Committee for Risk Assessment
RAC

Annex 2
Response to comments document (RCOM)
to the Opinion proposing harmonised classification and labelling at EU level of

hexyl 2-(1-(diethylaminohydroxyphenyl) methanoyl)benzoate;
hexyl 2-[4-(diethylamino)-2-hydroxybenzoyl]benzoate

EC Number: 443-860-6
CAS Number: 302776-68-7

CLH-O-0000001412-86-253/F

Adopted
30 November 2018

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.

All comments and attachments including confidential information received during the public consultation have been provided in full to the dossier submitter (Member State Competent Authority), the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the public consultation and are also published together with the opinion (after adoption) on ECHA's website. Dossier submitters who are manufacturers, importers or downstream users, will only receive the comments and non-confidential attachments, and not the confidential information received from other parties.

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Substance name: hexyl 2-(1-(diethylaminohydroxyphenyl)methanoyl)benzoate; hexyl 2-[4-(diethylamino)-2-hydroxybenzoyl]benzoate
EC number: 443-860-6
CAS number: 302776-68-7
Dossier submitter: Germany

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
09.01.2018	France		MemberState	1
Comment received				
France fully supports the proposal to modify the classification from Aquatic Chronic 4, H413 to Aquatic Chronic 1, H410 with a M-factor of 1000 due to the data on invertebrate long term NOEC reproduction.				
Dossier Submitter's Response				
Thank you for your supporting comment.				
RAC's response				
Thank you for your comment. RAC notes the support for the proposed environmental classification. Based on all available information including information made available in the original Public Consultation and targeted Public Consultation RAC considers the 21-d *Daphnia magna* reproduction study ((BASF, 2007) not valid due to uncertainties regarding the study design and therefore should not be taken in to account for classification. The study is considered as invalid based on the following: - RAC does not have any reliable information regarding the identitiy of precipitate in test media (i.e. analysis report). The precipitate was identified by laboratory asistant as iron. Based on the colour of the precipitate (brownish) and the fact that was associated with the magnetic stirrer in the test baker, it was considered to be iron(III)oxide. - Additional analytical investigations showed that stirring of the M4 medium reduces the iron content of the M4 medium and thus impacts the final medium composition				

used for the *Daphnia magna* reproduction test. This means that control and treatment groups within the BASF 2007 study have different nutrient compositions since all test solutions were stired for 2 to 3 days (not control). Therefore the results of the study can not be taken in to account.

- Iron deficiency in the M4 medium has a negative impact on the reproduction behaviour of daphnids. Fe is essential for Daphnia in hemoglobin synthesis and reproduction (Dave, 1984). Hudson et al. (2016) study showed a reduced (but non-significant) maturation rate in Daphnia fed reduced Fe diets. Results of the BASF 2018c study showed that the absence of soluble iron (Fe(II) from the M4 medium) affect the reproduction of *Daphnia magna* in form of delayed deposition of the brood. The similar delay on the average day of brood deposition was observed in the BASF 2007 study. Overall, based on the available data RAC is of the opinion that different availability of iron in the test media could have affected the organisms and therefore the study outcome.

When comparing the results of all four available chronic toxicity studies to *Daphnia magna*, RAC notes that NOEC$_S$ from three studies (BASF 2009, 2018a and 2018b) differe from the NOEC of the BASF 2007 study by a factor of more than 100 (0.1 μg/L vs. ≥14.3 μg/L, ≥ 11.4 μg/L and ≥ 12.7 μg/L). There are no differences in sensitivity of various daphnid strains when comparing the studies.

During the process of the preparation of the draft opinion, RAC became aware of two new *Daphnia magna* reproduction tests (OECD 211) with Uvinul A Plus (BASF 2018a and BASF 2018b). RAC assessed the studies and consideres them valid and reliable thus these studies should be used for the classifaication purposes. Both studies show no chronic toxicity to *Daphnia magna* up to the limit of water solubility. In the view of RAC, three reliable chronic toxicity studies on invertebrate *Daphnia magna* are relevant for classification, namely BASF 2009, 2018a and 2018b.

