Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

to the Opinion proposing harmonised classification and labelling at EU level of

succinic anhydride

EC Number: 203-570-0
CAS Number: 180-30-5

CLH-O-0000001412-86-123/F

Adopted

16 September 2016

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON SUCCINIC ANHYDRIDE

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.

All comments and attachments including confidential information received during the public consultation have been provided in full to the dossier submitter (Member State Competent Authority), the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the public consultation and are also published together with the opinion (after adoption) on ECHA's website. Dossier submitters who are manufacturers, importers or downstream users, will only receive the comments and non-confidential attachments, and not the confidential information received from other parties.

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Substance name: succinic anhydride
EC number: 203-570-0
CAS number: 108-30-5
Dossier submitter: Austria

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
25.01.2016	France		Individual	1
Comment received				
Labelling, page 6 As succinic anhydride is classified as Skin corr. 1, the risk of severe damage to eyes is considered implicit. The substance need to be classified for serious eye damage but not labelled for serious eye damage				
Dossier Submitter's Response				
It is correct that according to CLP guidance (Chapter 3.3) serious damage to eyes is implicit for substance or mixture already classified as Skin corrosive Category 1. Such substances are not to be tested for eye irritation and are classified but not labelled for serious eye damage in addition to skin corrosion. For succinic anhydride test data is available and therefore presented in the dossier. For succinic anhydride both classifications (Skin Corr. 1 and Eye Dam. 1) are required but the hazard statement H318 'Causes serious eye damage' does not have to be indicated on the label because of redundancy (CLP-regulation, Article 27).				
RAC's response				
RAC concurs with the respons given by the DS.				

Date	Country	Organisation	Type of Organisation	Comment number
22.01.2016	Netherlands		MemberState	2
Comment received				
NL agrees with classification for skin and respiratory sensitization, both Category 1				
Dossier Submitter's Response				
Thank you for the support.				
RAC's response				
The support is noted.				

Date	Country	Organisation	Type of Organisation	Comment number
25.01.2016	Germany		MemberState	3

Comment received

In general the German CA supports the proposed classification of succinic anhydride.

Annex III Read across justification
Page 50, section 1.1
It is noted that a double bond can strongly influence the reactivity of a compound. It is recommended to include some further explanation on this point in section 1.1.

Page 52, section 4.1
Please change "(see Table 2)" to "(see Table 3)"

Dossier Submitter's Response

Add Annex III page 50, section 1.1.:
Maleic anhydride displays a high structural similarity to succinic anhydride. Both chemicals are monocyclic anhydrides. The only structural difference is that maleic anhydride has a double bond in its ring structure. This double bond makes the structure of maleic anhydride easier accessable for an additional reaction. Maleic anhydride hydrolyses at a rate ten times higher than that of succinic anhydride. This has been explained either as a result of ring strain, or as been due to activation of one carbonyl group for nucleophilic attack by electronic relay through the double bond (Eberson, 1972). For the sensitizing property of succinic acid it can be concluded that the protein binding mechanism is given despite the the missing double bond in the chemical structure based on a positive LLNA for succinic anhydride.

Page 52, section 4.1
Thank you for this remark. The reference should be changed to "see Table 3".

Literature:

Eberson L and Landström L (1972). Studies on cyclic anhydrides. Acta Chemica Scandinavica 26 (1972) 239-249.

RAC's response

RAC notes the comment from the MS and agrees with the response from the DS. Although the reactivity of succinic anhydride might be lower than that of maleic anhydride, the LLNA data show that it is of biological relevance.

RESPIRATORY SENSITISATION

Date	Country	Organisation	Type of Organisation	Comment number
25.01.2016	France		Individual	4

Comment received

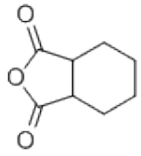
Toxicocinetic data on succinic anhydride and maleic anhydride would be very helpful in order to accept or reject the read-across proposal for respiratory sensitisation. There is no human data available with succinic anhydride and small changes in the structure of the substance could impact the reactivity and the respiratory sensitisation potential. In our opinion, read-across with maleic anhydride is not sufficiently justified to classify Succinic

anhydride resp sens 1.

