~~Confidential~~

Helsinki, 11 October 2023

Addressee(s)
Registrant(s) of JS_1,2-DCB as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
13 March 2023

Registered substance subject to this decision ("the Substance")
Substance name: 1,2-dichlorobenzene
EC/List number: 202-425-9

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 ***19 October 2026***.

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

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

1. 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 appendix 1 below, 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 related to the information under Annex X of REACH

1. Extended one-generation reproductive toxicity study

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.

1.1. Information provided

ECHA understands that you have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on the following:

(i) Two-generation reproductive toxicity study via inhalation (1989) with the Substance. You have disregarded this study "due to major methodological deficiencies";
(ii) Reproductive toxicity assay on sperm abnormalities (1985) with the Substance, reliability 4;
(iii) Sub-chronic toxicity study (1985), 13 weeks oral, with the Substance, reliability 2;
(iv) Combined repeated dose and carcinogenicity study (1985), with the Substance, reliability 2.

You have provided the following justification: "*Priority for this study is low based on the absence of toxicity to reproductive organs in the reliable oral sub-chronic and chronic studies, and based on observations on fertility in the unreliable 2-generation study only at maternally toxic concentrations > 10-fold higher than systemic toxicity.*"

You also indicate that you consider that "*Overall, based on the information gained from repeated dose toxicity studies and considering that a full risk assessment is possible even without this endpoint study, conducting of a two-generation reproductive toxicity study is scientifically not of high priority. In addition data need aspects might be balanced with animal welfare considerations*."

1.2. Assessment of the information provided

Annex XI, Section 1.2. states that there may be sufficient weight of evidence from several independent sources of information enabling, through a reasoned justification, a conclusion on the information requirement, while the information from each single source alone is insufficient to fulfil the information requirement.

The justification must have regard to the information that would otherwise be obtained from the study that must normally be performed for this information requirement.

According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude on the corresponding information requirement.

1.2.1. Lack of documentation justifying the weight of evidence adaptation

Annex XI, Section 1.2. requires that adequate and reliable documentation is provided to describe a weight of evidence approach. This documentation must include robust study summaries of the studies used as sources of information and a justification explaining why the sources of information together provide a conclusion on the information requirement.

You have not included a justification for your weight of evidence adaptation, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude on the information requirements under consideration.

1.2.2. Missing robust study summary of source of information (ii)

Annex XI, Section 1.2. requires that whenever weight of evidence is used adequate and reliable documentation of the applied method must be provided. Such documentation must include a robust study summary for each source of information used in the adaptations.

A robust study summary must provide a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study (Article 3(28)).

In addition, for weight of evidence adaptations, the robust study summary must clearly indicate which key parameters of the study normally required for the information requirement are investigated in the study.

The set of information on study (ii) included in your technical dossier is limited. You have only reported the name of the study, information on the identity of substance investigated and the dosing protocol applied. You indicate that only a short abstract of this study was available and you consider that the limited information available on this study does not allow to assess the reliability of this study.

The extent of the coverage of the key parameters associated with the information requirement by this study and the reliability of the contribution of this information on the key parameters cannot be evaluated based on the information provided.

In the absence of a robust study summary for this specific source study used in the adaptation as required by Annex XI, Section 1.2, this source of information cannot be considered as contributing to the overall weight of evidence for the information requirement under consideration.

Beside these critical deficiencies, ECHA has also assessed the other aspects of your adaptation.

Information that can be used to support weight of evidence adaptation for the information requirement of Annex X, Section 8.7.3 includes similar information that is produced by the OECD TG 443. The OECD TG 443 requires the study to investigate the following key parameters:

1. Sexual function and fertility
2. Toxicity to the offspring
3. Systemic toxicity

1.2.3. Sexual function and fertility

Sexual function and fertility on both sexes must include information on mating, fertility, gestation (length), maintenance of pregnancy (abortions, total resorptions), parturition, lactation, organ weights and histopathology of reproductive organs and tissues, oestrous cyclicity, sperm count, sperm analysis, litter sizes, nursing performance and other potential aspects of sexual function and fertility.

1.2.3.1. Relevance of the information provided

Source (i) may provide relevant information on mating, fertility, gestation (length), maintenance of pregnancy (abortions, total resorptions), parturition, lactation, organ weights and histopathology of reproductive organs and tissues, litter sizes, nursing performance but it does not provide information on oestrous cyclicity, sperm count and sperm analysis.

Source (ii) that is lacking robust study summary cannot be considered as contributing for this aspect with any relevant and reliable information.

Sources (iii) and (iv) may provide relevant information on organ weights and histopathology of reproductive organs in both sexes, but neither of these sources provide information on any other element of the sexual function and fertility.

1.2.3.2. Reliability of the information provided

1.2.3.2.1. Inadequate route of administration for study (i)

According to the information requirement of Annex X, 8.7.3, column 1, "*The route of administration shall be oral if the substance is a solid or liquid, and inhalation if the substance is a gas; deviations may be made if scientifically justified, for example through evidence of equivalent or higher systemic exposure via another relevant route of human exposure or route-specific toxicity*".

Study (i) is reported as a two-generation study which has been performed with the Substance via the inhalation route.

Since the Substance is a liquid, the default route of administration is the oral route, as explained above.

You have not provided any evidence of equivalent or higher systemic exposure via the inhalation route compared with the systemic exposure achieved using the default oral route. Therefore you have not established that deviation from the default route of administration is scientifically justified, and that testing of the Substance via the inhalation route would not lead to under-estimating the reproductive toxicity properties of the Substance.

