action involved in the sex hormonal pathways, examples of mechanistic/mode of action observations are decreased GnRH release *ex vivo* and increased luteinising hormone (LH) levels *in vivo*, decreased sex hormone levels *in vivo*, estrogenic activity *in vivo* and progesterone receptor antagonism *in vitro*. A decrease in sperm counts was observed in two *in vivo* rodent studies and a decrease in relative prostate weights was observed by Axelstad *et al.* (2011). However, no clear adverse effects were observed on sexual function and fertility, and development in standard studies in experimental animals (OECD CF 4/5).

Establishing a link between these changes and one specific endocrine mode of action is challenging since OMC may act through several modes of action at the same time. The uncertainty about which mode of action to investigate and the lack of effects in standard fertility and developmental toxicity studies makes further investigations for sex hormone disruption in mammals difficult to justify.

For fish, no relevant data are available from standard *in vivo* studies falling in OECD CF Levels 4 or 5 which would provide adequate information on apical effects in fish, such as fecundity, reproduction and development - alongside mechanistic effects to confirm cause and effect. In order to clarify the relevance of the reported interactions with the HPG axis in fish, a Level 4 Fish Sexual Development Study (FSDT) according to OECD TG 234 is therefore required to confirm these observations from the public domain data and determine whether such interactions could lead to actual adverse effects on fish (sub)populations at relevant environmental concentrations. It is possible that the requested fish study will provide additional information which can be used in conjunction

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with the current database and any new scientific or test method developments to evaluate whether additional testing may be necessary.

What is the possible regulatory outcome

Possible regulatory outcomes are that further information may be required to address the potential environmental hazard or risk, or that the registered substance may, or may not, be considered to be an environmental endocrine disruptor according to the current World Health Organisation/International Programme on Chemical Safety working definition (WHO/IPCS, 2002). This may trigger its consideration as a possible SVHC under REACH Article 57(f) along with further subsequent regulatory risk management activity.

Considerations on the test method and testing strategy

The test is required to be conducted according to OECD Test Guideline 234 (Fish Sexual Development Test). It should investigate potential endocrine-mediated (anti-) oestrogenic or androgenic effects resulting from exposure to the test substance according to recommendations in the test guideline. These effects should include (but not necessarily be restricted to) investigation of blood VTG levels, sex ratio, gonad histopathology (according to OECD Guidance document No. 123), including genetic sex determination. Because of the possibility for genetic sex determination, it may be preferable to conduct the study on Japanese medaka (*Oryzias latipes*), however the test guideline is also validated for Zebrafish (*Danio rerio*) and this species could be used instead since there are currently no clear indications of significant differences in species sensitivity. Histopathological examination of both liver and kidney should also be performed. The study should be conducted up to the limit of solubility of the registered substance in the test medium and close attention should be paid to the analysis and presentation of actual measured concentrations of the substance. Reference is made to OECD Guidance document (No. 23) on aquatic toxicity testing of difficult substances and mixtures. Based on pre- or range-finding tests, it may be possible to conduct this as a limit test, but if any potential ED-related effects are seen, then it would be desirable to determine a NOEC and/or EC_{10} value for these effects. If the full test is required, it should be performed using five test concentrations together with controls.

The full study report should be submitted to allow consideration of the raw data and their statistical analysis. Depending on the results of this and other studies requested in this Decision, further testing according to Level 5 in the OECD CF may be required (e.g. a Medaka Extended One Generation Reproduction Test (to OECD TG 240) or Full Fish Life-Cycle Test).

Consideration of alternative approaches

No other approaches have been presented in the registration dossier regarding effects of OMC on the fish HPG endocrine axis, but ECHA has assessed whether alternative approaches could be used to address the concern expressed in this Decision.

One approach would be to undertake testing first using a Level 3, 21-day Fish Screening Assay (to OECD TG 230) or a Fish Short Term Reproduction Assay (to OECD TG 229). However, if positive endocrine disruption results were seen in this alternative test, then the Fish Sexual Development Test would still be required and this would not be in the interests of animal welfare. A further Level 3 test would not investigate the range of mechanistic and apical endpoints of a Level 4 test, nor show how these are linked. ECHA also determines that there are sufficient reliable *in vitro* and *in vivo* mammalian and

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non-mammalian data already at Levels 2 and 3 in the OECD CF to indicate a plausible mechanistic endocrine mode of action of OMC on oestrogenic or androgenic hormones or pathways. Therefore further testing at these lower Levels is not justified as the concern would remain.

