Helsinki, 19 January 2024

Addressee(s)
Registrant(s) of JS_Furfurylalcohol as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
24 May 2016

Registered substance subject to this decision ("the Substance")
Substance name: furfuryl alcohol
EC/List number: 202-626-1

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 ***25 October 2027***.

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

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

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

2. Growth inhibition study on 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

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

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

4. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211).

5. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210).

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

6. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) by oral route, in a second species (rabbit).

7. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route, specified as follows:
    - Ten weeks premating exposure duration for the parental (P0) generation;
    - The highest dose level in P0 animals must be determined based on clear evidence of an adverse effect on sexual function and fertility without severe suffering or deaths in P0 animals as specified in request 9.3, or follow the

limit dose concept. The reporting of the study must provide the justification for the setting of the dose levels;
- Cohort 1A (Reproductive toxicity); and
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation.

You must report the study performed according to the above specifications. Any expansion of the study must be scientifically justified.

The reasons for the request(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 request(s)
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 request(s)

Reasons common to several requests

0.1. QSAR adaptation rejected

1 You seek to adapt the following standard information requirements by applying a (Q)SAR approach in accordance with Annex XI, Section 1.3.:

- 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 to fish (Annex VIII, Section 9.1.3.)

2 ECHA has considered the scientific and regulatory validity of your (Q)SAR adaptation in general before assessing the specific standard information requirements in the following appendices.

3 Under Annex XI, Section 1.3., the following conditions must be fulfilled whenever a (Q)SAR approach is used:

(1) the prediction needs to be derived from a scientifically valid model,

(2) the substance must fall within the applicability domain of the model,

(3) results need to be adequate for the purpose of risk assessment or classification and labelling, and

(4) adequate and reliable documentation of the method must be provided.

0.1.1. Inappropriate measures of robustness of the model

4 The Guidance on IRs and CSA R.6.1.3. states that for (Q)SAR models, to be scientifically valid, i.e. condition (1), they must fulfil the principles listed in the OECD Principles for (Q)SAR validation (ENV/JM/MONO(2007)2). The fourth of these principles requires that a model has appropriate measures of the internal performance (i.e. goodness-of-fit and robustness) and predictivity.

5 A model is considered robust when it is built from a training set which includes a sufficient number of substances. The minimum number of substances depends on the number of variables or descriptors included in the model. The ratio between the number of substances and the number of variables or descriptors must be at least 5.

6 The training set of your model is based on less than five chemicals.

7 Since the ratio between the number of substances and the number of variables or descriptors is less than five, you have not established the robustness, and thus the scientific validity, of the model.

8 Additional issues related to (Q)SAR are addressed request 4.

0.1.2. Conclusion

9 Based on the above, your (Q)SAR adaptations under Annex XI, Section 1.3. is rejected.

Reasons related to the information under Annex VII of REACH

1. Short-term toxicity testing on aquatic invertebrates

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

1.1. Information provided

11 You have provided:

(i) a short-term toxicity study on daphnia magna (1982) with the Substance;

12 In addition, you have adapted this information requirement by using Annex XI, Section 1.3. (Qualitative or Quantitative Structure-Activity Relationships ((Q)SARs). To support the adaptation, you have provided the following information:

(ii) a prediction from QSAR ECOSAR-US EPA (2000).

1.2. Assessment of the information provided

1.2.1. The provided study does not meet the specifications of the test guideline(s)

13 To fulfil the information requirement, a study must comply with OECD TG 202 (Article 13(3) of REACH). Therefore, the following specifications must be met:

Technical specifications impacting the sensitivity/reliability of the test

a) the test duration is 48 hours or longer.

Characterisation of exposure

b) analytical monitoring must be conducted. A reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available;

c) the concentrations of the test material are measured at least at the highest and lowest test concentration, at the beginning and end of the test;

d) the effect values can only be based on nominal or measured initial concentration if the concentration of the test material has been satisfactorily maintained within 20 % of the nominal or measured initial concentration throughout the test (see also Guidance on IRs and CSA, Section R.7.8.4.1).