Based on all available information RAC is of the opinion that no classification for chronic aquatic toxicity is warranted. In case of Uvinul A Plus, adequate chronic toxicity data are available for all three trophic levels (fish, daphnia and algae). The available information shows no adverse effects of the substance to aquatic organisms at concentrations up to the water solubility limit in all reliable tests. According to Table 4.1.0 of CLP Regulation, Aquatic Chronic 4 classification is assigned to poorly soluble substances for which no acute toxicity is recorded at levels up to the water solubility and which are not rapidly degradable and have an experimentally determined BCF ≥ 500 (or, if absent, a log Kow > 4), indicating a potential to bioaccumulate. As the latter is clearly not the case, Uvinul A Plus should no longer be classified as Aquatic Chronic 4. Aquatic Chronic 4 classification is not necessary if in addition to the above criteria other scientific evidence exists showing classification to be unnecessary. Such evidence includes chronic toxicity NOECs > water solubility or > 1 mg/L. In case of Uvinul A Plus the available NOECs are all equal to or greater than the water solubility for all three trophic levels.

RAC is of the opinion that no classification for chronic aquatic toxicity is warranted. In conclusion, RAC does not support the Dossier Submitter's proposal to classify the substance as Aquatic Chronic 1 (H410) with M-factor of 1000.

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON HEXYL 2-(1-(DIETHYLAMINOHYDROXYPHENYL)METHANOYL)BENZOATE; HEXYL 2-[4-(DIETHYLAMINO)-2-HYDROXYBENZOYL]BENZOATE

Date	Country	Organisation	Type of Organisation	Comment number
12.01.2018	Germany	BASF SE	Company-Manufacturer	2
Comment received				

BASF Comments on the CHL proposal for hexyl 2-(1-(diethylaminohydroxyphenyl)methanoyl)benzoate; hexyl 2-[4-(diethylamino)-2-hydroxybenzoyl]benzoate), EC Number: 443-860-6, CAS Number: 302776-68-7, Index Number: 607-693-00-4

Summary:

We disagree with the suggested re-classification of the substance as hazardous to the environment (Aquatic Chronic 1 and M-factor of 1000; H410). The proposal of the Dossier Submitter is based on a misinterpretation of a chronic daphnia toxicity study (IBACON 2007) which is considered invalid according to the OECD 211 test guideline (IBACON 2017, 2nd amendment to report; IBACON 2017, expert statement), adopted 21st September 1998 and the current version, adopted 2nd October 2012) as well as according to Commission Directive 2001/59/EC of 6 August 2001, Method C.20) due to the following severe shortcomings:

a) Adequate (solvent) control group is missing

b) Differences in the preparation of the test media led to differences in the nutrition composition of the M4-control group compared to the treatment groups

Due to these experimental weaknesses of the IBACON study, a confirmatory limit test study was carried out subsequently (BASF SE 2009; report submitted as confidential attachment). This follow-up study demonstrated clearly the absence of any chronic toxicity effects towards daphnia. In particular, the results of the study showed that

a) The control group (M4-medium only) was adequate for the test, as no solvent was used.

b) The mean reproduction rate of 20 Daphnids in the treatment group was slightly higher than the control group (163.8 versus 156.9 living young after 21 d).

c) No effects on the mean days to first brood, parental mortality and growth, mean dead young, or mean aborted eggs.

d) Average control reproduction rate within the historical control data.

e) The average measured test item concentration under flow-through conditions was much higher than in the IBACON study and revealed a concentration of 14.3 μg/l, which is within ± 20 % of the determined water solubility in pure water of 16 ± 3 μg/L

These results are furthermore supported by a weight of evidence taking into account the existing chronic toxicity data on fish as well as QSAR calculations (see attached expert statement BASF 2018). In conclusion, we do not agree with the CLH proposal as it is not justified by the existing data and applying a weight of evidence assessment. Instead, based on the absence of chronic toxicity towards algae, daphnia and fish in line with the low potential for bioaccumulation (BCF < 500), the existing classification (Chronic 4) for this substance should be removed.

Attachments

1. BASF 2009. Report Uvinul A Plus Daphnia magna reproduction test, unpublished data, report No. 52E0636/023040, 4th November 2009.

2. BASF 2018. BASF Comments on the CHL report by Federal Institute of Occupational Safety and Health (BAuA) on hexyl 2-(1-(diethylaminohydroxyphenyl)methanoyl)benzoate; hexyl 2-[4-(diethylamino)-2-hydroxybenzoyl]benzoate, EC Number: 443-860-6, CAS Number: 302776-68-7, Index Number: 607-693-00-4.

