CLH report

Proposal for Harmonised Classification and Labelling

Based on Regulation (EC) No 1272/2008 (CLP Regulation),
Annex VI, Part 2

International Chemical Identification:

2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate

EC Number: **-**

CAS Number: **83834-59-7**

Index Number: **-**

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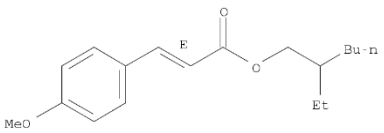
1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 1: Substance identity and information related to molecular and structural formula of the substance

Name(s) in the IUPAC nomenclature or other international chemical name(s)	2-Ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate
Other names (usual name, trade name, abbreviation)	2-ethylhexyl (2E)-3-(4-methoxyphenyl)acrylate 2-Ethylhexyl (2E)-3-(4-methoxyphenyl)prop-2-enoate 2-Ethylhexyl *trans*-4-methoxycinnamate 2-Ethylhexyl p-methoxycinnamate 2-Ethylhexyl *trans*-4-methoxycinnamate 2-Propenoic acid, 3-(4-methoxyphenyl)-, 2-ethylhexyl ester Octinoxate
ISO common name (if available and appropriate)	-
EC number (if available and appropriate)	-
EC name (if available and appropriate)	-
CAS number (if available)	83834-59-7
Other identity code (if available)	-
Molecular formula	$C_{18}H_{26}O_3$
Structural formula	
SMILES notation (if available)	CCCCC(CC)COC(=O)/C=C/C1=CC=C(C=C1)OC
Molecular weight or molecular weight range	290.397 g/mol
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	optical rotation = 0
Description of the manufacturing process and identity of the source (for UVCB substances only)	-
Degree of purity (%) (if relevant for the entry in Annex VI)	-

1.2 Composition of the substance

Table 2: Constituents (non-confidential information)

Constituent (Name and numerical identifier)	**Concentration range (% w/w minimum and maximum in multi-constituent substances)**	**Current CLH in Annex VI Table 3.1 (CLP)**	**Current self-classification and labelling (CLP)**
2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate	**≤ 100**	**-**	not classified, Aquatic Chronic 2, Eye Irrit. 2, Skin Irrit. 2, STOT SE 3

2 PROPOSED HARMONISED CLASSIFICATION AND LABELLING

2.1 Proposed harmonised classification and labelling according to the CLP criteria

Table 3: Proposed harmonised classification and labelling according to the CLP criteria

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current entry	No entry										
Dossier submitters proposal	tbd	2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate	-	83834-59-7	Aquatic Acute 1 Aquatic Chronic 1	H400 H410	GHS09 Wng	H410		M = 10 M = 10	
Resulting Annex VI entry if agreed by RAC and COM											

Table 4: Reason for not proposing harmonised classification and status under public consultation

Hazard class	Reason for no classification	Within the scope of public consultation
Explosives	hazard class not assessed in this dossier	No
Flammable gases (including chemically unstable gases)		
Oxidising gases		
Gases under pressure		
Flammable liquids		
Flammable solids		
Self-reactive substances		
Pyrophoric liquids		
Pyrophoric solids		
Self-heating substances		
Substances which in contact with water emit flammable gases		
Oxidising liquids		
Oxidising solids		
Organic peroxides		
Corrosive to metals		
Acute toxicity via oral route		
Acute toxicity via dermal route		
Acute toxicity via inhalation route		
Skin corrosion/irritation		
Serious eye damage/eye irritation		
Respiratory sensitisation		
Skin sensitisation		
Germ cell mutagenicity		
Carcinogenicity		
Reproductive toxicity		
Specific target organ toxicity-single exposure		
Specific target organ toxicity-repeated exposure		
Aspiration hazard		
Hazardous to the aquatic environment	harmonised classification proposed	Yes
Hazardous to the ozone layer	hazard class not assessed in this dossier	No

3 HISTORY OF THE PREVIOUS CLASSIFICATION AND LABELLING

There is no harmonised classification for this substance.

4 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

Reason for a need for action at Community level:

- Differences in self-classification
- Disagreement by DS with current self-classification

Current self-classifications (as of May 2023):

- Aquatic Acute 2: 62 of 188
- No classification for aquatic environment: 126 of 188

5 IDENTIFIED USES

The substance is a UV filter. It is used in the manufacture of cosmetics and personal care products. It is used "as such" in these products, e.g. as a UV filter in sun creams.

Futhermore the substance is used in perfumes and fragrances, air care products, biocides (e.g. disinfectants, pest control products), polishes and waxes, washing and cleaning products, paints and coating or adhesives and as processing aid.

6 DATA SOURCES

The primary sources of data used in this report are the available information on the website of ECHA and in the REACH registration dossier[1] as well as information from substance evaluation process.

7 PHYSICOCHEMICAL PROPERTIES

Table 5: Summary of physicochemical properties

Property	Value	Reference	Comment (e.g. measured or estimated)
Physical state at 20°C and 101,3 kPa	Liquid; pale yellow liquid	REACH registration data	Visual observation
Melting/freezing point	-68.3 °C at 101.3 kPa	REACH registration data	Measured (EU Method A.1; OECD Guideline 102)
Boiling point	382 °C at 101.3 kPa	REACH registration data	Measured (extrapolated based on vapour pressure determined by dynamic method)
Relative density	D^{20}_4 = 1.01	REACH registration data	Measured (EU Method A.; OECD Guideline 109)
Vapour pressure	0.3 hPa (at 154 °C) This is: 0.0675 Pa (at 25 °C) (not volatile)	REACH registration data	Measured (dynamic method)
Surface tension	The study does not need to be conducted because water solubility is below 1 mg/L at 20°C.	-	-
Water solubility	0.051 mg/L (at 20 °C, pH 6.7)	REACH registration data	Measured (OECD Guideline 105; column elution method) 0.046 mg/L (at 20 °C, pH 7.9) 0.048 mg/L (at 20 °C, pH 7.8)
	0.22 - 0.75 mg/L (at 21 °C) The substance is considered to be slightly soluble (0.1 – 100 mg/L)*	SEv conclusion	Measured (OECD Guideline 105; flask method)
Partition coefficient n-octanol/water	Log Pow >6 (at 23 °C)	REACH registration data	Measured (OECD Guideline 117 (Partition Coefficient (n-octanol / water), HPLC Method))

[1] https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15876 (last access: 10.01.2024)

Property	Value	Reference	Comment (e.g. measured or estimated)
Viscosity	dynamic viscosity: 99.8 mPa s (at 20 °C; 216 – 1130 s^{-1}) 31.6 mPa s (at 40 °C; 781 – 2050 s^{-1})	REACH registration data	Measured (OECD Test Guideline 114)

The information in this table marked with „REACH registration data“ is based on information taken from the REACH registration dossier and ECHA’s public registration information as accessed on 12-05-2023

*) The water solubility of OMC was investigated according to OECD Guideline 105 and was found to be 0.22 – 0.75 mg/L at 21 °C using the flask method. It is considered to be slightly soluble (0.1 – 100 mg/L). A new water solubility test was provided according to OECD TG 105. The result was 0.051 mg/L at 20 °C and pH of 6.7 using the column elution method.

8 EVALUATION OF PHYSICAL HAZARDS

Hazard class not assessed in this dossier

9 TOXICOKINETICS (ABSORPTION, METABOLISM, DISTRIBUTION AND ELIMINATION)

Hazard class not assessed in this dossier

10 EVALUATION OF HEALTH HAZARDS

Hazard class not assessed in this dossier

11 EVALUATION OF ENVIRONMENTAL HAZARDS

11.1 Rapid degradability of organic substances

Table 6: Summary of relevant information on rapid degradability

Method	Results	Remarks	Reference
SETAC. Procedures for assessing the environmental fate and ecotoxicity of pesticides Ed. M. Lynch, 1995); equivalent or similar to OECD Guideline 111	pH 4, pH 7, pH 9 20 °C, DT50 > 1 year Transformation products not fully identified	Reliability 2, GLP Since results with a flow-through test were unsatisfactory due to low recovery of radioactivity, a second closed test system was performed.	Registration dossier (Notox B.V., 2002a)
OECD Guideline 301 F	78 % O_2 consumption after 28 days	Reliability 1, GLP	Registration dossier (Givaudan-Roure SA, 1994b)
OECD Guideline 301 F	70 – 80 % O_2 consumption after 28 days	Reliability 1, GLP	Registration dossier (BASF AG, 1997)

11.1.1 Ready biodegradability

A ready biodegradability study according to OECD Guideline 301F was performed (Givaudan-Roure SA, 1994b). It used domestic, non-adapted activated sludge and was conducted using 100 mg/L of test substance and 30 mg/L (dry weight) activated sludge. Aniline was used as a reference substance, and the test temperature was 20 °C. 78 % biodegradation was observed by day 28, and the 10-day window was met (69 % biodegradation between days 6 and 16). Aniline exceeds 40 % degradation after 7 days and 65 % after 14 days.