14 In study (i):

Technical specifications impacting the sensitivity/reliability of the test

a) the test duration was 24 hours.

Characterisation of exposure

b) no analytical monitoring of exposure was conducted;

c) the concentration of the test material was not determined during the test;

d) the reported effect values are based on nominal concentrations. However, you have not provided any evidence that confirm that the concentration of the test substance has been satisfactorily maintained within ± 20 % of the nominal or measured initial concentration.

15 Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically the test duration of study (i) was shorter than that prescribed by the OECD TG 202 and the exposure concentrations were not measured. Both deviations may have resulted in the underestimation of the measured toxicity of the substance.

16 On this basis, the specifications of the OECD TG 202 are not met.

1.2.2. (Q)SAR adaptation rejected

17 As explained in Section 0.1., your adaptation based on Qualitative or Quantitative Structure-Activity Relationships ((Q)SARs) under Annex XI, Section 1.3. is rejected.

18 Therefore, the information requirement is not fulfilled.

19 In the comments on the draft decision you agree that further aquatic toxicity testing may be needed. You do not agree that both short- and long-term testing on aquatic invertebrates and fish are needed. Instead of performing a new OECD TG 202 study, you propose to perform the requested long-term toxicity study on aquatic invertebrates (OECD TG 211) (request 4) in order to adapt this information requirement.

20 Annex VII, Section 9.1.1, Column 2 specifies that the short-term toxicity study does not need to be conducted if a long-term aquatic toxicity study on invertebrates is available.

21 At present no long-term toxicity study on aquatic invertebrates is provided in the IUCLID dossier, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

1.3. Study design

22 The Substance is difficult to test due to the volatility of the substance (vapour pressure = 53 Pa). OECD TG 202 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 202. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

2. Growth inhibition study aquatic plants

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

2.1. Information provided

24 You have provided:

(i) Growth inhibition key study on aquatic plants/algae (1980) with the Substance;

25 In addition, you have adapted this information requirement by using Annex XI, Section 1.3. (Qualitative or Quantitative Structure-Activity Relationships ((Q)SARs). To support the adaptation, you have provided the following information:

(ii) a supporting prediction from QSAR ECOSAR-US EPA (2000).

2.2. Assessment of the information provided

2.2.1. The provided study does not meet the specifications of the test guideline(s)

26 To fulfil the information requirement, a study must comply with the OECD TG 201 and the specifications of the OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

Key parameter measured

a) the concentrations of the test material leading to a 50 % and 0% (or 10%) inhibition of growth at the end of the test are estimated. Growth must be expressed as the logarithmic increase in biomass (average specific growth rate) during the exposure period.

Technical specifications impacting the sensitivity/reliability of the test

b) the test duration is 72 hours. However for slow-growing species (i.e. specific growth rate < 0.92 day-1 in the control), the test duration must be extended until the biomass in the control cultures increases by at least 16-fold.

Characterisation of exposure

c) analytical monitoring must be conducted. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;

d) for some substances (*e.g.* adsorbing substances), the results may only be expressed based on nominal concentrations if the decrease in measured concentrations of the test substance during the test is not accompanied by a decrease in growth inhibition. If a reduction in growth inhibition is observed, a suitable model describing the decline of the concentration of the test material must be used.

Reporting of the methodology and results

e) the test design is reported (*e.g.*, number of replicates, number of test concentrations and geometric progression used);

f) the test conditions are reported (*e.g.*, composition of the test medium, test temperature, test species, biomass density at the beginning of the test);

g) the method for determination of biomass and evidence of correlation between the measured parameter and dry weight are reported. Algal biomass is normally determined based on dry weight per volume, or alternatively as cell counts or biovolume using microscopy or an electric particle counter. If an alternative method is used (e.g. flow cytometry, *in vitro* or *in vivo* fluorescence, or optical density), a satisfactory correlation with biomass must be demonstrated over the range of biomass occurring in the test;

h) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;

i) microscopic observation performed to verify a normal and healthy appearance of the inoculum culture are reported. Any abnormal appearance of the algae at the end of the test is reported.

