SUBSTANCE EVALUATION REPORT

Public Name: Succinic anhydride

EC Number: 203-570-0

CAS Number: 108-30-5

Submitting Member State Competent Authority:

Environment Agency Austria, Spittelauer Lände 5, 1090 Vienna, Austria

on behalf of Austrian Federal Ministry of Agriculture, Forestry, Environment and Water Management, Stubenring 1, 1010 Vienna, Austria

Year of evaluation: 2013

VERSION NUMBER: 0.1 **DATE: January 2015**

Conclusions of the most recent evaluation step	Tick relevant box(es)
Concern not clarified; Need to request further information from the Registrant(s) with the draft decision	
Concern clarified; No need of further risk management measures	
Concern clarified; Need for risk management measures; RMO analysis to be performed	
Need for harmonized classification	x

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Executive summary

Grounds for concern:

Succinic anhydride was proposed for substance evaluation based on Article 45(5) of REACH Regulation. The substance is produced at high tonnages (1,000 - 10,000 t/yr) and is mainly used as intermediate for the production of various other chemicals. The evaluation was targeted to all sections of the chemical safety assessment given in the IUCLID dossiers and chemical safety reports of the registrants. Following main concerns were identified before and during substance evaluation by the evaluating member state.

The following grounds for concern refer to the former version of the registration dossiers submitted to ECHA before start of substance evaluation (20th March 2013). The registration dossiers were updated in October 2013 during and in November 2014 after the first year of evaluation (current version).

Human health:

- Acute toxicity: Acute toxicity studies are available for the dermal and oral route (Experimental study 2, 1982, Experimental study 6, 2010). It was examined whether there are any concerns for toxicity via inhalation. The Registrant(s) waived inhalation testing based on not respirable particles without any provision of information on the particle size distribution. Furthermore, it is possible that relevant amounts of a substance enter air via gaseous release depending on its vapour pressure. In principle, this is also possible for solids at room temperature like succinic anhydride. Regarding this option, the given vapour pressure in the former dossier was estimated to be too low and gaseous release was disregarded as potential option by the registrants. Higher vapour pressures can be found in literature and are also predicted by QSAR-models like MPBPWIN (Episuite v.4.1). Besides, elevated process temperatures for some uses are also considered to be possible/likely increasing the potential for gaseous release (resulting in higher vapour pressures e.g. 1.2 hPa at 92°C, vapour pressure found in literature), as the processes and the temperatures were not specified in detail.

- Corrosion/Irritation: Succinic anhydride is harmonized classified as Eye Irrit. 2 and STOT SE 3 (respiratory tract irritation). For the endpoint skin irritation/corrosion experimental results with succinic anhydride has been submitted. In order to close data gaps, a read across with succinic acid (hydrolysis) has been applied for the endpoint skin irritation/corrosion by the registrant(s). No skin irritating effects were observed with the acid form (Experimental study 14., 1999b). During substance evaluation it was further examined, if the application of the read across approach was justified.

- Sensitisation: Read across to maleic anhydride and other cyclic anhydrides was supported by a positive local lymphnode assay (LLNA) with succinic anhydride (Experimental study 4, 2010) and by the structural similarity to the group of cyclic anhydrides, both for respiratory and skin sensitization. It was stated that the LLNA study for succinic anhydride is of insufficient quality to derive a quantitative DNEL for succinic anhydride. On the basis of data from other cyclic anhydrides it was also not possible to derive a DNEL. During substance evaluation it has been verified if a quantitative and/or qualitative risk assessment needs to be carried out and if applied risk management measures (RMM) are sufficient.

- Repeated dose toxicity: One oral 13 wk study for succinic anhydride is available (Melnick R., 1990). Route-to-route (RTR) extrapolation to dermal & inhalation route was proposed. For systemic effects RTR extrapolation from oral to inhalation route seemed justifiable. However, for dermal absorption it is necessary to first substantiate the dermal absorption value of 5% (see also dermal acute toxicity).

- Reproductive toxicity: Regarding the reproductive toxicity there were indications for effects (Fabro et al., 1982). The available studies carried out with succinic anhydride have severe deficiencies (Brown NA. et al., 1978, Fabro et al., 1976). It is stated that potential developmental toxicity could be related to the acetylating properties of succinic anhydride. This concern has been further considered under substance evaluation.