It may be possible for the test to be conducted on the structurally similar substance, isopentyl p-methoxycinnamate (IPMC) (CAS no. 71617-10-2), for which Substance Evaluation on similar issues has also been undertaken. However, a scientifically reasoned case justifying read-across of results from a study on IPMC to the registered substance would be necessary (according to ECHA's Read Across Assessment Framework, 2015 or later version). This would need to present evidence to allow conclusions to be drawn about relative potencies and bioavailability of the two substances in aquatic test systems.

ECHA has also considered whether to request the two ED tests in this decision in parallel or sequentially. Two different modes of action are investigated, and for any required risk management, this would need to be specifically protective of the adverse effects resulting from each mode of action. This means the outcome of both tests will be required as the sensitivity of each mode of action needs to be understood. If only one test was conducted, even if this indicated the substance was an SVHC, it would not be known if the second test indicated greater sensitivity (and hence require more stringent risk management). Therefore as both tests are required, there is no reason to request these sequentially.

Consideration of your comments on the draft decision and PfAs

In your comments you agreed to perform the FSDT test, and made several suggestions for the test design. Firstly you suggested to determine the water solubility of the substance under relevant test conditions. ECHA agrees that this would be useful to ensure the study can be performed at or up to the limit of solubility. ECHA highlights that the measurements should be made without the addition of test organisms.

You proposed to conduct a non-GLP OECD TG 210 Fish Early Life Stage (FELS) study at the limit of water solubility under relevant test conditions as a pre-test to evaluate chronic toxicity endpoints. Depending on the results, the FSDT test would be carried out either as a limit test or as a full test with at least five test concentrations and an appropriate control group. ECHA agrees that in the absence of chronic fish data for OMC, performing the non-GLP FELS test as proposed is a reasonable approach. The possibility of a limit test FSDT was already offered in the draft decision, and it is in principle reasonable and in the interests of animal welfare. If you do use this approach you will need to ensure that there are no statistically significant effects to allow a conclusion of "no effects" from the limit test, and provide justification for the statistical approach used. ECHA agrees that if the full test is performed this should be using at least five test concentrations and an appropriate control group.

You stated that the diagnosis of endocrine-related histopathology will be done according to the corresponding OECD guidance document. ECHA confirms this should be OECD GD 123, and the reference has been added to the test specification above.

You suggested to additionally include histopathological examination of both liver and kidney, highlighting that this will aid interpretation of general toxicity when assessing ED-related endpoints. ECHA agrees that this is a useful additional analysis, and have added this to the test specification above.

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You suggested (also in your subsequent comments on the PfAs) that the test is designed to provide a NOEC, rather than ECx.

While the decision was initially amended to reflect this comment, in a PfA made by a MSCA, it was highlighted that the OECD 234 test guideline can also be used to determine an ECx in relation to certain endpoints (e.g. for VTG measurements). Therefore, the decision has not been amended. The most appropriate response variables (ECx and/or NOEC) to include in the final study report are ultimately for you and for the conducting laboratory to determine.

Finally, you suggested sharing the draft study protocol and relevant pre-test results with the evaluating MSCA for approval of the protocol. The evaluating MSCA is ready to comment on the draft study protocol, although it will not be in a position to provide "approval" as the final responsibility for the test and assessment lies with you as the Registrants.

Three MSCAs made PfAs that the species to be used in the test should include Zebrafish as well as Japanese medaka. These PfAs cited a lack of current evidence that Zebrafish (despite the lack of a single genetic sex marker) are less sensitive than Japanese medaka, as well as the possibility for you to consider contract laboratory experience with the different species. Consequently the decision was amended to offer the option of either Japanese medaka or Zebrafish. In your subsequent comments, you agreed with these PfAs.

Additionally one MSCA proposed revisions to the text relating to the summary of the mammalian data used to justify this request. Taking your comments on this PfA into account the suggested text on the uncertainties in the current mammalian database has been revised.

Conclusion

Therefore, based on the substance evaluation and in accordance with Article 46(1) of the REACH Regulation, ECHA concludes that you are required to carry out the following study using the registered substance subject to this Decision:

A Fish Sexual Development Test using either Japanese medaka (*Oryzias latipes*) or Zebrafish (*Danio rerio*) according to OECD Test Guideline 234.

