Committee for Risk Assessment (RAC)

Committee for Socio-economic Analysis (SEAC)

Opinion on an Application for Authorisation for

Diarsenic trioxide

Industrial use of diarsenic trioxide to produce a copper concentrate in the purification of the leaching solution in a zinc electro winning process

ECHA/RAC/SEAC: AFA-O-0000004618-67-13/D

Consolidated version

Date: 15 October 2014

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Consolidated version of the
Opinion of the Committee for Risk Assessment
and
Opinion of the Committee for Socio-economic Analysis

on an Application for Authorisation

Having regard to Regulation (EC) No 1907/2006 of the European Parliament and of the Council 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (the REACH Regulation), and in particular Chapter 2 of Title VII thereof, the Committee for Risk Assessment (RAC) and the Committee for Socio-economic Analysis (SEAC) have adopted their opinions in accordance with Article 64(4)(a) and (b) respectively of the REACH Regulation with regard to an application for authorisation for:

Chemical name(s):	**Diarsenic trioxide**
EC No.:	**215-481-4**
CAS No.:	**1327-53-3**

for the following use:

Industrial use of diarsenic trioxide to produce a copper concentrate in the purification of the leaching solution in a zinc electro winning process

Intrinsic property referred to in Annex XIV:

Carcinogenic (Article 57[a] of the REACH Regulation)

Applicant

Nordenhamer Zinkhütte GmbH

Reference number

11-0000000338-75-0000

Rapporteur, appointed by the RAC: **Marianne van der Hagen**
Co-rapporteur, appointed by the RAC: **Sonja Kapelari**

Rapporteur, appointed by the SEAC: **Stavros Georgiou**
Co-rapporteur, appointed by the SEAC: **Janez Furlan**

This document compiles the opinions adopted by RAC and SEAC.

PROCESS FOR ADOPTION OF THE OPINIONS

On **13 November 2013 Nordenhamer Zinkhütte GmbH** submitted an application for authorisation including information as stipulated in Articles 62(4) and 62(5) of the REACH Regulation. On **23 January 2014** ECHA received the required fee in accordance with Fee Regulation (EC) No 340/2008. The broad information on uses of the application was made publicly available at http://echa.europa.eu/web/guest/addressing-chemicals-of-concern/authorisation/applications-for-authorisation on **12 February 2014**. Interested parties were invited to submit comments and contributions by 9 April 2014.

The draft opinions of RAC and SEAC take into account the comments of interested parties provided in accordance with Article 64(2) of the REACH Regulation as well as the responses of the applicant.

The draft opinions of RAC and SEAC take into account the responses of the applicant to the requests that the SEAC made according to Article 64(3) on additional information on possible alternative substances or technologies.

The draft opinions of RAC and SEAC were sent to the applicant on **25 September 2014.**

On **15 October 2014** the applicant informed that it did not wish to comment on the opinions and the draft opinions of RAC and SEAC were therefore considered as the final on **15 October 2014**.

ADOPTION OF THE OPINION OF RAC

The draft opinion of RAC

The draft opinion of RAC, which assesses the risk to human health and/or the environment arising from the use of the substance – including the appropriateness and effectiveness of the risk management measures as described in the application and, if relevant, an assessment of the risks arising from possible alternatives – was reached in accordance with Article 64(4)(a) of the REACH Regulation on **12 September 2014**.

The draft opinion of RAC was adopted by consensus.

The opinion of RAC

Based on the aforementioned draft opinion and in the absence of comments from the applicant, the opinion of RAC was adopted as final on **15 October 2014**.

ADOPTION OF THE OPINION OF SEAC

The draft opinion of SEAC

The draft opinion of SEAC, which assesses the socio-economic factors and the availability, suitability and technical and economic feasibility of alternatives associated with the use of the substance as described in the application was reached in accordance with Article 64(4)(b) of the

REACH Regulation on **13 June 2014**.

The draft opinion of SEAC was adopted by consensus.

The opinion of SEAC

Based on the aforementioned draft opinion and in the absence of comments from the applicant, the opinion of SEAC was adopted as final on **15 October 2014**.

THE OPINION OF RAC

RAC confirmed that it is not possible to determine a DNEL for the carcinogenic (category 1A) properties of the substance in accordance with Annex I of the REACH Regulation.

RAC confirmed that the exposure assessment in the application is demonstrated to be appropriate and effective in limiting the risk, provided that the risk management measures and operational conditions are as described in the application.

The duration for the review period has been suggested below.

THE OPINION OF SEAC

SEAC has formulated its opinion on the socio-economic factors and the availability, suitability and technical and economic feasibility of alternatives associated with the use of the substance as documented in the application and on information submitted by interested third parties as well as other available information.

The application included the necessary information specified in Article 62 of the REACH Regulation that is relevant to the Committee's remit.

SEAC took note of RAC's confirmation that it is not possible to determine a DNEL for the carcinogenic (category 1A) properties of the substance in accordance with Annex I of the REACH Regulation.

SEAC confirmed that there appear not to be suitable alternatives in terms of their technical and economic feasibility for the applicant.

SEAC considered that the applicant's assessment of (a) the potential socio-economic benefits of the use, (b) the potential adverse effects to human health or the environment of use and (c) the assessment used to compare the two is based on acceptable socio-economic analysis. Therefore, SEAC does not raise any reservations that would change the validity of the applicant's conclusion that overall benefits of the use outweigh the risk to human health or the environment, whilst taking account of any uncertainties in the assessment.

The duration for the review period has been suggested below.

