ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 19 July 2016

Addressee: [redacted]

Decision number: CCH-D-2114339024-59-01/F
Substance name: Exo-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl methacrylate
EC number: 231-403-1
CAS number: 7534-94-3
Registration number: [redacted]
Submission number: [redacted]
Submission date: 09.09.2013

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA requests you to submit information on

1. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2; test method: EU B.31/OECD TG 414) in a first species (rats or rabbits), oral route with the registered substance;**

2. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2; test method: EU B.31./OECD TG 414) in a second species (rats/rabbits), oral route with the registered substance;**

3. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3; test method: OECD TG 443) in rats, oral route, with the registered substance, specified as follows:**
   - **Ten weeks premating exposure duration for the parental (P0) generation;**
   - **Dose level setting shall aim to induce some toxicity at the highest dose level;**
   - **Cohort 1A (Reproductive toxicity);**
   - **Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation;**

4. **Identification of DNEL(s) and risk characterisation (Annex I, Section 1.4. and 6.): use the assessment factors recommended by ECHA and revise the risk characterisation accordingly or provide a detailed justification for not using the recommendations of ECHA Guidance R.8 for DNEL derivation;**

5. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment: use default release factors and revise the risk characterisation accordingly or provide a detailed justification for not using the default release factors, for instance based on risk management measures, operational conditions or substance properties;**

6. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for human health: generate exposure scenarios and exposure assessment for the uses which you have specified for which no exposure assessment for workers has been developed and revise the risk characterisation accordingly.**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **26 July 2019**. You shall also update the chemical safety report, where relevant.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2. Advice and further observations are provided in Appendix 3.

Appeal

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

Authorised[1] by Ofelia Bercaru, Head of Unit, Evaluation E3

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

Appendix 1: Reasons

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

A "pre-natal developmental toxicity study" for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of a pre-natal developmental toxicity study in the dossier that would meet the information requirement of Annex IX, Section 8.7.2.

In the technical dossier you have provided a study record for a "reproduction/ developmental toxicity screening test" (test method: OECD TG 421). However, this study does not provide the information required by Annex IX, Section 8.7.2., because it does not cover key parameters of a pre-natal developmental toxicity study like examinations of foetuses for skeletal and visceral alterations.

Furthermore, you have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation. You have provided four pre-natal developmental toxicity studies made with suggested structural analogues, methyl methacrylate (EC no 201-297-1) and butyl methacrylate (EC no 202-615-1). A reference has also been made to Weight of Evidence (WoE). However, no justification or documentation has been provided for the suggested read-across or WoE. The use of an the adaptation option under Annex XI, 1.5. requires you to justify and document your approach (Annex XI, 1.5. 4th indent, sentence of Annex XI, 1.2., introduction to Annex IX). Consequently the adaptation based on read-across and/or WoE cannot be accepted and there is an information gap for this endpoint.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test method EU B.31/OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default assumption ECHA considers testing should be performed with rats or rabbits as a **first species**.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, July 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a first species (rats or rabbits) by the oral route.

2. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species

Pursuant to Articles 10(a)(vi) and (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

Pre-natal developmental toxicity studies (test method EU B.31./OECD TG 414) on two species are part of the standard information requirements for a substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

The technical dossier does not contain information on a pre-natal developmental toxicity study with the registered substance.

In the technical dossier you have provided a study record for a "reproduction/ developmental toxicity screening test" (test method: OECD TG 421). However, this study does not provide the information required by Annex IX, Section 8.7.2., because it does not cover key parameters of a pre-natal developmental toxicity study like examinations of foetuses for skeletal and visceral alterations.

Furthermore, you have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation. You have provided four pre-natal developmental toxicity studies made with suggested structural analogues, methyl methacrylate (EC no 201-297-1) and butyl methacrylate (EC no 202-615-1). A reference has also been made to Weight of Evidence (WoE). However, no justification or documentation has been provided for the suggested read-across or WoE. The use of an the adaptation option under Annex XI, 1.5. or 1.2. requires you to justify and document your approach (Annex XI, 1.5. 4th indent, last sentence of Annex XI, 1.2., introduction to Annex X). Consequently the adaptation based on read-across and/or WoE cannot be accepted and there is an information gap for this endpoint.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test method EU B.31/OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default consideration, ECHA considers testing should be performed with rabbits or rats as a **second species**, depending on the species tested in the first pre-natal developmental toxicity study.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, July 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a second species (rabbits or rats) by the oral route.