27 In study (i):

Key parameter measured

a) the concentrations of the test material leading to a 50 % and 0% (or 10%) inhibition of growth at the end of the test were not estimated. The key parameter was reported to be the concentration where the substance had an effect ≥3%. In addition, this endpoint was based on cell number instead of growth rate.

Technical specifications impacting the sensitivity/reliability of the test

b) the test duration was 7 days. However *Scenedesmus quadricauda* is not a slow-growing species (i.e. specific growth rate < 0.92 day-1 in the control). You have not justified why the test duration had to be extended.

Characterisation of exposure

c) no analytical monitoring of exposure was conducted;

d) the reported effect values are based on nominal concentrations. However, you have not provided any evidence that confirm that the concentration of the test substance has been satisfactorily maintained within ± 20 % of the nominal or measured initial concentration;

Reporting of the methodology and results

e) to i) above. You have not provided any of the information listed under these points.

28 Based on the above, the key parameter of the OECD TG 201 is not covered.

29 Furthermore, there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, the analytical monitoring of exposure was not conducted. In addition, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, you have not reported key pieces of information (e.g. the results of algal biomass determined in each flask at least daily during the test period) that are relevant to the validity of the study On this basis, the specifications of the OECD TG 201 are not met.

2.2.2. (Q)SAR adaptation rejected

30 As explained in Section 0.1., your adaptation based on Qualitative or Quantitative Structure-Activity Relationships ((Q)SARs) under Annex XI, Section 1.3. is rejected.

31 Therefore, the information requirement is not fulfilled.

2.3. Study design

32 The OECD TG 201 specifies that, for difficult to test substances, the OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in "Study design" under request 1.

33 In your comments to the draft decision, you agree to perform the requested study.

Reasons related to the information under Annex VIII of REACH

3. Short-term toxicity testing on fish

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

3.1. Information provided

35 You have provided:

(i) a key short-term toxicity study on fish (1978) with the Substance;

36 In addition, you have adapted this information requirement by using Annex XI, Section 1.3. (Qualitative or Quantitative Structure-Activity Relationships ((Q)SARs). To support the adaptation, you have provided the following information:

(ii) a prediction from QSAR ECOSAR-US EPA (2000).

3.2. Assessment of the information provided

3.2.1. The provided study does not meet the specifications of the test guideline(s)

37 To fulfil the information requirement, a study must comply with OECD TG 203 (Article 13(3) of REACH). Therefore, the following specifications must be met:

Validity criteria

f) the analytical measurement of test concentrations is conducted.

38 Technical specifications impacting the sensitivity/reliability of the test

g) the test duration is 96 hours or longer.

Characterisation of exposure

h) in static tests, if the concentrations of the test material: are not expected to remain within ± 20 % of the nominal, then the test substance concentration is determined (in one replicate) in all concentrations at the beginning, at 48 hours and at the end of the test.

Reporting of the methodology and results

i) the test procedure is reported (e.g. composition of the test medium, fish loading);

j) the methods used to prepare stock and test solutions is reported;

k) in static tests, the results of at least daily measurements of dissolved oxygen, pH, salinity (if relevant) and temperature measured daily in each test vessel are reported. The results of hardness and TOC determinations at the beginning of the exposure in the dilution water are reported;

l) mortalities and sub-lethal effects (*e.g.* with regard to equilibrium, appearance, ventilator and swimming behaviour) are reported. The frequency of observations includes at least 2 observations within the first 24 hours and at least two observations per day from day 2 to 4.

39 In study (i):

Validity criteria

a) no analytical measurement of test concentrations was conducted.

