

Helsinki, 19 April 2024

**Addressee(s)**

Registrants of JS\_Cesium carbonate as listed in Appendix 3 of this decision

**Date of submission of the dossier subject to this decision**

27 January 2023

**Registered substance subject to this decision ("the Substance")**

Substance name: caesium carbonate

EC/List number: 208-591-9

**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 **25 January 2027**.

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

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

1. *In vivo* mammalian alkaline comet assay (triggered by Annex VIII, Section 8.4., Column 2; test method: OECD TG 489) combined with *in vivo* mammalian erythrocyte micronucleus test (test method: OECD TG 474) in rats, or if justified, in mice, oral route. For the comet assay the following tissues shall be analysed: liver, glandular stomach and duodenum. For the micronucleus test:
  - the aneugenic potential of the Substance must be assessed by using a centromere staining technique if the substance induces an increase in the frequency of micronuclei in the OECD TG 474;
  - target tissue exposure must be demonstrated if the result of the OECD TG 474 is negative.

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<sup>1</sup> 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

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<sup>1</sup> 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 VIII of REACH ..... 4**

1. *In vivo* mammalian alkaline comet assay combined with *in vivo* mammalian erythrocyte micronucleus test ..... 4

**References ..... 11**

**Reasons related to the information under Annex VIII of REACH****1. *In vivo* mammalian alkaline comet assay combined with *in vivo* mammalian erythrocyte micronucleus test**

1 Appropriate *in vivo* mutagenicity studies must be considered under Annex VIII, Section 8.4., Column 2 in case of a positive result in any of the *in vitro* genotoxicity studies under Annex VII or VIII.

*1.1. Triggering of the information requirement*

2 In relation to the first condition, your dossier contains positive results for the *in vitro* cytogenicity test (OECD Guideline 473 (In Vitro Mammalian Chromosome Aberration Test, 2007) with the Substance which raises the concern for chromosomal aberration.

3 Therefore, the information requirement is triggered.

*1.2. Information provided*

4 Your dossier contains the following information:

(i) an *in vivo* Mammalian Bone Marrow Chromosome Aberration Test (2008) conducted with the Substance.

5 In addition, you also have adapted this information requirement by using Annex XI, Section 1.5. (grouping of substances and read-across approach) based on experimental data from the following substances:

(ii) an *in vivo* Mammalian Bone Marrow Chromosome Aberration Test (2012) with the source substance Cesium Hydroxide monohydrate EC 627-088-9.

*1.3. Assessment of the information provided**1.3.1. The provided study (i) does not meet the specifications of the test guideline(s)*

6 To be considered adequate, the study has to meet the requirements of OECD TG 475. Therefore, the following specifications must be met:

- a) the mitotic index and the mean number of cells with aberrations per group are reported for each group of animals;
- b) a clear negative outcome is concluded when the data available shows that bone marrow exposure to the Substance, or its metabolite(s), occurred;
- c) the negative control data is ideally within the 95% control limits of the distribution of the laboratory's historical negative control database.

7 In study (i):

- a) the mitotic index and the mean number of cells with aberrations per group were not reported for each group of animals;
- b) you did not demonstrate that bone marrow exposure to the Substance, or its metabolite(s), occurred;
- c) you did not prove that the negative control showed a response within the historical control range of the laboratory.