No inhibition was indicated in the toxicity control. An abiotic sterile control was not included. Blank inoculum respiration was 24 mg O_2/L on days 6 and 33 on day 28, which is within the expected levels for the test. In conclusion, 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate is readily biodegradable.

A further study according to OECD Guideline 301F supports this conclusion (BASF AG, 1997). Domestic activated sludge (adaption not specified) was used as inoculum (30 mg/L). The initial concentration of 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate used in this study was 100 mg/L. After 28 days a biodegradation of 70-80 % was determined and the pass level was reached within the 10-day window.

11.1.2 BOD_5/COD

No data available.

11.1.3 Hydrolysis

The registration dossier contains a hydrolysis study in compliance with GLP using SETAC Procedures for assessing the environmental fate and ecotoxicity of pesticides (Notox B.V., 2002a). The test was performed with radio-labelled (phenyl ring) test substance at 20 °C for 30 days using pH 4, 7 and 9 under exclusion of light and oxygen. Since results with a flow-through test were unsatisfactory due to low recovery of radioactivity, a second closed test system was performed. The test substance concentration was 0.111 mg/L. There was variability in the concentration of2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate, the key degradant and other degradants at the different sampling points. The registrant was unable to fit kinetics to the available data and concluded that the half-life exceeds one year at all pH at 20 °C.

The registrant considered that the major metabolites most likely to be p-methoxycinnamic acid and ethylhexyl methoxycinnamate cis-isomer. This was based on co-chromatography (thin layer chromatography) using its reference substance on normal phase and reversed phase. However, identification could not be confirmed by both methods.

11.1.4 Other convincing scientific evidence

No data available.

11.1.4.1 Field investigations and monitoring data (if relevant for C&L)

No data available.

11.1.4.2 Inherent and enhanced ready biodegradability tests

No data available.

11.1.4.3 Water, water-sediment and soil degradation data (including simulation studies)

No data available.

11.1.4.4 Photochemical degradation

A study in compliance with GLP assessing the photodegradation of 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate in water is provided in the registration dossier (Notox B.V., 2002b). This was performed to an EPA test guideline[2] using radio-labelled (phenyl ring) test substance in a solution of 20 % acetonitrile and 80 % pH 7 buffer (acetonitrile was used to prevent hydrolysis). Solutions were irradiated with a xenon lamp (290-800 nm) for 23 days, which is indicated to be equivalent to 21 days sunlight (this appears to be corrected to 40 °N) and a temperature of 23.2 °C. DT50 between 5 and 9 days were determined based on

[2] EPA Guideline Subdivision N 161-2 (Photodegradation Studies in Water)

degradation from trans and cis-2-ethylhexyl 4-methoxycinnamate to transformation products. The mass balance decreased from 92 % (t=0) to 52 % (t = 23 days). The authors of the study assumed that this was due to adsorption.

11.2 Environmental fate and other relevant information

No experimental data on adsorption is available. Based on KOCWIN (version 2.01) a log Koc of 4.124 (estimate from predicted log Kow of 5.8) and a log Koc of 3.94 (MCI method) were estimated.

11.3 Bioaccumulation

Table 7: Summary of relevant information on bioaccumulation

Method	Results	Remarks	Reference
OECD Guideline 117 (HPLC method)	Log Kow > 6 (23°C)	Reliability 1, GLP	Registration dossier (Givaudan-Roure SA, 1994a)
OECD Guideline 305	BCF = 433 L/kg (at 0.07 mg/L) BCF = 175 L/kg (at 0.7 mg/L)	Reliability 3, GLP (Registrant: Reliability 1) Deviations from OECD Guidance: uptake period of 5 instead of 28 days; Test concentration much above water solubility limit	Registration dossier (Notox B.V., 2000b)

11.3.1 Estimated bioaccumulation

No data available.

11.3.2 Measured partition coefficient and bioaccumulation test data

The registrant performed a study according to OECD 117 (HPLC-method) to determine the log Kow. The log Kow for 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate was determined to be > 6 at 23 °C.

The key study in the registration dossier is a 14-day aqueous fish bioconcentration test in compliance with GLP, conducted according to OECD 305 in *Oncorhynchus mykiss* and flow-through conditions at 15 °C using radio-labelled (phenyl ring) test substance. A control and two test concentrations of 70 and 700 µg/L were used, with ethanol used at a concentration of 0.1 mL/L to help dissolve 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate. Each treatment was run as a single replicate with 40 fish per (stainless steel) vessel. Fish length and weight were measured at study initiation. No further growth measurements were made, being regarded as "irrelevant" due to the short period of the test growth according to the registration. There is no information on the lipid content of the fish. A 5-day uptake and 9-day depuration period was used. The test medium was sampled daily, including two days prior to exposure. This indicated the TWA (time weighted average), concentrations were 84±6.7 µg/L and 731±22 µg/L an exceed the water solubility limit of 50 µg/L. Fish were sampled five times during uptake, and four times during depuration. No abnormalities or mortalities were observed during the test.

BCF values were calculated at each time point and the registrant concludes that the BCF was 433 L/kg at the lower concentration at the final sampling point. At the higher test concentration, the BCF was low (64-72 L/kg) after the first day until 2.25 days. However, on the last day the concentration in the fish increased by more than a factor of two resulting in a final BCF of 175 L/kg. The DT50 (depuration) was stated to be 1.5 to 1.7 days.

Due to performance with a test concentration much above water solubility limit, the study should be considered as not valid. Hence, the study should not be used for classification purposes.

11.4 Acute aquatic hazard

Table 8: Summary of relevant information on acute aquatic toxicity

Method	Species	Results[1]	Remarks	Reference
OECD TG 203 Range-finding/ limit test	*Cyprinus carpio*	96h-LC_{50} > 100 mg/L (n) 96h- LC_{50} > 0.27 mg/L (m)	Reliability 3 (Registrant: Reliability 1) Number of fish per conc. half of those required by OECD TG	Registration dossier (Notox B.V., 2000a)
OECD TG 203	*Danio rerio*	96h-LC_{50} = 1216.1 mg/L (m)	Reliability 3 (Registrant: Reliability 1) Turbidity in all test conc.	Registration dossier (BASF AG, 1998)
OECD TG 202	*Daphnia magna*	48h-EC_{50} > 0.0271 mg/L (m)	Reliability 1	Registration dossier (BASF AG, 2003)
OECD TG 202	*Daphnia magna*	48h-EC_{50} = mg/L 0.57 (n) 48h-EC_{10} = 0.14 mg/L (n)	Reliability 2 No analytical verification of test conc.	(Sieratowicz et al., 2011)
OECD TG 202	*Daphnia magna*	48h-EC_{50} = 0.29 mg/L (n)	Reliability 2 No analytical verification of test conc.	(Fent et al., 2010)
Non-standard	*Siriella armata* Mysid crustacean	96h-EC_{50} = 0.199 mg/L (n) 96h-EC_{10} = 0.081 mg/L (n)	Reliability 2 seawater	(Paredes et al., 2014)
Non-standard	*Mytilus galloprovincialis* Mussel	48h-EC_{50} = 3.118 mg/L (n) 48h-EC_{10} = 0.431 mg/L (n)	Reliability 2 seawater	(Paredes et al., 2014)
Non-standard	*Paracentrotus lividus* Sea urchin	48h-EC_{50} = 0.284 mg/L (n) 48h-EC_{10} = 0.049 mg/L (n)	Reliability 2 seawater	(Paredes et al., 2014)
OECD TG 201	*Selenastrum capricornutum* (now: *Raphidocelis subcapitata*)	72h-ErC_{50} > 100 mg/L (n)	Reliability 3 (Registrant: Reliability 1) Test conc. much above water solubility limit	Registration dossier (Notox B.V., 2000c)
OECD TG 201	*Scenedesmus subspicatus* (now: *Desmodesmus subspicatus*)	96h-ErC_{50} > 100 mg/L (n) 5.8 % effect on growth at 100 mg/L	Reliability 3 (Registrant: Reliability 1) Test conc. much above water solubility limit	Registration dossier (BASF AG, 2001)
OECD TG 201	*Desmodesmus subspicatus*	72h-IrC_{50} > 0.25 mg/L (n) 72h-IrC_{10} = 0.07 mg/L (n)	Reliability 3 No validity information, fewer replicates used than TG, no analysis	(Sieratowicz et al., 2011)
Non-standard	*Scenedesumus vacuolatus* Uni-cellular chlorophyte	77h-EC_{50} = 0.19 mg/L (n) Decline of toxicity up to 72h	Reliability 4 Lack of information on validity criteria, pH changes	(Rodil et al., 2009)
Non-standard	*Isochrysis galbana* Marine uni-cellular microalgae	**72h-EC_{50} = 0.075 mg/L (n)**	Reliability 2 Drop in test substance concentration seawater	(Paredes et al., 2014)
OECD TG 221	*Lemna minor*	7d-EC_{50} > 0.0579 mg/L (m)	Reliability 1	Registration dossier (Fort Environmental Laboratories, 2021b)

n = nominal concentration; m = measured concentration; results in bold = relevant for classification and labelling