Technical specifications impacting the sensitivity/reliability of the test

b) the test duration was 48 hours.

Characterisation of exposure

c) the reported effect values are based on nominal concentrations. However, you have not provided any evidence that confirm that the concentration of the test substance has been satisfactorily maintained within ± 20 % of the nominal or measured initial concentration.

Reporting of the methodology and results

d) to i) you have not provided any of the information listed under these points above.

40 Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically, the test duration of study (i) was shorter than that prescribed by the OECD TG 202 and the exposure concentrations were not measured. Both deviations may have resulted in the underestimation of the measured toxicity of the substance. Furthermore, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, you have not reported key pieces of information (e.g. mortality and sub-lethal effects) that are relevant to the validity of the study. Because of this, ECHA cannot independently verify if study (i) is valid.

41 On this basis, the specifications of the OECD TG 203 are not met.

3.2.2. (Q)SAR adaptation rejected

42 As explained in Section 0.1., your adaptation based on Qualitative or Quantitative Structure-Activity Relationships ((Q)SARs) under Annex XI, Section 1.3. is rejected.

43 In addition, ECHA identified endpoint-specific issue(s) addressed below.

3.2.2.1. The substance is outside the applicability domain of the model

44 Under Annex XI, Section 1.3., the following conditions must be fulfilled whenever a (Q)SAR approach is used:

(1) the substance must fall within the applicability domain of the model,

45 You have used the benzyl alcohol model from ECOSAR to predict the aquatic toxicity of the Substance. The applicability domain of the model you used is defined by the Log Kow of the substances in the training set of the model. The lowest logKow for fish in the training set for benzyl alcohol model as predicted by EPISuite, is 0.45.

46 The Log Kow of the Substance is 0.3.

47 The Substance has a log Kow lower than the lowest log Kow of the substances in the training set.

48 You have not demonstrated that the Substance falls within the applicability domain of the model.

49 Therefore, the information requirement is not fulfilled.

50 In the comments on the draft decision you agree that further aquatic toxicity testing may be needed. You do not agree that both short- and long-term testing on aquatic invertebrates and fish are needed. Instead of performing a new OECD TG 203 study, you propose to perform the requested long-term toxicity study on fish (OECD TG 210) (request 5) in order to adapt this information requirement.

51 Annex VIII, Section 9.1.3, Column 2 specifies that the short-term toxicity study does not need to be conducted if a long-term aquatic toxicity study on fish is available.

52 At present no long-term toxicity study on fish is provided in the IUCLID dossier, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

3.3. Study design

53 The OECD TG 203 specifies that, for difficult to test substances, the OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in "Study design" under request 1.

Reasons related to the information under Annex IX of REACH

4. Long-term toxicity testing on aquatic invertebrates

54 Long-term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

4.1. Information provided

55 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided the following information:

(i) 'In accordance with column 2 of REACH Annex IX, no long term toxicity testing is proposed (required in section 9.1.5) as the chemical safety assessment does not indicate a need to further investigate the effects on aquatic invertebrates. There are no adverse effects in the short term studies and the substance is readily biodegradable'

4.2. Assessment of the information provided

56 Under Annex IX, Section 9.1., Column 2 is not a basis for omitting information on long-term toxicity to aquatic invertebrates referred to under Column 1, Section 9.1.5.

57 Your adaptation is therefore rejected and the information requirement is not fulfilled.

4.3. Study design

58 The OECD TG 211 specifies that, for difficult to test substances, the OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in "Study design" under request 1.

59 In your comments to the draft decision, you agree to perform the requested study.

5. Long-term toxicity testing on fish

60 Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

5.1. Information provided

61 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided the following information:

(i) 'In accordance with column 2 of REACH Annex IX, no long term toxicity testing is proposed (required in section 9.1.6) as the chemical safety assessment does not indicate a need to further investigate the effects on fish. There are no adverse effects in the short term studies and the substance is readily biodegradable'.