8 The information provided does not cover the specifications required by the OECD TG 475.

- 9 In your comment to the draft decision, you indicate that the study was in line with the respective OECD Test Guideline in place at the time the study was performed.
- 10 ECHA acknowledges that the study (i) should have been assessed according to the Test Guideline applicable at the time the study was performed. Based on the decision of the Board of Appeal (A-001-2022 decision), ECHA has modified the assessment accordingly.
- 11 In your comments to the draft decision, you indicate that you will provide the missing information under points a) and c) above in a future update of your registration dossier. You however claim that this information "*not a mandatory field in IUCLID*" and that "*ECHA's own guideline was not listing these specific details*".
- 12 ECHA takes note of your intention to provide additional information on the existing study from your dossier. However, this information is not yet available in your dossier, no assessment can currently be made. Furthermore, ECHA emphasizes that OECD TG 475 specifies the information that needs to be reported in order to adequately describe the methodology applied and the results obtained in a specific study. These reporting requirements includes points a) to c) as listed above.
- 13 Regarding point b) above, you mention that "*systemic bioavailability of Cs administered by gavage after acute and repeated dose exposure has clearly been shown*" and you will include this information in your dossier.
- 14 ECHA understand from your comments that you consider that providing information on point b) above is not necessary. However, ECHA emphasizes that the examination of the bone marrow exposure to the tested substance is one the mandatory conditions listed in the paragraph 44 of the OECD TG 475. This condition must be fulfilled to confirm the reliability of the conclusion drawn from such study when negative results are obtained. Therefore, ECHA maintains that this information must be provided.
- 15 On this basis, your comments on the draft decision do not change the assessment's outcome.
- 16 Therefore, ECHA maintain that study (i) does not meet the information requirement.

*1.3.2. Your read-across adaptation is rejected (study (ii))*

- 17 You provide a read-across justification document in IUCLID Section 13.
- 18 You predict the properties of the Substance from information obtained from the following source substance:
- Cesium hydroxide monohydrate, EC 627-088-9.
- 19 You provide the following reasoning for the prediction of toxicological properties: "*Inorganic cesium salts used in this read across statement are all well water soluble and completely dissociate in aqueous media forming the cesium cation and a corresponding counter ion. The counterions are generally of low toxicity or their toxicity (e.g. local effects) can be regarded as negligible for the endpoint under consideration. Therefore, the cesium moiety represents the relevant species triggering the toxicological profile with regard to systemic toxicity*".
- 20 ECHA understands that your read-across hypothesis is based on the formation of common (bio)transformation products. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

*1.3.2.1. Inadequate or unreliable study (ii) on the source substance*

- 21 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the

corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 475. Therefore, the following specifications must be met:

- a) the mitotic index and the mean number of cells with aberrations per group are reported for each group of animals;
- b) a clear negative outcome is concluded when the data available shows that bone marrow exposure to the Substance, or its metabolite(s), occurred;
- c) the negative control data is ideally within the 95% control limits of the distribution of the laboratory's historical negative control database.

22 In study (ii):

- a) the mitotic index and the mean number of cells with aberrations per group were not reported for each group of animals in study;
- b) you did not demonstrate that bone marrow exposure to the Substance, or its metabolite(s), occurred in study;
- c) you did not report if the negative control showed a response within the historical control range of the laboratory in study.

23 In your comments to the draft decision, you indicate that you will provide the missing information under points a) and c) above in a future update of your registration dossier. You also specify that this information "*not a mandatory field in IUCLID*" and that "*ECHAs own guideline was not listing these specific details*".

24 ECHA takes note of your intention to provide additional information on the existing study from your dossier. However, this information is not yet available in your dossier, no assessment can currently be made. Furthermore, ECHA emphasizes that OECD TG 475 specifies the information that needs to be reported in order to adequately describe the methodology applied and the results obtained in a specific study. These reporting requirements includes points a) to c) as listed above.

25 Regarding point b) above, your comment has already been addressed above for study (i).

26 On this basis, your comments on the draft decision do not change the assessment's outcome.

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

28 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance. On this basis, your read-across approach under Annex XI, Section 1.5. is rejected.

29 Therefore, the information requirement is not fulfilled.

30 In your comments to the draft decision, you state that you will "*carefully assess, if a new animal study (being the last resort under REACH) is really the only option taken into account all the information available already*". You also state that you have "*received the same data request for several soluble Cs salts based on more or less the same rational [...]*" and that you "*will certainly consider the read across option for soluble Cs salts*".

31 As this strategy relies on a read-across approach that has not yet been fully described and justified, as well as on data which is yet to be provided for the source substance(s) (including bridging studies and supporting information), no conclusion on the compliance of the proposed adaptation can be made. You remain responsible for complying with this decision by the set deadline.

