~~Confidential~~

Helsinki, 4 May 2022

Addressees
Registrant(s) of 4-methylbenzophenone as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
17/03/2020

Registered substance subject to this decision ("the Substance")
Substance name: 4-methylbenzophenone
EC number: 205-159-1

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***11 May 2023***.

Requested information must be generated using the Substance unless otherwise specified.

Information required from all the Registrants subject to Annex VII of REACH

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: OECD TG 471, 2020);

2. Skin sensitisation (Annex VII, Section 8.3.; test methods):
   i) *In vitro/in chemico* skin sensitisation information on molecular interaction with skin proteins and inflammatory response in keratinocytes and activation of dendritic cells (OECD TG 442C and OECD TG 442D and EU B.71/OECD TG 442E); and
   ii) Only in case no conclusion on the skin sensitisation potency can be made for the Substance based on the newly generated in vitro/in chemico data, in vivo skin sensitisation study must be performed and the murine local lymph node assay (EU Method B.42/OECD TG 429) is considered as the appropriate study for the potency estimation.

3. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: EU C.2./OECD TG 202);

4. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3./OECD TG 201);

Information required from all the Registrants subject to Annex VIII of REACH

5. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487);

6. If negative results are obtained in the test performed for the information requirement of Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490);

7. Short-term repeated dose toxicity (28 days; Annex VIII, Section 8.6.1.) to be combined with the Screening for reproductive/developmental toxicity below;

8. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.64/OECD TG 422) by oral route, in rats;

9. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: EU C.1./OECD TG 203).

The reasons for the decision(s) are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

How to comply with your information requirements

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also **update the chemical safety report, where** relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general requirements for testing and reporting new tests under REACH, see Appendix 4.

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of -Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the decision
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[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 for the decision

Contents

0. Reasons common to several requests

0.1. Assessment of the read-across approach

1 You have adapted the following standard information requirements by using grouping and read-across approach under Annex XI, Section 1.5:

- Skin sensitisation (Annex VII, Section 8.3.)
- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

2 ECHA has considered the scientific and regulatory validity of your read-across approach(es) in general before assessing the specific standard information requirements in the following sections.

3 Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group.

4 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

0.1.1. Predictions for (eco)toxicological properties

5 You have provided a justification for the read-across under the respective endpoint study records in IUCLID.

6 You predict the properties of the Substance from information obtained from the following source substance: benzophenone, EC No. 204-337-6.

7 You provide the following reasoning for the prediction of (eco)toxicological properties:”M*uch more information is available on benzophenone, a substance with a closely related chemical structure. 4-Methylbenzophenone and benzophenone are aromatic ketones with a comparable molecular weight (196 or 182 g/mol, respectively). Both substances share a conjugated structure, with a carbonyl group bridging two phenyl rings. The only difference is an additional methyl group in 4-Methylbenzophenone. 4-Methylbenzophenone is expected to be metabolised by the same metabolic pathways as benzophenone, with the addition of oxidation of the 4-methyl group to the corresponding alcohol and further oxidation to the carboxylic acid with its glycine and glucuronide conjugates. From these considerations, it is very likely that 4-methylbenzophenone will also exhibit very similar effects as benzophenone*”.

8 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

9 We have identified the following issue(s) with the prediction(s) of toxicological properties:

0.1.1.1. Missing supporting information

10 Annex XI, Section 1.5 of the REACH Regulation states that "physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)". For this purpose "it is important to provide supporting information to strengthen the rationale for the read-across" (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.). The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

11 Supporting information must include bridging studies to compare properties of the Substance and source substances.

12 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm that both substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

13 You have not provided bridging studies to compare the properties of the Substance and the source substance. In the absence of such information, you have not established that the Substance and the source substances are likely to have similar properties.

14 Furthermore, ECHA notes that the source substance has hazardous properties as identified in the Committee for Risk Assessment Opinon proposing harmonised classification and labelling at EU level of Benzophenone (EC 204-337-6)[2]. Due to the lack of supporting information on the Substance, it is not possible to determine if other and/or more severe effects would be observed with the Substance, and your predictions may underestimate the hazards of the Substance. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

0.1.1.2. Adequacy and reliability of source studies

15 According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must:

a. be adequate for the purpose of classification and labelling and/or risk assessment;

b. have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3);

c. cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

16 Specific reasons why the studies on the source substance do not meet these criteria are explained further below under the applicable information requirement sections 1.2.1.1, 1.2.1.2, 2.2.1.1, 4.2.1.1, 5.2.1.2 and 6.2.1.1. Therefore, no reliable predictions can be made for these information requirements.