- Read across: Succinic anhydride is harmonized classified for oral acute toxicity, eye irritation and respiratory tract irritation. Succinic anhydride is self-classified by the registrants for skin and respiratory sensitization on the basis of read across to the structurally similar substance maleic anhydride. The toxicity database for succinic anhydride is partly incomplete. The registrants attempted to close these data gaps by applying read across to the structurally related substance maleic anhydride and other cyclic anhydrides for several endpoints. In general, this read across was insufficiently justified.

- Derived no effect levels (DNELs)

  DNEL long term & acute, inhalation, systemic: 10 mg/m^3
  A DNEL of 14 mg/m^3 was derived based on the NOAEL from the oral sub-chronic study for succinic anhydride (Melnick R., 1990). As this value exceeds the time-weighted average (TWA) of 10 mg/m^3 for non-toxic dust, 10 mg/m^3 was used instead. The applied assessment factors (AFs) were however not in line with the recommendations of the REACH guidance[1]. If AFs are reduced from the default this has to be justified adequately. Justifications were missing. Further the DNEL was based on systemic long-term effects and therefore does not cover the sensitising effects of succinic anhydride for which no quantitative DNEL can be derived.

  DNEL long term & acute, inhalation, local: 0,41 mg/m^3
  This value is based on read across from maleic anhydride. It is based on the evaluation by the German MAK commission who used a 6 months study where local irritating effects were observed in rats, hamsters and rhesus monkeys to derive this value. Two case reports of occupational respiratory sensitisation with unclear exposure (maleic anhydride as well as phthalic anhydrate) lead the MAK commission to review their MAK value, however, they concluded not to change their value. The MAK commission stated, however, that there exists no reliable quantitative information on maleic anhydride concentrations which can be related to sensitisation or elicitation. Therefore, the sensitising effects of maleic anhydride and in consequence also of succinic anhydride are not covered by this DNEL.

  AFs: see above.

[1] ECHA (2012). Guidance on information requirements and chemical safety assessment. Chapter R.8: Characterisation of dose [concentration]-response for human health; pp. 186 (available at: http://echa.europa.eu/documents/10162/13632/information_requirements_r8_en.pdf)

DNEL acute, dermal, local & systemic: 167 mg/kg bw/day
The value of 5% for dermal absorption needed better justification in order to increase reliability of this DNEL for systemic effects. It was not clearly demonstrated that also local irritant effects are covered by this DNEL.

AFs: see above

DNEL long-term, dermal, local & systemic: 0,04 mg/cm^2

As the LLNA for succinic anhydride is not suitable for quantitative risk assessment this DNEL is based on read across from maleic anhydride. The value was derived from an EC3 value from a LLNA on maleic anhydride. The information presented in the former registration dossier was insufficient to conclude whether this value was derived correctly. An EC3 value can be regarded as a LOAEL value. The REACH guidance on CSA & IR chapter R.8 recommends to apply several AFs (vehicle or matrix effects: 1-10, occasionally higher; exposure conditions: 1-10, occasionally higher; interspecies difference: 1-10, occasionally higher) in order to derive DNELs from EC3 values. No AFs were applied to derive this DNEL, and no justification was provided for that.

Based on the available information it is not sure if maleic anhydride and succinic anhydride have a comparable potency with regard to their sensitising properties. Therefore it cannot be concluded that the DNEL of 0.04 mg/cm^2 is sufficiently low to cover the sensitising effects of succinic anhydride.

The registrant applied the DNELs described above in the former risk characterisation. As the resulting RCRs are below 1 (though quite close to 1 in some cases) the registrant concluded that the uses and tasks performed by workers are sufficient to guarantee safe use conditions. However, the most critical effects have no threshold and it seems that the sensitising properties of succinic anhydride were not adequately covered by the quantitative risk assessment approach prepared.

Procedure

The evaluation of the toxicity of succinic anhydride is based on data/information submitted within REACH registration (IUCLID dossiers, CSRs). The registrants granted access to the original studies used for the registration and data on uses and risk management. In addition, comprehensive reviews performed by international bodies/regulatory programs and original publications have been taken into consideration. Original publications and/or study reports have been considered for evaluation. Furthermore, scientific databases have been screened to gather further information (e.g., Hazardous Substances Data Bank (HSDB), Integrated Risk Information System (IRIS), Chemical Carcinogenesis Research Information System (CCRIS), Toxline, CHEMIDPLUS and ToxNet). The evaluation was targeted to all sections of the chemical safety assessment.