Dossier Submitter's Response

For respiratory sensitisation as local effect (observed at the site of first contact, but considering that respiratory sensitisation via dermal exposure is possible) toxikokinetic data are of limited value nevertheless additional information on toxicokinetics can be provided (ad Chapter 4.1).

A comparison of physico-chemical properties and mammalian toxicity for succinic anhydride and maleic anhydride has been provided in the CLP dossier, Annex III. No toxicokinetic data is available for succinic anhydride or maleic anhydride itself but Kim, 2009 reviewed toxicokinetic data for cyclic anhydrides. Most of the available information is based on exposure to Hexahydrophthalic anhydride.



Hexahydrophthalic anhydride, CAS 85-42-7

ABSORPTION: No human data is available on the oral or gastro-intestinal absorption of cyclic acid anhydrides.
Investigations with hexahydrophthalic anhydride showed that during inhal. exposure at 80 µg/m^3 1–4% was found in exhaled air. Urinary analysis of worker exposed to an 8-h time-weighted average concentration of 30 µg/m^3 indicate that more than 85% of the inhaled dose was excreted in urine as hexahydrophthalic acid.

DISTRIBUTION: The distribution was evaluated with (3H2)-hexahydrophthalic anhydride (inhalated) in guinea-pigs and rats. Lung tissue contained negligible levels of radioactivity, whereas the mucosa of the nasal region and trachea contained medium to high levels. The gastrointestinal tract and conjunctiva possessed tissue-bound radioactivity, although the amount was not described. Low levels of tissue-bound radioactivity were found in the kidney cortex of rats, but not guinea-pigs. Radioactivity persisted for at least 7 days after the end of exposure. Tissue-bound radioactivity could be only partially extracted by organic solvents and water, suggesting that radioactive chemical was covalently bound to tissue macromolecules. Radioactivity in dialysed plasma was primarily found in the same fraction as albumin.

METABOLISM: The anhydride moiety of acid anhydrides readily reacts with amino acids and conjugates with plasma proteins and haemoglobin. Cyclic acid anhydrides are hydrolysed to corresponding dicarboxylic acids (succinic anhydride → succinic acid) and effectively excreted in urine. The urinary half-time for the dicarboxylic acid of phthalic anhydride was 14 h, whereas half-times for the dicarboxylic acids of hexahydrophthalic anhydride, methyl hexahydrophthalic anhydride, and methyl tetrahydrophthalic anhydride were generally shorter (between 2 and 7 h).
Sera from hexahydrophthalic anhydride– and methyl hexahydrophthalic anhydride–exposed workers have measurable plasma protein and albumin adduct levels that correlated with exposure. The half-time for these adducts in vivo was about 20 days.
In vitro and in vivo exposure tests on guinea-pig lung found that methyl tetrahydrophthalic anhydride was conjugated primarily to lysine in the collage.
Experiments using human erythrocytes exposed to hexahydrophthalic anhydride or

methyl hexahydrophthalic anhydride demonstrated conjugation with haemoglobin. The major amino acid bound to hexahydrophthalic anhydride was lysine.

Cyclic acid anhydrides have been observed to cause IgE-mediated contact urticaria in humans. The formation of protein adducts is hypothesized to be the first step in sensitization. This has been demonstrated by total protein and albumin adducts of hexa-hydrophthalic anhydride and methyl hexahydrophthalic anhydride in the plasma of exposed workers (Kim, 2009).

Beside the proposed read across (maleic anhydride displays a high structural similarity to succinic anhydride) and the structural alert (anhydride structure) for respiratory sensitising property it is evident that succinic anhydride has sensitising properties (LLNA pos). Information on sensitizing activity of substances can also be taken into consideration and used in a weight of evidence assessment, because there may be a relationship between the skin sensitising properties of a substance and the respiratory sensitising properties (CLP guidance, ECHA 2015). This positive result with succinic anhydride also indicated that the protein binding mechanism of succinic acid is given despite the missing double bond – the only difference in the chemical structure.