You have disregarded the source (i) as unreliable due to major methodological deficiencies related to the use of the inhalation route of administration. Your conclusions are in agreement with ECHA's assessment that the information obtained from study (i) cannot reliably contribute to your weight of evidence adaptation.

1.2.3.3. Conclusion on sexual function and fertility

As indicated above, the study (i) provide relevant information on some of the elements of the key parameter sexual function and fertility, but for the reasons presented above this information cannot be considered reliable.

Studies (iii) and (iv) are the only sources of reliable information on sexual function and fertility. However these studies only inform on organ weights and histopathology of reproductive organs and do not cover all elements of sexual function and fertility.

Taken together, there is no information on oestrous cyclicity and sperm count and no reliable information on sperm analysis, mating, fertility, gestation (length), maintenance of pregnancy (abortions, total resorptions), parturition, lactation, litter sizes and nursing performance.

1.2.4. Toxicity to the offspring

Toxicity to offspring must cover information on deaths before, during or after birth, growth, external malformations, clinical signs, sexual maturity, oestrous cyclicity, organ weights and histopathology of reproductive organs and tissues in adulthood and other potential aspects of toxicity to offspring.

1.2.4.1. Relevance of the information provided

The study (i) may provide relevant information on toxicity to offspring, but it does not provide information on oestrous cyclicity, organ weights and histopathology of reproductive organs in adulthood, individual pup weights, clinical signs by pup number, pup organ weights.

The study (ii) that is lacking robust study summary cannot be considered as contributing for this aspect with any relevant and reliable information.

Studies (iii) and (iv) do not provide relevant information on toxicity to the offspring as the design of these studies do not include mating and generation of offpsring.

1.2.4.2. Reliability of the information provided

As explained above on section 1.2.2.2.1, the results obtained from the study (i) cannot reliably contribute to your weight of evidence adaptation.

1.2.4.3. Conclusion on toxicity to the offpsring

As indicated above, the study (i) provide relevant information on some of the elements of the key parameter toxicity to the offspring, but for the reasons presented above this information cannot be considered reliable.

Taken together, there is no reliable information in your weight of evidence adaptation on any of the elements of the key parameter toxicity to the offspring.

1.2.5. Systemic toxicity

Systemic toxicity must include information on clinical signs, survival, body weights, food consumption, haematology (full-scale), clinical chemistry (full-scale), organ weights and histopathology of non-reproductive organs and tissues (full-scale) and other potential aspects of systemic toxicity in the parental P and F1 generation up to adulthood.

1.2.5.1. Relevance of the information provided

Study (i) may provide relevant information on systemic toxicity for the parental P and F1 generation up to adulthood. However it does not provide information on histopathology of non-reproductive organs and tissues in the F1 generation.

Source (ii) that is lacking robust study summary cannot be considered as contributing for this aspect with any relevant and reliable information.

The studies (iii) and (iv) may provide relevant information on systemic toxicity for the parental P generation. However the studies (iii) and (iv) do not inform on any element of systemic toxicity (clinical signs, survival, body weights, food consumption, haematology (full-scale), clinical chemistry (full-scale), organ weights and histopathology of non-reproductive organs) in the F1 generation up to adulthood.

1.2.5.2. Reliability of the information provided

As explained above on section 1.2.2.2.1, the results obtained from the study (i) cannot reliably contribute to your weight of evidence adaptation.

1.2.5.3. Conclusion on systemic toxicity

As indicated above, the study (i) provides relevant information on some of the elements of the key parameter systemic toxicity. However the study (i) cannot be considered a reliable source of information that could contribute to the conclusion on systemic toxicity for the reasons presented above.

Therefore, studies (iii) and (iv) are the only sources of reliable information on systemic toxicity. However these studies do not cover all elements of systemic toxicity.

Taken together, there is no information on haematology (full-scale), clinical chemistry (full-scale), organ weights and histopathology of non-reproductive organs and tissues for F1 generation up to adulthood and no reliable information on clinical signs, survival, body weights and food consumption for F1 generation up to adulthood.

1.2.6. Conclusion on weight of evidence

Taken together the sources of information as indicated above do not cover all elements of the key parameters:, the following is missing:

- sexual function and fertility: no information on oestrous cyclicity and sperm count
- toxicity to offspring: no information on oestrous cyclicity, organ weights and histopathology of reproductive organs in adulthood, individual pup weights, clinical signs by pup number, pup organ weights
- systemic toxicity: no information on haematology (full-scale), clinical chemistry (full-scale), organ weights and histopathology of non-reproductive organs and tissues for F1 generation up to adulthood

Even for the elements of the key parameters that are covered, this information cannot be considered as reliable.

Therefore, it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for Extended one-generation reproductive toxicity study.

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

1.3. Study design

1.3.1. Route selection

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).

1.3.2. Pre-mating exposure duration

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.

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.).

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

1.3.3. Dose-level setting

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.

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.

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.

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.

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

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.

1.3.4. Cohorts 1A and 1B

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

1.3.4.1. Histopathological investigations in Cohorts 1A and 1B

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,

- the test substance is a suspected reproductive toxicant or
- the test substance is a suspected endocrine toxicant.

1.3.4.2. Splenic lymphocyte subpopulation analysis

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

1.3.4.3. Investigations of sexual maturation

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.

1.3.5. Further expansion of the study design

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 (2012).
***Guidance on intermediates*;** ECHA (2010).
All guidance documents are 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 07 July 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 did not amend the request.

ECHA notes that during the decision-making process you have changed your registration to a lower tonnage band and provided documentary evidence on the production volume for the preceding years (2021-2022) and the estimated production volume of the present year (2023). However, that tonnage band change is not considered for this decision-making process as the data shows that within the year preceding the adoption of this decision you were still operating at the higher tonnage band.

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]

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).