A detailed review of the registration data, available studies and studies provided by the registrants was performed. Comments and recommendations for changes were sent to the registrants. The identified concerns and recommendations for amendments were discussed between the experts of the evaluating member state and registrants. An update of the registration data (IUCLID files, CSRs) was uploaded in October 2013- covering concerns that could be clarified within the first year of substance evaluation. A draft decision requesting data

for not clarified concerns was sent to the registrants for comments in April 2014. The registrants agreed with the data requests described in the draft. A second update of the registration dossier (IUCLID files, CSRs) containing the requested data was uploaded by the registrants in November 2014. Referring to this version, the concerns indicated in the draft decision were targeted and clarified by the registrants. Thereafter, missing data required for evaluation were provided by the registrants and assessed by the evaluating member state. Therefore, the draft decision was withdrawn. Substance evaluation of succinic anhydride was concluded, as no reasons for requesting further data were found.

The updated dossiers are considered to be a main output of the substance evaluation performed by the evaluating member state. The following section summarizes sections of the new dossier updates and presents the drawn conclusions.

Summary of human health hazard assessment:

For the endpoint acute toxicity an oral toxicity study was submitted by the registrants (Experimental study 2, 1982). Data confirm the harmonized classification of succinic anhydride as Acute Tox 4 (H302: harmful if swallowed) according to Regulation (EC) No 1272/2008. Succinic anhydride does not possess acute toxicity potential via the dermal route (Experimental study 6, 2010), indicating that dermal absorption is lower than absorption via the oral route. Beside the dermal route, workers might also be exposed to the substance via inhalation. However, for the inhalation route, no testing is required if the vapour pressure is very low (< 0.1 Pa at 20°C) or the particle size is > 100 µm. The original data on particle size distribution have been provided by the registrants. Approximately 13 % of the particles are in the range of 0-500 µm. A L_{10} of 377 µm has been deduced. This means that the diameter of particles representing 10% of the particle mass is below 377 µm. Percentage of particles which are below 100 µm cannot be determined exactly based on these values, but it is lower than 10% and considered to be a comparatively small fraction. It is stated in the ECHA guidance (Chapter R.7a: Endpoint specific guidance) that if particle size is > 100 µm for the inhalation route, no testing is required. The vapour pressure indicated by the registrants is 0.000381 Pa at 25°C. Based on the low volatility and the particle size distribution of the substance as manufactured and used, it can be reasonably assumed that inhalative route is of minor relevance and no further tests are considered to be required.

Cyclic anhydrides are known to possess irritative and/or corrosive potential. Tests demonstrating the eye corrosive potential of succinic anhydride were submitted (Carpenter CP and Smyth HF, 1946, Experimental study 15, 1999, Experimental study 5, 1950). Succinic anhydride is a harmonized classified as Eye Irrit. 2 (H319: causes serious eye irritation). However, the present data suggest that succinic anhydride warrants a classification as Eye Dam. 1 (H318: causes serious eye damage). Therefore, the evaluating member state suggests a revision of the recent Annex VI entry of the Regulation (EC) No 1272/2008. Furthermore, the read across approach with succinic acid aiming to demonstrate the lack of irritative/corrosive potential (Experimental study 15, 1999b) has not been accepted due to following reasons: (1) transformation step from the anhydride to its corresponding acid is a step in which exposed cellular structures (e.g., skin, eye) can be damaged; thus, hydrolysis of anhydrides is a critical step, which possesses irritating potential, (2) cyclic anhydrides (structural analogues to succinic anhydrides) possess moderate to severe skin irritation potential (Kim et al., 2009), (3) the most similar structural analogue maleic anhydride is harmonized classified as Skin Corr. 1B compound, (4) the acute dermal toxicity study indicates irritation potential of succinic anhydride (Experimental study 6, 2010).

Therefore, further *in vitro* skin irritation/corrosion tests were requested by the evaluating member state in the draft decision. The draft decision was submitted to the registrants for comments in April 2014.