3. **Long-term toxicity testing on aquatic invertebrates (test method: Daphnia magna reproduction test, EU C.20./OECD 211)**

4. **Growth inhibition study aquatic plants (test method: Alga, growth inhibition test, EU C.3./OECD 201** or **Lemna Growth Inhibition Test, OECD 221)**

The concern(s) identified

ECHA is concerned that OMC may pose a risk to the environment, but there are insufficient data available to allow a reliable conclusion to be drawn. Studies available in the open literature suggest that, contrary to the ecotoxicity data in your registration dossiers, acute aquatic toxicity might occur at concentrations below 1 mg/L. A tentative predicted no effect concentration (PNEC) derived from these data and combined with the estimated local predicted environmental concentration (PEC) in your registration dossiers

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([redacted]), indicates that the aquatic risk characterisation ratio (RCR) would exceed one.

OMC is supplied at high tonnage between 1000 and 10000 tonnes/year with all professional and consumer applications stated to be wide dispersive use in the chemical safety reports (CSRs). It is also used in consumer products that are either "down-the-drain" applications or result in direct environmental exposure. It is therefore very important to clarify any environmental risk that OMC might pose, and ensure any risk management is adequate.

Why new information is needed

ECHA does not consider that it is possible to draw conclusions about the acute aquatic toxicity of OMC using any of the ecotoxicity data in the registration dossiers. There are also no chronic/long-term aquatic toxicity data provided in your registration dossiers, and instead the endpoints are waived.

ECHA's considerations of the available aquatic data are provided below.

The key fish acute toxicity study detailed in the registration dossiers is a 96-h test performed using static conditions. The measured initial concentrations suggest saturation was achieved at the highest treatment (measured concentration = 0.71 mg/L). No effects were observed at this treatment level, but the analysis shows that the measured concentration declined significantly during the test (concentration at 96-h = 0.075 mg/L). It therefore cannot be concluded that no adverse effects occur in fish up to the saturation limit. A second supporting 96-h acute fish test was also conducted using static conditions. Nominal concentrations of up to 1422 mg/L were used with solutions indicated to be "turbid" in the robust study summary. Effects were seen at the two highest test concentrations although as both the NOEC and LC50 significantly exceed the reported water solubility value of OMC, ECHA concludes it is not possible to determine whether these effects indicate intrinsic toxicity or physical effects.

There is one invertebrate acute toxicity test in the registration dossiers, which is a static 48-h *Daphnia magna* study. Chemical analysis shows that the initial concentration of the highest treatment was 0.035 mg/L, which subsequently declined to 0.019 mg/L at 48-h. Although no significant effects were observed at any concentration, the organisms were not exposed to concentrations up to the water solubility limit of the substance (i.e. 0.22 – 0.77 mg/L). Therefore, similar to the key fish acute test, it is not known whether adverse effects could occur at concentrations between the maximum achieved in the test and the water solubility limit.

ECHA has found two further acute *Daphnia magna* studies in the scientific literature (Sieratowicz *et al.*, 2011 and Fent *et al.*, 2010), which were both 48-h static tests. Results are based on nominal concentrations as no analysis was performed. The 48-h EC50 values were 0.57 mg/L and 0.29 mg/L, respectively. In the absence of chemical analysis, and given the difficulties in maintaining concentrations in the tests summarised in the registration dossier, ECHA considers that the actual exposure concentrations were uncertain. However, as effects were observed at (nominal) concentrations close to the saturation limit, these data justify a requirement for further information about acute toxicity of OMC to invertebrates.

Two 21-d *Daphnia magna* tests using semi-static conditions have been published in the scientific literature by Sieratowicz *et al.* (2011) and Fent *et al.* (2010). Neither is

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included in the registration dossiers, but both have been reviewed by ECHA. They have procedural deficiencies, in particular, neither is performed using concentrations up to the water solubility of the substance. Chemical analysis to measure test concentrations was only performed by Sieratowicz *et al.* (2011), and this indicated very significant reductions in test substance concentration during the renewal period. This means the actual exposure is uncertain and would be even further from the limit of saturation than the nominal concentrations suggest. Each paper also included an acute toxicity study (see above). Mortality was observed in both, with 48-h EC50 values below 1 mg/L (nominal concentrations). This suggests that chronic effects cannot be excluded below the water solubility value.