3. Galloway, T. 2017. Expert statement on the validity of the IBACON 2007 test to determine the influence of Uvinul A Plus on Daphnia magna, especially in relation to reproduction,

4. IBACON 2007. Influence of Uvinul A Plus to Daphnia magna in a Reproduction test, unpublished data, project no. 34541221, BASF report No. 51E0636/029036, 25th June, 2007.

5. IBACON 2007. First amendment to Final Report, Influence of Uvinul A Plus to Daphnia magna in a Reproduction Test, unpublished data, project no. 34541221, BASF report No. 51E0636/029036, 5th September 2007.

6. IBACON 2017. Second amendment to Final Report, Influence of Uvinul A Plus to Daphnia magna in a Reproduction Test, project no. 34541221, BASF report No. 51E0636/029036, 8th December 2017.

7. IBACON 2017. Expert statement, Re-Evaluation of the Daphnia Reproduction Test on Uvinul A Plus, project no. 34541221, BASF report No. 51E0636/029036, 8th December 2017.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Public comments Uvinul A Plus.zip
ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Confidential comments Uvinul A Plus.zip

Dossier Submitter's Response

Thank you for your comment.
You consider (IBACON/BASF 2007) invalid due to in your opinion severe shortcomings:

a) In your opinion an adequate (solvent) control is missing. You explain in the attachment 2 and 3 that in (IBACON/BASF 2007), no solvent control was used although acetone was used for the test concentration preparation. It is correct that according to OECD 211 a solvent control has to be used, when a solvent is used for the preparation of the test concentrations. In this test as well as in (BASF 2009) (the limit test study) the test substance was dissolved in acetone. This solution was applied on the test vessel glass surface (walls) (IBACON/ BASF 2007) or on glass wool (BASF 2009). After acetone completely evaporated, test media was added to the test vessels and stirred for 2 to 3 days (IBACON/BASF 2007). In (BASF 2009) the glass wool was included in a glass column. The packed column was rinsed with demineralized water for approx. 48h and then with M4 medium again for approx. 48 h. The rinse water was discarded. M4 medium was pumped circularly through the column to be used as the test solution for the flow-through test. As acetone evaporated and therefore is not part of the test solution, a solvent control is not necessary. Moreover, both tests (IBACON/ BASF 2007 as well as BASF 2009) used acetone to expose the test vessels with the test substance and evaporated acetone.

b) You state that the nutrition composition of the M4 control group differed from the treatment groups. In attachment 7 IBACON stated in December 2017 that "After 2 to 3 days of stirring, precipitation was observed either floating on the surface (exposure day 0), or being stuck to the magnetic stirrer (exposure day 2, 9 and 12). This observation only occurred in the test concentrations and not in the control. The precipitation was not determined analytically, but identified by the laboratory assistant as iron. Therefore, it can be concluded that the test media composition was different for the daphnia of the test concentration compared to the test medium for

the control group." This observation was not described in the test report (IBACON/ BASF 2007 – attachment 4). In chapter 8.3 (pH, dissolved oxygen concentrations, water temperature and behaviour of the test item in test water) it was stated under "Behaviour of the test item:" "No remarkable observations (see Table 6)". In Table 6 observation like "2: Turbidity caused by the test item" or "5: Test item at the surface". In the whole table "0: No remarkable observations, clear test medium" was filled in. In attachment 3 (Expert statement Galloway December 2017) it is described that this precipitation of iron was noted in the raw data report (not in IBACON/ BASF 2007). According to Galloway, the observation of precipitations in the test medium but not in the control medium could point towards differences in nutrient content between test and control media. It is explained (in Galloway) that variations in metal concentration, including iron, can affect growth and reproduction in *Daphnia* species (Biesinger and Christensen, 1972, Bosnir et al., 2013, Hudson et al., 2016). In (Biesinger and Christensen, 1972) the 3-week 16 % reproductive impairment concentrations of different metals on *Daphnia* was examined (Fe^{3+}: 4.38 mg/L). (Bosnir et al. 2013) examined the acute toxic effects of iron ($EC_{50}= 46.9$ mg/L). Both publications deal with the toxic effects of iron on *Daphnia* and do not provide information on the effects of different iron levels in the test medium. (Hudson et al. 2016) examined the effects of a low iron diet together with a methylmercury exposure. The different iron contents (no, low, high) in the diet did not result in significant effects on time to first reproduction, average brood size or reproduction rate. Therefore, the potential difference in the iron content of test medium is likely to have no consequence for toxicity of the test substance to *Daphnia*. For the development of the Elendt M4-Medium itself, according to (Elendt and Bias 1990), the selenium not the iron content was essential for a better growth and reproduction of *Daphnia*.