0.1.2. Conclusion on the read-*across approach*

[2] Committee for Risk Assessment, RAC. Opinion proposing harmonised classification and labelling at EU level of Benzophenone. EC Number: 204-337-6; CAS Number: 119-61-9. CLH-O-0000006808-62-01/F. Adopted 11 June 2020

17 For the reasons above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Your read-across approach under Annex XI, Section 1.5. is rejected.

Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

18 Skin sensitisation is an information requirement under Annex VII to REACH (Section 8.3.). Under Section 8.3., Column 1, the registrants must submit information allowing (1) A) a conclusion whether the substance is a skin sensitiser and B) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A), and (2) risk assessment, where required.

1.1. Information provided

19 You have adapted this information requirement by using a Grouping of substances and read-across approach based on the following experimental data from the source substance benzophenone, EC No. 204-337-6:

(i) Modified Draize test in guinea pigs, similar to OECD TG 406 (Sharp et al., 1978);

(ii) Guinea pig maximisation test, similar to OECD TG 406 (Calas et al., 1977);

(iii) Human patch test (Opdyke, 1979).

1.2. Assessment of the information provided

20 We have assessed this information and identified the following issue(s):

1.2.1. Read-across adaptation rejected

21 As explained in Sections 0.1.1.1 and 0.1.1.2, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint-specific issue(s) addressed below.

1.2.1.1. Adequacy and reliability of studies on the source substance

22 As explained in the Appendix on Reasons common to several requests, under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 406. Therefore, the following specifications must be met:

a. Dose level selection rationale;
b. The induction concentration should be the highest causing mild-to-moderate irritation to the skin and the challenge dose should be the highest non-irritation concentration (GPMT: OECD TG 406, paragraph 14);
c. Positive and negative controls to establish the sensitivity and reliability of the experimental technique (OECD TG 406, paragraph 11).

23 However, ECHA notes that in the provided studies (i and ii):

- No dose level selection rationale was provided;
- The concentration used for induction did not cause mild-to-moderate irritation;
- No information on positive and negative controls was provided.

24 Therefore, the studies (i and ii) submitted in your adaptation, as currently reported in your dossier, do not provide an adequate and reliable coverage of the key parameter(s) of the corresponding OECD TG.

1.2.1.2. Adequacy of the study for hazard identification

25 As explained in the Appendix on Reasons common to several requests, under Annex XI, Section 1.5., the results to be read across must be adequate for the purpose of classification and labelling and/or risk assessment. The ECHA Guidance defines adequacy as "the usefulness of data for hazard/risk assessment purposes".

26 Study (iii) appears to have been conducted on humans for the purpose of risk assessment and with the objective of identification of safe levels for specific intended uses such as fragrances, as it is specified in the title 'Monographs on fragrance raw materials'.

27 Whilst the study appears to have been designed to establish safe levels for specific intended uses, it does not investigate the intrinsic properties of the Substance as required for the purpose of hazard identification. The study has to meet the general requirements for human studies[3]. Among others, the key parameters for these studies include:

- Information on the test protocol used (study design, controls);
- Information on the extent of exposure (dose per square centimetre or concentration, frequency and duration);
- Information on the presence of interfering factors (e.g. pre-existing dermal health effects, medication, presence of other skin sensitisers); and
- Information on the health status of the exposed volunteers (the healthy worker effect).

28 Information as specified above was not provided. Therefore, the study does not allow to make a conclusion whether the source substance causes skin sensitisation.

29 Therefore, study (iii) does not provide information on the intrinsic properties of the substance and does not allow to make a conclusion whether the Substance causes skin sensitisation. As a conclusion, it is not adequate for the purpose of classification and labelling.

30 On this basis, the information requirement is not fulfilled.

1.3. Specification of the study design

31 To fulfil the information requirement for the Substance, information on molecular interaction with skin proteins and inflammatory response in keratinocytes and activation of dendritic cells (OECD TG 442C and OECD TG 442D and EU B.71/OECD TG 442E) must be provided. Furthermore an appropriate risk assessment is required as a result of the classification of the Substance as a skin sensitiser (Cat 1A or 1B).

32 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the newly generated in vitro/in chemico data, in vivo skin sensitisation study must be performed and the murine local lymph node assay (EU Method B.42/OECD TG 429) is considered as the appropriate study for the potency estimation.