Use

The authorisation is considered for the following use:

Industrial use of diarsenic trioxide to produce a copper concentrate in the purification of the leaching solution in a zinc electro winning process

SUGGESTED CONDITIONS AND MONITORING ARRANGEMENTS

Conditions

The following conditions are recommended in case the authorisation is granted:

In the case of reapplication the applicant is requested to improve the exposure assessment to both workers and man via the environment.

Monitoring arrangements

The following monitoring arrangements are recommended in case the authorisation is granted:

No additional monitoring arrangements to those described in the application are proposed.

REVIEW

Taking into account the information provided in the analysis of alternatives prepared by the applicant and the comments received on the broad information on use the duration of the review period for the use is recommended to be twelve (12) years.

JUSTIFICATIONS

Substance name:	Diarsenic trioxide
Name of applicant(s):	Nordenhamer Zinkhütte GmbH
Use name:	Industrial use of diarsenic trioxide to produce a copper concentrate in the purification of the leaching solution in a zinc electrowinning process
Reference number:	11-0000000338-75-0000

The justifications for the opinion are as follows:

1. The substance was included in Annex XIV due to the following property / properties:

- ☒ Carcinogenic (Article 57(a))
- ☐ Mutagenic (Article 57(b))
- ☐ Toxic to reproduction (Article 57(c))
- ☐ Persistent, bioaccumulative and toxic (Article 57(d))
- ☐ Very persistent and very bioaccumulative (Article 57(e))
- ☐ Other properties in accordance with Article 57(f) [please specify]:

2. Is the substance a threshold substance?

- ☐ YES
- ☒ NO

Justification:

The cancer mode of action of arsenic and its inorganic compounds has not been established, but it appears not to be related to direct DNA reactive genotoxicity and therefore it is possible that the arsenic carcinogenicity has a threshold exposure level. However, the available data do not allow the identification of threshold exposure levels for key events in the modes of action proposed in the scientific literature (RAC/27/2013/07 Rev. 1.).

3. Hazard assessment. Are the DNEL(s) appropriate?

Justification:

RAC has established a reference dose response relationship for lung carcinogenicity of inorganic arsenic compounds (RAC/27/2013/07 Rev. 1.). Dose response relationships were derived by linear extrapolation. Extrapolating outside the range of observation inevitably introduces uncertainties. As the mechanistic evidence is suggestive of non-linearity, it is acknowledged that the excess risks in the low exposure range might be an overestimate. RAC has not derived DMEL values for inorganic arsenic compounds.

In the SEA the remaining human health risks are evaluated based on the dose-response relationship adopted by RAC.

4. Exposure assessment. Is the exposure from the use adequately described?

☒ YES

☐ NO

Justification:

- ***Exposure scenario***

The applicant described one exposure scenario:

"Industrial use of diarsenic trioxide to produce a copper concentrate in the purification of the leaching solution in a zinc electrowinning process (Scenario for workers and environment)."

The applicant described the following steps for this exposure scenario:

WCS[1]1: Preparation of arsenious acid solution (PROC 3)
WCS2: Use in purification process (PROCs 1/2/3)
WCS3: Packing, transport and storage of copper concentrate (PROCs 1/2/3/9/26)
WCS4: Cleaning work and handling of waste (PROC 8b/9/26)
WCS5: Maintenance work (PROC 8b)
ECS[2]1: Industrial use of diarsenic trioxide to produce copper concentrate (ERC 6a)

Amounts, duration and frequency of exposure in the contributing scenarios:

WCS1: 400 kg/d, 20 minutes/8h shift, maximum 2 preparation per 24h, about 600 preparations per year.

WCS2: Continuous process. As_2O_3 consumption is ca. 300-400 kg/day

WCS3: 4000-5000 kg/day, <1h/day in closing/changing bags. One packing, transport, storage takes 10 minutes, max 3 times per shift

WCS4: 365 days/year, 0.5h/shift (cleaning barrels, handling waste materials). Landfill area: Authorised waste management company.

WCS5: Variable tasks and amount of substances, duration of specific maintenance tasks 15min-8h/day/person.

ECS1: 140 t/year As_2O_3 continuous use, 365 days/24h

The same worker may be involved in multiple tasks covered by more than one WCS.

- ***Methodology used by applicant***

Worker exposure:

Measured data on As concentration in NZH workplace air is available. The routine method used is static sampling. The location of the sampling points and the frequency of the measurements are fixed by the plant safety officer as a result of the risk assessments. Personal air samplers are used as a supplementary measure and will be the routine way

[1] Worker Contributing Scenario
[2] Environmental Contributing Scenario

of monitoring in the future.

On-site measurement data are available for the WCSs. Also modelled data have been submitted by the applicant. For WCS1, 4 and 5 the tool ECETOC-TRA version 3.1.0 (The ECETOC Targeted Risk Assessment (TRA) tool, also called TRAM) was used. The new tool MEASE (version of TRA developed for metals) was used for workers exposure in WCS2, 3, 4 and 5. For WCS3 the higher tier model ART was applied but the input data are not available, so the results have not been used by RAC. Dermal exposure assessment is not available for WCS3.

In the exposure assessment the use of protective clothing including gloves are assumed for all WCS. For WCS1 respiration protective equipment (RPE) is always used. The use of personal protective equipment (PPE) (including RPE) was assumed by the applicant to reduce the exposure by 95 %. In the dermal estimates the use of PPE is taken into consideration in the modelling.

Effectiveness of ventilation was described in the CSR as 90 % for general ventilation by referring to defaults used in ECETOC-TRA.

Available exposure data for workers is summarised in Annex I.