Literature:

Kim, J. H., Gibb, H. J., Iannucci, A (2009). Concise International Chemical Assessment Document 75. Cyclic acid anhydrides: Human Health Aspects. World Health Organisation

RAC's response

RAC notes that toxicokinetic data on succinic anhydride itself (and possibly maleic anhydride) could have been helpful, but agree with the response that toxicokinetic data is less important in the case of local effects such as respiratory sensitisation.

Date	Country	Organisation	Type of Organisation	Comment number
22.01.2016	Netherlands		MemberState	5

Comment received

Skin sensitization
We agree with classification for skin sensitization Category 1.

Respiratory sensitization
We agree with classification for respiratory sensitization Category 1.

Dossier Submitter's Response

Thank you for the support.

RAC's response

The support is noted.

Date	Country	Organisation	Type of Organisation	Comment number
25.01.2016	Sweden		MemberState	6

Comment received

The DS proposes to classify succinic anhydride as Resp. Sens. 1. The classification proposal is based on a QSAR structural alert for respiratory sensitisation (cyclic anhydrides), positive skin sensitisation data and read-across to maleic anhydride

(analogue approach). Maleic anhydride has a harmonised classification as Resp. Sens. 1.

The read-across approach is scientifically sound and the Swedish CA agrees with the DS that it is very likely that succinic anhydride has respiratory sensitising properties. However, we are uncertain as to whether the available evidence fulfils the criteria for classification as Resp. Sens. according to the regulation (EC) No 1272/2008.

In section 3.4.2.1.1.4., Table 3.4.1 of the regulation it is stated that substances shall be classified as respiratory sensitisers (Category 1) where data are not sufficient for sub-categorisation in accordance with the following criteria: (a) if there is evidence in humans that the substance can lead to specific respiratory hypersensitivity; and/or (b) if there are positive results from an appropriate animal test. Structural similarity to substances known to cause respiratory hypersensitivity is mentioned in the legal text, however only as supportive evidence to human data (section 3.4.2.1.2.3 a) iv). These issues are also up for discussion at the GHS –level.

In the Guidance on the Application of the CLP criteria (version 4.1 – June 2015) – section 3.4.2.1.3. - it is stated that substances shall be classified as respiratory sensitisers if there is evidence in humans and/or animals that the substance can lead to specific respiratory hypersensitivity. Further, that no formally recognised and validated animal tests currently exist for respiratory sensitisation, but that data from some animal studies may provide supportive evidence in case human evidence is available. This information may also be combined with information on structural alerts for respiratory sensitisation and information on the skin sensitising properties of a substance and used in a weight of evidence assessment.

Thus, from the wording in the CLP and the Guidance, it seems that human data from the chemical substance itself is required in order to fulfil the criteria.