The key algal growth inhibition study in the registration dossiers was performed with nominal concentrations that exceeded the reported water solubility limit. As a result the initial measured concentrations also exceeded the water solubility limit (apart from one treatment). The test was performed for 96 h with the vessels kept in the dark for the first 24 h, before exposure to standard OECD TG 201 lighting conditions for the remaining 72-h period. A significant decline in test substance concentration was seen for all treatments during the first 24-h period in the dark. This meant that the effective initial concentration for the main 72-h period of the test was well below the limit of water solubility. Limited inhibition was observed in the test, so similar to the key fish acute toxicity test, it is not known whether adverse effects sufficient to produce an ErC50 could have occurred at concentrations between the maximum achieved in this test and the water solubility limit. While ECHA appreciates that by its nature the algal study is performed using static conditions, the additional 24-h period in the dark at the start of the test has contributed to the difficulty in performing the test with a degradable and adsorptive substance. A supporting 72-h algal growth inhibition study provided in the registration dossiers was performed without chemical analysis of test concentrations, so the measured exposure concentrations are unknown. Slight inhibition was observed at the highest test concentration (nominally 100 mg/L), but there was no assessment of whether this was statistically significant.

ECHA has found three further relevant studies in the scientific literature: Sieratowicz *et al.* (2011), Rodil *et al.* (2009) and Paredes *et al.* (2014). These were 72-h or 77-h non-GLP studies without chemical analysis. The tests indicate variable results: effects were observed in all three studies at nominal concentrations below the water solubility limit of OMC. In the absence of chemical analysis, and given the significant decline in concentrations in the key algal test in the registration dossier, ECHA considers that the exposure concentrations in these tests was uncertain. However, as more severe effects were observed in contrast to the key study in the registration dossier, and at (nominal) concentrations closer to the saturation limit, these data justify a requirement for further information on the toxicity of OMC to aquatic algae/plants.

Further ecotoxicity data in the literature, and not currently included in your registration dossiers, suggest that acute effects may occur in other taxa. For example Parades *et al.* (2014) found EC50 values of 0.075 mg/L, 0.199 mg/L and 0.284 mg/L for *Isochrysis galbana* (marine microalgae 72-h test), *Siriella armata* (mysid crustacean 96-h test) and *Paracentrotus lividus* (sea urchin 48-h test) respectively. ECHA is uncertain whether these data are of sufficient quality to use for a definitive PNEC, for example they lack measured substance concentrations. However, using an assessment factor of 1000, a tentative aquatic PNEC would be 0.000075 mg/L. The two PECs derived by [redacted] were 0.001 mg/L and 0.025 mg/L (indoor and outdoor use), which means risks (RCR > 1) would result from both PECs using this PNEC.

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Overall ECHA does not consider that an aquatic PNEC can be derived with confidence using the current data, but there are concerns that the value of the PNEC may be much lower than you currently estimate. Therefore as a starting point, ECHA requires you to provide new ecotoxicity data: a 21-d *Daphnia magna* reproduction toxicity study and an algal growth inhibition study. Together these will provide reliable aquatic ecotoxicity information for these two endpoints, and the results can be used to determine an aquatic PNEC (together with information for fish toxicity requested in this decision).

What is the possible regulatory outcome?

These data will be used together with the requested environmental exposure assessment to confirm whether there are environmental risks. If there are, these will need to be addressed through additional data gathering, involving either ecotoxicity or exposure assessment, as part of a follow-up decision. If it is not possible to refine the risk assessment with further data, risk management will be needed, for example by limiting the amounts of substance that can be used in final products.

As indicated above, ECHA has concerns that several other taxa may be sensitive to the substance, for example from studies published in the scientific literature such as Kaiser *et al.* (2012) and Paredes *et al.* (2014). A further assessment of the other ecotoxicological data will be made in light of the results of the requested studies above and environmental exposure assessment, to determine whether there is a sufficient concern to request additional testing to repeat these studies (for example to obtain results with measured concentrations). This includes molluscs and marine invertebrates.

There are also no terrestrial ecotoxicity data and limited benthic organism toxicity data available for OMC. Again the need for further testing will depend on the outcome of the requested studies above and of the environmental exposure assessment.