Man via the environment:

Exposure of man via the environment (inhalation and oral) was modelled using EUSES (version 2.1). Model input parameters (partition co-efficients) were described and justified by the applicant. Their assessment included site-specific emission factors derived from monitoring data. Measured data on local exposure via inhalation were also available and were used preferably to modelled data. It should be noted that partition-based models are designed to work best with organic chemicals; the input values for inorganic arsenic may be less reliable.

- ***Values used in the SEA:***

Worker exposure:

WCS1, 4 and 5 are identified by the applicant to be tasks with the highest potential for exposure, especially WCS 1 and 5. For WCS1 there is a risk to get accidentally in contact with diarsenic trioxide, and for WCS5 because repairs and cleaning of the equipment lead to potential direct contact with As compounds. In the SEA, for practical reasons, the exposure is assumed by the applicant to be below 4 µg/m^3, a value equal to the applicant´s DMEL.

The exposure level used in the SEA is lower than the exposure levels presented in the exposure scenarios, resulting from modelling. Following the trialogue meeting the applicant provided a justification for the use of a level of 4 µg/m^3 for high exposure tasks based on the lower level measured data (stationary measurements), and installed RMMs such as negative-pressure, use of scrubber and effective containment. The additional justifications support using this value in the SEA. The tasks with high exposure potentials involve 8-10 (average 9) workers.

The other WCSs have the lower exposure potential, and are generally covered in the SEA by applying a background concentration of < 1 µg/m^3 in the working environment. There are about 30 workers involved in the tasks with the low exposure. Exposure data are presented in the Annex.

Even if RAC agrees to use the exposure of 4 µg/m^3 in the SEA, some of the modelled data indicate higher concentration in the working environment. A realistic worst case scenario could be to assume that the potential high exposure WCS 1, 4, 5 would be 1.2 µg/m^3 via inhalation (maximum values measured for WCS1 before adjusting to the use of RPE in WCS1). A realistic worst case scenario for the low exposure WCS 2 and 3 could be based on the measurements from WCS2, i.e. 0.22 µg/m^3. Equally a realistic worst case scenario for dermal exposure could be 34 µg/kg/day (which could be reduced to 1.7 µg/kg/day by applying an APF of 20 for wearing gloves), for WCS 1, 4, 5 and 0.2 µg/kg/day for WCS 2, 3, all for 8 hours/day and 40 years.
Based on the dose response relationship established by RAC the excess lifetime lung cancer mortality risk for workers is **1.4 x 10^{-4} per µg As/m^3** for the inhalable particulate fraction (based on a 40 year working life) and **6.4 x 10^{-6} per µg As/kg bw/day** for the dermal route (based on a 40 years working life)[3].

The numbers of workers are described in the SEA with 8-10 (average 9) workers involved with the high exposure tasks and 30 with the low exposure tasks.

Realistic worst case scenario for high exposed workers:
All workers (n=10) exposed to 1.2 µg/m3 and to ECETOC-TRA estimated dermal exposure of 34 µg/kg/day for 8 hours.
Realistic worst case scenario for low exposed workers:
All workers (n=30) exposed to 0.22 µg/m^3 and to ECETOC-TRA estimated dermal exposure of 0.2 µg/kg/day for 8 hours.

The table 1 gives an overview over the exposure and the corresponding risk level.

Table 1: overview of the exposure and the corresponding risk level

WCS	Exposure via Inhalation (measured) (µg/m^3)	Risk level without RPE	Skin exposure (estimated) (µg/kg/d)	Risk level with protective clothing, gloves
1, 4, 5	1.2	1.68 x 10^{-4}	34	2.18 x 10^{-4}
2, 3	0.22	3.08 x 10^{-5}	0.2	1.28 x 10^{-6}

RAC notes that the resulting risk level for high exposed workers is relatively high. It should be noted that the risk level from inhalation would decrease by 95% if RPE was taken into account. It should also be noted that not all of the WCS takes place the full shift, so this would also drive the risk in a decreasing direction.

[3] The risk from dermal route was calculated from the risk level for the general population according to the RAC dose-response relationship: 1.7 x 10^{-5} divided by 70 years (of exposure for the general population) and multiplied by 40 years (of exposure for workers), divided by 52 weeks and multiplied by 48 working weeks, divided by 7 days and multiplied by 5 working days per week, resulting in a risk level of 6.4 x 10^{-6} for the workers.

It is not always clear from the CSR and the additional information received if the use of PPE including RPE were assumed when estimating the exposure with models or if the need for it arose from the resulting RCR based on the exposure estimate. However RAC in its assessment used predominantly measured data, not taking into account potential use of RPE.

Man via the environment:

Arsenic is released to the air from NZH primarily in the form of AsH_3. In 2012 the average AsH_3 concentration in NZH exhaust air was 0.18 mg/Nm^3. In local air 0.0011 µg/m^3 was measured as the annual mean concentration of arsenic. The EUSES modelled estimate of a concentration in air was found to be 0.0533 µg/m^3 for the local exposure.

An initial exposure estimate for the combined inhalation and oral routes (diet) of exposure was calculated using EUSES as 4.81 µg/kg/day. This estimate was based on the default EUSES food basket approach and an assumption that all consumed food was produced locally (i.e. in the immediate vicinity of the zinc smelter). The principal source of exposure in this estimate comes from the intake of local leaf crops (98.5 % of total exposure). This initial exposure estimate was subsequently refined by the applicant by using representative estimates of the intake rates of leaf crops (rather than EUSES defaults) and an assumption that only 20 % of the leaf crops consumed were grown locally (as the applicant reports that there is no production of leaf crops in the vicinity of the zinc smelter). After these further refinements the oral exposure was estimated as 0.55 µg/kg/day. The local exposure via the inhalation was reported as 0.022 µg/day based on a measured concentration of 1.1 ng/m^3 (PM10 particulate fraction). RAC notes that this equals to 0.00031 µg/kg bw/day when assuming the default inhalation for general population of 20 m^3/day and a body weight of 70 kg. Combined exposure from oral and inhalation routes was therefore estimated by the applicant as 0.55 µg/kg/day. The applicant considers that the exposure estimates reported are over-estimates of the likely exposure via the oral route.