Dossier Submitter's Response

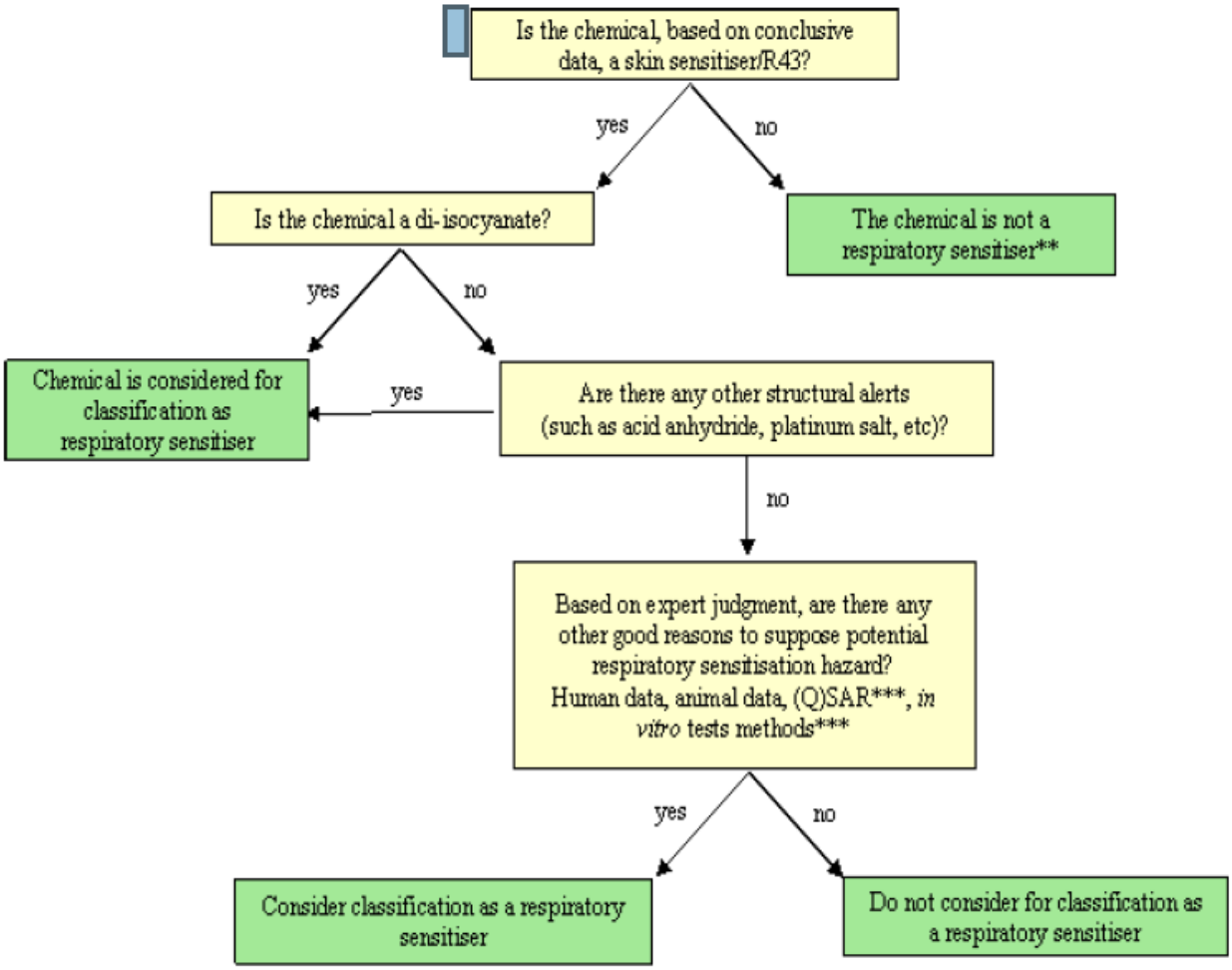
Due to missing appropriate, validated testing methods for respiratory sensitisation and the fact that testing is not necessary under REACH the evaluation of this endpoint is difficult. Nevertheless from our point of view the available data fulfill the formal criteria for classification. For the application of the criteria for classification as Resp. Sens. also Annex I (Chapter 1.1.1) of Regulation 1272/2008 has to be considered: "*Where the criteria cannot be applied directly to available identified information, or where only the information referred to in Article 6(5) is available, the weight of evidence determination using expert judgment shall be applied in accordance with Article 9(3) or 9(4) respectively.*
A weight of evidence determination means that all available information bearing on the determination of hazard is considered together, such as the results of suitable in vitro tests, relevant animal data, information from the application of the category approach (grouping, read-across), (Q)SAR results, human experience such as occupational data and data from accident databases, epidemiological and clinical studies and welldocumented case reports and observations. The quality and consistency of the data shall be given appropriate weight. Information on substances or mixtures related to the substance or mixture being classified shall be considered as appropriate, as well as site of action and mechanism or mode of action study results. Both positive and negative results shall be assembled together in a single weight of evidence determination."