c) (second a in comment) (BASF 2009) as well as (IBACON/ BASF 2007) used acetone to dissolve the test substance and bring it into the test vessels. In both test the test medium was poured in after evaporation of acetone.

d) (second b to c) Yes, you are right.

e) (d in comment) The average number of live offspring produced per surviving adult within 21 days of exposure was in the control of (BASF 2009) 156.9 and in the historical control (see BASF/ IBACON 2007) 107.1. In (BASF/ IBACON 2007) it was 130.1. There seems to be a bigger difference between the historical control and the control of (BASF 2009) than between the historical control and the control of (BASF/ IBACON 2007).

f) (e in comment) The recovery of the test substance in the highest test concentration in BASF/ IBACON 2007 seems to be in good consistence with the ones of BASF 2009, keeping in mind the different nominal concentrations (see table below).
Concerning the QSAR calculations (Expert statement Galloway December 2017), there is no information if the structure falls into the applicability domain. It is difficult to apply reliable QSAR for a chronic toxicity, therefore a QSAR calculation should not replace the result of a valid experimental result.

Some core data from the two long-term toxicity test on *Daphnia* for comparison:

	BASF/ IBACON 2007	BASF 2009
animals	10 animals held individually per concentration	20 animals (5 per vessel) per concentration
Nominal concentrations tested	1, 3.2, 10, 32, and 100 µg/L	Limit-test: 15 µg/L
Measured	0.1, 0.43, 1, 3.5, and 15.4	14.2 µg/L mean measured

concentrations	µg/L mean measured (14 %= mean of recovery rates of the upper two conc. used for lower; recovery rate highest test concentration: 3 – 41 %)	(recovery rate: 35 – 218%)	
Analytical method	LC-MS/MS (LOQ= 2 µg/L)	GC-MS (LOD= 2 µg/L)	
Temperature	19 – 20 °C	19 – 21 °C	
pH	7.2 – 8.3	8.0 – 8.2	
	semi-static (renewal after 2-3d)	Flow-through	
Dissolved oxygen	7.7 – 10.0 mg/L	8.4 – 8.9 mg/L	
Light per day	16 h (60 – 120 lux)	16 h (680 – 741 lux)	
Medium used	M4	M4	
Test concentration preparation	- Test substance dissolved in acetone 200 µL of the acetonic solution were distributed on the glass surface of each empty test vessel - Acetone was evaporated - Test vessels were filled with M4 medium and stirred for 2 to 3 days	- Test substance dissolved in acetone - Acetonic solution was poured over glass wool in a stainless steel pan - Acetone was evaporated - Glass wool with substance was packed into a glass column - The packed column was rinsed with demineralized water and with M4 medium - After 4 days, M4 medium was pumped through the saturation column for 1d	

As a result of the reflections above, in our opinion both long-term toxicity tests are valid and reliable equally. As the DE CA considers both chronic studies on invertebrates valid, the lowest value should be considered for classification.

RAC's response

Thank you for your comments.

a) RAC notes that in the BASF 2007 study the solvent (aceton) was used for the preparation of test slution but no solvent control was performed what is not in accordance with OECD 211 test guideline. Since, the solvent was completely evaporated before the test media was added to the test vessels RAC is of the opinion that missing solvent control does not make the BASF 2007 study invalid but just decrease the reliability of the study. RAC agrees with Dossier Submitter's explanation regarding the lack of solvent control in the BASF 2007 study and BASF 2009 study.

b) RAC notes that the reported deviations regarding test media (precipitation of iron) are not consistant. The precipitation of iron were reported in the 2nd Amendment to Final Report (attachement 7) and in raw data report (Galloway, 2017) but not in Final Report (attachement 4). Regarding the identity of the precipitation RAC is of the opinion that due to missing analitical report demonstrating the presenc of the iron in the test media such statement cannot be considered scientifcaly valid.

c) Noted.

d) Noted.

e) Dossier Submitter comapred the average control reproduction rate in the BASF 2009 study (156.9) and BASF 2007 study (130.1) with the historical control data from BASF 2007 study (107.1). RAC noticed that in the attacmnet 2 (BASF 2018, BASF Comments on the CHL) under the headline Detailed discussion of the individual studies, 2. Chronic daphnia toxicity – flow-through test design (BASF 2009) it is described that the average reproduction rate of the parental Daphnids (156.9 living young) was well within the range of the historical control data (136.8±31.4 living young; n=93). The study was carried out in the laboratories of BASF.

f) QSAR calculations
In the BASF comments on CLH-dossier (BASF, 2018) the QSAR predictions for chronic fish and chronic Daphnia toxicity are provided. The results are presented in ODD. RAC considers that the QSAR predictions as presented by the company are not well documented and justified (i.e. no detailed assessment of applicability domain and reliability). Based only on prediction results, as provided, it is difficult to assess the reliability and relevance of the predicted chronic values. RAC agrees with DS that QSAR calculations should not replace the results of a valid experimental results.