5.2. Assessment of the information provided

62 Under Annex IX, Section 9.1., Column 2 is not a basis for omitting information on long-term toxicity to fish referred to under Column 1, Section 9.1.6.

63 Your adaptation is therefore rejected and the information requirement is not fulfilled.

5.3. Study design

64 To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (Guidance on IRs and CSA, Section R.7.8.2.). The OECD TG 210 specifies that, for difficult to test substances, the OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in "Study design" under request 1.

65 In your comments to the draft decision, you agree to perform the requested study.

66 In the comments to the draft decision, you propose to conduct the requested aquatic plants growth inhibition study (request 2) and the long term aquatic invertebrates study (request 4) before initiating the requested fish study according to OECD TG 210. You indicate that the results of these two studies would potentially enable the refinement of the fish testing with the aim of reducing the number of animals sacrificed. However, you do not explain how you intend to refine the fish testing using the results from OECD TG 201 and 211.

67 In this regard, ECHA wishes to draw your attention to the specifications laid down in point 22 of the OECD TG 210. Based on that test method, normally five concentrations of the test chemical, with a mimimum of four replicates per concentration, spaced by a constant factor not exceeding 3.2 are required. If available, information on the acute testing, preferable with the same species and/or a range finding test should be considered when selecting the range of test concentrations. However, all sources of information should be considered when selecting the range of test concentrations, including sources like e.g., read across, fish embryo acute toxicity test data. A limit test, or an extended limit test, with fewer than five concentrations (and thus with lower number of test organisms) may be conducted as a definitive test to establish empirical NOECs. Justification should be provided if fewer than five concentrations are used. Furthermore, concentrations of the test chemical higher than the 96 hour LC50 or 10 mg/L, whichever is the lower, need not be tested.

Reasons related to the information under Annex X of REACH

6. Pre-natal developmental toxicity study in a second species

68 Pre-natal developmental toxicity (PNDT) studies (OECD TG 414) in two species is an information requirement under Annex X, Section 8.7.2.

6.1. Information provided

69 You have not submitted any information for this requirement in your dossier.

70 In your comments on the draft decision you have provided a read-across justification for an adaptation where you predict the pre-natal developmental toxicity properties of the Substance using available information on the analogue substance furfural (EC 202-627-7). You express your intentions to include this read-across justification document together with a pre-natal developmental toxicity study on the analogue substance furfural in a dossier update, in order to fulfil this information requirement.

6.2. Assessment of the information provided

71 Annex XI, Section 1.5. requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must include robust study summary for each source study used in the adaptation.

72 As the information from the pre-natal developmental toxicity study on the analogue substance furfural referred to in your comments is neither provided as part of your comments nor available in your registration dossier, the read-across adaptation is not complete and cannot be assessed. Therefore, the data gap remains.

6.3. Study design

73 A PNDT study according to the test method OECD TG 414 should be performed in rabbit or rat as preferred second species. The study in the first species was carried out by using a rodent species (rat). Therefore, a PNDT study in a second species must be performed in the rabbit as preferred non-rodent species.

74 As the Substance is a liquid, the study must be conducted with oral administration of the Substance (Annex X, Section 8.7.2., Column 1).

75 Based on the above, the study must be conducted in rabbits with oral administration of the Substance.

7. Extended one-generation reproductive toxicity study

76 An extended one-generation reproductive toxicity (EOGRT) study (OECD TG 443) is an information requirement under Annex X, Section 8.7.3. Furthermore Column 2 defines the conditions under which the study design needs to be expanded.

7.1. Information provided

77 You have provided:

(i) a 14-week toxicity study via inhalation in rats (1999) with the Substance;

(ii) a 14-week toxicity study via inhalation in mice (1999) with the Substance.