Notes for your consideration

You are reminded that before performing a pre-natal developmental toxicity study in a second species you must consider the specific adaptation possibilities of Annex X, Section 8.7.2., column 2 and general adaptation possibilities of Annex XI. If the results of the test in the first species enable such adaptation, testing in the second species should be omitted and the registration dossier should be updated containing the corresponding adaptation statement.

3. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

The basic test design of an extended one-generation reproductive toxicity study (test method EU B.56./OECD TG 443 with Cohorts 1A and 1B, without extension of Cohort 1B to include a F2 generation, and without Cohorts 2A, 2B and 3) is a standard information requirement as laid down in column 1 of 8.7.3., Annex X. If the conditions described in column 2 of Annex X are met, the study design needs to be expanded to include the extension of Cohort 1B, Cohorts 2A/2B, and/or Cohort 3. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

a) The information requirement

In the technical dossier you have provided a study record for a "reproduction/developmental toxicity screening test" (test method: OECD TG 421). However, this study does not provide the information required by Annex X, Section 8.7.3., because it does not cover key parameters of an extended one-generation reproductive toxicity study. For example, the size of animal groups is 20 animals per dose and sex in the extended one-generation reproductive toxicity study, whereas the group size is 10 animals in the reproduction/developmental toxicity screening test. Furthermore, haematology, urinalysis and clinical chemistry data including TSH and T4, phenotypic analysis of spleen cells and bone marrow cellularity, time to mating, percentage of male pups, sexual maturation of F1 animals, sperm parameters, and data on follicles contained in the ovaries are recorded in an extended one-generation reproductive toxicity study, but are not recorded in the reproduction/developmental toxicity screening test.

Furthermore, you have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation. You have provided a two-generation reproductive toxicity study made with a suggested structural analogue, methyl methacrylate (EC no 201-297-1). However, no justification or documentation has been provided for the suggested read-across. The use of an the adaptation option under Annex XI, 1.5. requires you to justify and document your approach (Annex XI, 1.5. 4th indent, introdcution to Annex X). Consequently, the adaptation based on read-across cannot be accepted.

You have also provided two sub-chronic toxicity studies with a reference to Weight of Evidence. A Weight of Evidence approach pursuant to Annex XI, 1.2. requires that there are several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property. However, the information related to reproductive toxicity, in particular to sexual function and fertility, provided by the reported repeated dose toxicity studies is limited to morphological findings of the gonads and lacks information on effects on functional reproduction such as mating, functional fertility, gestation, parturition, litter data, nursing and sexual development. Because

information on key elements on reproduction is not provided it is not possible to conclude/assume that the registered substance has or has not dangerous properties regarding to reproduction, in particular concerning the hazard "sexual function and fertility".

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

b) The specifications for the study design

Premating exposure duration and dose-level setting

To ensure that the study design adequately addresses the fertility endpoint, the duration of the premating exposure period and the selection of the highest dose level are key aspects to be considered. According to ECHA Guidance, the starting point for deciding on the length of premating exposure period should be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

Ten weeks premating exposure duration is required because there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA Guidance on information requirements and chemical safety assessment R.7a, chapter R.7.6 (version 4.0, July 2015).

Species and route selection

According to the test method EU B.56/ OECD TG 443, the rat is the preferred species. On the basis of this default assumption, ECHA considers that testing should be performed in rats.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, July 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

a) Outcome

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Extended one-generation reproductive toxicity study (test method EU B.56./OECD TG 443), in rats, oral route, according to the following study-design specifications:

- Ten weeks premating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce some toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation;

Notes for your consideration

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3 if new information

becomes available after this decision is issued to justify such an inclusion. Inclusion is justified if the new information shows triggers which are described in column 2 of Section 8.7.3., Annex X and further elaborated in ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 4.0, July 2015). You may also expand the study to address a concern identified during the conduct of the extended one-generation reproduction toxicity study and also due to other scientific reasons in order to avoid a conduct of a new study. The justification for the expansion must be documented. The study design must be justified and, thus, the existence/non-existence of the conditions/triggers must be documented in the dossier.

