~~Confidential~~

Helsinki, 13 October 2023

Addressee(s)
Registrant(s) of Reaktiv-Gelb F-68072 FW as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
01/09/2022

Registered substance subject to this decision ("the Substance")
Substance name: lithium sodium 2-amino-4-{[4-(cyanoazanidyl)-6-[(3-sulfonatophenyl)amino]-1,3,5-triazin-2-yl]amino}-5-(2-{4-[2-(sulfonatooxy)ethanesulfonyl]phenyl}diazen-1-yl)benzene-1-sulfonate
EC/List number: 413-090-5

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 ***20 October 2025***.

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

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

1. Skin sensitisation (Annex VII, Section 8.3.)

   a) *in vitro/in chemico* skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (OECD TG 442E) (Annex VII, Section 8.3.1.); and

   b) only if the *in vitro/in chemico* test methods specified under point a) above are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429);

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

2. Adsorption/desorption screening (Annex VIII, Section 9.3.1.; test method: EU C.18/OECD TG 106)

3. Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.; test method: EU C.7./OECD TG 111) at pH values between 7 and 8.5 and at least at pH values of 8 and 8.5

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 addressee of the decision and its

corresponding information requirements based on registered tonnage band are listed in Appendix 3.

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)

Contents

Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

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

1.1. Information provided

2 You have provided:

(i) a Guinea Pig Maximisation Test (1993) with the Substance;

1.2. Assessment of the information provided

1.2.1. Assessment whether the Substance causes skin sensitisation

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

3 To fulfil the information requirement, and to enable concluding whether the Substance causes skin sensitisation, a study must comply with the EU Method B.6/OECD TG 406 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the induction (intradermal and topical) concentration is the highest causing mild-to-moderate irritation to the skin;

b) the challenge dose is the highest non-irritation concentration;

c) a justification for the concentration selected, including the results of a dose-range finding study.

4 In study (i):

a) you have not reported whether the concentration used for topical induction caused mild-to-moderate irritation while you have reported a concentration of 5% for intradermal induction as the highest one causing mild-to-moderate irritation;

b) you have not reported whether the challenge concentration was the highest non-irritating concentration;

c) you claim that 25% concentration is the highest concentration for topical induction causing mild-to-moderate irritation, but also that the same concentration is the highest non-irritating concentration;

c) you have not provided the results of the dose-range-finding study.

5 Therefore, first, the requirement for setting the concentration for topical induction is not fulfilled.

6 Second, for topical induction, your claims a) and c) are conflicting, as the same concentration (25%) cannot be both i.e. concentration causing mild-to-moderate irritation and non-irritant concentration.

7 Third, you have not submitted supporting information to assess the reliability of the information provided for setting the dose concentrations.

8 Threrefore, the information provided does not cover the specification(s) required by the EU Method B.6/OECD TG 406.

9 On this basis, it cannot be concluded whether the Substance causes skin sensitisation.

1.2.1.2. Comments on the draft decision

10 In the comments to the draft decision, you have provided additional information to justify the dose level selection for both topical induction and challenge exposures. You have proposed to update your dossier with the modified robust study summary.

11 The information provided as part of your comments addresses the incompliances identified above. However, as the information is currently not available in your registration dossier, the data gap remains. You should submit this information in an updated registration dossier by the deadline set in the decision.

1.2.2. No assessment of potency

12 To be considered compliant and enable a conclusion in cases where the substance is considered to cause skin sensitisation, the information provided must also allow a conclusion whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

13 As the currently available data does not allow to conclude whether the Substance causes skin sensitisation (see section 1.2..1. above), this condition cannot be assessed.

14 Therefore, the information requirement is not fulfilled.

1.3. Specification of the study design

15 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 OECD TG 442E) must be provided. Furthermore an appropriate risk assessment is required if a classification of the Substance as a skin sensitiser (Cat 1A or 1B) is warranted.

16 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the existing data or 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.