Considerations on the test method and testing strategy

ECHA notes the difficulties in maintaining the concentration of the test substance, particularly in the available algal study included in the registration dossiers. This may be due (at least in part) to the methodology used for that test. However, if you find that concentration maintenance in the study is not feasible, you may alternatively choose to perform a 7-d Lemna growth inhibition test (OECD TG 221), since this can also be performed using semi-static or flow-through conditions.

Prior to conducting either test you should refer to the OECD Difficult Substances guidance (OECD Guidance Document 23), paying particular attention to advice for substances which degrade in the test system or are adsorptive.

The maximum test concentrations shall be equivalent to the measured water solubility value of the substance, unless you can show that the solubility in the test medium is lower (in which case the maximum concentration shall be the limit of solubility in the test medium). Efforts shall be made to maintain test concentrations as close to the nominals as far as technically feasible throughout the experiment. You must justify the exposure conditions used to achieve this, for example flow-through or semi-static.

Consideration of alternative approaches

ECHA has considered several alternatives to the requests in the Decision. One is to try to replicate the original test solution preparation (registration and literature data), and

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perform chemical analysis on these. However, there is considerable uncertainty for whether such an exact replication is possible given the different possibilities for losses to occur, and the documentation available. In any case one of the studies may be confounded by solvent effects. Therefore this alternative is not considered addressing the concern.

A second option could be to conduct an acute rather than chronic *Daphnia magna* study. Due to the low water solubility and high adsorption potential, ECHA considers a chronic study to be more appropriate, as potentially the substance may not be sufficiently bioavailable to exhibit toxic effects in the short time period of an acute test. Effects were also observed in the chronic study performed by Sieratowicz *et al.* (2011). Therefore, if there were no effects in a new acute study, this would not provide adequate confidence that there would be no effects in a new chronic study.

A third alternative is a repeat of the water solubility test to check the ecotoxicity results are being compared against the correct value. Two GLP tests are detailed in the registration dossiers. The key study is a shake flask test giving a result of 0.22-0.75 mg/L. A supporting study using column elution gives a result of 0.041 mg/L. You prefer the shake flask result as it is a more recent study. ECHA agrees that the shake flask result should be used, but this is because the column elution method is not applicable for liquids. Therefore, ECHA is satisfied with the current water solubility data.

A final option could be to take a worst case value for the PNEC based on the available data from the scientific literature. However, the uncertainty in the exposure concentrations make it impossible to determine a PNEC value with any confidence.

ECHA has also considered whether read-across from the structurally similar substance, IPMC (isopentyl p-methoxycinnamate, EC no. 275-702-5) is possible. However, on review ECHA is unconvinced about the suitability of read-across due to the current log Kow values being different by around an order of magnitude of 1.3. Despite this, it does seem reasonable to consider the two substances as a category due to their overall structural similarity, and therefore likely having a trend in environmental hazard properties. As IPMC is toxic to aquatic organisms, there is a possibility that OMC is also acutely toxic within its water solubility limit despite having a higher log Kow and lower water solubility, although this cannot be determined using the current data set. Overall in the absence of any reliable ecotoxicity data for OMC, it is not possible to use a category approach at present. If there are new data addressing the cited issues, the situation may change.

ECHA also considers there is a need for fish toxicity data to address the concern. However, as endocrine testing using fish is already requested in this decision, ECHA proposes to await those results as they may also address the chronic fish toxicity endpoint. This is in the interests of proportionality as well as minimising the number of vertebrates used in testing.

If, the apical NOEC from either test requirement (1) or (2) occurs at measured concentrations at or above 1 mg/l, or the water solubility of the substance, whichever is lower (this is the threshold for hazard classification for chronic toxicity towards aquatic life), you are required to provide the *Daphnia* and algae tests (3 and 4).

ECHA notes that if requirements (3) and (4) are not triggered in this decision, this does not preclude the tests being requested at a later stage on the basis of new information.

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Consideration of registrants' comments on the draft decision

In your comments you agreed to perform both tests. ECHA confirms that you can do this voluntarily. For the algae test, you indicated that you would choose to perform the 7-d Lemna Growth Inhibition Test according to OECD TG 221 due to the expectation of significant substance concentration decline under the static conditions of an algal study. This option was already offered in the draft decision, but Decision has been clarified in this regard.