11.4.1 Acute (short-term) toxicity to fish

The key acute fish toxicity test in the registration dossier (Notox B.V., 2000a) is a static 96-h test performed in compliance with GLP using *Cyprinus carpio*. It is stated to be a combined range-finding/Limit test. Water accommodated fractions (WAF) were prepared at nominal loadings of 10 and 100 mg/L by stirring nominal concentrations in the dark for 48 hours. Following overnight settling the water phase was decanted for testing. The treatments of 0.1 and 10 mg/L were prepared by diluting the 10 mg/L WAF. Due to a film being observed in the 100 mg/L concentration, this was further settled for an hour and then decanted through glass wool. All final test solutions were observed to be clear and colourless. The test was performed at 20 °C, and pH was between 7.5 and 8.0. Fish loading was below 1 g fish per litre. Aeration was introduced after 72 hours of exposure. 7 fish were used for the control and 100 mg/L treatments, with 3 fish used for the 0.1, 1.0 and 10 mg/L treatments. One replicate for each treatment was used. No mortality or behavioural abnormalities were observed in the test. Analytical measurements (HLPC-UV) were made only for the 100 mg/L solution, which showed a marked concentration decline during the test: 0.71 mg/L (t=0), 0.36 mg/L (t=24 h), 0.075 mg/L (t=96 h). This results in a geometric mean measured concentration of 0.27 mg/L. While the registrant assesses the study to be Klimisch 1, the eMSCA considers it as Klimisch 3 based on the number of fish used for the concentrations of 0.1, 1 and 10 mg/L, which is half those required in the OECD TG.

A supporting 96-h OECD TG 203 study performed in compliance with GLP is provided (registration dossier (BASF AG, 1998)). *Brachydanio rerio* (now *Danio rerio*, Zebrafish) was exposed using a static system. Solutions of nominal concentrations of 0, 100, 215, 464, 1000, 2150, 4640 mg/L were prepared using an Ultra-turrax stirrer for 25 minutes prior to placing the fish in the solutions. Concentrations were chosen based on two range-finding studies. 10 fish were used per vessel, with one replicate per treatment. The robust study summary (RSS) indicates all treatments were turbid, with “fat-like” droplets visible on the surface. The level of turbidity increased with concentration to the extent that at the two highest concentrations fish had to be driven to the front of the aquaria to observe them. Analysis was performed on both unfiltered and filtered solutions. In the unfiltered solutions, concentrations were initially between 29.5 % and 59.5 % of nominal concentrations, which fell to between 1.2 and 4.4 % after 96 hours. For the filtered solutions, initial concentrations were between 0.6 and 2.0 % and dropped to between 0.0 - 1.0 % after 96 hours. All fish died at the highest concentration, and two fish died at the second highest concentration. The mean concentration (analysis at start and end of study) of the unfiltered solutions (16.8, 33.8, 101.5, 271.3, 604.5 and 1422.3 mg/L) were used to calculate the results. The NOEC was 271.3 mg/L and the LC_{50} was 1216.1 mg/L. The registrant assesses the study to be Reliability 1 for2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate, but in the view of the Dossier Submitter based on the above concerns the test is Reliability 3 as the solution preparation is considered to be unsuitable (longer pre-stir period required, turbidity observations indicate substance present in excess of the water solubility limit, it is not possible to determine if effects at the two highest test concentrations indicate intrinsic toxicity or physical effects).

11.4.2 Acute (short-term) toxicity to aquatic invertebrates

Daphnia magna (crustacean 48 h)

A 48-h study in compliance with GLP using *Daphnia magna* (BASF AG, 2003) according to OECD TG 202 was performed using static conditions. Very limited information about the test is available in the registration dossier. Nominal concentrations of 12.5, 25, 50 and 100 mg/L together with a control were prepared. 5 animals per vessel and four replicates per treatment were used and the test medium was prepared with (q.v.) *an aqueous extract of the test substance (eluate)*. To prepare the test solutions, the substance was stirred for 20 hours at 20 °C in M4 medium. Undissolved test substance was subsequently removed by centrifuging (20 minutes at 17700 G) to provide a stock solution of nominal concentration 100.2 mg/L. Further M4 medium was added to dilute the stock solution to provide the remaining treatments. Chemical analysis was performed on the control and highest concentration only, at the start and end of the test. This shows that the starting concentration for the nominal 100 mg/L treatment was 0.035 mg/L, and at 48-h was 0.0191 mg/L (mean measured: 0.0271 mg/L). The report indicates that all four test guideline validity criteria were met, and the test substance showed no inhibitory effects at any concentration (apart from one Daphnid death at 12.5 mg/L). The registrant assesses the study to by Klimisch 1. According to the updated water solubility value (0.051 mg/L) cited in the

registration dossier, the measured solubility in the study is not as far from this water solubility value as previously assumed (with the old data). Therefore, the eMSCA agrees to the rating of the study.

Sieratowicz et al. (2011) performed a non-GLP 48-h acute Daphnia study according to OECD TG 202 using a number of UV filters including Ethylhexyl methoxycinnamate (EHMC, CAS 5466-77-3). This was part of a battery of three ecotoxicity tests (also chronic Daphnia and algal inhibition studies) conducted to provide data for a risk assessment of the substances. The purity of the substance was not described. It was a static test using nominal concentrations of 0.08, 0.16, 0.31, 0.63, 1.25 and 2.5 mg/L and M4 test media. A range finding test is not mentioned. Ethanol (0.05 %) was used as a solvent, but a solvent control is not mentioned for this experiment (it was used for the other studies performed by the authors in the same paper, so this may just be an editorial omission). There were 4 replicates per treatment with 5 animals per replicate. Immobilisation was observed at 24 and 48 hours. The results are stated as 48-h EC_{50} = 0.57 mg/L and 48-h EC_{10} = 0.14 mg/L. No analysis was conducted to verify the measured concentrations, but some information can be taken from the chronic Daphnia test which was performed in the same research lab (and described below). This had significant issues for the concentration maintenance in the limited analysis performed. The results would suggest that significant test substance loss is likely to have occurred in the acute study as well, albeit the test period was half the renewal period of the chronic test. On this basis the quoted 48-h EC_{50} value may well be lower than 0.57 mg/L. As there was no analytical verification of the test concentrations and the issues for concentration maintenance revealed in the chronic Daphnia test from the same lab, the reliability of the study was rated with Klimisch 2.

Fent et al. (2010) reports the findings of an acute Daphnia study, which is a 48-h non-GLP acute Daphnia toxicity study performed in accordance with OECD TG 202 for four UV filters including the substance. No deviations from the test guideline were reported. Five concentrations between 0.1 and 1 mg/L were used. It appears to have been performed under static conditions without analysis. The 48-h EC_{50} is stated as 0.29 mg/L, and so it could have been lower. Therefore, the reliability was rated with Klimisch 2.

Siriella armata (mysid crustacean 96-h)

The test conducted by Paredes et al. (2014) evaluated the effects on four organisms, which are separately described in the following. The test was performed according to a method described in another reference (Pérez et al., 2010a), which has not been reviewed by the Dossier Submitter. Single newly released neonates were incubated in 20 mL glass vials for 96h at 20 °C using a 16/8 light/dark photo period. 20 animals were used per concentration and they were fed daily for the first half of the test. Dead neonates were counted every 24h.
Results were stated as EC_{50} = 0.199 mg/L; EC_{10} = 0.081 mg/L, NOEC = 0.063 mg/L and LOEC = 0.125 mg/L.