RAC considers that the exposure estimates derived by the applicant for the oral route (underpinned by modelling) are considerably more uncertain than the exposure estimates derived for the inhalation route (from monitoring). In addition, RAC acknowledges that the use of EUSES is likely to overestimate the exposure via the oral route in this application and that further refinement of model parameters or use of alternative models or techniques may allow a more definitive description of the exposure to man via the environment for this use. However, despite these limitations, RAC considers that the combined exposure estimate of 0.55 µg/kg bw/d for the local exposure via the environment presented by the applicant is suitable for use as a worst-case in impact assessment by SEAC.

5. If considered a threshold substance, has adequate control been demonstrated?

☐ YES

☐ NO

Justification:

Not relevant (non-threshold substance)

6. If adequate control is not demonstrated, is the remaining risk reduced to as low a level as is technically and practically possible?

Justification and concluding on the remaining risk:

The remaining human health risks are evaluated in the SEA based on the dose-response relationship published by RAC (RAC/27/2013/07 Rev. 1) and the estimated exposure levels. The overall risks are counted for two main population groups: risks to employees in NZH due to the exposure through inhalation; and risks to the general population of Nordenhamer town due to the exposure through inhalation and oral intake.

- **Workers**

For the purposes of the SEA, the applicant calculated an illustrative estimate of the presumed lung cancer cases from inhalation exposure. In addition, RAC calculated an illustrative estimate of the presumed lung cancer cases from the dermal exposure based on the exposure modelled by the applicant. The resulting exposure level and the corresponding risk level is not expected to give rise to any cases of the occupational cancer in the company from both the exposure via inhalation and the dermal exposure for 40 years exposure based on an assumption that high exposed workers were exposed to 1.2 µg/m^3 via inhalation, and dermally to 34 µg/kg/day, and low exposed workers to 0.22 µg/m^3 via inhalation, and dermally to 0.2 µg/kg/day.

The workers exposure has been evaluated under the assumption that sufficiently efficient general ventilation is in use in the process halls (operational with 90% effectiveness (default ECETOC-TRAM modelling value)).

In addition to training, job rotation, general ventilation and local exhaust ventilation the use of personal protective equipment (PPE) reduces the risk to the individual worker. For all WCS protective clothing including gloves are used. For WCS1 respiration protective equipment (RPE) is always used. For all other WCS RPE is not normally needed but still available if necessary if dust is generated. Effectiveness of both RPE and gloves was assumed by the applicant to be minimum 90% in the CSR.

Assuming the tasks would be carried out during the whole working day, and without RPE the inhalation by the exposure described above would theoretically result in a risk level of 1.68 x 10^{-4} for the high exposed workers in WCS 1, 4 and 5. As RPE is always used for WCS1 the actual risk would be tenfold lower, i.e. 1.68 x 10^{-5}. The inhalation by the exposure for the low exposed workers in WCS 2 and 3 would result in a risk level of 2.8 x 10^{-5}. As dermal protection is always used for all WCSs the additional risk from the dermal exposure would be 2.36 x 10^{-4} for the high exposed workers in WCS 1, 4 and 5 and 1.28 x 10^{-6} for the low exposed workers. If the effect of gloves is not considered, the exposure and corresponding risk levels would be 20 times higher (with assigned protection factor of 20 for the gloves). Table 2 summarises the risk estimates for

workers.

Table 2: Risk estimated from exposure of workers at NZH

WCS	Route	PPE/RPE	Exposure	Excess risk	Persons exposed[4]
1, 4, 5 high exposed	Inhalation	RPE	0.12 µg/m^3	1.68 x 10^{-5}	10
	Inhalation	-	1.2 µg/m^3	1.68 x 10^{-4}	10
	Dermal	PPE	34 µg/kg/day	2.36 x 10^{-4}	10
2, 3 low exposed	Inhalation	RPE	0.02 µg/m^3	-	-
	Inhalation	-	0.22 µg/m^3	3.08 x 10^{-5}	30
	Dermal	PPE	0.2 µg/kg/day	1.28 x 10^{-6}	30

The estimated exposure level is not expected to give rise to any cases of occupational cancer in the company. However, for the purposes of the SEA, RAC calculated the illustrative estimate of presumed lung cancer cases based on the realistic worst case exposure of 40 years.

High exposed workers (10 workers):
Inhalation: 10 x 1.2 µg/m^3 x 1.4 x 10^{-4} per µg As/m^3 = 0.00168 = 1.7 x 10^{-3}
Dermal: 10 x 34 µg/kg/day x 6.4 x 10^{-6} per µg As/kg bw/day = 0.00235 = 2.4 x 10^{-3}

Low exposed workers (30 workers):
Inhalation: 30 x 0.22 µg/m^3 x 1.4 x 10^{-4} per µg As/m^3 = 0.000924 = 9.2 x 10^{-4}
Dermal: 30 x 0.2 µg/kg/day x 6.4 x 10^{-6} per µg As/kg bw/day = 0.0000384 = 3.8 x 10^{-5}