Reasons related to the information under Annex VIII of REACH

2. Adsorption/ desorption screening

17 Adsorption/desorption screening is an information requirement under Annex VIII to REACH (Section 9.3.1).

2.1. Information provided

18 You have provided a study conducted with the Substance, using test method EU C.19 / OECD TG 121.

2.2. Assessment of the information provided

19 To fulfil the information requirement, a study must comply with the OECD TG 121 (Article 13(3) of REACH). Therefore, the following specifications must be met:

20 Applicability domain

a) The method is applicable to substances having a log K_{oc} between 1.5 and 5.

21 Your registration dossier provides an OECD TG 121 showing the following:

22 Applicability domain

a) The Substance has a log K_{oc} < 1.3.

23 In your comments on the draft decision, you acknowledge that a value for LogKoc of <1.3 falls outside the applicability domain of OECD 121.

24 Based on the above, the Substance is outside of the applicability domain of the corresponding test guideline.

25 Therefore, the specifications of OECD TG 121 are not met.

2.3. Comments on the draft decision

26 In your comments to the draft decision you state that under Annex VIII, column 2 the study may be omitted if the substance can be expected to have a low potential for adsorption, in your case demonstrated by an estimated low octanol-water partition coefficient of LogKow <-6.

2.4. Assessment of your comments on the draft decision

27 In order to adapt this information requirement based on low octanol-water partition coefficient (log K_{ow}), lipophilicity must be the sole characteristic driving the adsorption potential of a substance. However, for some groups of substances (e.g. ionisable substances, surfactants) other mechanisms than lipophilicity may drive adsorption.

28 You have not provided any other evidence or argument that the Substance can be expected to have a low potential for adsorption.

29 In Section 4.7 of your dossier, you report that the substance is ionised because 'since the measurement of log Pow of the test substance can not be performed in its non-ionised form as required by OECD guideline 117'. Additionally your Substance is a well soluble organic salt (water solubility of 113 g/L) which dissociates in water, as you indicated yourself.

Because of the ionised form of the Substance other mechanisms than lipophilicity may drive adsorption.

30 You have not demonstrated that lipophilicity is the sole characteristic driving adsorption potential, and that log K_{ow} is a valid descriptor for assessing the adsorption potential of the Substance.

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

2.5. Specification of the test selection and study design

32 The OECD TG 106 Batch Equilibrium Method is the appropriate method to study the adsorption of the Substance. This method uses a range of actual soils and so represents a more realistic scenario than the HPLC (OECD TG 121) method. The ionisable properties of the Substance should be considered when selecting the appropriate test design. For ionisable substances, soil types should cover a wide range of pH.

3. Hydrolysis as a function of pH

33 Hydrolysis as a function of pH is an information requirement under Annex VIII to REACH (Section 9.2.2.1.).

3.1. Information provided

34 You have provided one key study:

(i) a hydrolysis study (1993) according to 84/449/EWG Anhang V, Teil C: Methoden zur Bestimmung der Ökotoxizität; C. 10: Abbaubarkeit - Abiotischer Abbau - Hydrolyse in Abhängigkeit vom pH, with the Substance;

3.2. Assessment of the information provided

3.2.1. The provided studies do not meet the specifications of the test guideline

35 To fulfil the information requirement, a study must comply with OECD TG 111 (Article 13(3) of REACH). This TG is designed as a tiered approach and each tier is triggered by the results of the previous tier. Therefore, the following specifications must be met:

36 Hydrolysis testing (Tier 2)

a) the test is required if more than 10 % hydrolysis occurs after 5 days in the preliminary test (Tier 1);

b) the test must be performed at the pH value(s) at which the test material was found unstable in the preliminary test (i.e. > 10 % hydrolysis in Tier 1 test);

37 Identification of hydrolysis products (Tier 3)

c) all major hydrolysis products observed in Tier 2 testing (i.e. at least those representing > 10% of the applied dose) must be identified using an appropriate analytical method (Tier 3);

38 Testing at pH values other than 4, 7, 9

d) additional tests at pH values other than 4, 7 and 9 may be required for a hydrolytically unstable test substance.