Table 9: Nominal and measured concentrations for the 96h-time period (*Siriella armata*, (Paredes et al., 2014))

Nominal concentration, mg/L	**Measured concentration, µg/L**	
	0 h	**96 h**
0.050	0.015	n.d.
0.200	0.027	n.d.
0.800	0.126	0.018

n.d. = not detected

The paper contains limited information about the test methods, validity criteria and controls. In addition, significant losses are suggested from the analytical work conducted in parallel to the experiment in controls without animals. This makes it very difficult to assess the concentration at which effects occurred. However, the available data do suggest that the substance affects the mysid crustacean with some indication that actual effect concentrations are even lower than suggested by the authors. As the study documentation is acceptable for assessment, the reliability was rated with Klimisch 2.

Mytilus galloprovincialis (mussel 48-h test)

Paredes et al. (2014) induced the mussels to spawn by thermal stimulation, and subsequently fertilised eggs were transferred to the experimental vials and incubated at 20 °C until the second larval stage at 48-h. 40 eggs/ml were used, but the paper does not indicate the water volume of the test vessels. Toxicity was assessed based on percentage of normal (second stage) larvae at test completion. The test was performed according to a method described in another reference (Bellas et al., 2005), which has not been reviewed by the Dossier Submitter. The test appears similar in principle to a US EPA test guideline[3] where the test commences 4-h after fertilisation and continues for 48-h. Results were stated as EC_{50} = 3.118 mg/L, EC_{10} = 0.431 mg/L, NOEC = 0.500 mg/L and LOEC = 1 mg/L. The Dossier Submitter notes that the NOEC is above the EC_{10}, although this may well be an outcome of the statistical derivation. As the study documentation is acceptable for assessment and the test procedure similar to a standard method, the reliability was rated with Klimisch 2.

Table 10: Nominal and measured concentrations for the 48h-time period (*M. galloprovincialis* and *P. lividus*, (Paredes et al., 2014))

Nominal concentration, mg/L	**Measured concentration, mg/L**	
	0 h	**48 h**
0.050	0.039	0.023
0.200	0.111	0.044
0.600	0.463	0.093

Paracentrotus lividus (sea urchin 48-h test),

The test conducted by Paredes et al. (2014) was performed according to a method described in another reference (Saco-Álvarez et al., 2010), which has not been reviewed by the Dossier Submitter. Fertilized eggs (density 40/ml) were incubated in vials at 20 °C for 48-h. At test completion these were fixed with formalin, and analysed under a microscope. Toxicity was assessed using larval growth (by subtracting the average diameter of the fertilized eggs from the maximum dimension of the first 35 larvae in each vial at 48-h. Results were stated as EC_{50} = 0.284 mg/L; EC_{10} = 0.049 mg/L, NOEC = 0.600 mg/L and LOEC = 0.800 mg/L. There was a large difference between the NOEC and EC_{10} in the sea urchin test. Apparently, effects at 600 µg/L were not significantly different from control; yet exciting > 80 % effect. This results in a NOEC that is markedly higher than the EC_{50}. The Dossier Submitter notes that the EC_{50} and EC_{10} are below the values of the NOEC and LOEC, suggesting a possible error. As the study documentation is acceptable for assessment, the reliability was rated with Klimisch 2.

All four studies had good concentration-effect curves. Here are some specific points influencing their reliability highlighted below:

- Not all nominal test concentrations are described (should have been 5 to 7 concentrations according to concentration-effect curves), only the analysed concentrations are listed in Table 1 of the publication.
- Recoveries of the substance at test start were highly variable between the different tests: 56-151 % for algae, mussel, and sea urchin; measured start concentrations were much lower for the mysid test (recovery 14-30 %). The latter test was performed under light/dark conditions. However, this would not explain the lower start concentrations. Another explanation might be that possibly the same stock solutions were used over a longer period of time and that the mysid test was performed at the end of the project.

[3] OPPTS 850.1055 Bivalve Acute Toxicity Test (Embryo-Larval), 1996.

11.4.3 Acute (short-term) toxicity to algae or other aquatic plants

A 72-h algal inhibition toxicity test was performed in compliance with GLP using *Selenastrum capricornutum*, now *Raphidocelis subcapitata* (Notox B.V., 2000c) according to OECD TG 201. The first 24-h were performed in the absence of light, and the remaining 72-h were performed in light (TLD lamp yielding 3100 – 3300 lux). Water accommodated fractions (WAF) were prepared for nominal concentrations of 10, 18, 32, 56 and 100 mg/L 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate together with a control. The test was originally a range-finding-limit test, with the range-finding using 0.1, 1, 10 and 100 mg/L WAFs. It then appears to have been extended to include loadings at 18, 32 and 56 mg/L. The study report describes the preparation of the 0.1, 1, 10 and 100 mg/L loading WAFs. The 10 and 100 mg/L loadings were prepared by 48-h stirring in a closed vessel in the dark (because of known photodegradation of the substance). After settling the aqueous phase was decanted off for the test. However, as an oily layer remained, a volumetric pipette was used to remove portions of the middle of the solution. The 0.1 and 1 mg/L WAFs were prepared by dilution of the 10 mg/L WAF. It is unclear how the concentrations at 18, 32, 56 mg/L were prepared (dilution of the 100 mg/L WAF, or preparation of individual WAFs). Final test solutions are described as clear and colourless to opalescent. According to the study report there were "3 +2" replicates of each test concentration, "6+3" replicates of treatment control with algae, one replicate of each test concentration without algae and two extra replicates of the highest concentration without algae. The pH ranged from 7.9 to 9.7, with the temperature around 23 °C. Chemical analysis was conducted at 0, 24, 48 and 96-h. At the start of the test substance concentrations exceeded the water solubility limit of 51 µg/L for all treatment levels. After 24-h in the dark, measured concentrations had fallen significantly, with further reductions indicated at 48 and 96-h so that all treatments were below the detection limit (0.001 mg/L) except 56 mg/L (measured: 0.0603 mg/L). The validity criteria were fulfilled (study report), for example exponential growth occurred in the controls within three days. In the robust study summary (RSS) no information is given on fulfilment of validity criteria. The results are expressed based on nominal concentrations for the light exposure (24-96-h). The 72-h ErC_{50} is >100 mg/L. The test is assigned by the registrant to be Reliability 1. The Dossier Submitter assigns this test to be Reliability 3, due to very high test concentrations above solubility limit of 0.051 mg/L (and also the former valid solubility limit) and the use of WAF for a single component substance.

A second, supporting, algal inhibition study is a 96-h OECD TG 201 test performed in compliance with GLP using *Scenedesmus subspicatus*, now *Desmodesmus subspicatus* (BASF AG, 2001). Nominal concentrations of 6.25, 12.5, 25, 50, 100 mg/L 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate and a control were tested, but the number of replicates is not stated. Solutions were prepared in the same way as for the acute Daphnia study (BASF AG, 2003) (20-h stirring, and centrifuging at 17700 G). This provided a stock solution of a nominal concentration of 125 mg/L. This was diluted to 100, 50, 25, 12.5 and 6.25 mg/L nominal concentrations. No analytical monitoring was conducted. Validity criteria (study report) were indicated to have been met as the control growth was exponential, pH change was "less than 2 pH units", and the positive control results were in line with expectation. In the robust study summary (RSS) no information is given on fulfilment of validity criteria. Contrary to the pH rise in the other algal test, pH at the end of the study was pH 8.0. As a result of the test, 5.8 % effect on growth was observed at 100 mg/L. However, there is no analysis to indicate whether this was statistically significant. No effects on growth were observed for the remaining concentrations.

The registrant assesses this study to be Reliability 1. In the view of the Dossier Submitter based on the above lack of information the test is Reliability 3. This is mainly because the absence of an analytical verification of the test concentrations means it is unclear what concentration the algal were exposed to. The effect values based on nominal concentrations given in the robust study summary (RSS) do not represent the reality as they are highly above the very low solubility limit. Furthermore, information on the number of replicates is lacking.

Sieratowicz et al. (2011) performed a non-GLP 72-h algal inhibition test according to OECD TG 201 using *Desmodesmus subspicatus*. This used nominal concentrations of 0.015, 0.03, 0.06, 0.13 and 0.25 mg/L, together with a control and solvent control (ethanol (0.05 %)). There were 5 replicates for the control and 3 replicates per treatment and solvent control. Cell density was assessed at 24, 48 and 72 hours. The maximum observed inhibition of the growth rate was 23.9 %, therefore the 72h-IrC_{50} is higher than 0.25 mg/L. The 72h-IrC_{10} was 0.07 mg/L. No validity information, such as confirmation of exponential growth, is provided in the paper. This test used fewer replicates than the OECD TG 201 guideline. Hence, the statistical confidence of the results is lower. No analysis was conducted to verify the measured concentrations, but some information

can be taken from the chronic Daphnia test performed by the same authors in the same paper (described above). The Daphnia study had significant issues for the concentration maintenance in the limited analysis performed, which suggests that significant test substance loss is likely to have occurred in the algal study as well. Therefore, the stated results should be treated with caution. The test is assigned to Reliability 3, as the fulfilment of validity criteria is unclear and fewer replicates are used.