- **Man via the environment**

During the trialogue meeting, the applicant clarified that the calculation of an illustrative estimate of presumed lung cancer cases based on the modelled exposure at a regional level was not considered necessary, because As_2O_3 would be deposited in precipitation as inorganic As or As compounds in the vicinity of the emission source, and the risk from regional exposure to man via the environment would be very low. In the SEA the citizens of Nordenham town (population 26,700) was used as the exposed population. The oral exposure to man via the environment was estimated as 0.55 µg/kg/day and the exposure from inhalation was estimated as 0.00031 µg/kg bw/day. The combined exposure was therefore estimated as 0.55 µg/kg/day. By applying the RAC reference dose-response relationship (RAC/27/2013/07 Rev. 1.) an excess lifetime cancer risk in a 70 year exposure for the general population was estimated to be:

Oral: 0.55 x 1.7 x 10^{-3} = 9.35 x 10^{-4}

Inhalation: 0.0011 x 1.0 x 10^{-3} = 1.1 x 10^{-6}

For the purposes of the SEA, the applicant has calculated an illustrative estimate of the presumed lung cancer cases based on the population in Nordenham by exposure of 70

[4] 10 + 30 persons, totally 40 persons, with or without PPE.

years which is 0.03 for the inhalation route and 22.91 for the oral route.

The applicant states that the risk level via the oral route should be interpreted with caution because of the conservative exposure assessment (described in section 4). RAC considers that the approach used to estimate the oral exposure is likely to have an overestimated exposure, but is adequate to estimate the worst case impacts for consideration by SEAC.

Table 3: Risk estimated from exposure to man via the environment for 70 years

Route	Exposure	Excess risk	Persons exposed
Inhalation	0.022 µg/day	1.1×10^{-6}	26.700
Oral	0.55 µg/kg/day	9.35×10^{-4}	26.700

- **Plausibility of risk management measures**

The occupational RMMs described in the application seem appropriate/adequate to protect the workers (closed systems where possible, general and local exhaust ventilation, job rotation, training, PPE), and will reduce the exposure. For workers a summary of the biomonitoring data was available in the CSR. These data were not used by RAC but it was noted that almost all values were below the guidance value of 50 µg/g creatinine reported by the applicant.

The company has implemented the IPPC and IED directives and comply with the emission limit value based on the Best Available Techniques. The on-site environmental protection equipment such as filters, exhaust gas washing facility, scrubbers and WWTP, and the waste treatment procedures, which is carried out in accordance with local regulations and permissions as well as guidelines to European legislation on waste and pollution prevention, results in a release factor for As of 0.0072 % for water, 0.05 % for air and 0 % to soil. The release of As to surface water is well below the limit value of 50 µg/l in the BREF/BAT document for this industry. The company comply with site specific environmental permissions set by the national authorities. According to the applicant the values of emissions of As to air are below national permission limit values as well as the limit value in Directive 2004/107/EC on air quality. The deposition of As was significantly lower than the national limit of 4 µg/m^2/day.

- **Conclusion**

RAC agrees that due to the differences in the population sizes (workers vs. general population), the majority of the theoretically estimated cancer cases would result from the exposure to man via the environment. For exposure to man via the environment RAC agrees that the quantification carried out by the applicant leads to overestimation of the cancer cases but can still be used as a worst case estimate in the SEA.

Furthermore, RAC agrees that the operational conditions and risk management measures in place are appropriate in reducing the exposures and the risk.

7. Justification of the suitability and availability of alternatives

7.1 Would the alternatives lead to overall reduction of risk?

☐ YES

☐ NO

☒ NOT APPLICABLE

It is not clear to RAC if the alternatives would result in a lower risk to workers and humans exposed via the environment. There is not enough information on hazards nor on the resulting exposure should these substances be used instead of As_2O_3. However, as the applicant has presented arguments that the alternatives are not economically feasible to justify that the alternatives are not suitable, the assessment of the risk from alternatives is not assessed further by RAC.

7.1.1 Are the risks of alternatives adequately described and compared with the Annex XIV substance?

☐ YES

☒ NO

☐ NOT APPLICABLE

Justification:

Justification: Two industrial scale alternatives were identified by the applicant as possible candidates, which could perform the function of eliminating metal impurities from the leaching solution (the impure electrolysis solution). The main alternative substances used in such processes are:

1) Diantimony trioxide, Sb_2O_3; or
2) Antimony potassium tartrate, $K_2Sb_2(C_4H_2O_6)_2$.

These two antimony compounds can be used interchangeably in the so-called antimony compound based process.

Hazard profile

Diantimony trioxide has a harmonized classification in CLP Annex VI as Carcinogenic in category 2 (Carc.2) with H351 (Suspected of causing cancer).

There is no harmonized classification in CLP for Antimony potassium tartrate but there is a harmonized classification for acute toxicity and aquatic chronic toxicity for index no 051-003-00-9 i.e. for antimony compounds with the exception of the tetroxide (Sb_2O_4), pentoxide (Sb_2O_5), trisulphide (Sb_2S_3), pentasulphide (Sb_2S_5) and those specified elsewhere in Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation).

According to the applicant the literature review of the toxicological information on antimony potassium tartrate ($K_2Sb_2(C_4H_2O_6)_2$) indicates that the existing data raises some health concerns. There is indication that the substance may induce mutations in

human and there is also concern about potential carcinogenicity. In general, the available information on $K_2Sb_2(C_4H_2O_6)_2$ is very limited and relatively old. Thus, the hazard assessment of most endpoints is based on published results of the experiments that often do not fulfil the current guideline requirements of the toxicological studies.

7.2 Are the alternatives technically and economically feasible for the applicant?

☐ YES

☒ NO

Justification:

The analysis of alternatives undertaken by the applicant sets out the possible alternatives that might be considered for replacing diarsenic trioxide. The applicant reaches the conclusion that whilst it would be technically feasible to replace their use of diarsenic trioxide, it would not be economically feasible to replace their use of diarsenic trioxide by the sunset date with an alternative.