2. In vitro gene mutation study in bacteria

33 An in vitro gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

2.1. Information provided

34 You have adapted this information requirement by using a Grouping of substances and read-across approach based on the following experimental data from the source substance benzophenone, EC No. 204-337-6:

[3] ECHA Guidance R.7a

(i) *In vitro* gene mutation study in bacteria, similar to OECD TG 471 (Mortelmans et al., 1986);

(ii) *In vitro* gene mutation study in bacteria, similar to OECD TG 471 (Seifried et al., 2006);

(iii) *In vitro* gene mutation study in bacteria (Martinez et al., 2000);

(iv) *In vitro* DNA damage and repair study in bacteria (Fluck et al., 1976).

2.2. Assessment of the information provided

35 We have assessed this information and identified the following issue(s):

2.2.1. Read-across adaptation rejected

36 As explained in Sections 0.1.1.1 and 0.1.1.2, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint-specific issue(s) addressed below.

2.2.1.1. Adequacy and reliability of studies on the source substance

37 As explained in the Appendix on Reasons common to several requests, under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 471 (2020). Therefore, the following specifications must be met:

a) The test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101)
b) Triplicate plating must be used at each dose level.
c) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.
d) The mean number of revertant colonies per plate must be reported for the treated doses and controls.

38 Studies (i)-(iv) are described as in vitro gene mutation tests in bacteria. However, the studies have the following deficiencies in comparison to the requirements of OECD TG 471 (2020):

a) No results for the appropriate 5 strains, that is in TA98/TA100/TA1535/TA1537 or TA97a or TA97/the required fifth strain, *S. tyhimurium* TA102 or *E. coli* WP2 uvrA (pKM101) (studies i, ii).
b) No triplicate plating at each dose level (studies i, iii,).
c) Not clearly specified which positive control was used (studies ii, iii).
d) No data on the number of revertant colonies per plate for the treated doses and the controls (studies ii, iii).

39 Study (iv) is an *in vitro* DNA damage and repair study in the *E. coli* PolA+ and PolA− (DNA polymerase-deficient) strains. This test provides an indication of induced damage to DNA, but does not show direct evidence of gene mutation. Therefore, study (iv) does not provide relevant information for this endpoint.

40 Therefore, the studies (i)-(iv) submitted in your adaptation, as currently reported in your dossier, do not provide an adequate and reliable coverage of the key parameters of the corresponding OECD TG.

41 On this basis, the information requirement is not fulfilled.

2.3. Specification of the study design

42 To fulfil the information requirement for the Substance, the in vitro gene mutation study in bacteria (OECD TG 471, 2020) is considered suitable.

3. Short-term toxicity testing on aquatic invertebrates

43 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.).

3.1. Information provided

44 You have adapted this information requirement by using a Grouping of substances and read-across approach based on the following experimental data from the source substance benzophenone, EC No. 204-337-6:

(i) a key study according to the OECD TG 202 ([redacted], 2011).

3.2. Assessment of the information provided

45 We have assessed this information and identified the following issue:

3.2.1. Read-across adaptation rejected

46 As explained in Sections 0.1.1.1 and 0.1.1.2, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

47 On this basis, the information requirement is not fulfilled.

4. Growth inhibition study aquatic plants

48 Growth inhibition study on aquatic plants is an information requirement under Annex VII to REACH (Section 9.1.2.).

4.1. Information provided

49 You have adapted this information requirement by using a Grouping of substances and read-across approach based on the following experimental data from the source substance benzophenone, EC No. 204-337-6:

(i) a key study according to the OECD TG 201 (Peer reviewed database, [redacted] 2010).

4.2. Assessment of the information provided

50 We have assessed this information and identified the following issue:

4.2.1. Read-across adaptation rejected

51 As explained in Section 0.1.1.1 and 0.1.1.2, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint-specific issue(s) addressed below.

52 As explained in the Appendix on Reasons common to several requests, under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

4.2.1.1. Study not adequate for the information requirement

53 To fulfil the information requirement, the study must meet the requirements of the OECD TG 201. Therefore, the following specifications must be met:

a) analytical monitoring must be conducted. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;
b) sthe test design is reported (*e.g.*, number of replicates, number of test concentrations and geometric progression used);
c) the test conditions are reported (*e.g.*, composition of the test medium, test temperature, test species, biomass density at the beginning of the test);
d) the method for determination of biomass and evidence of correlation between the measured parameter and dry weight are reported.
e) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form.

54 Your registration dossier provides an OECD TG 201 study showing the following:

a) no analytical monitoring of exposure was conducted.
b) on the test design, you have not specified the number of replicates, number of test concentrations, or geometric progression used;
c) on the test conditions, you have not specified the composition of the test medium, test temperature, or biomass density at the beginning of the test;
d) the method used to determine algal biomass is not reported;
e) tabulated data on the algal biomass determined daily for each treatment group and control are not reported.