Date	Country	Organisation	Type of Organisation	Comment number
12.01.2018	Belgium		MemberState	3
Comment received				

Aquatic Acute toxicity :
BE CA agrees that, based on the results of the available studies with the 3 trophic levels, a classification for aquatic acute toxicity is not warranted.

Aquatic Chronic toxicity :
BE CA agrees with the proposed classification as Aquatic Chronic 1, H410 with M=1000.
Key study : chronic study with Daphnia magna (BASF, 2007), OECD211
- Physical effects :
The substance has a low water solubility (WS of test item=0.01mg/L).
With a log Koc=5.1 you might expect adsorption to organic matter.
However BE CA agrees with BAuA that it cannot be excluded that observed effects are due to exposure to the substance because no physical effects on the test organisms by non-dissolved test material were reported in the study.

- The registrant commented that an "unusually high" reproduction rate was seen in the control when compared to the historical control data. Therefore test results were compared to the historical control data instead. However the same study conditions are applied for control and test concentration, so BE CA is also of the opinion that test results should be compared to the control data of the study and not with the historical control data.

- BE CA considers both chronic studies on invertebrates (BASF 2007 and BASF, 2009) valid and thus the lowest value should be considered for classification : NOEC of 0.14µg/L (extrapolated mean measured; corresponding to 1µg/L nominal)

In conclusion : BE CA agrees with the proposed environmental classification by BAuA.

Dossier Submitter's Response
Thank you for your supporting comment.
RAC's response
Thank you for your comments. Aquatic acute toxicity RAC agree with Dossier Submitter and BE CA that based on the results of the available studies in the CLH report no classification for acute aquatic toxicity is warranted. Aquatic chronic toxicity RAC notes the support for the proposed environmental classification. Please see the RAC response under Comment number 1. Physical effects Noted. Concurrent/historical control According to OECD 211 test guidance the data from treated animals should be compared with concurrent study control data. Therefore RAC agrees with DS and commenting member state. Validity of BASF (2007) and BASF (2009) RAC is of the opinion that the BASF 2009 study is valid and should be used for classification purposes. Regardin the validity of the BASF 2007 study please see the RAC response under Comment number 1.

Date	Country	Organisation	Type of Organisation	Comment number
29.12.2017	Finland		MemberState	4
Comment received				
Toxicity tests with water fleas are valid for classification purposes of aquatic hazards. The key study for this proposal is Daphnia magna reproduction test (OECD 211). It was carried out using five concentrations between 1-100 µg/l. However, only two of the highest concentrations fell within the detection limits and 87,8-93,1 % reductions of nominal concentrations were measured. According to statistical analysis including lower concentration values extrapolated from the highest concentrations, the chronic toxicity NOEC value is 0,1 µg/l. FI CA supports the conclusions that the substance is neither rapidly degradable nor bioaccumulative. Based on the available information and the classification criteria FI CA supports modifying the current classification of Aquatic Chronic 4, H413 to Aquatic Chronic 1, H410 with M-factor of 1000 for Hexyl 2-[4-(diethylamino)-2-hydroxybenzoyl]benzoate.				
Dossier Submitter's Response				
Thank you for your supporting comment.				
RAC's response				
RAC notes the support for the proposed environmental classification. Please see the RAC response under Comment number 1.				