#### 1.4. Test selection

- 32 The positive *in vitro* results available in the dossier indicate a concern for chromosomal aberration.
- 33 The *in vivo* mammalian erythrocyte micronucleus test ("MN test", OECD TG 474) and the *in vivo* mammalian alkaline comet assay ("comet assay", OECD TG 489) can be combined in a single study (OECD TG 474, paragraph 37c; OECD TG 489, paragraph 33; Guidance on IRs & CSA, Section R.7.7.6.3). While the MN test can detect both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy), the comet assay can detect primary DNA damage that may lead to gene mutations and/or structural chromosomal aberrations.
- 34 The combined study, together with the results of the *in vitro* mutagenicity studies, can be used to make definitive conclusions about the mechanism(s) inducing *in vivo* mutagenicity and lack thereof. Furthermore, the combined study can detect effects in both distant organs, such as the bone marrow or the liver, and at site(s) of contact, such as the glandular stomach, the duodenum or the lung. Investigating several genotoxic endpoints and different tissues in a combined study is necessary to reduce the uncertainties of not testing all organs and to generate complementary information that provides a comprehensive overview of the genotoxic potential of the Substance. Moreover, the combined study can help reduce the number of tests performed and the number of animals used.
- 35 Therefore, the comet assay combined with the MN test is the most appropriate study for the Substance.
- 36 In your comments to the draft decision, you claim that there is no specific OECD TG for combining the *in vivo* comet assay and the *in vivo* micronucleus test into a single study and that this situation, according to you, causes "legal uncertainty".
- 37 However, ECHA notes that both the OECD TG 474 (paragraphs 36 and 37) and the OECD TG 489 (paragraphs 7 and 33) contain detailed recommendations on how to combine the *in vivo* comet assay and the *in vivo* micronucleus test into a single study as well as references to scientific publications demonstrating the successful combination of both tests.

#### 1.5. Study design

- 38 According to the test method OECD TG 489, rats are the preferred species. Other rodent species can be used if scientifically justified. According to the test method OECD TG 474, the test may be performed in mice or rats. Therefore, the combined study must be performed in rats, or if justified, in mice.
- 39 Having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.
- 40 In line with the test method OECD TG 489, the test must be performed by analysing tissues from liver as primary site of xenobiotic metabolism, glandular stomach and duodenum as sites of contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the Substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.
- 41 In your comments to the draft decision, you argue that the Substance does not raise any concern for gene mutation from the *in vitro* test results in bacteria and mammalian cells and that the *in vivo* comet assay is not appropriate to address the chromosomal aberration concern coming from the positive *in vitro* chromosomal aberration study (1994). You repeat

your argument that performing a new *in vivo* study is not necessary as the provided OECD TG 475 (2012) with the Substance and toxicokinetic information available in your dossier on other cesium substances are sufficient to address the chromosomal aberration concern identified *in vitro* for the Substance. You further disagree with testing both the glandular stomach and the duodenum as sites of contact in the comet assay and consider analysis of the glandular stomach as sufficient since concentrations of the Substance are expected to be higher than in the duodenum after oral administration. You base your argument on the OECD TG 489 and a publication from Kirkland *et al.* (2015), which both indicate that only one site of contact needs to be investigated to detect genotoxic substances.