55 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, no information on test design, test conditions, method used to determine algae biomass or data on determined algal biomass were provided. Furthermore, no analytical monitoring nor justification for technical feasibility were provided. On this basis, an independent assessment of the reliability of the study is not possible. Therefore, the requirements of the OECD TG 201 are not met.

Reasons related to the information under Annex VIII of REACH

5. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

56 An in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

5.1. Information provided

57 You have adapted this information requirement by using Column 2 of Annex VIII, Section 8.4.2. To support the adaptation, you have provided following information:

(i) Summary of justification: an *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is not scientifically necessary because an *in vivo* cytogenicity study is available.

(ii) *In vivo* mammalian somatic cell study: micronucleus assay (Zetterberg and Svensson, 2011), with the source substance, benzophenone, EC No. 204-337-6.

(iii) *In vivo* mammalian erythrocyte micronucleus test, according to OECD TG 474 ([redacted] 2000), with the source substance, benzophenone, EC No. 204-337-6.

5.2. Assessment of the information provided

58 We have assessed this information and identified the following issue(s):

5.2.1. Column 2 adaptation criteria not met

59 Under Section 8.4.2., column 2 of Annex VIII to REACH, the study usually does not need to be conducted "if adequate data from an in vivo cytogenicity test are available". The Guidance on IRs and CSA, Section R.7.7.6.3 and Table R.7.7–3 clarifies that the *in vivo* somatic cell cytogenicity test must be either a micronucleus test or a chromosomal aberration test, performed according to OECD TG 474 or 475, respectively.

5.2.1.1. Read-across adaptation rejected

60 As explained in Sections 0.1.1.1 and 0.1.1.2, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint-specific issue(s) addressed below.

5.2.1.2. Adequacy and reliability of studies on the source substance

61 As explained in the Appendix on Reasons common to several requests, under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 474 (2020). Therefore, the following specifications must be met:

a) Each group must have a minimum of 5 analysable animals (the test can be performed in either sex).
b) The proportion of immature erythrocytes among total erythrocytes and the mean number of micronucleated immature erythrocytes must be reported for each group of animals.
c) In order to provide a clear negative outcome, the data available must show that "*bone marrow exposure to the test Substance occurred*".

62 Study (ii) is described as an in vivo micronucleus test. However, the study has the following deficiencies in comparison to the requirements of the OECD TG 474:

a) Less than 5 animals per group were used
b) No data on the proportion of immature erythrocytes among total erythrocytes and the mean number of micronucleated immature erythrocytes for each group of animals
c) No demonstration of the systemic or target tissue (bone marrow) exposure to the source substance or its metabolites.

63 Therefore, the study (ii) submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameters of the corresponding OECD TG.

64 On this basis, the information requirement is not fulfilled.

5.3. Specification of the study design

65 To fulfil the information requirement for the Substance, the in vitro cytogenicity study in mammalian cells (OECD TG 473, 2016) or the in vitro micronucleus study (OECD TG 487, 2016) are considered suitable.

6. In vitro gene mutation study in mammalian cells

66 An in vitro gene mutation study in mammalian cells is an information requirement under Annex VIII to REACH (Section 8.4.3.) in case of a negative result in the in vitro gene mutation test in bacteria and the in vitro cytogenicity test.

67 The result of the request for information in Sections 2 and 5 will determine whether the present requirement for an in vitro mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

~~68~~ Consequently, you are required to provide information for this endpoint, if the *in vitro* gene mutation study in bacteria, the *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study provide a negative result.

6.1. Information provided

69 You have adapted this information requirement by using a Grouping of substances and read-across approach based on the following experimental data from the source substance benzophenone, EC No. 204-337-6:

(i) *In vitro* mammalian cell gene mutation, similar to the OECD TG 476 (Seifried et al., 2006).

6.2. Assessment of the information provided

70 We have assessed this information and identified the following issue(s):

6.2.1. Read-across adaptation rejected

71 As explained in Sections 0.1.1.1 and 0.1.1.2, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint-specific issue(s) addressed below.

6.2.1.1. Adequacy and reliability of studies on the source substance

72 To fulfil the information requirement, the study must meet the requirements of the OECD TG 476 or OECD TG 490 (Guidance on IRs and CSA, Table.7.7-2). Therefore, the following specifications must be:

a) At least 4 concentrations must be evaluated, in each test condition.
b) The response for the concurrent negative control must be inside the historical control range of the laboratory.
c) Data on the cytotoxicity and the mutation frequency for the treated and control cultures must be reported.