78 In your comments on the draft decision you have provided a read-across justification for an adaptation where you predict the reproductive toxicity properties of the Substance using

available information on the analogue substance furfural (EC 202-627-7). You express your intentions to include this read-across justification document together with a two-generation reproductive toxicity study on the analogue substance furfural in a dossier update, in order to fulfil this information requirement.

7.2. Assessment of the information provided

7.2.1. Assessment of Annex XI, Section 1.1.2. adaptation

79 Under Annex XI, Section 1.1.2., data from experiments generated prior to the 1st of June 2008 and not carried out according to GLP or the test guideline normally required for the information requirement must be considered equivalent to data generated from the test method if the following condition(s) are met, including:

(1) adequacy for the purpose of classification and labelling and/or risk assessment; and/or

(2) adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3).

80 For this information requirement, the data from the experiment must have adequate and reliable coverage of the key parameters of the OECD TG 443. Therefore, the following specifications must be met:

a) the relevant life stages (mating, gestation, lactation and exposure of the F1 generation starting in utero and continuing up to adulthood) are examined.

81 In studies (i) and (ii):

a) the animals were not exposed during gestation, during lactation, *in utero*, and postnatally.

82 Therefore, the data provided do not have adequate and reliable coverage of the key parameters of the OECD TG 443.

83 Consequently, the data is not adequate for the purpose of classification and labelling and/or risk assessment because not all potential hazards of the substance have been investigated.

84 Based on the above, the adaptation is rejected and the information requirement is not fulfilled.

7.2.2. Assessment of the read-across adaptation described in your comments

85 Annex XI, Section 1.5. requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must include robust study summary for each source study used in the adaptation.

86 As the information from the two-generation reproductive toxicity study on the analogue substance furfural referred to in your comments is neither provided as part of your comments nor available in your registration dossier, the read-across adaptation is not complete and cannot be assessed. Therefore, the data gap remains.

7.3. Study design

7.3.1. Species and route selection

87 As the Substance is a liquid, the study must be conducted with oral administration of the Substance (Annex X, Section 8.7.3., Column 1).

7.3.2. Pre-mating exposure duration

88 The length of pre-mating exposure period must be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

89 Ten weeks pre-mating exposure duration is required to obtain results adequate for classification and labelling and/or risk assessment. There is no substance specific information in the dossier supporting shorter premating exposure duration (Guidance on IRs and CSA, Section R.7.6.).

90 Therefore, the requested pre-mating exposure duration is ten weeks.

7.3.3. Dose-level setting

91 The aim of the requested test must be to demonstrate whether the classification criteria of the most severe hazard category for sexual function and fertility (Repr. 1B; H360F) and developmental toxicity (Repr. 1B; H360D) under the CLP Regulation apply for the Substance (OECD TG 443, paragraph 22; OECD GD 151, paragraph 28; introductory part of Annex IX/X to REACH; Annex I, Section 1.0.1. to REACH and Recital 7, Regulation 2015/282), and whether the Substance meets the criteria for a Substance of very high concern regarding endocrine disruption according to Art.57(f) of REACH as well as supporting the identification of appropriate risk management measures in the chemical safety assessment.

92 To investigate the properties of the Substance for these purposes, the highest dose level must be set on the basis of clear evidence of an adverse effect on sexual function and fertility, but no deaths (i.e., no more than 10% mortality; Annex I, Section 3.7.2.4.4. of the CLP Regulation) or severe suffering such as persistent pain and distress (OECD GD 19, paragraph 18) in the P0 animals.

93 In case there are no clear evidence of an adverse effect on sexual function and fertility, the limit dose of at least 1000 mg/kg bw/day or the highest possible dose level not causing severe suffering or deaths in P0 must be used as the highest dose level. A descending sequence of dose levels should be selected to demonstrate any dose-related effect and aiming to establish the lowest dose level as a NOAEL.