- 42 ECHA disagrees with your statement that an *In vivo* mammalian alkaline comet assay combined with *in vivo* mammalian erythrocyte micronucleus test is not an adequate follow-up study to investigate further concern for chromosomal aberration when no concern for gene mutation is indicated. ECHA considers the *in vivo* comet assay as a suitable test to investigate chromosomal aberrations *in vivo*, in particular when combined with the *in vivo* micronucleus test. The *in vivo* comet assay can detect genotoxic effects that can potentially lead to gene mutations and/or chromosomal aberrations and can be used to investigate different tissues, including sites of contact. As the Substance has been shown to induce chromosomal aberrations and not gene mutations *in vitro*, positive *in vivo* comet assay results can be assumed to reflect the potential of the Substance to induce chromosomal aberrations *in vivo*, in the liver and at site-of-contact tissues. Additionally, combination of the *in vivo* comet assay with the *in vivo* micronucleus test will provide information on the mutagenic effects of the Substance in the bone marrow, a distant target organ, and allow a clarification of its chromosomal aberration mechanism(s), *i.e.* clastogenicity and/or aneugenicity.
- 43 Regarding ECHA's request to investigate, in addition to the liver, both the glandular stomach and the duodenum as site-of-contact tissues in the *in vivo* comet assay, is based on physiological differences between the various tissues and uncertainty regarding differences in exposure following oral administration. As you indicate in your comments to the draft decision, the glandular stomach may be more exposed to the Substance than the duodenum. However, ECHA notes that the Substance is corrosive and that you self-classified it as Skin Corr. 1A. In your comments to the draft decision, you also refer to the corrosive properties of the Substance that can cause massive local tissue damage in the gastro-intestinal tract. On that basis, a higher toxicity is expected in the glandular stomach than in the duodenum. According to paragraph 54 of OECD TG 489, positive findings in the comet assay can be due to genotoxicity but may also result from target tissue toxicity and subsequent increases in DNA migration [...] and increases in DNA migration in the presence of clear evidence of cytotoxicity should be interpreted with caution. For these reasons, ECHA disagrees that an analysis of the glandular stomach is sufficient and considers that investigation of two sites of contact, with potentially different levels of confounding cytotoxicity, is necessary and will help in the interpretation of the findings in the *in vivo* comet assay.
- 44 According to the test method OECD TG 474, in order to demonstrate the ability of the study to identify clastogens and aneugens, you must include two concurrent positive controls, one known clastogen and one known aneugen (OECD TG 474, paragraph 25, Table 1).
- 45 The combination of the OECD TGs 489 and 474 should not impair the validity of and the results from each individual study. Careful consideration should be given to the dosing, and tissue sampling for the comet analysis alongside the requirements of tissue sampling for the mammalian erythrocyte micronucleus test (see OECD TG 489, e.g. Bowen et al. 2011 [1]).



[1] Bowen DE *et al.* (2011) Evaluation of a multi-endpoint assay in rats, combining the bone-marrow micronucleus test, the comet assay and the flow-cytometric peripheral blood micronucleus test. *Muta Res*;722:7–19.