As part of their investigation of several UV filters Rodil et al. (2009) assessed the phytotoxicity of 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate[4] to the uni-cellular chlorophyte *Scenedesmus vacuolatus*. The cells were cultured using a 14/10 light/dark cycle so that a full reproduction cycle occurred after 24 h. A 24-h test was performed using a concentration range for the substance of 0.024 to 0.400 mg/L together with three solvent controls (DMSO, 0.1 %) and three controls. No further details on the exact concentrations or number of replicates of these are provided. A second test was performed using test substance solutions exposed to UV light for 14, 28, 42 and 77 h. The irradiated solutions were diluted with algal medium and contained then 5.6, 11.3, 22.5, 45 and 90 % of the original volume. Per dilution level six controls and two replicates were used. For both experiments cell density was determined after 24 h and used to assess inhibition. No information is provided in the paper about validity criteria such as exponential growth in the controls, or pH changes (although the study is otherwise well reported, for example the initial cell density is provided). Therefore, the study is rated with Klimisch 4.

Results: The 24-h EC_{50} was stated to be 0.19 mg/L although it was not described whether this is a growth or biomass result. For the UV-degraded solutions, toxicity declined with time (up to 72 h) and the authors conclude that the degradants of the substance are less toxic than the parent substance.

A test with *Isochrysis galbana*, a marine unicellular microalgae, with exposure duration of 72 h exists (Paredes et al. 2014). The test was performed according to a method described by (Pérez et al., 2010b) at 20°C with a 24-h light cycle and an initial cell density of 7000 cells/ml. Three replicates per concentration and three controls were used. Cell density and growth rate were calculated at 72 h. The calculation of growth rate (comparing initial and final numbers of cells) is described in the publication with reference to (Pérez et al., 2010a). Therefore, it is assumed that the results stated in the paper are based on growth rate. These were EC_{50} = 0.075 mg/L, EC_{10} = 0.052 mg/L, NOEC = 0.010 mg/L and LOEC = 0.030 mg/L (all based on nominal concentrations). The Dossier Submitter notes that the EC_{10} and EC_{50} values suggest a very steep dose-response curve. There was a 99 % drop in test substance concentration over the duration of the test. Therefore, the real effect values are much lower than specified above based on nominal values. The eMSCA rated the study with Klimisch 2.

Summary of algal toxicity data

A summary of available toxicity data for algae is provided in Table 11. Effects are observed in all available studies, but there is significant variation in the severity. It is not clear if this is due to the actual exposure concentration (which are in in most studies unknown) or differences in the quality of the study, or a difference in species sensitivity. It seems surprising that concentration maintenance would have been any better in the academic studies than the lab ones in compliance with GLP: the algae study is static, and it is clear that 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate either degrades or adsorbs to the test vessel.

Table 11: Summary of available toxicity data for algae

Reference	Algae species	EC_{50} (mg/L)	Nominal / measured concentration
Notox, 2000	*Selenastrum capricornutum*	>100	N
BASF, 2001	*Selenastrum capricornutum*	>100	N
Sieratowicz et al, 2011	*Desmodesmus subspicatus*	>0.25	N
Rodil et al, 2009	*Scenedesmus vacuolatus*	0.19	N
Paredes et al, 2014	*Isochrysis galbana*	0.075	N

[4] The earlier part of their work assed the photodegradation.

11.4.4 Acute (short-term) toxicity to other aquatic organisms

A 7-d-toxicity test on *Lemna minor* according to OECD TG 221 was performed using a semi-static test type(Fort Environmental Laboratories, 2021b). GLP compliance was stated. The substance purity was 99.8 %. Analytical monitoring was conducted using LC-MS (LOQ = 0.00324 mg/L). The limit concentration was 0.0637 mg/L (measured: 0.0579 mg/L). No solvent was used. The test temperature was 24 ± 2 °C and the pH 6.5 to 9 (with a variability less than 1.5 units). 16 hours light per day with an intensity of 6500 to 10000 lux were provided. Six replicates per treatment and control were used. The initial fonds number was 10 per replicate. No significant effects on dry weight, growth rate, or fond area were observed. There were no visual signs of phytotoxicity. The validity criteria described in OECD TG 221 were fulfilled. The substance was stable in the test medium (94.3 to 100.4 % measured compared to nominal concentrations). The study is assigned by the registrant to be Klimisch 1. The eMSCA agrees on this rating.

11.5 Long-term aquatic hazard

Table 12: Summary of relevant information on chronic aquatic toxicity

Method	Species	Results[1]	Remarks	Reference
OECD TG 234	*Danio rerio*	63d-NOEC < 0.0469 mg/L (m) (gonadal histology, length + weight) 63d-NOEC ≥ 0.0469 mg/L (m) (mortality, sex ratio, number of hatch)	Reliability 1	Registration dossier: (Fort Environmental Laboratories Inc., 2020b)
Non-Standard	*Danio rerio*	**125d-NOEC = 0.001 mg/L (n)**	Reliability 2	(Zhou et al., 2019b)
Non-Standard	*Oncorhynchus mykiss*	154d-NOEC < 0.05 mg/L (n)	Reliability 2	(Lee et al., 2019)
OECD TG 231	*Xenopus laevis*	21d-NOEC ≥ 0.0442 mg/L (m)	Reliability 1	Registration dossier: (Fort Environmental Laboratories Inc., 2020a)
OECD TG 211	*Daphnia magna*	21d-NOEC ≥ 0.06 mg/L (n)	Reliability 1	Registration dossier: (Fort Environmental Laboratories Inc., 2021a)
OECD TG 211	*Daphnia magna*	21d-NOEC = 0.04 mg/L (n) (growth)	Reliability 2 Solvent influence possible	(Sieratowicz et al., 2011)
OECD TG 211	*Daphnia magna*	21d-NOEC ≥ 0.02 mg/L (n)	Reliability 2 No analytical verification of test conc.	(Fent et al., 2010)
OECD TG 201	*Selenastrum capricornutum* (now: *Raphidocelis subcapitata*)	72h-ErC_{10} = 65 mg/L (n) 72h-NOErC = 32 mg/L (n)	Reliability 3 (Registrant: Reliability 1) Test conc. much above water solubility limit	Registration dossier (Notox B.V., 2000c)
OECD TG 201	*Scenedesmus subspicatus* (now: *Desmodesmus subspicatus*)	5.8 % effect on growth at 100 mg/L	Reliability 3 (Registrant: Reliability 1)	Registration dossier (BASF AG, 2001)

			Test conc. much above water solubility limit	
OECD TG 201	*Desmodesmus subspicatus*	72h-IrC_{10} = 0.07 mg/L (n)	Reliability 3 No validity information, fewer replicates used than TG, no analysis	(Sieratowicz et al., 2011)
Non-standard	*Isochrysis galbana* Marine uni-cellular microalgae	72h-EC_{10} = 0.052 mg/L (n) 72h-NOEC = 0.010 mg/L (n)	Reliability 2 Drop in test substance concentration	(Paredes et al., 2014)
Non-standard	*Acropora sp.* Red sea, Egypt Zooxanthellae – form of unicellular algae *Acropora pulchra* Andaman Sea, Thailand 3 experiments	33 µl/L: bleaching initiation after 2h, bleaching rate: 91 % at 24h, 86 % Zooxanthellae released 50 µl/L: bleaching initiation after 48h, bleaching rate: 91 % at 96h, 90 % Zooxanthellae released	Reliability 2	(Danovaro et al., 2008)

[1] n = nominal concentration; m = measured concentration; results in bold = relevant for classification and labelling

11.5.1 Chronic toxicity to fish

There are several studies available examining the long-term toxicity of the substance to fish. Amongst these some also address endpoints relevant for the assessment of endocrine disrupting properties without evaluating adverse effects (as e.g. Christen et al. (2011); Chu et al. (2021); Inui et al. (2003); Lee et al. (2019); Zhou et al. (2019a); Zucchi et al. (2011)). These are only briefly described here (but in more detail in the conclusion document of the SEV).

In the study conducted 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/L for 14 days. ERα, AR, 3β-HSD regulation in males and females was measured as well as changes in gene expression and plasma vitellogenin (VTG) levels. Effects on spermatogenesis were observed in males exposed to 394 µg/L.