The requested data were provided by the registrants in November 2014. As it was indicated in the draft decision, a top down approach (start with an *in vitro* skin corrosion test followed by an *in vitro* skin irritation test) was proposed (OECD, 2014). The guideline conforming *in vitro* skin corrosion test conducted under GLP condition demonstrates corrosive potential (Experimental study 12, 2014). Although not necessarily required a further in vitro skin irritation test has been conducted, which did not indicate irritative properties (Experimental study 1, 2014). This, somehow contradictory result can be explained by differences in the exposure times of the two test systems. Thus, it cannot be excluded that in some situations a skin corrosive chemical is correctly identified as corrosive in the in vitro RhE-based skin corrosion test methods but identified as being non-irritant in the in vitro RhE-based skin irritation test methods (OECD, 2014). Based on the outcome of these tests, a classification of succinic anhydride as Skin Corr. 1B (H314: Causes severe skin burns and eye damage) according to the CLP Regulation is proposed by the evaluating member state.

A recently conducted guideline and GLP conforming study demonstrates that succinic anhydride has skin sensitizing potential (Experimental study 4, 2010). Therefore, succinic anhydride has to be classified accordingly to Regulation (EC) No 1272/2008 as Skin Sens. 1 (H 317: may cause an allergic skin reaction).

Furthermore, succinic anhydride might possess respiratory sensitising potential supported by a read across approach to maleic anhydride (Experimental study 13, 1991), which is harmonized classified as Resp. Sens.1 (H334: may cause allergy or asthma symptoms or breathing difficulties if inhaled) and due to the fact that succinic anhydride has skin sensitising potential, which gives evidence that also respiratory sensitisation might be observed. Present data and information indicate that succinic anhydride has skin and also respiratory sensitizing potential. Available data on sensitising potential do not allow deriving accurate DNELs. Therefore, a qualitative risk assessment approach has been proposed and the registrants have carried out this approach in the revised version of the CSR.

A guideline comparable oral repeated dose toxicity study (duration 90 days) has been submitted for evaluation (Melnick R., 1990). For the inhalative and dermal route no repeated dose toxicity studies have been submitted. Since succinic anhydride has corrosive and sensitizing (skin and respiratory) potential further testing is not deemed justified. Route-to-route extrapolation has been considered. The assumption that the dermal absorption rate is lower than the oral absorption rate is substantiated by acute toxicity data. The deduction of the registrants of the dermal NOAEL (of 2000 mg/kg bw) is not regarded as appropriate, because the dermal absorption rate was assumed to be 5%. This assumption is based on a study carried out with three volunteers to which hexahydrophtalic anhydride (a bicyclic anhydride) has been dermally administered and the excretion of the acid form was an indicator for dermal absorption of the anhydride. Data indicate that anhydrides are absorbed dermally and are distributed throughout the body and that not only local effects (such as irritation) are of relevance. The study description however is rather poor to determine unambiguously absorption rates. The conservative estimation (default value) that the bioavailability of oral and dermal exposure is in the same order of magnitude is not substantiated by the oral acute toxicity studies. These studies indicate that there is poor availability via the skin and leads to the assumption that an estimation of 10% dermal absorption rate is appropriate (IGHRC, 2006). Therefore, taken into consideration an oral systemic NOAEL of 100 mg/kg bw (rat, 90 day

study) and a dermal absorption rate of 10%, a dermal systemic NOAEL of 1000 mg/kg bw can be estimated. A route-to-route extrapolation using default values for absorption is justified in the case of inhalation repeated toxicity since the substance has irritating potential. Present data and drawn assumptions are sufficient for the hazard identification and risk characterisation and no further repeated dose toxicity testing is considered to be justified.

For the evaluation of the mutagenic potential of succinic anhydride no further data are required. Taken into consideration the presented data of the registrants and data from literature succinic anhydride lacks mutagenic potential, which is consistent with the *in vivo* carcinogenicity data. The carcinogenic potential of succinic anhydride has been studied in a two-year oral feeding guideline comparable study carried out with rats and mice (Melnick R., 1990). There is no indication that maleic anhydride has a carcinogenic potential. It is agreed on the registrants evaluation that based on the presented data a lack of carcinogenic potential of succinic anhydride can be assumed.

Regarding the developmental and fertility endpoint further information on the read across approach has been requested in the draft decision (submitted to the registrants for comments in April 2014).