Concerning the three information requests (points 1-3) as specified above you have proposed the following in your comment to the draft decision: "*Regarding the animal testing requirements, we see the opportunity for an in-depth weight-of-evidence approach, which involves read-across and limits animal testing*". However, you have provided no new studies or data, and no further justification or documentation for a weight of evidence or for a read-across adaptation. Therefore, ECHA has not revised the draft decision.

4. Identification of DNEL(s) and risk characterisation (Annex I, Sections 1.4. and 6.)

Pursuant to Articles 10(b) and 14(1) of the REACH Regulation, the registration shall contain a chemical safety report which shall document the chemical safety assessment conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

Annex I, Section 1.4.1 of the REACH Regulation requires that the following factors shall, among others, be taken into account when deriving DNELs:

- the uncertainty arising, among other factors, from the variability in the experimental information and from intra- and inter-species variation;
- the nature and severity of the effect;
- the sensitivity of the human (sub-)population to which the quantitative and/or qualitative information on exposure applies;
- and that the DNELs reflect the likely route(s), duration and frequency of exposure.

ECHA Guidance on information requirements and chemical safety assessment Chapter R.8 provides further details and specifically provides default factors which should be applied to derive DNELs in the absence of substance specific information to fulfil the REACH obligations. ECHA notes that you derived some of the assessment factors (AF) not in accordance to the default assessment factors recommended in the ECHA Guidance R.8 for DNEL derivation.

You justified the deviations from the default AFs of the DNEL for workers, as follows:

1. Concerning Remaining interspecies differences, you claim that "Methacrylates are metabolised via general metabolic pathways that are common and very similar to rodents and humans and the absence of any specific target organs indicating a specific MOA at high concentrations there is no reason to believe that an additional AF of 2.5 for remaining differences is justified." However, ECHA finds that you have not documented that metabolism in human is similar with that seen in rodents. Therefore, you should apply the AF of 2.5 for the remaining interspecies variation.
2. Concerning Duration: from sub-acute to chronic, you have not justified the deviation from the default AF. Therefore, you should apply the AF of 6.

You have justified the deviations from the default AFs for DNEL for the general population, as follows:

1. Concerning Remaining interspecies differences, you claim that "Methacrylates are metabolised via general metabolic pathways that are common and very similar to rodents and humans and the absence of any specific target organs indicating a specific MOA at high concentrations there is no reason to believe that an additional AF of 2.5 for remaining differences is justified." However, ECHA finds that you have not documented that metabolism in human is similar with that seen in rodents. Therefore, you should apply the AF of 2.5.
2. Concerning Duration: from sub-acute to chronic, you have not justified the deviation from the default AF. Therefore, you should apply the AF of 6.
3. Concerning intraspecies difference, you claim that "*Known mode of action involving ubiquitous and non-specific enzyme systems (initial carboxylesterase cleavage followed by rapid oxidation to carbon dioxide) makes a lower variability likely, hence the AF of 5 by ECETOC (2010) is sufficiently conservative for the general population.*" However ECHA finds that variation of the metabolism can be wide in the general population (e.g. due to the genetic polymorphism) and you have not provided information to show otherwise. Therefore, you should apply the AF of 10.

The following table lists assessment factors (AF) applied in the registration compared to the default factors recommended in ECHA Guidance R.8.

DNEL		AFs applied	ECHA AFs
[Workers/General population], long-term, dermal, systemic effects	interspecies allometric	4	4 (rat to human)
	interspecies remaining	1	2.5
	Intraspecies	3	[5/10]
	exposure duration	2	6 (sub-acute to chronic)
	Quality of the data base	1	1
General population, long-term, oral, systemic effects	interspecies allometric	4	4 (rat to human)
	interspecies remaining	1	2.5
	intraspecies	5	10
	exposure duration	2	6 (sub-acute to chronic)
	Quality of the data base	1	1

Annex I, Section 1.4.1 of the REACH Regulation requires that the likely routes of exposure are reflected in establishing the DNEL(s). In your Chemical Safety Report (CSR) you have reported a DNEL, oral route, which was based on the NOAEL of 25 mg/kg obtained from a reproduction/developmental toxicity screening test (OECD 421). However, you have not obtained a DNEL for the inhalation route. Considering the exposure scenarios given in the CSR, ECHA is of the view that inhalation exposure is possible and furthermore, it was found that the vapor pressure is sufficient to consider volatilization of the substance (7.5 Pa) and even more so when considering Registrant's conclusion on the Henry's constant where he states that the Henry's law constant for the substance "*suggests that volatilization from the water phase is expected to be high*".

Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation you are requested to obtain a DNEL, inhalation route (workers) and apply that in the characterization for the exposure scenarios, where inhalation exposure may occur.

5. Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment

Pursuant to Annex I, Section 5.2.1 of the REACH Regulation the exposure estimation entails three elements: emission estimation, assessment of chemical fate and pathways and estimation of exposure levels. Emission estimation shall be performed under the assumption that the risk management measures (RMMs) and operational conditions (OCs) described in the exposure scenario (ES) have been implemented. These RMMs and OCs should be included in the ESs provided in a CSR.

The registration dossier contains 8 exposure scenarios: ES1: Manufacture of substance, ES2: Use in production of formulations, ES3: End use as monomer in formulations, ES4: Use as intermediate, ES5: End use as monomer in polymerisation (dry process), ES6: End use as monomer in polymerisation (wet process, emulsion polymerisation), ES7: End use as monomer in polymerisation (wet process, bead polymerisation), ES8: Professional end use in formulation.

The release factors you have used, deviation from the factors provided in the ECHA Guidance, justification for the deviating factors you have applied, and the outcome of ECHAs evaluation are detailed below per each relevant factor:

Deviations on the assumed number of release days per year

You have assumed the following values for the number of release days: 300 days/year for ES1, ES5, ES6, ES7 and 200 days/year for ES2, ES3. However, the default number of release days recommended in guidance R.16 (see page 14) are: 100 days/year for ES1, ES2, ES5 and 20 days/year for ES3, ES6, ES7. You state that "release times per year referred to industrial standard of high tonnage production" (for ES1) or "release times per year referred to industrial standard of polymer industry" (for ES2, ES3, ES5, ES6, ES7). However these statements are not substantiated by any factual evidence or actual data.

Deviations on the assumed fraction used at the main source (i.e. annual use at a site)

You have assumed that the amount of substance used in one site and in one year for ES1 and ES4 was [redacted]% of the total registered tonnage. You indicate that "[redacted] tonnes/year is estimated as maximum amount used of generic site" (for ES1 for which total tonnage is [redacted] tonnes/year) or that "[redacted] tonnes/year is estimated as maximum amount used of generic site" (for ES4 for which total tonnage is [redacted] tonnes/year).

ECHA Guidance R.16 (see page 15) recommends that the annual use at a site be set, by default, to 100%. ECHA Guidance R.16 specifies that the default value of 100% for the annual use at a site can be overwritten by a registrant, on the basis of site specific information or of information on the actual amount used by the largest downstream user. However no such information is provided in the dossier.

Deviations on the assumed fraction for the tonnage used in the region

For ES3, ES5, ES6, ES7, you have assumed as tonnage fraction going to the region [redacted]% of the total tonnage, whereas the ECHA Guidance R.16 (see page 16) recommends that the tonnage at the regional level for the industrial settings (i.e. ERC 1-7, 12)) was be set equal to 100% of a registrant's supply volume at EU level. The percentage of [redacted]% should normally only apply for wide dispersive uses. ES3, ES5, ES6, ES7 are only concerning industrial settings, not wide dispersive uses and therefore the value of [redacted]% should not be

applied. You have not provided a justification for this deviation for any of the respective exposure scenarios.

Deviations on the release factors

ECHA notes that you have used release factors that deviate from those recommended in guidance R.16, as follows:

- the numbers of release days per year for ES1, ES2, ES3, ES5, ES6 and ES7;
- the fraction used at main source (*i.e.* annual use at a site) for ES1 and ES4;
- the fraction tonnage to region for ES3, ES5, ES6 and ES7
- the release factors applied for ES1 (to waste water), ES3 (to air), ES4 (to waste water), ES6 (to waste water), and ES7 (to waste water)

For ES3, you have used a release factor of [redacted]% to air (default recommended in guidance R.16 is 50%) by making reference to SpERC FEICA7. According to the FEICA website, SpERC FEICA 7 is defined as applicable for "Industrial Use of Substances other than Solvents in Transportation (Automotive/aircraft/rail vehicles) / industrial Building Construction Adhesives". However, you have not provided any explanation why SpERC FEICA 7 would be relevant for exposure scenario ES3 (defined as "End use as monomer in formulations").