In a study with *Danio rerio* conducted by Chu et al. (2021) two tests were performed: with adult male fish exposed for 1 d and with larvae exposed from 4 hpf to 5 dpf. The exposure concentrations were in both tests 1, 3, 10, 30 µM OMC. Plasma T3 as well as T4 levels were measured and the gene expression regarding the thyroid system was investigated.

Inui et al. (2003) investigated the potential oestrogenic effects of 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate on adult male Japanese Medaka (*Oryzias latipes*). The fish were exposed to nominal concentrations of 0.034, 0.34, 3.4 and 34 mM 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate (9.87, 98.7, 987, 9877 mg/L) and a solvent control (ethanol: 0.1%) for seven days, but maintenance of the concentrations was not analytically verified. Effects on plasma VTG levels, mRNA expression of oestrogen mediated genes for VTG and choriognen proteins and for ERα were observed.

In the study by Zucchi et al. (2011), adult male zebrafish (*Danio rerio*) were exposed to median measured concentrations of 2.2 and 890 µg/L 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate for 14 days. The regulation of the key genes associated with hormonal pathways was observed.

Zhou et al. (2019a) exposed adult D. rerio for 21 days at the concentrations 1, 10, 100 µg 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate /L (nominal). The measured concentrations were 0.87, 8.5, 79.5 µg/L (3, 29.3, 273.7 nmol/L). E2, testosterone and VTG were determined in the visceral mass of fish. The gene expression

levels of ER, AR, PR, VTG1, CYP17a1, CYP19a1, 17β-HSD1, and 17β-HSD3 were also determined in the visceral mass. Additional oxidative stress markers were examined. The concentration of 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate in fish muscle tissue exposed to 100 µg/L 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate increased with exposure time from about 3000 ng/g wet weight after 7 days to about 17500 ng/g wet weight after 21 days. At exposure to 10 µg/L the OMC concentration increased from about 300 ng/g wet weight (7 d) to 1500 ng/g wet weight (21 d).

The study by (Zhou et al., 2019b) was conducted with Zebrafish (*D.rerio*). The nominal concentrations were 1, 10 and 100 µg/L and not analytical verified. However, the study by Zhou et al. (2019a) showed, that the measured concentrations could be maintained at about 80 % or higher of nominal using a similar exposure media preparation. In the actual study the exposure media was even replaced twice a day, whereas in the study by Zhou et al. (2019a) it was replaced once a day. Zebrafish embryos were exposed to 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate from 2 hpf (hours post-fertilisation) for 4 months until sexual maturation. At 120 dpf (days post-fertilisation) male and female fish were paired. F1 eggs were divided into 2 groups: with and without continued the substance exposure until 5 dpf.

Effects on VTG and E2 levels are not reported here as the information is not relevant for this classification.

The malformation rate after 5 dpf was significantly increased at 100 µg/L in the F0 generation. Body weight decreased dose dependently (significantly decreased at 100 µg/L at 40 dpf (F0)).

The 3-d hatching rates were significantly decreased in the F0 generation and in the not further exposed F1 generation at 10 and 100 µg/L, whereas in the further exposed F1 groups the hatching rate was significantly decreased at 1, 10 and 100 µg/L (see

Table 13). In the blank and solvent control the hatching rates were higher than 80 % fulfilling the validity criterium of OECD TG 234. 5-day survival was decreased at 100 µg/L in the F0 generation, but not in the F1 generations.

Table 13: 3-d hatching rates (%) (Zhou et al., 2019b)

3-d hatching rates (%)								
F0	BC	82.1	F1 (without further expo)	BC	84.7	F1 (with further expo)	BC	-
	SC	84.3		SC	82.1		SC	80.7
	1 µg/L	80.2		1 µg/L	78.7		1 µg/L	72.4*
	10 µg/L	76.5*		10 µg/L	72.9*		10 µg/L	70.5*
	100 µg/L	74.8*		100 µg/L	72.1*		100 µg/L	68.3*

Asterisk indicates significant differences between the exposure group and the control group.

In the F1-group with continued exposure 5-day malformation rates were increased at 10 and 100 µg/L, whereas no effect on malformation was seen in the F1-group without continued exposure. In the F0 generation the 5-day malformation rates were increased at 100 µg/L. The result relevant for classification and labelling is the F1-$NOEC_{3d\text{-}hatching\ rates}$ is 1 µg/L (n).

Table 14: Results from (Zhou et al., 2019b)

Method	**Results**
Danio rerio F0: Zebrafish embryos exposed for 4 months until sexual maturation, fish were paired at 120 dpf. Embryo age at test begin: 2 hpf	F0 and F1: Hatching rates 3 dpf: F0 and F1 (without continued exposure): sign. decreased at 10 and 100 µg/L F1 (with continued exposure): sign. decreased at 1, 10 and 100 µg/L, (in controls: 80.7 to 84.7 %)

F1: two groups with and without continued exposure for 5 dpf F0 and F1: 50 embryos per beaker, 3 replicates for treatments and controls Exposure solution replaced twice a day, Solvent: DMSO (0.01 %), Temperature: 28 ± 1°C, pH 7.4 Photoperiod 16:8 h light/dark Test media was aerated (24 h) Concentrations: 1, 10, 100 µg/L (nom)	Malformation 5dpf: F0: sign. increased at 100 µg/L, F1: at 10 and 100 µg/L with continued exposure sign. increased, without continued exposure no effect on malformation Survival 5 dpf: sign. decreased at 100 µg/L in the F0 generation, no effects in F1 Body weight 40 dpf: F0: sign. decreased at 100 µg/L, no effect on length, (F1: no data on growth) Possibly indication for neurotoxicity: acetylcholinesterase activity sign. increased at all concentrations in the brain of F0 parents (120 d) and in F1 (5 dpf, homogenate, with and without further exposure) Content of 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate in fish (F0) and eggs (F1): Fish: Control: 2.11 ng/g ww (incomplete cleaning of instruments or mistake in operation) 1 µg/L: 102.2 ng/g ww 10 µg/L: 925.7 ng/g ww 100 µg/L: 6514.9 ng/g ww F1 eggs from exposed parents: 1 µg/L: 22.2 ng/g ww 10 µg/L: 146.1 ng/g ww 100 µg/L: 1184.5 ng/g ww → parental transfer of 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate to eggs

Lee et al. (2019) conducted a 2-generation study with *O.latipes* (OECD CF level 5 study). The test concentrations were 50, 158, 500, 1580, 5000 µg/L (nominal concentrations; no chemical analysis). This study was conducted according to OECD TG 234 with slight modifications. During the exposure, the test solution was renewed three times per week, and water quality parameters (dissolved oxygen (DO), pH, temperature, and conductivity) were measured shortly before and after the renewal. Exposure was conducted under the following conditions: 6.9 ± 1.2 mg O_2/L (DO), 7.5 ± 0.3 (pH), 26 ± 2 °C (temperature), 158 ± 18 µS/cm (conductivity) and under 15:9 h light:dark photoperiod. The eggs were randomly distributed into the glass beakers of 50 mL volume with 20 eggs per replicate and four replicates per control, solvent control (0.01% DMSO) or each treatment. The parents were exposed from 24 hpf (hours post-fertilisation) until 154 dpf (days post-fertilisation). At 106 dpf the fish were paired and a mating period of 49 d began, the number of eggs was determined until 154 dpf. At 120 dpf eggs (F1) were further exposed and the F1 generation was examined until 38 dpf. There were no significant effects on hatchability and survival. However effects on reproduction appeared: the number of eggs (per brood per day) was significantly decreased at 50 µg/L and higher concentrations. Growth was decreased at 500 and 1580 µg/L at 38 dpf (only compared to solvent control). Effects on hormones or similar are not reported in this CLH report.

A fish sexual development test according to OECD TG 234 was conducted (Fort Environmental Laboratories Inc., 2020b) with 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate with the species zebrafish (*Danio rerio*) and a duration of 60 dph. Survival and hatching success were not affected. The test showed significant effects on body weights and length which were both reduced in male and female fish at the single concentration of

46.9 µg/L (measured). The test revealed decreased mean ovarian stage score (stage 0.0 ovaries in 66 % of treated females, whereas 61 % of control females were in ovarian stage 1.0, no statistics). The study authors connected this with treatment-induced decrease in somatic growth. A statistically not significant increase in the ratio of females to males was seen, which was -according to the study authors- related to the delayed transition from the female to male phenotype and treatment-induced decrease in somatic growth. The result relevant for classification and labelling is the 63d-$NOEC_{lengh+weight}$, which is lower than 0.0469 mg/L (m).