Date	Country	Organisation	Type of Organisation	Comment number
10.01.2018	United Kingdom		MemberState	5

Comment received
The environmental classification hinges on the reliability of the NOEC from the 21-day Daphnia magna reproduction study (BASF, 2007). We feel there are two areas which need to be considered to determine the NOEC reliability: whether the study control data is an outlier and ii) whether mean measured endpoints are reliable. The CLH report does not present the raw data and only summary data is available in the online registration RSS. Therefore the number of animals in individual replicates is unclear along with details of the laboratory historical control data. From our experience, the number of animals per surviving adult in controls can vary greatly with 130 and more being observed. If additional data are available to support the study controls as outliers, this should be provided. Based on the CLH report it is unclear what treatments were analysed and what the measured concentrations were. This information should be provided to consider if the mean measured range quoted in the CLH are reliable. In addition, we note this range is different to the mean measured range in the online registration RSS. On this basis, it is unclear at present if Reliability score 1 is applicable. We note the online registration includes QSAR predictions for the chronic toxicity to invertebrates endpoint. Further details and the reliability of such QSARs would be useful given the conflicting NOECs from BASF, 2007 and BASF 2009.

Dossier Submitter's Response
Thank you for your comment. For details of the two *Daphnia magna* reproduction studies please see also the table in our response to comment 2. For (BASF/ IBACON 2007) the number of live offspring produced per surviving adult within 21 days of exposure was:

21,0d	Replicates	Control	Historical control	0.1 µg/L	0.43 µg/L	1 µg/L	3.5 µg/L	15.4 µg/L
	1	116	101.1	123	101	88	111	153
	2	135	121.7	109	109	109	102	68
	3	134	125.7	142	71	110	92	86
	4	124	99.2	91	129	112	78	102
	5	137	116.2		102	124	141	118
	6	136	85.2	98			102	100
	7	153	108.6	96	101	90	95	77
	8	127	98.6	133	88	121	96	72
	9	133	Data from last 8 reproduction studies	120		105	96	101
	10	106		152	108	125	108	65
	#Replicates	10	8	9	8	9	10	10
	Mean	130,10	107.1	118,22	101,13	109,33	102,10	94,20
	Std.Dev	12,83	13.5	21,45	16,76	13,47	16,45	27,00
	CV%	9,9		18,1	16,6	12,3	16,1	28,7

For BASF 2009 the number of live offspring produced per surviving adult within 21 days of exposure was (5 individuals per replicate):

21,0d	Replicates	control sum	Sum 14.3 µg/L	Control mean value	Mean value 14.3 µg/L
	1	774	860	154.8	172
	2	721	804	144.2	160,8
	3	787	789	157,4	157,8
	4	685	823	171,25	164,6
	#Replicates	4	4	4	4
	Mean			156,9	163,8
	Std.Dev			30,2	

There was a typing error in the CLH report for the reported mean measured concentrations of BASF/ IBACON 2007. The correct ones are: 0.1, 0.43, 1, 3.5, and 15.4 µg/L (arithmetic mean measured, as reported in BASF/IBACON 2007). Normally, in a semi-static test the geometric mean would have to be used resulting in the following concentrations: 0.09, 0.27, 0.85, 2.73, and 8.52 µg/L (geometric mean measured). The two highest test concentrations were analysed. The mean recovery rates from the two highest test concentrations were used for the lower concentrations. The mean of the recovery rates for nominal 100 µg/L are 16 % (arithmetic mean), respectively 9% (geometric mean) and for nominal 32 µg/L is 11% (arithmetic mean), respectively 9% (geometric mean). This resulted in a mean recovery rate of 14%, according to BASF/IBACON 2007 using the arithmetic mean. The mean recovery rate using the geometric mean would be 9%. The range of recovery rates for the highest test concentration was 3 – to 41 % with a nominal concentration of 100 µg/L..

Concerning QSAR predictions, there is no information if the structure falls into the applicability domain. It is difficult to apply reliable QSAR for a chronic toxicity, therefore a QSAR calculation should not replace the result of a valid experimental result.

RAC's response

RAC appreciate the clarification provided by the DS regarding the analysis of the test item concentrations.

QSAR predictions
In the BASF comments on CLH-dossier (BASF, 2018) the QSAR predictions for chronic fish and chronic Daphnia toxicity are provided. The results are presented in ODD. RAC consideres that the QSAR predictions as presented by the company is not well documented and justified (i.e. no detailed assessment of applicability domain and reliability). Based only on prediction results, as provided, it is difficult to assess the reliability and relevance of the predicted chronic values. RAC agrees with DS that QSAR calculations should not replace the results of a valid experimental results.

PUBLIC ATTACHMENTS
1. Public comments Uvinul A Plus.zip [Please refer to comment No. 2]

CONFIDENTIAL ATTACHMENTS
1. Confidential comments Uvinul A Plus.zip [Please refer to comment No. 2]