ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 5 April 2019

Addressee: [redacted]

Decision number: TPE-D-2114465857-31-01/F
Substance name: Potassium cyanate
EC number: 209-676-3
CAS number: 590-28-3
Registration number: [redacted]
Submission number: [redacted]
Submission date: 31/10/2018
Registered tonnage band: Over 1000

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation ((EC) No 1907/2006) (the REACH Regulation), ECHA examined your testing proposal(s) and decided as follows.

Your testing proposal is accepted and you are requested to carry out:

Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route with the registered substance specified as follows:

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

You have to submit the requested information in an updated registration dossier by **12 April 2022**. You also have to update the chemical safety report, where relevant.

In the draft decision communicated to you the time indicated to provide the requested information was 24 months from the date of adoption of the decision. In your comments on the draft decision, you requested an extension of the timeline to 36 months. You sought to justify this request by providing an explanation from the indicative contract laboratory including their explanation on their capacity to conduct this test. Therefore, ECHA has granted the request and set the deadline to 36 months.

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

Appeal

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

Authorised[1] by Ofelia Bercaru, Head of Unit, Hazard Assessment C4

[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

The decision of ECHA is based on the examination of the testing proposals you submitted and scientific information submitted by third parties.

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

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

The basic test design of an extended one-generation reproductive toxicity study (Cohorts 1A and 1B, without extension of Cohort 1B to include a F2 generation, and without Cohorts 2A, 2B and 3) is a standard information requirement as laid down in column 1 of 8.7.3., Annex X of the REACH Regulation, whereas column 2 defines when the study design needs to be expanded.

The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

You have submitted a testing proposal for an extended one-generation reproductive toxicity study according to OECD TG 443 in rats, by the oral (dietary) route to be performed with the registered substance with the following justification and specification of the study design:
"-To cover the full spermatogenesis and maturation as well as the folliculogenesis, ten weeks premating exposure duration for male and female rats is proposed.
- The maximum dose in the diet will be set to induce some systemic toxicity, but no death or severe suffering of the animals.
- No effects on reproductive organs are expected which are not of secondary nature. Thus, the extension of cohort 1B to include the F2 generation will not lead to new information [...]. Therefore, and also considering animal welfare reasons, an extension of cohort 1B to include the F2 generation is scientifically not justified. However, in case effects on reproductive organs/ performance will be observed[...], the study will be extended by the second generation.
- No concern on (developmental) neurotoxicity is indicated in the existing repeated dose toxicity studies [...].
- [...] no particular concern justifying the inclusion of the developmental immunotoxicity cohort."

ECHA requested your considerations for alternative methods to fulfil the information requirement for Reproductive toxicity (extended one-generation reproductive toxicity study). ECHA notes that you provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement. Thus, an extended one-generation reproductive toxicity study according to columns 1 and 2 of 8.7.3., Annex X is required. The following refers to the specifications of this required study.

Premating exposure duration and dose-level setting

You proposed ten weeks premating exposure duration "*to cover the full spermatogenesis and maturation as well as the folliculogenesis*".

Based on reported wide-spread or even wide dispersive uses for the registered substance in your registration dossier (submission number [redacted]), ECHA initially considered an extension of Cohort 1B to produce the F2 generation, based on the provision of Column 2 of Section 8.7.3 in Annex X, and therefore also a premating exposure duration of at least two weeks.

However, in your comments to the draft decision you explained that you do not longer support any wide-spread or even wide dispersive uses for the registered substance. You have also submitted an updated dossier on 31 October 2018 (submission number [redacted]) and removed all the professional and wide dispersive uses. Therefore, the condition for the extension under Column 2 of Section 8.7.3 in Annex X is no longer met.

Consequently, ECHA agrees with you that the duration of pre-mating exposure shall be ten weeks, as you proposed.

You also proposed that "*the maximum dose in the diet will be set to induce some systemic toxicity, but no death or severe suffering of the animals*". ECHA agrees with your proposal. The highest dose level shall aim to induce systemic toxicity, but not death or severe suffering of the animals, to allow comparison of reproductive toxicity and systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels.

If there is no relevant data to be used for dose-level setting, it is recommended that a range-finding study (or range finding studies) is performed and that its results are reported with the main study. This will support the justifications of the dose-level selections and interpretation of the results.

Species and route selection

You proposed testing by oral (dietary) route in rats. ECHA agrees with your proposal.

Extension of Cohort 1B

If the column 2 conditions of Section 8.7.3., Annex X are met, Cohort 1B must be extended by mating the Cohort 1B animals to produce the F2 generation.

You proposed no extension of Cohort 1B to produce the F2 generation. In the initial draft decision, ECHA modified the proposed study design and requested to include an extension of Cohort 1B to produce the F2 generation. ECHA considered on the basis of the information in the registration dossier that the column 2 conditions of Section 8.7.3., Annex X for the extension were met, because (i) the uses of the registered substance might have lead to the significant professional exposure and (ii) ECHA considered that toxicity of the analogue substance sodium cyanate in endocrine organs (adrenals) was an indication for one or more modes of action related to endocrine disruption.

As already outlined above, in your comments to the draft decision you explained that you do not longer support any wide-spread or even wide dispersive uses for the registered substance. Furthermore, you have expressed your doubts on ECHA's considerations regarding possible endocrine disruption properties of the analogue substance and provided detailed scientific arguments. You have also submitted an updated dossier on 31 October 2018 (submission number [redacted]) and removed all the professional and wide

dispersive uses. Based on this updated information, ECHA considers that the condition (a) of Column 2, Section 8.7.3 Annex X is no longer met and consequently, the extension of cohort 1B to include the F2 generation is not required. ECHA therefore has amended its draft decision.

b) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal during the third party consultation. The third party provided their considerations of the study design and stated that the basic study design (Cohorts 1A and 1B without extension) "*is considered to be appropriate in the absence of any triggers or conditions necessitating the inclusion of additional cohorts or a further generation*". However, the third party did not provide any scientific data which would fulfil this information requirement.

c) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study with the registered substance subject to the present decision as specified above.

Appendix 2: Procedural history

ECHA received your registration containing the testing proposals for examination in accordance with Article 40(1) on 2 October 2017.

ECHA held a third party consultation for the testing proposals from 23 April 2018 until 7 June 2018. ECHA received information from third parties (see Appendix 1).

This decision does not take into account any updates after **5 November 2018**, 30 calendar days after the end of the commenting period.

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

ECHA took into account your comments and amended the request and the deadline. You updated your registration on 31 October 2018. ECHA took the information in the updated registration into account, and amended the draft decision. The updated information is reflected in the Reasons (Appendix 1).

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

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided in your registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the registration at a later stage.

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of the Member States.

3. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition.

   In addition, it is important to ensure that the particular sample of the substance tested in the new tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.