SEAC concurs with this conclusion based on its assessment of the applicant's analysis. The applicant has searched for and investigated a number of alternatives based on either making the function performed by diarsenic trioxide redundant (i.e. use an alternative production process to electro winning), or finding an alternative substance that can perform the same function as diarsenic trioxide (i.e. elimination of metal impurities from the electrolysis solution that is integral to production under the electro winning process).

In terms of alternatives that make the function redundant, possible alternatives include pyrometallurgy and solvent extraction technologies. In both cases, the production facilities are very different from those used by the applicant and based on electro winning, and hence are not considered further by the applicant.

Two alternatives were identified by the applicant as being able to perform the same function as diarsenic trioxide in eliminating metal impurities under the electro winning process, both based on so-called antimony compound based processes. Whilst the applicant concludes that both these alternatives are technical feasible and available, they result in a reduction on overall production efficiency, as well as requiring a further purification step in order to equivalently utilise the bi-product metals produced as under the process using diarsenic trioxide. The economic feasibility of these alternatives was thus assessed by the applicant in terms of the increased investment costs and impact on production efficiency (and associated economic losses) associated with the switch to these alternatives. Specifically the applicant considers the additional machinery investment costs (including temporary production shutdown costs during machinery installation), working capital increases, higher operating costs and changes in sales revenues (net losses) associated with the use of the alternatives. The applicant notes that there are also some financial benefits from using the alternatives in terms of reductions in reagents and sales increases of copper.

Regarding machinery investment costs, the applicant claims that although the required reaction volume in the zinc solution purification is lower under the alternative process, a thickener is required and the processing of the primary precipitate is more complicated. In order then to produce a saleable copper concentrate, more reaction volume and more filtration capacity is necessary, thereby necessitating the additional machinery

investment. The machinery investment costs required for the modifications to the purification process are provided by the applicant, based on an in-house assessment of the costs, broken down by cost item. The applicant provided further information on the breakdown of these costs in the course of the trialogue and further questions from SEAC. This helped clarify the exact nature of the costs and provided SEAC with additional confidence in the quality of the assessment. As a result, SEAC considers them to be a sufficiently robust estimate. As part of the cost of the investment required, the applicant also estimated the losses that would be incurred as a result of the temporary 1 week production shutdown that would be necessary to install the new machinery and the ensuing reduction in production during a start-up period for the machinery of 3 months. The applicant confirmed during further questioning and clarification at the trialogue that the losses represent the loss in profit (EBIT) having accounted for production costs, etc. The level of detail was sufficient for SEAC to have confidence in the magnitude of these losses and SEAC considers them to be robust. The remaining components of the costs of switching to an alternative substance estimated by the applicant relate to the increase in working capital required to finance the additional zinc required in the process, the increases in operating costs and the changes in revenues (net losses) arising from an increase in zinc powder consumption and corresponding 3.2 % decrease in production capacity. The costs arising from the first two of these components are relatively modest, whereas the net losses from the change in sales of copper, cadmium and zinc (due to the increased zinc dust consumption) represent the main part of the total costs associated with the applicant having to switch to the alternative process. The calculation of the net losses from the change in sales is relatively straightforward based on the revenue structure of the applicant's business model, and hence SEAC has confidence in the magnitude of these losses given the level of transparency in their estimation by the applicant.

Taking into account the magnitude and robustness of the various components in the applicant's assessment of costs, SEAC agrees with the applicant's conclusion that there are significant net present costs of switching to the alternatives, such that these are not considered to be economically feasible.

7.2.1 Are the technical and economic feasibility of alternatives adequately described and compared with the Annex XIV substance?

☒ YES

☐ NO

Justification:

The applicant describes the technical and economic feasibility of two alternative substances. Although other technologies for production of zinc exist based on pyrometallurgy and solvent extraction, the applicants production facilities are based around the hydrometallurgical "electro winning" process (as is more than 80% of the world's production of zinc). The production facilities in the pyrometallurgical and solvent extraction processes are very different from the applicant's facilities, and hence their search for an alternative was focussed on finding a substance that can perform the same function as diarsenic trioxide, rather than on seeking a different process to electro

winning under which elimination of impurities from the electro winning process is made redundant. SEAC considers that the costs of an entirely new production facility would be relatively prohibitive as compared to the costs of an alternative to perform the same function as under the electro winning process, hence SEAC agrees with the applicant's rationale for restricting their search for an alternative.

The search for alternative substances which can perform the function of eliminating metal impurities from the electro winning solution has to be considered in the context that the electro winning process based on diarsenic trioxide purification technology has been the state of the art production process since the early 20th century. No significant developments have apparently been made in the fundamental technology over this period. As such the applicant undertook relevant and appropriate data searches and consultation with a specialist engineering and metals and mineral processing technology consultancy, who advised that there were only 2 alternatives that could perform the same function in the electro winning process as diarsenic trioxide. The two alternatives suggested were taken forward by the applicant for the assessment of technical and economic feasibility.

The two alternatives are based in essence on the same process and hence can be used interchangeably by industry. The assessment of technical and economic feasibility is thus identical for each. The description of technical feasibility of the alternatives identifies the technical differences with the diarsenic trioxide process, and describes the qualitative consequences for production (and hence on costs). Since the alternatives are considered by the applicant to essentially be technically feasible, SEAC are content with the description and comparison.