For ES1, ES4, and ES7 you have used a release factor of [redacted]% to waste water indicating that because the value of the water solubility of IBOMA is estimated of being ca. 5 mg/L (i.e. 5 ppm), the maximum residual concentration in releases to waste water cannot theoretically exceed that concentration of 5 ppm. ECHA notes that your assumption would not be valid if the release water contained suspended matter, onto which the registered substance could have adsorbed or the substance could be suspended on its own. Moreover, other substances present in the release water could modify the actual solubility of the registered substance in the effluent. From the available information in the dossier (including attached documents) it is not clear whether suspended particulate matter (SPM) is eliminated from the released water (e.g. by filtration or sedimentation?) for ES1, ES4 and ES7. ECHA notes that 5 ppm would translate into a value of [redacted]% and not [redacted]%. ECHA considers that the justification for the release factor of [redacted]% is contradicting standard mathematics and insufficiently justified with regard to the potential role of SPM and others substance in the effluent.

For ES6 you have used a release factor of [redacted]% to waste water indicating that this release factor was estimated based on data of wet polymerisation process. Attached to the IUCLID dossier, you have provided a document ("Supporting file regarding environmental assessment - wet polymerisation"). However ECHA notes that this document does not refer to the registered substance but to another substance (MMA). It is not clear why the information provided for MMA should be considered relevant for the substance subject to this decision.

Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation you are requested to revise the exposure assessment and the risk characterisation using the default assumptions for the number of release days, fraction used at main source, fraction tonnage to region, and release factors and to revise the risk characterisation accordingly **or** to provide a detailed justification for not using the default assumptions, for instance based on risk management measures , operational conditions, substance properties, or site specific information.

Note for your consideration

Please note that ECHA Guidance R.16 has been revised recently (version 3.0, released in February 2016). In particular, the default release factors recommended for ERC 8C and ERC 8F have been amended. More specifically, ECHA notes that for exposure scenario ES8, you have applied a release factor to water of [redacted]%, in line with the recommendations of Guidance R.16 version 2.1. however, version 3.0 of ECHA Guidance recommends a release factor to water of 5% for ERC 8F. You should take these new recommendations into account when updating your dossier.

6. Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for human health

Annex I, Section 5. of the REACH Regulation requires a registrant to generate exposure scenarios and exposure estimations for the registered substance. The exposure assessment shall consider all stages of the life-cycle of the substance resulting from the manufacture and identified uses and shall cover any exposures that may relate to the identified hazards.

In the regisrtration dossier, you have identified the following Exposure scenarios:

- M-1: 1: Manufacture
- F-2: 2: Use in production of formulations
- IW-4:4: Use as intermediate
- IW-6: 6: End use as monomer in polymerisation (wet process)
- IW-5: 5: End use as monomer in polymerisation (dry process)
- IW-7: 7: End use as a monomer in polymerisation (wet process, bead polymerisation)
- IW3: 3: End use as monomer in formulations
- PW-8: 8: Professional end use in formulations

However, you have not provided assessment of worker exposure in these scenarios.
You have provided the following justification: "*As no human health hazard has been identified no worker-related exposure assessment and risk characterization was performed.*"
Since there were relevant histopathological findings in the parental animals in the OECD 421 screening study at 100 mg/kg (biliary proliferation/hypertrophy associated with fibrosis in liver and acidophilic globules in kidneys) and at 500 mg/kg (necrosis in the parenchyma in liver), ECHA does not agree with your opinion that no health hazard was identified.
Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to provide a exposure assessment for workers demonstrating the likelihood that health effects are avoided for the identified uses and to detail the appropriate operational conditions and risk management measures and revise the risk characterisation accordingly.

Appendix 2: Procedural history

ECHA notes that the tonnage band for one member of the joint submission is 1000 tonnes or more per year.

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 15 October 2015.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

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

ECHA took into account your comments and did not amend the request(s).

ECHA notified the draft decision to the competent authorities of the Member States for proposal(s) for amendment.

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

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

ECHA referred the draft decision to the Member State Committee.

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

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-48 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This compliance check decision does not prevent ECHA from initiating further compliance checks on the present registration at a later stage.

2. Failure to comply with the request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In relation to the information required by the present decision, the sample of substance used for the new test(s) must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance composition manufactured or imported by the joint registrants. It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of substance tested in the new test(s) is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new test(s) must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.