For reproductive toxicity (fertility and development) read across to maleic anhydride has been applied with the exemption of supportive intraperitoneal screening tests (Fabro S. et al., 1982, Fabro S. et al., 1976, Brown N.A et al., 1978). These supportive tests are not guideline and GLP conform and two of them are classified as not assignable for evaluation (Klimisch 4) (Fabro S. et al., 1976, Brown N.A. et al., 1978). Furthermore, the application route is regarded not appropriate for the indented uses (worker exposure: inhalative or dermal route). The irritant effect of succinic anhydride might produce artificial responses, if applied intraperitoneal. Beside the fact that the studies have some drawbacks, it has been shown, that succinic anhydride only induces a significant incidence of malformations at doses within the adult lethality range (relative teratogenicity index is close to 1) (Fabro et al., 1982).

Due to lack of reproductive toxicity as designated under REACH (Annex X) carried out with succinic anhydride a read across approach has been applied to fill the data gaps (REACH, Annex XI). The approach has been described only very briefly in the previous versions of the CSRs. Therefore, in the prepared draft decision an elaboration of the read across approach has been requested pursuant to Article 46(1) of the REACH Regulation to address the concern.

The read across approach has been elaborated in the revised version of the registration and a data matrix of relevant substances (maleic anhydride, succinic anhydride and the hydrolysis product maleic acid, succinic acid) is provided. In the present form of the IUCLID dossiers an attachment is provided, which illustrates the proposed read across approach.

Besides, the demonstration of the structural similarity to maleic anhydride, also the physicochemical parameters are given. The toxicological patterns of maleic anhydride and succinic anhydride are identical; both have sensitising as well as corrosive properties and hydrolyse rapidly under aqueous condition.

The two generation toxicity study comparable to OECD TG 416 (Two-generation reproduction toxicity study) carried out with the source substance maleic anhydride (Short et al., 1986) does not give evidence that maleic anhydride has negative effects on the reproductive system (fertility and development) and does not trigger classification.

It is described in the supplementary document that succinic anhydride is hydrolysed rapidly to succinic acid. Succinic acid is present ubiquitously in mammalian cells. It is part of the citrate

cycle. The body of evidence described in the supplementary document that succinic acid does not possess adverse effects on the reproductive system is plausible and valid. Furthermore, there is no evidence in the literature that anhydrides elicit adverse effects on the reproductive system (Kim et al., 2009).

The evaluating member state concludes that there is sufficient information provided to determine the hazard profile of succinic anhydride in respect to developmental toxicity. The provided read across approach by the registrants together with supplementary teratogenicity studies and the complementary information on the hydrolysis product is regarded as sufficient to conclude that reproductive system is not a target organ of succinic anhydride.

DNEL derivation: Data analysis revealed that DNEL derivation for the sensitizing effect (skin or respiratory) is not feasible. For the respiratory sensitizing effects no valid model is available so far. For the skin sensitizing properties the animal and also the human data do not allow to determine a DNEL. In the revised version of the CSRs the risk characterization has been carried as out applying a qualitative approach. This approach attempts to demonstrate that any (significant, relevant) contact of persons with the material is avoided by the nature of processes or by risk management measures, as no thresholds can be derived for the most critical effects.

Summary of human exposure assessment

Succinic anhydride is considered to be a skin and respiratory sensitizer and causes harm to the skin. As it has not been possible to derive quantitative hazard reference values and thus a qualitative exposure and risk assessment was performed for demonstrating safe use by the registrants. The goal of the envisaged qualitative approach is to keep exposure to the substance as low as feasible and at levels leading to no effects.

Succinic anhydride is intended for following uses under the scope of REACH. The substance is used only by workers at industrial sites. Professional and consumer uses are not registered and are not expected based on the uses described.

Registered uses:

1) Manufacture of succinic anhydride
2) Industrial use as intermediate for production of substances and other intermediates
3) Industrial use as monomer for production of resins
4) Laboratory use

Based on the chemical form of succinic anhydride, the most likely routes of worker exposure are via dermal contact and inhalation. Oral exposure is not considered to be relevant for workers and would only occur under intentional exposure which is outside the scope of REACH.

Exposure of the general public is expected to be unlikely as succinic anhydride is transformed/consumed during its industrial application for the synthesis of other chemicals. Release of succinic anhydride as waste to the environment is not intended and attempted to be low, as this would be a loss of raw material for the covered uses. Considering some release to the environment as potential situation, it is also considered to be unlikely that humans will be exposed indirectly either via air, water, soil, drinking water or through exposure in the food chain, as succinic anhydride is readily biodegradable in atmospheric, aquatic and soil compartments and does not bio-accumulate.