39 In the study:

40 Tier 2 and 3

a) the preliminary test (Tier 1) indicates that > 10 % hydrolysis occurs after 5 days at pH 9;

b) and c) hydrolysing testing (Tier 2) was performed at pH 4 but not at pH 7 and 9 while the test material was found unstable in the preliminary test (Tier 1) already at pH 7 (the Substance reached > 99% decomposition after 5 days at 50°C and > 50% decomposition in 4.25 hours at 50°C in the study);

41 Testing at pH values other than 4, 7, 9

d) The studies provided indicate substantial hydrolytical degradation of the Substance in alkaline pH. At pH 7 based on tier 1 test results the estimated half-life is 1.8 days at 25°C. Based on Tier 1 test results at pH 9 the half-life is estimated to be only < 1 day at 25°C.

42 In your comments to the draft decision you argue that further testing of the hydrolysis behaviour of the Substance would not lead to the new knowledge of the environmental hazard because the Substance is fully hydrolysed in this process and as such is not released in the environment based on an explanation of the mechanism of the dyeing reaction according to the literature and knowledge of "common industrial dyeing process."

43 Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results, specifically:

- The hydrolysis was not investigated at pH 7 and 9 (Tier 2 test was not performed for pH 7 and 9 in the study); however the estimated results for pH 7 and 9 based on tier 1 indicate significant depletion of the test substance between pH 7 and 9 and implies hydrolytical instability of the Substance in alkaline pH. However, you have not considered testing hydrolysis at pH values other than 4.

  Regarding your claim in the comments on the draft decision that testing at such pH would not result in new knowledge, the OECD TG does not provide for any exception. Further, you refer to information on use, which is irrelevant for the investigation of intrinsic properties, as is the case here, except in the case of exposure-based adaptation under Annex XI, Section 3, which you have not submitted. In any case, your claim is based on generic considerations (literature and knowledge), rather than being substantiated on the basis of your registration dossier, in particular on the basis of a rigorous exposure assessment.

- You have not investigated the hydrolysis behaviour of the Substance between pH 7 and 9. An abrupt change of the hydrolytical behaviour is expected for the Substance between pH 7 and 9. This pH range is relevant both for the environmental assessment and for the interpretation of ecotoxicological tests. The pH of wastewater or sewage water is typically between 6–8 but can reach 8.5, implying that the Substance may be hydrolysed in the wastewater or sewage water before it reaches the environment[2]. Test guidelines for aquatic toxicity tests tolerate pH of up to 8.5 and even beyond for some of them. Therefore, investigating further the

[2] The pH of domestic wastewater is typically between 6–8 but is largely related to the alkalinity of the carriage water. In areas having soft water (alkalinity between 50 and 100 mg/L as $CaCO_3$), the pH of domestic wastewater is around 6.0 to 6.5. In areas having moderately hard water (alkalinity between 100 and 300 mg/L as $CaCO_3$) it is between 7.0 and 8.0. In areas having hard water (alkalinity higher than 300 mg/L as $CaCO_3$) it is between 7.5 and 9.0. Some industrial wastewaters can be quite acidic or alkaline. The optimum pH range for aerobic biodegradation lies between 6.5 and 8.5. Any wastewater beyond that range would need to be neutralised by the operator of the wastewater treatment system.

hydrolysis behaviour of the Substance between pH 7 and 8.5 is necessary for the environmental risk assessment of the Substance and for interpreting the results of the ecotoxicity tests.

The objective of this test is to investigate an intrinsic property, hydrolysis, in pH that may be relevant for the environment, including in waste treatment. It is in light of this objective that this decision discusses pH in sewage water, i.e. in light of the objective of the OECD TG for hydrolysis. However, your claim in the comments on the draft decision that testing at such pH would not result in new knowledge is a use consideration specific to your Substance which must be assessed on the basis of and rejected on the basis of the considerations set above.

44 On this basis, the specifications of OECD TG 111 are not met.

45 Therefore, the information requirement is not fulfilled.

3.3. Study design

46 The hydrolysis test must be performed under slightly alkaline conditions at pH values between 7 and 8.5 and at least at pH values of 8 and 8.5.

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 01 August 2022.

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

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

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 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[3].

(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

(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 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.

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) .

[3] https://echa.europa.eu/practical-guides