For succinic anhydride despite of available human data there is strong evidence for classification (positive LLNA, structural alert, read across). The Guidance on Information Requirements (Chapter R.7a: Endpoint specific guidance) gives clear guidance:

- *Cyclic anhydride is listed as example for a structural alert in the Guidance (Table R.7.3–1).*
- *R.7.3.7.2: Although no testing strategy for respiratory sensitizers is available, a substance could be classified as respiratory sensitizer by following the flow chart*

for integrated evaluation strategy (IES) reported in Guidance on IR, Section R.7.3.8.3 which is based on existing evidence (see figure below). Following this flow chart succinic anhydride must be classified.

Figure R.7.3–2 Integrated evaluating strategy for respiratory sensitisation data*



* In contrast to tests for skin sensitisation, the performance of tests for respiratory sensitisation is currently not required under REACH. Therefore the present IES scheme depicts a strategy for evaluating existing data.
** This does not discount the possibility that the chemical may induce respiratory hypersensitivity through non-immunological mechanisms. Chemicals that act through such mechanisms are usually identified on the basis of evidence from human exposure.
*** not yet available

From our point of view beside the toxicological evidence also the formal criteria for classification of succinic anhydride as Resp.Sens 1 are fulfilled.

RAC's response
RAC concurs with the response provided by the DS.

Date	Country	Organisation	Type of Organisation	Comment number
25.01.2016	Germany		MemberState	7
Comment received				
Based on the data presented the classification as Resp. Sens. 1 is supported.				

Please clarify the following statement made in table 14 column "results" (Study: Lee et al. 1991): "Outcome: Worker had positive challenge test to maleic anhydride but reacted negatively to maleic anhydride." Did the worker react positive or negative to maleic anhydride? Please indicate in table 14 if the studies of Graneek et al. 1988 and Lee et al. 1991 are supporting or key studies.
Dossier Submitter's Response
Thank you for the support. The correct wording in Table 14, column results (Lee, 1991) should be: Outcome: Worker had positive bronchial challenge test to maleic anhydride but reacted negatively to phthalic anhydride. Both studies mentioned above (Graneek et al., 1988 and Lee et al., 1991) should be flagged as supporting studies.
RAC's response
The support is noted.

OTHER HAZARDS AND ENDPOINTS – Acute Toxicity

Date	Country	Organisation	Type of Organisation	Comment number
25.01.2016	Germany		MemberState	8
Comment received				
Page 19, section 4.2.4: The deduced ATE value used for classification should be based on the lowest observed LD50 value in a valid and reliable study. In the present case, for classification it is proposed to refer to the LD50 value of bw found for female rats rather than 1794.9 mg/kg bw deduced as an averaged value from female and male rats. As the DS did not consider the acute inhalation toxicity in the dossier, the evidence on respiratory tract irritation cannot be assessed by the data presented. As the classification as Corr. 1 is proposed by the DS, this may cover STOT SE3 for respiration tract irritation and STOT SE 3 may then be superfluous. If appropriate data on acute inhalation toxicity are available, EUH071 may also be considered. It is noted that EUH071 can also be applied to inhaled corrosive substances not tested for acute inhalation toxicity. According to CLP Annex II, Section 1.2.6 (which states 'For substances and mixtures in addition to classification for skin corrosivity, if no acute inhalation test data are available and which may be inhaled.'). EUH071 may then be appropriate without a corresponding classification for acute inhalation toxicity				
Dossier Submitter's Response				
Thank you for this comment. For classification the lowest available valid LD50 should be taken into account. In the study it has been demonstrated that females with an LD50 of 1510.5 mg/kg are more sensitive than males (LD50=2157.2 mg/kg bw). The LD50 value for males and females was calculated to be 1794.9 mg/kg bw. Therefore the first paragraph of Chapter 4.2.4 has to be amended as follows: *"According to the CLP criteria, classification as Acute Toxicity 4 needs to be assigned if the* *acute toxicity value expressed as LD50 value or as acute toxicity estimates is between 300*				

and 2000 mg/kg bw. The LD50 deduced from the existing studies is 1510.5 mg/kg bw and *thus a classification for Acute oral Toxicity 4 is deemed appropriate."* For the discussion on STOT SE3 please see response to comment number 13. According to the CLP-criteria EUH071 ist appropriate für succinic acid (see also comment number 13).
RAC's response
RAC concur with the comment provided by the MS and acknowledge the revised position by the DS.