The listed industrial uses cover the following processes: PROC 1, PROC 2, PROC 3, PROC 4, PROC 8b and PROC 15.

PROC 1 - Use in closed process, no likelihood of exposure
PROC 2 - Use in closed, continuous process with occasional controlled exposure
PROC 3 - Use in closed batch process (synthesis or formulation)
PROC 4 - Use in batch and other process (synthesis) where opportunity for exposure arises
PROC 8b - Transfer of chemicals from/to vessels/ large containers at dedicated facilities
PROC 15 - Use of laboratory reagents in small scale laboratories

Succinic anhydride is manufactured and applied as coarse powder.

Referring to the properties of the substance, succinic anhydride reveals a low vapour pressure (0.038 hPa at 25°C). Based on the low volatility of succinic anhydride, exposure to gaseous releases and vapours are expected to be not relevant.
The potential of inhalation of substance particles is also considered to be limited by the low dustiness of the powders manufactured and used, as particles set to air are expected to settle down within a short time and are unlikely to be inhaled. Considering this behaviour, the potential for dermal exposure is also expected to be limited, as formation of dust clouds is hampered. Direct handling and contact without dermal protection (e.g. manual handling without gloves or similar personal protective equipment) is not foreseen. The registrants indicated the following diameters for the granulometry of succinic anhydride powders manufactured and used.

L10 [µm]	L50 [µm]	L90 [µm]
377	1197	2309

Nevertheless, any potential exposure to the substance needs to be prevented by appropriate measures, if contact with the substance cannot be excluded and is considered to be possible (see following section).

The industrial manufacture processes using/producing succinic anhydride are performed in closed, semi-closed systems. Nevertheless, some potential for inhalation and dermal exposure may still arise due to these contained processes (PROC 1, 2, 3, 4) and due to required tasks like transfer of chemicals (PROC 8b), maintenance, etc. Therefore, local exhaust ventilation and engineering controls are applied in addition, if the used systems are considered to be not fully closed and release and exposure are considered to be possible. Workers involved in the production, handling, sampling and transfer of materials are trained in these procedures and the use of eye goggles, plastic gloves (no specific requirements but for example neoprene and coated neoprene /rubber / nitrile rubber gloves) and clothing with long sleeves and long legs, is required in order to minimize exposure. If inhalation exposure to succinic anhydride dust is considered to be possible, full face respirators are applied by the workers.

Based on the received data and descriptions provided by the registrants, the qualitative approach for the exposure and risk assessment was accepted. Referring to the explanations of the registrants, efficient risk management measures (RMM), personal protective equipment (PPE) and respiratory protective equipment (RPE) are used, if potential for exposure is possible. The degree and likeliness of human exposure is kept low during all processes. The currently applied measures are considered to be applicable for ensuring safe use and protecting

workers. The covered industrial uses are considered to be without any harm or health risk to workers.

Summary of environmental fate properties and environmental hazard assessment

The assessment of the environmental part of the succinic anhydride dossier did not reveal a concern which would lead to the necessity to ask for more data.

Succinic anhydride hydrolyses fast (half-life in the range of minutes, maybe seconds or up to hours depending on the pH and temperature) forming the hydrolysis product succinic acid (Experimental study 3, 2010 and SRC, 2006). Succinic acid fulfils the criteria for ready biodegradability (96.6% degradation after 28 days of incubation) (Experimental study 16, 2010). Therefore, succinic anhydride can be regarded as readily biodegradable, persistence is not expected.

The bioaccumulation potential can be regarded to be low, as the log Kow values of the substance succinic anhydride (logKow: 2.44) and its hydrolysis product succinic acid are low. Also the provided information on toxicokinetics in humans indicates no bioaccumulating potential.

Estimations for the Henry´s law constants for succinic anhydride and its hydrolysis product succinic acid indicate very low values suggesting that succinic anhydride or succinic acid will not likely evaporate from water surfaces to the air.