Table 15: Results from (Fort Environmental Laboratories Inc., 2020b)

Method	**Results**
Danio rerio FSDT, OECD 234 Duration 60 dph Embryo age at test begin: ca. 4hpf Four replicates with 30 embryos each Flow-through: 6.5 volume exchanges per day 25.8 – 27.1°C pH 6.7 – 7.6 Photoperiod 16:8 h light/dark Limit test: 50 µg/L (nominal), 46.9 µg/L (measured)	Hatching and survival: - at 46.9 µg/L (measured) no effect Sex ratio: - At 46.9 µg/L (measured): Female: Male: undiff. fish is 55.1 : 34.7 : 10.2 - In the control: Female: Male: undiff. fish is 51.5 : 44.4 : 4 → Less males and more undifferentiated fish, but not significantly changed. Length and body weight: - significantly decreased length in males and females (not in undifferentiated fish) - significantly decreased body weight in females and males; - undifferentiated fish: mean weight 41 % of mean control weight, but very high standard deviation in control, not sign. VTG: no effects Histopathology of gonads: - At 46.9 µg/L: decreased mean ovarian stage score: 0.3 - in control: 0.9 Intersex: - in the control 3 (6.8 %) males with testicular oocytes (minimal), none in 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate treated males; - one female fish with ovarian spermatogenesis was seen in the treatment and control each Intersex-like finding: - two control males showed a gonadal duct with a female phenotype (attachment of the testis to the dorsal coelomic mesothelium at two sites, not as normal at one site, forming an intervening space), it was not stated that this also appeared in the treatment Germ cell degeneration and oocyte atresia appeared in control and treatment, in control minimal, in treatment mostly minimal, in a few cases mild Histopathology kidney: - No exposure related effects Histopathology liver: - Hepatocytes, karyomegaly (mostly minimal) in males and females in treatment, none in control; - single cell necrosis in males and females in treatment, and some in control

	(mostly minimal), - some cases of oval cell proliferation in treated females (6 %)

11.5.2 Chronic toxicity to aquatic invertebrates

A chronic Daphnia test with 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate was conducted (Fort Environmental Laboratories Inc., 2021a). The test was conducted according to OECD TG 211. The purity of the substance was 99.8 %. Analytical monitoring was conducted using LC-MS/MS (LOQ = 0.00324 mg/L). The test was semi-static with renewal of the test solutions in 24-hour intervals. The test solution was prepared using saturator columns. There was no evidence of undissolved material. M4 medium was used. The exposure duration was 21 d. The nominal concentration was 0.06 mg/L (Limit test). No vehicle was used. The measured concentrations were initial 0.06 mg/L and in 24h old test solution 0.0582 mg/L (arithmetic mean). The nominal concentration can be used. The hardness was 216 to 224 mg $CaCO_3$/L, the test temperature 20.6 to 20.9 °C, the pH values were between 6.5 and 9 and the dissolved oxygen was above 3.0 mg/L. One organism per test vessel and 10 replicates were used. The light intensity was 1000 to 1500 lux with 16 hours light per day. The validity criteria of the OECD TG 211 were fulfilled. No effects on mortality, reproduction and growth appeared up to 60 µg/L.

Sieratowicz et al. (2011) performed a non-GLP 21-d *Daphnia magna* reproduction toxicity study according to OECD 211 for four different UV filters including 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate. The test was performed under semi-static conditions with renewal twice a week. There were 10 replicates with one Daphnid per replicate. Reproductive output (number of neonates) as well as length was assessed. Nominal 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate concentrations were 0.005, 0.01, 0.02, 0.04 and 0.08 mg/L, together with a control and solvent control (ethanol (0.05 %) in M4 media. Chemical analysis was HPLC with UV detection. The paper indicates that the method achieved a 51.9 % recovery rate for 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate. The results of the analysis of the two concentrations 0.05 and 0.8 mg/L indicate significant decreases in test substance concentration: ~100 % at the lowest concentration (as it could not be detected after 4 days) and 93 % at the highest concentration. The authors note the difficulties with the analysis suggest the exposure conditions would require amendment and caution about interpretation of the calculated "time-weighted mean concentrations" made in the paper from the fresh and expired media. No statistically significant effects on reproduction were observed for 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate. The paper notes that the non-solvent control had a significantly increased parental length compared to the solvent control for this chemical (compared to the other three UV-filter tests) at the highest treatment. A graph for these data is provided in the paper, and (by eye) it appears that the control length was 4.1 mm, the solvent control length was 3.8 mm and the highest concentration length was 3.7 mm. The standard deviation of the solvent control and highest concentration may coincide. Results are stated as being based on nominal concentrations: 21-d NOEC = 0.04 mg /L and 21-d LOEC 0.08 mg/L. An EC_{10} could not be calculated.

Fent et al. (2010) reports the findings of a chronic Daphnia study. There are few details in the publication itself but the test can be summarised as a 21-d non-GLP Daphnia reproduction toxicity study performed in accordance with OECD TG 211 for four UV filters including 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate. It used 48-h static renewal. Four concentrations of the substance were used (0.00128, 0.0032, 0.008 and 0.02 mg/L). The exposure concentrations were based on the acute test described above (Fent et al., 2010). No effects on reproduction or body length were observed for 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate. There is no mention of chemical analysis, so the Dossier Submitter assumes the quoted vales are nominal concentrations. The apparent lack of analysis in this study makes interpretation of the results difficult as it may be that little if any test substance was present particularly towards the end of the renewal period for such low concentrations.

11.5.3 Chronic toxicity to algae or other aquatic plants

The descriptions of the test conditions were provided in section 11.4.3.

In the 72-h algal inhibition toxicity test performed in compliance with GLP using *Selenastrum capricornutum*, now *Raphidocelis subcapitata* (Notox B.V., 2000c) according to OECD TG 201, the long-term result based

on nominal concentrations were: the 72-h NOE_rC being 32 mg/L and the E_rC_{10} being 65 mg/L. The test is assigned by the registrant to be Reliability 1. The Dossier Submitter assigns this test to be Reliability 3, due to very high test concentrations above solubility limit of 0.051 mg/L (and also the former valid solubility limit) and the use of WAF for a single component substance.

In the second, supporting, algal inhibition study, a 96-h OECD TG 201 test performed in compliance with GLP using *Scenedesmus subspicatus,* now *Raphidocelis subcapitata* (BASF AG, 2001), similar to the short term results the long-term results showed no effects besides 5.8 % effect on growth observed at 100 mg/L. However, there is no analysis to indicate whether this was statistically significant. The registrant assesses this study to be Reliability 1. In the view of the Dossier Submitter based on the above lack of information the test is Reliability 3. This is mainly because the absence of analysis means it is unclear what concentration the algal were exposed to. The effect values based on nominal concentrations given in the robust study summary (RSS) do not represent the reality as they are highly above the very low solubility limit. Furthermore, information on number of replicates is lacking.

Sieratowicz et al. (2011) performed a non-GLP 72-h algal inhibition test according to OECD 201 using *Desmodesmus subspicatus*. This used nominal concentrations of 0.015, 0.03, 0.06, 0.13 and 0.25 mg/L, together with a control and solvent control (ethanol (0.05 %). There were 5 replicates for the control and 3 replicates per treatment and solvent control. Cell density was assessed at 24, 48 and 72 hours. The 72h-I_rC_{10} was 0.07 mg/L. No validity information, such as confirmation of exponential growth, is provided in the paper. This test used fewer replicates than the OECD 201 guideline. Hence, the statistical confidence of the results is lower. No analysis was conducted to verify the measured concentrations, but some information can be taken from the chronic Daphnia test performed by the same authors in the same paper (described above). The Daphnia study had significant issues for the concentration maintenance in the limited analysis performed, which suggests that significant test substance loss is likely to have occurred in the algal study as well. Therefore, the stated results should be treated with caution. The test is assigned to Reliability 3, as the fulfilment of validity criteria was not assessed and fewer replicates are used.

A test with *Isochrysis galbana*, marine unicellular microalgae, with exposure duration of 72 h exists (Paredes et al., 2014). The test was performed according to a method described by (Pérez et al., 2010b) at 20 °C with a 24-h light cycle and an initial cell density of 7000 cells/ml. Three replicates per concentration and three controls were used. Cell density and growth rate were calculated at 72 h. The calculation of growth rate (comparing initial and final numbers of cells) is stated in the publication with reference to (Pérez and Beiras, 2010). Therefore, it is assumed that the results stated in the paper are based on growth rate. These were EC_{50} = 0.075 mg/L, EC_{10} = 0.052 mg/L, NOEC = 0.010 mg/L and LOEC = 0.030 mg/L (all based on nominal concentrations). The Dossier Submitter notes that the values of EC_{10} and EC_{50} suggest a very steep dose-response curve. There was a 99 % drop in test substance concentration over the duration of the test. Therefore, the real effect values are much lower than specified above, since nominal values were used.