You made two further suggestions for the test specification. Firstly, you suggested to determine the water solubility of the substance in both Daphnia and Lemna test media. In more general comments, you also suggested to determine the water solubility of the substance in pure water. ECHA agrees that these data will be useful to ensure the studies can be performed at or up to the limit of solubility under relevant conditions. ECHA highlights that the measurements should be made without the addition of test organisms.

Secondly, you suggested sharing the draft study protocol and relevant pre-test results with the evaluating MSCA for approval of the protocol. The evaluating MSCA is in principle ready to comment on the draft study protocol, although given the test is a standard REACH requirement and well established, it is not fully clear why this is necessary for these two tests. As above, please note that the evaluating MSCA will not be in a position to provide "approval" as final responsibility for the test and assessment lies with you as the Registrants.

Conclusion

Therefore, based on the substance evaluation and in accordance with Article 46(1) of the REACH Regulation, ECHA concludes that you are required to carry out one of the following studies using the registered substance subject to this decision:

- Long-term toxicity testing on aquatic invertebrates (test method: Daphnia magna reproduction test, EU C.20./OECD 211); or
- Growth inhibition study aquatic plants (test method: Alga, growth inhibition test, EU C.3./OECD 201 or Lemna Growth Inhibition Test, OECD 221).

5. Environmental exposure assessment

The concern(s) identified

ECHA is concerned that OMC may pose a risk to the environment, but there are insufficient data available to allow a reliable conclusion to be drawn. Studies available in the open literature suggest that, contrary to the ecotoxicity data in your registration dossiers, acute aquatic toxicity might occur at concentrations below 1 mg/L. As described above, a tentative PNEC derived from these data and combined with the estimated local PEC in your registration dossiers ([redacted]), indicates that the aquatic RCR would exceed one.

OMC is supplied at high tonnage between 1000 and 10000 tonnes/year with all professional and consumer applications stated to be wide dispersive use in the CSRs. It

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is also used in consumer products that are either "down-the-drain" applications or result in direct environmental exposure. It is therefore very important to clarify any environmental risk that OMC might pose.

A second concern relates to whether OMC is an environmental ED substance as described above. If the substance is determined to meet the REACH Article 57(f) criteria (equivalent level of concern) a decision will be needed on the most appropriate risk management measure. In making this decision, it is important for ECHA to understand the use patterns and be certain about the environmental exposure. This is required to ensure the effectiveness of any risk management measure proposed.

Why new information is needed

There is no environmental exposure assessment in your CSRs, and the only sources of information are two references in the dossiers ([redacted]). ECHA considers these do not provide sufficient information to assess environmental exposure resulting from the supply and use of OMC.

[redacted] collated two sets of data, one from a monitoring study of OMC at three sites in Switzerland, which was used to build a model to predict concentrations for large Swiss lake and a small Dutch recreational pond. The second was monitoring and modelling of concentrations in an English river catchment (monitoring of influent and effluent at two wastewater treatment plants (WWTPs) together with a prediction of the River Aire catchment concentration using the GREAT-ER model). ECHA considers that neither provide data that is sufficiently representative to provide a value that is reliable for use as either a regional or local PEC. This is because of the extremely limited number and geographical spread of sampling sites, and the very limited sampling performed at those sites. The information is also more than fifteen years old so there is no information about environmental concentrations relevant to current supply volumes.

[redacted] provides estimated concentrations for indoor and outdoor release of OMC as 0.001 and 0.025 mg/L in surface water. The PECs are indicated to have been calculated using the Cosmetics Europe specific environmental release category (spERC) for wide dispersive use of down the drain products (hair and skin care products). The spERC uses non-default emission values, but there is no justification for these refined emission parameters accompanying the spERC or in your CSR. If default values are used, these local PECs would increase (and so would any RCR values). Therefore, if the spERC is to be used, further information is needed to support its use for OMC.

Data are needed to provide information on the split in consumer use for OMC, for example sun screen applications vs. other cosmetic applications. This is important as some applications of OMC, such as sun screen, are likely to be seasonal in use, and may well also vary more latitudinally, for example within a "region".

Data are also needed to provide information on environmental exposure resulting from formulation. As well as being local emissions, these will also potentially contribute to the background (regional) concentrations, which will affect the local PECs calculated for consumer use. This means that, even if ECHA accepts the local PECs derived by [redacted], these may be underestimated as the whole lifecycle has not been assessed. Finally, there are no PECs provided for the sediment or terrestrial compartments for any part of the lifecycle.