#### 1.5.1. Assessment of aneugenicity potential

- 46 If the result of the *in vivo* MN test is positive, i.e. your Substance induces an increase in the frequency of micronuclei, you must assess the aneugenic potential of the Substance. In line with the OECD TG 474 (paragraph 42), you should use one of the centromere labelling or hybridisation procedures to determine whether the increase in the number of micronuclei is the result of clastogenic events (i.e. micronuclei contain chromosome fragment(s)) and/or aneugenic events (i.e. micronuclei contain whole chromosome(s)).
- 47 In the comments to the draft decision, you argue that aneugenicity assessment in case of positive results in the requested combined *in vivo* comet assay and *in vivo* micronucleus test is not necessary as (i) clastogenic effects were shown in the *in vitro* chromosomal aberration test with the Substance, (ii), there is no difference in the hazard assessment, risk assessment or classification and labelling between substances inducing aneugenic effects or clastogenic effects *in vivo*, and (iii) there are technical challenges to chromosome centromere staining in the *in vivo* micronucleus test.
- 48 Regarding point (i), you indicate in your dossier that the *in vitro* chromosomal aberration test with the Substance (1994) shows the induction of structural chromosomal aberrations as well numerical chromosomal aberrations (polyploid cells) at the maximum concentration of 1500 µg/mL in the 48h-treatment without metabolic activation. ECHA agrees with your conclusions that the study results raise a concern for chromosomal aberration. However, while the OECD TG 473 stresses the fact that the test is not designed to measure aneuploidy and that polyploidy alone does not necessarily indicate an aneugenic potential and can simply reflect cell cycle perturbation or cytotoxicity, ECHA considers that potential aneugenic properties of the Substance cannot be excluded based on the study results.
- 49 Regarding point (ii), ECHA disagrees that there is no difference in the hazard and risk assessment of aneugenic substances and clastogenic substances since aneugenic effects are considered as having a non-linear dose (concentration)-response curve and a threshold could in principle be identified for aneugenic substances and trigger specific risk management measures, contrary to clastogenic effects. However, ECHA acknowledges the fact that, if the Substance is confirmed to have both clastogenic and aneugenic properties, risk assessment would normally be based on its clastogenic effects as worst case. As the *in vitro* and *in vivo* data in your dossier are not sufficient to conclude on the mutagenic properties of the Substance and the *in vivo* micronucleus test can detect both clastogenic and aneugenic substances, ECHA considers it as the most appropriate *in vivo* follow up test to clarify the chromosomal aberration mechanisms of the Substance, in particular when combined with the *in vivo* comet assay, which will allow a broader coverage of target organs compared to the *in vivo* micronucleus test alone.
- 50 Regarding (iii), and as highlighted in the OECD TG 473, an *in vitro* micronucleus test would be recommended for the detection of aneuploidy *in vitro*. As an *in vitro* micronucleus test with the Substance was not conducted and the exact mechanism of chromosomal aberration is not fully clarified, aneugenicity assessment in case of positive results *in vivo* is necessary. According to OECD TG 474 (paragraph 42), 'anti-kinetochore antibodies, FISH with pancentromeric DNA probes, or primed *in situ* labelling with pancentromere-specific primers, together with appropriate DNA counterstaining, can be used to identify the nature of the micronuclei (chromosome/chromosomal fragment) in order to determine whether the mechanism of micronucleus induction is due to clastogenic and/or aneugenic activity. Other methods for differentiation between clastogens and aneugens may be used if they have been shown to be effective.'

### 1.5.2. Investigation of target tissue exposure

- 51 The applicable test method OECD TG 474 states that "If there is evidence that the test substance(s), or its metabolite(s), will not reach the target tissue, it may not be appropriate to use this test". Additionally, a negative test result can be considered reliable only if "Bone marrow exposure to the test substance(s) occurred".
- 52 Therefore, to ensure that the data generated are adequate for hazard identification, you must take blood samples at appropriate times and measure plasma levels of the Substance and/or its metabolites (OECD TG 474, paragraph 40), unless exposure of the bone marrow can be demonstrated through other means, e.g. by showing a depression of immature to mature erythrocyte ratio (OECD TG 474, paragraph 48).
- 53 If the Substance is negative in this test, but it is not possible to demonstrate that bone marrow exposure to the Substance occurred, then ECHA will consider any remaining uncertainty concerning the mutagenic potential of the Substance and whether to request any further information.
- 54 In your comment to the draft decision, you indicate that "There are enough data at hand about the bioavailability of the Cs salts after single and repeated dosing in rats. Therefore, additional data are not required to address this issue." ECHA reminds you that a "blood sample should be taken at appropriate time(s) in order to permit investigation of the plasma levels of the test substances for the purposes of demonstrating that exposure of the bone marrow occurred, where warranted and where other exposure data do not exist" (OECD TG 474, paragraph 40). The examination of the bone marrow exposure to the substance is one of the conditions listed in the paragraph 48 of the OECD TG 474 that must be fulfilled in order to assess if the results are clearly negative.

### 1.5.3. Germ cells

- 55 You may consider collecting the male gonadal cells from the seminiferous tubules in addition to the other aforementioned tissues in the comet assay, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2 months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells in the comet assay, you should consider analysing the slides prepared with gonadal cells.
- 56 This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

## 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 October 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 did not amend the requests.

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.

<b>Registrant Name</b>	<b>Registration number</b>	<b>Highest REACH Annex applicable to you</b>
[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>).