Summary of algal toxicity data

A summary of available toxicity data for algae is provided in Table 16. Effects are observed in all available studies, but there is significant variation in the severity. It is not clear if this is due to the actual exposure concentration which are for most studies unknown) or differences in the quality of the study, or a difference in species sensitivity. It seems surprising that concentration maintenance would have been any better in the academic studies than the lab ones in compliance with GLP: the algae study is static, and it is clear that 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate either degrades or adsorbs to the test vessel.

Table 16: Summary of available toxicity data for algae

Reference	Algae species	EC10 / mg/L	Nominal / measured concentration
(Notox B.V., 2000c)	Selenastrum capricornutum	65	N
(BASF AG, 2001)	Selenastrum capricornutum	> 100	N
(Sieratowicz et al., 2011)	Desmodesmus subspicatus	0.07	N
(Paredes et al., 2014)	Isochrysis galbana	0.052	N

11.5.4 Chronic toxicity to other aquatic organisms

A 21-d Amphibian Metamorphosis Assay (AMA) with the African Clawed Frog (*Xenopus laevis*) was conducted with 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate (Fort Environmental Laboratories Inc., 2020a). Three concentrations up to 0.0442 mg/L (measured) were tested. The median developmental stage, snout-vent length, hind limb development and body weight were not statistically different from control on SD day 7 and 21. No treatment-related histopathologic findings in the thyroids of tadpoles exposed to 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate were seen. In summary no thyroid effects were seen and no other signs of toxicity.

Danovaro et al. (2008) investigated coral bleaching resulting from exposure to a number of sun screens and individual UV filters including 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate. They conducted in-situ studies in four locations in the world: Siladen, Celebes Sea (Indonesia, Pacific Ocean), Akumal, Caribbean Sea (Mexico, Atlantic Ocean), Phuket, Andaman Sea (Thailand, Indian Ocean) and Ras Mohammed, Red Sea (Egypt, Indian Ocean). Three species of hard coral were investigated: *Acropora* (different species of this genus: *A. divaricata, A. cervicornis, pulchra, A. aspera, A. intermedia*), *Stylophora pistillata* and *Millepora complanata*. 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate was only assessed in two locations: Phuket (*Acropora pulchra)* and Ras Mohammed (*Acropora spathulata)*. Nubbins of *Acropora* were collected and incubated in-situ in polyethylene bags containing 2-L of virus free seawater. The test used concentrations of 10, 33, 50, 100 µl/L seawater together with a control of untreated seawater. Three replicates each containing more than 300 polyps were used for each treatment. The exact length of the experiments is not specified but appears to be 96h, with observations made periodically during that time. No chemical analysis was performed.

Bleaching was assessed using a colorimetric analysis from digital photographs taken during the study. These were analysed using photo-editing software to assess colour composition (cyan, magenta, yellow and black). Changes in each colour were assessed relative to the control to establish the level of bleaching. Adverse effects to the Zooxanthellae (protozoa which live on the coral) was also assessed. These microalgae were extracted using artificial seawater, and the number of cells counted and their health assessed (based on colour and condition). A final aspect of the study was the observation of effects of sunscreen on causing viral infections. However, this aspect used only (unspecified) sunscreen mixtures, rather than specific chemicals such as 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate.

The results for 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate can be found in the following table.

Table 17

Coral	Quantity	Bleaching initiation / h	Bleaching rate	% Zoozanthellae released
Phuket (*Acropora pulchra)*	33 µl/L	2	24 (91)	86
Ras Moohammed (*Acropora sp.)*	50 µl/L	48	96 (91)	90

Commentary

It can be seen that there was a marked difference between the bleaching initiation time for the two corals. Although the paper compares the control Zooxanthellae cell condition with the exposed cells, specific quantification of toxicity to Zooxanthellae from 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate is not reported.

While there are no standard guidelines for this type of test, on the basis of comparison to the controls, effects were observed. It is known that many causes have been suggested for coral bleaching (for example temperature

changes due to global warming). It is beyond the scope of this evaluation to assess this impact. However, the Dossier Submitter does note that the toxic effects on the Zooxanthellae (which are a form of unicellular algae) do not in principle appear to be out of step with other studies described above where 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate caused adverse effects on algae.

11.6 Comparison with the CLP criteria

11.6.1 Acute aquatic hazard

Table 18: Comparison with criteria for acute aquatic hazards

	Criteria for acute environmental hazards	**2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate**	**Conclusion**
Acute Aquatic Toxicity	Cat. 1: $LC_{50}/EC_{50}/ErC_{50} \leq 1$ mg/L	Fish: not available (all studies Reliability 3) Freshwater Crustacean: 48h-EC_{50}= 0.29 mg/L (n) (*Daphnia magna*) (Fent et al., 2010) Seawater Crustacean: 48h-EC_{50}= 0.199 mg/L (n) (*Siriella armata*) (Parades et al., 2014) Algae: Seawater: 72h-$EC_{50,\ growth}$= 0.075 mg/L (n) (*Isochrysis galbana*) (Parades et al., 2014)	**Aquatic Acute 1, M=10** Based on *Isochrysis galbana*

11.6.2 Long-term aquatic hazard (including bioaccumulation potential and degradation)

Table 19: Comparison with criteria for long-term aquatic hazards

	Criteria for environmental hazards	2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate	Conclusion
Rapid Degradation	Half-life hydrolysis < 16 days Readily biodegradable in a 28-day test for ready biodegradability (> 70 % DOC removal or > 60 % theoretical oxygen demand, theoretical carbon dioxide)	Half-life hydrolysis > 1 year 78 % after 28 days → readily biodegradable	**Rapidly degradable**
Bioaccumulation	Log Kow ≥ 4 BCF ≥ 500	Log Kow > 6 BCF: no valid data available	**High potential for bioaccumulation**
Aquatic Toxicity	rapidly degradable substances: Cat. 1: NOEC ≤ 0.01 mg/L Cat. 2: NOEC > 0.01 ≤ 0.1 mg/L Cat. 3: NOEC > 0.1 ≤ 1 mg/L (based on Table 4.1.0 (b) (ii) of the CLP Regulation)	Fish (both *Danio rerio*): 63d-$NOEC_{lengh+weight}$ < 0.0469 mg/L (m) (Fort Environmental Laboratories, Inc., 2020) 125d-F1-$NOEC_{hatching\ rates}$= 0.001 mg/L (n) (Zhou et al., 2019b) Aquatic Invertebrates: 21d-$NOEC_{growth}$= 0.04 mg/L (n) (Sieratowicz et al., 2011) Algae: 72h- EC_{10} = 0.052 mg/L (n) (*Isochrysis galbana*) (Parades et al., 2014)	**Aquatic Chronic 1, M = 10** Based on *Danio rerio* F1 hatching rates

11.7 CONCLUSION ON CLASSIFICATION AND LABELLING FOR ENVIRONMENTAL HAZARDS

Acute aquatic hazard:

There is no valid E/LC_{50} value from the short-term toxicity tests on fish available.

The valid E/LC_{50} values from the short-term toxicity tests on aquatic invertebrates (freshwater and saltwater) are between 0.1 and 1 mg/L.

The valid E_rC_{50} from the algae toxicity test is 0.075 mg/L (*Isochrysis galbana*) and therefore < 1 mg/L.

The proposed acute aquatic classification is Aquatic Acute 1 (H400) with a M-factor of 10 based on the criteria given in Table 4.1.0 (a) and Table 4.1.3 of the CLP Regulation.

Chronic aquatic hazard:

2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate is rapidly degradable and has a high potential for bioaccumulation in the aquatic environment, as the log Kow is higher than 4.

Chronic toxicity data is available for all three trophic levels. The most sensitive valid long-term toxicity value is the F1-$NOEC_{hatching\ rates}$ of 0.001 mg/L (n) for the fish *Danio rerio*. This results in a classification of 2-ethylhexyl (2*E*)-3-(4-methoxyphenyl)acrylate as Aquatic Chronic 1 (M= 10) based on the criteria given in Table 4.1.0 (b) (ii) and Table 4.1.3 of the CLP Regulation.

12 EVALUATION OF ADDITIONAL HAZARDS

12.1 Hazardous to the ozone layer

Not assessed in this dossier.

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