Helsinki, 21 April 2016

Addressee: [redacted]

Decision number: CCH-D-2114329769-33-01/F
Substance name: A mixture of: propan-2-one-O,O'(methoxyvinylsilandiyl)dioxime; propan-2-one-O-(dimethoxyvinylsilyl)oxime; propan-2-one-O,O',O''-(vinylsilantriyl)trioxime
EC number: 458-680-3
CAS number: 797751-44-1
Registration number: [redacted]
Submission number: [redacted]
Submission date: 20.10.2011

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA requests you to submit information on

1. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2; test method: EU B.26/OECD TG 408) in rats; with the registered substance;**

2. **Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1; test method: OECD 421/422) with the registered substance;**

3. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2; test method: EU B.31/OECD TG 414) in a first species (rats or rabbits), oral route with the registered substance;**

4. **Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1; test method: EU C.7/OECD TG 111) with the registered substance;**

5. **Adsorption/desorption screening (Annex VIII, Section 9.3.1.; test method: Adsorption/desorption using a batch equilibrium method, OECD TG 121);with the hydrolysis and/or degradation products, whichever are the most relevant, of the registered substance;**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **29 October 2018**. You shall also update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2. 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, shall 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 Guilhem de Seze, Head of Unit, Evaluation E1

[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

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

A "sub-chronic toxicity study (90 day)" is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of a sub-chronic toxicity study (90 day) in the dossier that would meet the information requirement of Annex IX, Section 8.6.2.

You have sought to adapt this information requirement according to Annex IX, Section 8.6.2., column 2. You provided the following justification for the adaptation *"According to REACH Annex IX, the 90 days study does not need to be conducted because the substance hydrolyses very fast and very high molecular weight polymer molecules are formed in that process. Their big molecular size is a barrier for the cell absorption. The reaction mass molecules have very low water solubility. The polymer formed (dimers, trimers, tetramers and higher structures) are not soluble in water. The 28-days toxicity study shows no toxic effects. The exposition to humans is unlikely".*

The specific rules for adaptation of Annex IX, Section 8.6.2, column 2, 3rd and 4th indents state that the sub-chronic toxicity study (90 days) does not need to be conducted if:

- A substance undergoes immediate disintegration and there are sufficient data on the cleavage products (both for systemic effects and effects at the site of uptake), or
- The substance is unreactive, insoluble and not inhalable and there is no evidence of absorption and no evidence of toxicity in a 28-day 'limit test', particularly if such a pattern is coupled with limited human exposure.

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 8.6.2., column 2, 3rd or 4th indents because:

- Although the substance has a half-life of under <1 hour in the hydrolysis study, this does not show that the substance undergoes *immediate disintegration.*
- Regardless of the half-life of the substance, the requirements of the 3rd indent are not met as the dossier does not contain sufficient data on the cleavage products (both of systemic effects and effects at the site of uptake). In fact, as pointed out above, there is no information on the identity of the cleavage products, and no information has been provided to support the assertion that polymers or very high molecular weight products cannot be absorbed.
- No toxicokinetics data were provided to support that no absorption occurs. On the contrary, the available 28-d study (OECD 407) indicates toxicity at the mid and high doses, with a NOEL 20 mg/kg bw/d indicating already an adverse effect and the possibility for absorption of the parent substance, the hydrolysis products, or both.
- No exposure assessment is provided in the dossier/CSR; only an attachment with exposure estimates related to production and to use indicating that exposure related to use for consumers are *"Not known, the substance hydrolyses very fast" and for production "filling the final product: placing in the open air - workers should be protected correctly".*

ECHA notes that the substance has uses in formulation, by professional workers and consumers (adhesives, sealants, intermediate, coatings and paints, paint removes and modelling clay). A low release is seen in ERC but for workers a clear potential for exposure is seen in the PROCS (e.g. transfer of substance or preparation; roller application and brushing; and non-industrial spraying). Hence, limited exposure is not demonstrated.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, July 2015) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration. More specifically, even though the information indicates that human exposure to the registered substance by the inhalation route is likely, the available oral 28-day study indicates a concern for systemic toxicity (high dosed males had a significantly lower body weight and test substance caused damage to mature erythrocytes in the peripheral blood, resulting in alterations in virtually all erythrocyte-related parameters at the haematological examination) that requires further information on repeated dose toxicity by the oral route. Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

According to the test method EU B.26/OECD TG 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Repeated dose 90-day oral toxicity study (test method: EU B.26./OECD TG 408) in rats.

2. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Screening for reproductive/developmental toxicity" (test method OECD TG 421 or 422) is a standard information requirement as laid down in Annex VIII, Section 8.7.1. of the REACH Regulation if there is no evidence from available information on structurally related substances, from (Q)SAR estimates or from *in vitro* methods that the substance may be a developmental toxicant. No such evidence is presented in the dossier. Therefore, adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of a screening for reproductive/developmental toxicity in the dossier that would meet the information requirement of Annex VIII, Section 8.7.1.

You have sought to adapt this information requirement according to Annex IX, Section 8.7., column 2. You provided the following justification for the adaptation *"According to REACH Annex IX, Column 2, the study does not to be conducted is the substance is of low toxicological activity (no evidence of toxicity was seen in any of the tests available), and the human exposure is unlikely".*

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 8.7., column 2, third indent because:

- The provided 28-day study in the technical dossier indicates toxicity at the mid- and high doses.
- There are no toxicokinetics data available in the dossier to support that no absorption occurs.
- In addition, the substance is used in finger paints and modelling clay. You also report uses where opportunity for exposure arises and you indicate applications were brushing and non-industrial spraying occurs. Therefore, the unlikely exposure is not demonstrated in the technical dossier.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.
According to the test methods OECD TG 421/422, the test is designed for use with rats. On the basis of this default assumption ECHA considers testing should be performed with rats.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, July 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Reproductive/developmental toxicity screening test (test method: OECD TG 421) *or* Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (test method: OECD TG 422) in rats by the oral route.

Notes for your considerations

For the selection of the appropriate test, please consult ECHA *Guidance on information requirements and chemical safety assessment*, Chapter R.7a, section R.7.5 and 7.6 (version 4.0, July 2015).

3. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

A "pre-natal developmental toxicity study" (test method EU B.31./OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.
You have not provided any study record of a pre-natal developmental toxicity study in the dossier that would meet the information requirement of Annex IX, Section 8.7.2.

You have sought to adapt this information requirement according to Annex IX, Section 8.7., column 2. You provided the following justification for the adaptation *"According to REACH Annex IX, Column 2, the study does not to be conducted is the substance is of low toxicological activity (no evidence of toxicity was seen in any of the tests available), and the human exposure is unlikely."*

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 8.7., column 2, third indent because:

- The provided 28-day study in the technical dossier indicates toxicity at the mid- and high doses.
- There are no toxicokinetics data available in the dossier to support that no absorption occurs.
- In addition, the substance is used in finger paints and modelling clay. You also report uses where opportunity for exposure arises and you indicate applications were brushing and non-industrial spraying occurs. Therefore, the unlikely exposure is not demonstrated in the technical dossier.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test method EU B.31/OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default assumption ECHA considers testing should be performed with rats or rabbits as a first species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, July 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a first species (rats or rabbits) by the oral route.

4. Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Hydrolysis as a function of pH" is a standard information requirement as laid down in Annex VIII, Section 9.2.2.1 of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You reported 3 endpoint study records addressing each of the 3 main constituents performed according to EU C7 method (2005). The results provided were a half-life or DT 50 < 1 hr at 25 °C, for all 3 constituents and at pH of 4.0, 7.0, and 9.0. No replicate was done for the constituents' half-life hydrolysis measurements and no data on the hydrolysis products was provided in the robust study summary.
The only information provided in the robust study summary on the hydrolysis products or transformation was:*" The test substance is composed of several compounds, including the 3 main components. They polymerise, triggered by hydrolysis."*

The technical dossier contains information on hydrolysis rate but not on the identity of the hydrolysis products. According to the test guidelines OECD TG 111 "*The hydrolysis test is performed to determine the rate of hydrolysis of the test substance as a function of pH and temperature and to identify or nature and rates of formation and decline of hydrolysis products to which organisms may be exposed*". As the information reported in the technical dossier does not contain information on the identification and quantification of the hydrolysis products as prescribed in tier 3 by the method, the information provided is not adequate to fulfil the standard information requirement.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

The analysis of hydrolysis or transformation products of the 3 main constituents of the registered substance are of paramount importance as these products are the ones to which all aquatic organisms and the various environmental compartments will be exposed to. According to the ECHA Guidance on Information Requirement and Chemical Safety Assessment, Chapter R.11: PBT/vPvB assessment, careful consideration will need to be given to the formation of stable degradation products with potential PBT/vPvB properties. Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Hydrolysis as a function of pH (test method: EU C.7/OECD TG 111). This shall include identification and quantification of the hydrolysis products, as described by the test guideline.