73 The study (i) is described as an in vitro mammalian cell gene mutation test. However, the study has the following deficiencies in comparison to the requirements of OECD TG 476:

a) Not clearly stated if at least 4 concentrations were evaluated in each test condition.
b) Not stated if a negative control with a response inside the historical control range of the laboratory was used.
c) No data on the cytotoxicity and the mutation frequency for the treated and control cultures.

74 The information provided does not cover key parameters required by OECD TG 476.

75 Therefore, the information requirement is not fulfilled.

6.3. Specification of the study design

76 To fulfil the information requirement for the Substance, either the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

7. Short-term repeated dose toxicity (28 days)

77 A short-term repeated dose toxicity study (28 days) is an information requirement under Annex VIII to REACH (Section 8.6.1.).

7.1. Information provided

78 You have adapted this information requirement by using a Grouping of substances and read-across approach based on the following experimental data from the source substance benzophenone, EC No. 204-337-6:

(i) Repeated dose toxicity study in rats, similar to OECD TG 408 ([redacted] 2000);
(ii) Repeated dose toxicity study in mice, similar to OECD TG 408 ([redacted] 2000);
(iii) Repeated dose toxicity study in rats, similar to OECD TG 408 (Burdock et al., 1991).

7.2. Assessment of the information provided

79 We have assessed this information and identified the following issue(s):

7.2.1. Read-across adaptation rejected

80 As explained in Sections 0.1.1.1 and 0.1.1.2, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

81 On this basis, the information requirement is not fulfilled.

7.3. Specification of the study design

82 When there is no information available neither for the 28-day repeated dose toxicity endpoint (OECD TG 407), nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to

ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG 407, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, 8.6.1 and that of REACH Annex VIII, 8.7.1. (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

83 Therefore, a study according to the test method EU B.64/OECD TG 422 must be performed in rats with oral administration of the Substance.

8. Screening for reproductive/developmental toxicity

84 A screening for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII to REACH (Section 8.7.1.), if there is no evidence from analogue substances, QSAR or *in vitro* methods that the substance may be a developmental toxicant.

8.1. Information provided

85 You have adapted this information requirement by using a Grouping of substances and read-across approach based on the following experimental data from the source substance benzophenone, EC No. 204-337-6:

(i) A two-generation study according to the OECD TG 416 (Hoshino, 2005).

8.2. Assessment of the information provided

86 We have assessed this information and identified the following issue(s):

8.2.1. Read-across adaptation rejected

87 As explained in Sections 0.1.1.1 and 0.1.1.2, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

88 On this basis, the information requirement is not fulfilled.

8.3. Specification of the study design

89 When there is no information available neither for the 28-day repeated dose toxicity endpoint (OECD TG 407), nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG 407, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, 8.6.1 and that of REACH Annex VIII, 8.7.1. (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

90 Therefore, a study according to the test method EU B.64/OECD TG 422 must be performed in rats with oral administration of the Substance.

9. Short-term toxicity testing on fish

91 Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.).

9.1. Information provided

92 You have adapted this information requirement by using a Grouping of substances and read-across approach based on the following experimental data from the source substance benzophenone, EC No. 204-337-6:

(i) OECD TG 203 key study ([redacted] 1984);

(ii) A non-guideline supporting study (Marchini S, Tosato M, Norberg-King TJ, Hammermeister DE and Hoglund MDAuthor, 1992);

(iii) OECD TG 203 supporting study (Peer reviewed database, [redacted] 2010).

9.2. Assessment of the information provided

93 We have assessed this information and identified the following issue(s):

9.2.1. Read-across adaptation rejected

94 As explained in Sections 0.1.1.1 and 0.1.1.2, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

95 On this basis, the information requirement is not fulfilled.

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; (ECHA 2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).

All Guidance on REACH is available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

RAAF, 2017 Read-across assessment framework (RAAF), ECHA (2017)
RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs), ECHA (2017).

The RAAF and related documents are available online: https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

***OECD Guidance documents* (OECD GDs)**

OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: Procedure

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

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 02 September 2021.

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

ECHA did not receive any comments within the commenting period.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix 3: Addressees of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1. Test methods, GLP requirements and reporting

(1) Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

(2) Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

(3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[4].

1.2. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

(1) Selection of the Test material(s)
The Test Material used to generate the new data must be selected taking into account the following:
- the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

(2) Information on the Test Material needed in the updated dossier
- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[5].

[4] https://echa.europa.eu/practical-guides
[5] https://echa.europa.eu/manuals