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Overall, the available data are insufficient to allow an accurate assessment of environmental exposure to be made. ECHA considers that all these missing elements form part of a standard environmental exposure assessment. Therefore, you are required to provide an assessment according to ECHA Guidance R16 on Environmental Exposure assessment (version 3.0, February 2016).

What is the possible regulatory outcome?

These data will be used together with the requested 21-d *Daphnia magna* and aquatic algae/plant toxicity testing to confirm whether there are environmental risks. If there are, these will need to be addressed through additional data gathering, involving either ecotoxicity or exposure assessment, as part of a follow-up decision. If it is not possible to refine the risk assessment with further data, risk management will be needed, for example by limiting the amounts of substance that can be used in final products.

Secondly, the environmental exposure assessment will inform any future risk management decisions if the substance is determined to be SVHC due to ED properties. Information on the use patterns and environmental exposure at different lifecycle stages will ensure the most appropriate risk management measure is chosen.

As indicated above, ECHA has concerns that several other taxa may be sensitive to the substance, for example studies published in the scientific literature such as Kaiser *et al.* (2012) and Paredes *et al.* (2014). A further assessment of the other ecotoxicological data will be made in light of the results of the requested studies above and environmental exposure assessment, to determine whether there is a sufficient concern to request additional testing to repeat these studies (for example to obtain a results with measured concentrations). This includes molluscs and marine invertebrates.

There are also no terrestrial ecotoxicity data and limited benthic organism toxicity data available for OMC. Again the need for further testing will depend on the outcome of the requested studies above and environmental exposure assessment.

Considerations on the test method and testing strategy

In preparing the environmental exposure assessment, you shall include justification for the values used for the following:

- On-site treatment efficiency (if included) at formulation sites;
- Regional tonnage fraction and Fraction Main Local Source; and
- Emissions based on a spERC, if used. This should include, for example, a supporting background document for the spERC, or publicly available references that provide the data on which the values are based.

In preparing the environmental exposure assessment, you shall include information for the following:

- For any direct environmental emission such as sunscreen use, an explanation for what scenario is being modelled, for example a beach of 1000 people. By way of explanation, in normal modelling the private use is modelled with discharge via a WWTP. The standard WWTP receives effluent from 10000 people, and discharges to a river with a flow of 18000 m^3/day. The modelling provides a local aquatic PEC at the edge of the mixing zone of the WWTP discharge in the river. Where direct emission is modelled, it is less clear what any output represents. This is an important factor to

explain if the scenario is effectively demonstrating safe use at a coastal or lake shoreline location.

- The per cent weight/weight concentration of OMC used in consumer products (including typical mean concentrations in specific product types, if there is significant variation, and the range).

- Separate supply volumes for cosmetics with:
  - immediate emissions to water (e.g. during bathing in swimming pools, rivers, lakes or the sea)
  - delayed emissions (e.g. due to application without exposure to water, followed by showering).

The risk assessment should also include the output of any modelling programme, for example the ECETOC TRA spreadsheet, CHESAR file or EUSES file. This is needed to understand the inputs to the assessment chosen by you so that ECHA can test their sensitivity. From experience this is not possible using the standard information in the CSR template.

Consideration of alternative approaches

No alternatives are available: the request for an environmental exposure assessment is suitable and necessary to obtain information that will allow to clarify whether there is an environmental risk. More explicitly, there is no equally suitable alternative way available of obtaining this information.

This request has been tiered in a sequential order so that the hazard data are produced first. This is because of the different obligations that may or may not arise as result of the tests.

If the results of any of the ecotoxicity tests (requirements 1-4) show adverse effects that would result in environmental classification, you are required to provide the environmental exposure assessment. ECHA highlights that apical effects observed in the OECD 234 and 231/241 would be relevant for the classification if these effects occurred up to 1 mg/l or the water solubility limit (whichever is lower).

Based on the current wider literature, for example Parades *et al.* (2014), adverse effects occur at classifiable concentrations for several aquatic taxa. In correspondence between you and the evaluating MSCA, you assessed the tests performed in Kaiser *et al.* (2012) and Paredes *et al.* (2014) to be reliability 2 (except the *Potamopyrgus antipodarum* assay (which you assess to be reliability 3). As a consequence, you should update your registration dossier with summaries of these studies and assess any change in (self) classification accordingly. This may then affect your current waiver for the environmental exposure assessment. If you do decide that this assessment is required, ECHA recommends that you consider the points noted in this decision (under *Considerations on the test method and testing strategy*) when producing the assessment.