5. Adsorption/desorption screening (Annex VIII, Section 9.3.1.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

"Adsorption/desorption screening" is a standard information requirement as laid down in Annex VIII, Section 9.3.1. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement by providing waiver as per column 2 of REACH Annex VIII, section 9.3.1.:*"An experimental determination of the adsorption coefficient KOC could not be performed, because: 1) the test substance rapidly degrades with a half-life time of <1 hour at 25 °C and 2) the test substance is a mixture of several compounds and reacts with water as part of the eluent. EPI Suite v3.12 was therefore used for each constituent and log Koc of 3.6, 4.3 and 5.0 were provided."*

The specific rules for adaptation of Annex VIII, Section 9.3.1, column 2, 2nd indent states that the adsorption/desorption screening does not need to be conducted if:

- the substance and its relevant degradation products decompose rapidly.

However, ECHA notes that your adaptation does not meet the specific rules for adaptation as the hydrolysis products or degradation products are not proven to decompose rapidly either under hydrolysis test results or for the readily biodegradation test results provided.

Furthermore, you gave QSAR results showing that the log Koc of the three main constituents is 3.6, 4.3 and 5.0.
Annex XI, Section 1.3 of the REACH Regulation states that results of (Q)SARs may be used instead of testing when the following conditions are met:

- results are derived from a (Q)SAR model whose scientific validity has been established,
- the substance falls within the applicability domain of the (Q)SAR model,
- results are adequate for the purpose of classification and labelling and/or risk assessment, and
- adequate and reliable documentation of the applied method is provided.

Adequate and reliable documentation should provide information on the scientific validity of the approach. The justification for using the (Q)SAR information should be based on the use of the QSAR Reporting Formats described in ECHA Guidance on information requirements and chemical safety assessment (May 2008), Chapter R.6 (Section R.6.1.6.):

- The description of a particular (Q)SAR model (i.e. description of the algorithm, its development and validation based on the OECD principles) will be stored in the (Q)SAR Model Reporting Format (QMRF).
- The (Q)SAR Prediction Reporting Format (QPRF) will explain how an estimate has been derived by applying a specific model or method to a specific substance. This should include information on the model prediction(s), including the endpoint, a precise identification of the substance modelled and the relationship between the modelled substance and the defined applicability domain.

This QSAR prediction based on the structures you used does not fulfill REACH requirements for Annex XI 1.3 adaptations and should be rejected based on the following conditions that according to REACH Annex XI, 1.3:

- the substance does not fall within the applicability domain of the (Q)SAR model as the substance is a multiconstituent with 3 components (used as representative of the registered substance) for which, in addition, there are no close analogues in the training sets for all representative structures;

- the results are not adequate for the purpose of classification and labelling and/or risk assessment, the substance being a multiconstituent, either several representative structures of the parent compound should have been used for prediction or an explanation why you think you used a worst-case representative structure; and

- adequate and reliable documentation is not provided as no QMRF and QPRF were provided.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

In your comments on the draft decision, you reiterated the technical difficulties in conducting any testing due to fast hydrolysis of the registered substance, as confirmed by an OECD 111, GLP study. Although the study does not contain replicates and does not identify the hydrolysis products, ECHA reconsidered this knowledge and agrees that the value of obtaining adsorption/desorption information (whether via an experimental study or QSAR method) on the registered substance is not relevant. Nevertheless, there is a lack of information for the hydrolysis and/or degradation products for this endpoint, which is still necessary to address the environmental fate of the substance. This is clearly indicated in the ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) R.7a, chapter R.7.1.15 and the ECHA *Guidance on PBT assessment* (Chapter R.11, November 2014). As the technical dossier currently does not contain any data on the hydrolysis and/or the degradation products of the substance, ECHA has amended the request in the draft decision accordingly.
Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the hydrolysis and/or degradation products depending on their relevance, of the registered substance subject to the present decision: Adsorption/desorption screening. Guidance for determining appropriate test methods for the adsorption/desorption screening is available in the ECHA Guidance on information requirements and chemical safety assessment (version 2.3., December 2013), Chapter R.7a, Section R.7.1.15.3.

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 23 October 2015.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation:

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

ECHA took into account your comment and amended the request.

On 3 March 2016 ECHA notified the Competent Authorities of the Member States of its draft decision and invited them pursuant to Article 51(1) of the REACH Regulation to submit proposals for amendment of the draft decision within 30 days of the receipt of the notification.

As no proposal for amendment was submitted, ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. The substance subject to the present decision is provisionally listed in the Community rolling action plan (CoRAP) for start of substance evaluation in 2018.

2. This compliance check decision does not prevent ECHA from initiating further compliance checks on the present registration at a later stage.

3. Failure to comply with the request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

4. In carrying out the test(s) required by the present decision it is important to ensure that the particular sample of substance tested 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. If the registration of the substance covers different grades, the sample used for the new test(s) must be suitable to assess these. Furthermore, there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.