The level of detail provided by the applicant on economic feasibility was generally sufficient, although where it was not, further questioning and clarifications during the trialogue elicited a more detailed and transparent breakdown of costs to allow the magnitude of costs to be confirmed. SEAC thus has confidence in the estimates and considers the description of economic feasibility to adequately describe the current status of the substitution possibilities available to the applicant.

7.3 If alternatives are suitable, are they available to the applicant?

☐ YES

☐ NO

☒ NO SUITABLE ALTERNATIVES EXIST

Justification:

Although the alternatives considered by the applicant are considered by the applicant to be essentially technically feasible, as discussed in section 7.2, SEAC agrees that the alternatives are not economically feasible, and hence they cannot be considered suitable.

Given the long-standing historical profile of the technological process used by the

applicant, imminent change towards an alternative with no significant impacts on the production process and need for significant investments is unlikely. According to the applicant, the time period for considering investments in zinc production process technologies is of the order of 20 years, and hence the availability of alternatives, including those based on pyrometallurgy and solvent extraction must be considered in this context. This makes it unlikely that the economic feasibility and hence the suitability of alternatives will change in the near future. However, where such change to occur, the alternatives can be considered to be available, given that they are based on established industrial scale operating technology.

8. For non-threshold substances, have the benefits of continued use been adequately demonstrated to exceed the risks of continued use?

☒ YES

☐ NO

☐ NOT RELEVANT

Justification:

The assessment of impacts associated with this authorisation application and which has been undertaken by the applicant is based on a quantitative monetary assessment of the societal costs and benefits associated with the “non-use” of diarsenic trioxide. As such the perspective of the analysis is such that it aims to provide net cost estimates as the necessary corollary that the benefits of continued use exceed the risks of continued use. The net cost estimates are assessed on a net present value basis using a 20 year time horizon as the temporal scope of analysis for costs and a 70 year time horizon for benefits associated with health impacts to the local population, whilst a 40 year time horizon is used for workers health impacts. Although this is not ideal in terms of a consistent comparison of benefits and costs, the choice of different time periods is driven by the respective time frames under which: on the costs side, investments are considered (based on the lifetime of the capital equipment); on the benefits side, exposure time period used to derive the dose-response relationship for the health outcome of interest (in this case cancer). Irrespective, the approach is acceptable, since to the extent that the difference in time periods used cannot be factored formally into the analysis, any bias introduced will tend to induce conservatism (overestimation) in the health benefit estimates derived for the “non-use” scenario. This will have the effect of reducing the net cost estimates required as the necessary corollary that the benefits of continued use exceed risks. The analysis of the economic costs of the “non-use” scenario follows established procedures for the calculation of financial costs of switching to an alternative substance. The analysis of human health benefits is based on established procedures for the calculation of economic welfare changes as a result of human health risk reductions. An acceptable general methodological approach thus underpins the assessment of impacts. Moreover, the analysis can be considered to be proportionate, taking into account the relative size of costs and risks.

Costs

The analysis of the costs of "non-use" is based on data from the assessment of alternatives. The available information indicates that the switch to either one of the two technically feasible alternatives would result in the applicant incurring additional direct costs associated with the need for modifications to the purification steps in the production process, as well as an increase in zinc powder consumption and resulting 3.2% decrease in production capacity. In addition the installation of new machinery associated with the modification to the purification steps would necessitate the temporary closure and production shutdown of the plant facility, an increase in the working capital requirements of the applicant, as well as an increase in other operating costs. The costs associated with these impacts have been estimated in terms of the additional machinery investment equipment costs, the loss in profits from the temporary production shutdown, the change in sales (net losses) of copper, cadmium and zinc due to the 3.2% decrease in production capacity, as well as the costs of financing the working capital increase and the increase in additional operating costs. In its assessment (see *Assessment of Costs in* Annex) SEAC consider only the direct economic losses to the applicant as relevant for the comparison with the (health) benefits of the non-use scenario. The total direct economic costs associated with the non-use scenario are thus estimated by the applicant at €48.8 million (PV in 2013 for 20 year time period). SEAC confirms that the cost assessment undertaken by the applicant and embodied in the total cost estimate of €48.8 million provides a proportionate analysis and a methodologically and empirically appropriate estimate of the costs of non-use of diarsenic trioxide.

Benefits

The quantitative analysis of the benefits associated with the "non-use" of diarsenic trioxide is based on a health impact assessment using an 'impact pathway' type methodology. This estimates the change in physical health impacts (disease burden) due to changes in exposures as a result of the "non-use" scenario. The approach is based on linking quantitative relationships between exposure and the health impact of interest. This general procedure is widely used for the assessment of benefits related to pollutants and is considered to be an appropriate methodological approach. The sole health endpoint considered in the quantitative health impact assessment is the number of excess cancer cases. SEAC is unaware of any other relevant human health endpoints or environmental concerns. The number of cases of excess cancer has been estimated by the applicant at 0.0042 cases for workers at the applicant's facility based on an exposure time period of 40 years and 22.91 cases for the local population around the applicants facility based on an exposure time period of 70 years. Although there are uncertainties with the disease burden analysis, SEAC in its assessment (see *Assessment of Benefits* in Annex) considers the estimates are likely to be conservative, with a tendency to be an overestimate of the expected level of cancer cases relevant to the length of review periods considered for authorisation applications.

Concerning the estimation of economic welfare losses associated with this number of excess lung cancer cases, the applicant uses a Willingness To Pay (WTP) value of €1.34 million to avoid a fatal cancer case and €536,891 for a non-fatal cancer case. Aside from the conservatism noted above in estimating the cancer disease burden, SEAC additionally

considers this may also be a significant overestimate as a result of the failure to account for the latency of cancer (see *Assessment of Benefits* in Annex). In conclusion, SEAC find that the approach and assumptions used to derive the health benefits of "non-use" are on the whole clear and transparent. Moreover, although there are some issues and uncertainties with the analysis as discussed above, the methodology, assumptions and studies used to derive the benefit estimates can be considered on the whole acceptable and proportionate, albeit likely to result in a significant overestimate.