Consideration of registrants' comments on the draft decision

In your comments you acknowledge that an environmental exposure assessment might become necessary for the substance. You also indicate that together with the evaluating MSCA, you are going to work towards the development of a SpERC for the direct release of UV filters into the environment.

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ECHA notes your acknowledgement, and that the evaluating MSCA agreed to work with the registrants on the spERC development as a general initiative resulting from the industry/ECHA workshop on UV filters on 7 March 2017.

ECHA notes that OMC is on the EU Watch list under the Water Framework Directive, which requires EU Member States to monitor the substance. The results of the first year of Member State monitoring will be published by the JRC (https://ec.europa.eu/jrc/en) and may be useful for you to consider in preparing your exposure assessment. You should take account of the seasonal variation in use and types of water that were monitored when interpreting this information.

Conclusion

Therefore, based on the substance evaluation and in accordance with Article 46(1) of the REACH Regulation, ECHA concludes that you are required to provide an environmental exposure assessment for the registered substance subject to this decision.

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Appendix 2: Procedural history

On the basis of an opinion of the ECHA Member State Committee and due to initial grounds for concern relating to potential endocrine disruption, PBT concerns, wide dispersive use/consumer use/environmental use, 2-ethylhexyl trans-4-methoxycinnamate (OMC) CAS No 83834-59-7 (EC No 629-661-9) was included in the Community rolling action plan (CoRAP) for substance evaluation to be evaluated in 2016. The updated CoRAP was published on the ECHA website on 22 March 2016. The competent authority of the United Kingdom (hereafter called the evaluating MSCA) was appointed to carry out the evaluation.

In accordance with Article 45(4) of the REACH Regulation, the evaluating MSCA carried out the evaluation of the above substance based on the information in your registration(s) and other relevant and available information. An additional concern for risks in the aquatic environment was identified during the evaluation.

The evaluating MSCA considered that further information was required to clarify the abovementioned concerns. Therefore, it prepared a draft decision under Article 46(1) of the REACH Regulation to request further information. It subsequently submitted the draft decision to ECHA on 20 March 2017.

The decision making followed the procedure of Articles 50 and 52 of the REACH Regulation as described below.

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

Registrant(s)' commenting phase

ECHA received comments from you and forwarded them to the evaluating MSCA without delay.

The evaluating MSCA took the comments from you, which were sent within the commenting period, into account and they are reflected in the reasons (Appendix 1).

Proposals for amendment by other MSCAs and ECHA and referral to the Member State Committee

The evaluating MSCA notified the draft decision to the competent authorities of the other Member States and ECHA for proposal(s) for amendment.

Subsequently, the evaluating MSCA received proposal(s) for amendment to the draft decision and modified the draft decision. They are reflected in the reasons (Appendix 1).

ECHA referred the draft decision, together with your comments, to the Member State Committee.

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

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

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MSC agreement seeking stage

The Member State Committee reached a unanimous agreement on the draft decision during its MSC-58 meeting and ECHA took the decision according to Article 52(2) and 51(6) of the REACH Regulation.

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Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided by you in the registration(s) is in compliance with the REACH requirements. The decision neither prevents ECHA from initiating compliance checks on your dossier(s) at a later stage, nor does it prevent a subsequent decision under the current substance evaluation or a new substance evaluation process once the present substance evaluation has been completed.

2. Failure to comply with the request(s) in this decision, or to otherwise fulfil 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 relation to the required experimental study/ies, the sample of the substance to be used ('test material') has to 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 material to be subjected to the test(s) subject to this decision and to document the necessary information on the 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.

4. In relation to the experimental stud(y/ies) the legal text foresees the sharing of information and costs between registrant(s) (Article 53 of the REACH Regulation). You are therefore required to make every effort to reach an agreement regarding each experimental study for every endpoint as to who will carry out the study 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. 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/regulations/reach/registration/data-sharing . If ECHA is not informed of such agreement within 90 days, it will designate one of the registrants to perform the stud(y/ies) on behalf of all of them.