94 In summary: unless limited by the physical/chemical nature of the Substance, the highest dose level in P0 animals must be as follows:

(1) in case of clear evidence of an adverse effect on sexual function and fertility without severe suffering or deaths in P0 animals, the highest dose level in P0 animals must be determined based on such clear evidence, or

(2) in the absence of such clear evidence, the highest dose level in P0 animals must be set to be the highest possible dose not causing severe suffering or death, or

(3) if there is such clear evidence but the highest dose level set on that basis would cause severe suffering or death, the highest dose level in P0 animals must be set to be the highest possible dose not causing severe suffering or death, or

(4) the highest dose level in P0 animals must follow the limit dose concept.

95 You have to provide a justification with your study results demonstrating that the dose level selection meets the conditions described above.

96 Numerical results (i.e. incidences and magnitudes) and description of the severity of effects at all dose levels from the dose range-finding study/ies must be reported to facilitate the assessment of the dose level section and interpretation of the results of the main study.

7.3.4. Cohorts 1A and 1B

97 Cohorts 1A and 1B belong to the basic study design and must be included.

7.3.4.1. Histopathological investigations in Cohorts 1A and 1B

98 In addition to histopathological investigations of cohorts 1A, organs and tissues of Cohort 1B animals processed to block stage, including those of identified target organs, must be subjected to histopathological investigations (according to OECD TG 443, paragraph 67 and 72) if

- the results from Cohort 1A are equivocal, or
- the test substance is a suspected reproductive toxicant or
- the test substance is a suspected endocrine toxicant.

7.3.4.2. Splenic lymphocyte subpopulation analysis

99 Splenic lymphocyte subpopulation analysis must be conducted in Cohort 1A (OECD TG 443, paragraph 66; OECD GD 151, Annex Table 1.3).

7.3.4.3. Investigations of sexual maturation

100 To improve the ability to detect rare or low-incidence effects, all F1 animals must be maintained until sexual maturation to ensure that sufficient animals (3/sex/litter/dose) are available for evaluation of balano-preputial separation or vaginal patency (OECD GD 151, paragraph 12 in conjunction with OECD TG 443, paragraph 47). For statistical analyses, data on sexual maturation from all evaluated animals/sex/dose must be combined to maximise the statistical power of the study.

7.3.5. Further expansion of the study design

101 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 relevant information becomes available from other studies or during conduct of this study. Inclusion is justified if the available information meets the criteria and conditions which are described in Annex X, Section 8.7.3., Column 2. You may also expand the study due to other scientific reasons in order to avoid a conduct of a new study. The study design, including any added expansions, must be fully justified and documented. Further detailed guidance on study design and triggers is provided in Guidance on IRs & CSA, Section R.7.6.

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).
Guidance for monomers and polymers; ECHA (2023).
Guidance on intermediates; ECHA (2010).
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 23 August 2022.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 12 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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

ECHA took into account your comments and amended the request(s).

In your comments on the draft decision, and in a subsequent dossier update, you have provided information addressing the deficiencies listed in the draft decision regarding the information requirement of Annex IX, 8.7.2 for a pre-natal developmental toxicity study in a first species. As your updated dossier is compliant for this information requirement, the conditions for an adaptation according to Annex VIII, 8.7.1, column 2, fourth indent for the information requirement of Annex VIII, 8.7.1 for a screening study for developmental/reproductive toxicity are also met. Therefore, the requests for a screening study for developmental/reproductive toxicity and for a pre-natal developmental toxicity study in a first species have been removed from the decision.

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: Addressee(s) 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 Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[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 (https://echa.europa.eu/practical-guides).

(4) Under the introductory part of Annexes VII/VIII/IX/X to REACH, where a test method offers flexibility in the study design, for example in relation to the choice of dose levels or concentrations, the chosen study design must ensure that the data generated are adequate for hazard identification and risk assessment.

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 variation in compositions reported by all members of the joint submission,
- the boundary composition(s) of the Substance,
- 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.

With that detailed information, ECHA can confirm 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 (https://echa.europa.eu/manuals).