Comparison of benefits and risks of continued use

Overall, given the modest level of risks (which are most probably overestimated) associated with the applicants use of diarsenic trioxide, the benefits of the "non-use scenario are likewise modest, whilst the additional costs (stemming largely from the loss in revenues to the applicant) associated with the use of any alternative substance are relatively substantial, such that the benefits of continued use of diarsenic trioxide exceed the risks of continued use. SEAC thus finds that the total net cost of the "non-use" scenario (and hence the net benefits from granting the authorisation) are of the order of around €18-37 million over the 20 year cost time horizon considered (even whilst not taking into account the need to discount the health benefits of "non-use") over the relevant 40/70 year time period considered. Although there are some uncertainties, these arise mainly in relation to the health benefits of non-use and are likely to have resulted in these being conservative (overestimated). The magnitude by which benefits of continued use outweigh the risks is likely to be even greater if account if taken of the conservatism in the health impact estimates. Moreover, the applicant has included a sensitivity analysis for some of the parameters used on the cost side of the analysis. This indicates that for the range of values of those parameters considered, the conclusion that benefits outweigh the risks of continued use is robust.

9. Do you propose additional conditions or monitoring arrangements

☒ YES

☐ NO

Considering that the implemented risk management measures and existing operational conditions appear to be appropriate in reducing the exposures and the risk, additional monitoring arrangements are not considered necessary. However, in the case of reapplication the applicant is requested to improve the exposure assessment to both workers and man via the environment.

10. Proposed review period:

☐ Normal (7 years)

☒ Long (12 years

☐ Short (…years)

☐ Other:

Justification for the suggested review period:

In identifying the proposed review period SEAC took note of the following considerations:

- RAC recommends a short review period due to the deficiencies in the exposure assessment. In the case of reapplication, RAC expects that this should include an improved exposure assessment for both workers and man via the environment.
- The risks associated with continued use are not negligible. At the same time, although the applicant estimated that there was a modest level of risk associated with the continued use (and corresponding modest benefits of "non-use") of diarsenic trioxide, this is likely to have been significantly overestimated;
- There are technically feasible alternatives available, even though they are economically infeasible;
- The possibilities for the applicant to switch to an alternative as a result of technological change are likely to remain limited, particularly in view of the fact that the basic technology in use has remained fundamentally the same since the early 20th century.
- The applicant's has suggested a 20 year review period, based on their use of an investment time horizon of this length, as well as the desire to avoid the cost of re-applying for a follow-up authorisation if a shorter review period is granted.

Taking into account these points, SEAC recommends a "long" review period of **twelve (12) years.** Whilst SEAC has the freedom to recommend a review period outside of the defaults, the risks from continued use are not negligible, and it is not felt that the arguments for a longer period are sufficient to override the standards grounds on which the long default period is granted.

Annex I

Table A1: Available exposure data for workers

WCS	Title	Route of exposure	Number of measurements or model applied	Maximum	90th percentile	Mean/Median	Duration	Frequency	Persons/shift	PPE/RPE normally used in WCS	Exposure adjusted with RPE; APF 10/20?	Table no. in CSR
1	**Preparation of arsenious acid solution**	Inhal µg/m^3	Stationary	1.2		0.5-1.2	20 min/ shift	2 preparations/ 24 h 600 preparatio	2	PPE incl RPE (APF1000)	0.5-1.2#	49
1		Dermal µg/kg/d	Ecetoc-TRA			34						
2	**Use in purification process**	Inhal µg/m^3	5 (personal monitoring)	0.25	0.22	0.15	8h	continuous	2 16 p/y	PPE used RPE not normally needed		50
2		Inhal µg/m^3	Stationary	4.4 (min-max 0.9-4.4)								

2		Inhal µg/m^3	MEASE			1						
2		Dermal µg/kg/d	MEASE			0.2						
3	**Packing, transport and storage of copper concentrate**	Inhal µg/m^3	Stationary			<1	<1 h/d		2 16 p/y (same as in WCS2)	PPE used RPE when closing/changing big bags not normally needed		51
3		Inhal mg/m^3	MEASE	>100 (peaks)						The high exposure demands RPE*		
4	**Cleaning work and handling of waste**	Inhal µg/m^3	Ecetoc-TRA			35	0.5 h/shift Landfill: 8h NB! all data for WCS4 modelled for >4h)	365 d/y	2 (process hall) Landfill outsourced	PPE, Gloves APF 10 RPE normally not required for <4h		52
4		Inhal µg/m^3	MEASE			50						52
4		Inhal µg/m^3	Ecetoc-TRA									
4		Dermal µg/kg/d	Ecetoc-TRA			69						
4		Dermal µg/d	MEASE			5						

5	**Maintenance work**						15min -8h/d)		2 p/shift (total 12p) 6p in separate workshop 0600-1330 5d/wk Cleaning of tanks every 3 months – 3p/2d/8h/d**	PPE as clothing, gloves (APF 20) and goggles, RPE in tanks if necessary (APF 40)		
5		Inhal µg/m^3	Ecetoc-TRA			15	15 min-1h			PPE, RPE		53
5		Inhal µg/m^3	MEASE			1				RPE APF 20		53
5		Dermal µg/kg/d	Ecetoc-TRA			68				PPE		53
5		Dermal µg/d/shift	MEASE			48						