No test data on fish, daphnia, algae or microbiological activity were provided for succinic anhydride, but for its hydrolysis product succinic acid, which is formed fast coming into contact with water. Data for fish provided in a limit test revealed no effect at 100 mg/L after 96h (Experimental study 7, 2010). Data for daphnia demonstrate a 48-hour EC50 of 63 mg/L for the test in which no pH adjustment of the stock solution has taken place. In a test with pH-adjustment of the stock solution no effect was detected at 100 mg/L (Experimental study 8, 2010, Experimental study 9, 2010). Data for algae provided a 72h-EC_{50} of 40.7 mg/L and a 72h-NOEC of 25 mg/L (growth rate) for the test with succinic acid without pH adjustment (with pH-adjustment the 72h-EC_{50} value is > 100 mg/L and the 72h-NOEC is $\geq$ 100 mg/L) (Experimental study 10, 2010).

The microbiological activity in sewage treatment systems revealed low toxicity with an EC_{50} of > 300 mg/L for the hydrolysis product succinic acid (Experimental study 11, 2010).

The derived PNECs for freshwater (0.1 mg/L), for marine water (0.01 mg/L), for intermittent releases to water (1 mg/L) and for the sewage treatment plant (3 mg/L) can be supported.

For sediment and soil no PNECs have been derived with the argument that no exposure is expected, although no environmental exposure assessment has been provided. Against evaluating Member states´ advise no PNECs using Partitioning Equilibrium Method were derived. The eMSCA recommends that this data is provided in the next update of the dossier.

Regarding the classification of succinic anhydride for the environment the evaluating member state agrees with the registrants that no data are available providing a basis for classification.

Summary of environmental exposure assessment

A quantitative assessment was not performed by the registrants. Nevertheless, the registrants provided detailed information on the uses and the risk management measures at sites.

Regarding the indicated industrial uses, significant releases of succinic anhydride to the environment are not expected. The substance is consumed during their final uses. Losses during manufacture and use are avoided as far as feasible and estimated to be not relevant referring to the waste management at sites (e.g. treatment of emissions to water and air). Regarding the indicated uses and the properties of the substance, the sewage treatment plant is expected to be the main receiving compartment. Rapid hydrolysis and readily biodegradability suggest that small amounts of release will rapidly disappear from water and soil via mineralization. Furthermore, the low log Kow suggests that the substance is not bioaccumulative. The indicated uses of the substance give no reason for concern and for requesting further data.

Conclusions

A draft decision to request further information was prepared by the evaluating member state and sent to the registrants for comments in April 2014. In order to close data gaps the registrants submitted further information and study results. Revised registration data including the requested data have been submitted. Therefore, the data request stipulated in the draft decision was withdrawn. Available and submitted data and information are considered to be sufficient for chemical safety assessment. The identified concerns have been addressed and clarified during substance evaluation process and to date no further information is required. The evaluating member state considers a harmonized classification proposal according to Regulation (EC) No 1272/2008 as the appropriate further risk management measure.

Succinic anhydride has an Annex VI entry (Index Number 607-103-00-5) according to the CLP Regulation and is harmonized classified as Acute Tox. 4* (H302: harmful if swallowed), Eye Irrit. 2 (H319: causes severe skin burns and eye damage) and STOT SE 3 (H335: May cause respiratory irritation). Evaluation of the individual endpoints revealed that the Annex VI entry is incomplete and needs revision. Data are available which demonstrate that succinic anhydride requires further harmonized classification for its sensitizing properties (Skin Sens. 1; H317: may cause an allergic skin reaction; Resp. Sens. 1; H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled). Furthermore, data demonstrate that succinic anhydride has corrosive properties and needs to be classified as Skin Corr. 1B (H314: Causes severe skin burns and eye damage) and Eye Dam. 1 (H318: Causes serious eye damage).

A comparison between already harmonized classification entry in Annex VI of the Regulation (EC) No 1272/2008 and the further proposed harmonized classification is depicted in the following table.

Table: Overview of harmonized classification entry[1] and proposed amendment of the entry

	Classification		**Labelling**
	Hazard Class and Category Code(s)	**Hazard Statement Code(s)**	**Hazard Statement Code(s)**
Harmonised classification[1]	Acute Tox 4* Eye Irrit. 2 STOT SE 3	H302 H319 H335	H302 H319 H335
Proposed amendment of the entry	Acute Tox 4 (removal of asterisk) Resp. Sens. 1 Skin Sens. 1 Eye Dam. 1[2] Skin Corr. 1B	H302 H334 H317 H318 H314	H302 H334 H317 H314

[1]Regulation (EC) No 1272/2008, Annex VI (Table 3.1.)

[2] instead of Eye Irrit 2 (H319: Causes serious eye irritation)

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