OTHER HAZARDS AND ENDPOINTS – Skin Hazard

Date	Country	Organisation	Type of Organisation	Comment number
25.01.2016	Germany		MemberState	9
Comment received				
Please indicate in table 11 if the study of Verbaan 2014 is a supporting or key study.				
Dossier Submitter's Response				
The study from Verbaan, 2014 is neither a key nor a supporting study for the corrosive property of succinic anhydride. This test on skin irritation was negative and it should be noted that the test design is not intended to identify corrosive substances. The Test Guideline 439 (Verbaan, 2014) does not provide adequate information on skin corrosion. OECD TG 431 on skin corrosion (Buskens, 2014 - with positive result for succinic acid) is based on the same RhE test system, though using another protocol.				
RAC's response				
Noted				

OTHER HAZARDS AND ENDPOINTS – Eye Hazard

Date	Country	Organisation	Type of Organisation	Comment number
25.01.2016	Germany		MemberState	10
Comment received				
Page 27/28, table 12/section 4.4.2.1: As succinic anhydride has been classified as skin corrosive it shall be considered as leading to serious damage to the eyes as well (CLP Regulation, section 3.3.2.3.). Hence, including the study by Carpenter and Smyth, 1946, the evidences for succinic anhydride are sufficient warranting classification as Eye Dam. 1 (H318). The performed read across to succinic acid is considered to be superfluous and could be omitted. If the read across is intended to be still included, it is recommended to amend a discussion on the acid reserves of succinic anhydride and succinic acid. The study by Bernat, 1999 should be mentioned as supporting study rather than key study. Page 29, section 4.4.2.4 It is recommended to include the following phrases: "According to the CLP Regulation (section 3.3.2.3) skin corrosive substances shall be considered as leading to serious damage to the eyes as well (Category 1). Succinic anhydride has been classified as Skin Corr. 1. Hence, classification of succinic anhydride as Eye Dam. 1 (H318) is warranted as well. Moreover, the study of Carpenter…."				

Dossier Submitter's Response
It is correct that according to CLP regulation (Chapter 3.3.2.3) and CLP guidance (Chapter 3.3) serious damage to eyes is implicit for substance or mixture already classified as Skin corrosive Category 1. For succinic anhydride and succinic acid test data is available and therefore presented in the dossier. Carpenter, 1946 should be flagged as key study and Bernat, 1999 as supporting study. The key study with positive results for Eye Dam. is a non-GLP and non-TG conform study therefore the study from Bernat, 1999 and the knowledge that under aqueous conditions (like in eyes) succinic anhydride hydrolyses to succinic acid was used to support the adverse effects on eyes. For succinic anhydride both classifications (Skin Corr. 1 and Eye Dam. 1) are required but the hazard statement H318 'Causes serious eye damage' does not have to be indicated on the label because of redundancy (CLP-regulation, Article 27). To consider the legal requirements the first paragraph of Chapter 4.4.2.4 (Comparison with criteria) should be amended as follows: *According to the CLP Regulation (section 3.3.2.3) skin corrosive substances shall be considered as leading to serious damage to the eyes as well (Category 1). Succinic anhydride has been classified as Skin Corr. 1. Hence, classification of succinic anhydride as Eye Dam. 1 (H318) is warranted as well. Moreover, the study of Carpenter (1946) indicates that application of succinic anhydride…..*
RAC's response
RAC concur in general with the response provided by the DS. However RAC is of the opinion that the key study for the evaluation of this endpoint is the study by Bernat which is a robust study of high quality and this study confirms the result from the study by Carpenter. There are limitations in the reporting of the Carpenter study and it is not clear if the undiluted substance perhaps was applied as a solid substance. In addition, when succinic anhydride was applied as a solution, it appears that water (or propylene glycol) was used as vehicle when preparing the test solutions. Considering that succinic anhydride will hydrolyse in an aqueous media it is likely that the results from the experiments on succinic anhydride more likely reflect the eye damaging properties of succinic acid.

OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard

Date	Country	Organisation	Type of Organisation	Comment number
25.01.2016	Sweden		MemberState	11
Comment received				
The Swedish CA supports the proposed classification of succinic anhydride as Skin Sens. 1. With stimulation indexes greater than 3 for all tested concentrations, the results of the LLNA assay demonstrate that Succinic anhydride has skin sensitising properties. Since the nonlinearity between dose and response rendered it impossible to derive an EC3 value, we agree with the DS that the available data does not allow for subcategorization.				
Dossier Submitter's Response				
Thank you for the support.				
RAC's response				
The support is noted.				

Date	Country	Organisation	Type of Organisation	Comment number
25.01.2016	Germany		MemberState	12
Comment received				
Page 37, section 4.6.2.1 (last section beginning with "Succinic anhydride has been tested in the local lymph node assay …"): Please also refer to the Guidance on the Application of the CLP Criteria (section 3.4.2.1.3.2.).				
Dossier Submitter's Response				
A reference to the CLP criteria can be included as follows Page 37, section 4.6.2.1 (last paragraph): *Succinic anhydride has been tested in the local lymph node assay (LLNA) test (Weber et al., 2010). The study demonstrates that succinic anhydride has skin sensitising properties (for details see Chapter 4.6.1.1.).* According to GLP guidance (ECHA, 2015) information on the skin sensitising properties of a substance should be used in a weight of evidence assessment because there may be a relationship between the skin sensitising properties of a substance and the respiratory sensitising properties. *Although the LLNA test was developed and validated for identification of contact allergens, there is evidence that chemical respiratory allergens will also elicit positive responses in this assay (Kimber, 1995). Chemicals known to cause respiratory allergy and occupational asthma have been shown to test positive in the LLNA. Among such chemicals are acid anhydrides (such as trimellitic anhydtide and phthalic anhydride). In the ECHA guidance on information reqirements it is stated that the current view is that most, if not all, chemical respiratory allergens are able to elicit positive responses in the LLNA (or in other skin sensitisation test). Maleic anhydride is harmonised classified as Resp. Sens. 1 (H 334: may cause allergy or asthma symptoms or breathing difficulties if inhaled). The read across approach to maleic anhydride is plausible, beside the structural similarity, the toxicity pattern of the two compounds is identical (for details see non-confidential Annex III) and both possess the structural alert (anhydride group) for its sensitising properties. The sensitising properties of succinic anhydride have been demonstrated in the LLNA test described under section 4.6.1.1.*				
RAC's response				
Noted				

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Single Exposure

Date	Country	Organisation	Type of Organisation	Comment number
25.01.2016	Germany		MemberState	13
Comment received				
Page 19, section 4.3 The data justifying STOT SE3 were not presented in the dossier. The source of STOT SE3 remains unknown. Succinic anhydride has been identified as corrosive substance. It is noted that according to the Guidance on the Application of the CLP Criteria (section 3.8.2.5) concerning classification of substances for STOT SE a classification for corrosivity is considered to				

implicitly cover the potential to cause respiratory tract irritation and the additional STOT SE Category 3 classification is then be considered as superfluous. Hence, it should be assessed whether the already existing classification of STOT SE 3, H335 ("May cause respiratory irritation") should remain considering the proposed new classification.

Dossier Submitter's Response

No information on the discussion leading to the current classification as STOT SE3 (12th ATP to Directive 67/548/EEC) is available. According to the registrant and a literature search no studies for this endpoint are available. There are currently no standard tests and no OECD TGs available for acute respiratory tract irritation and there is no testing requirement for respiratory tract irritation under the REACH Regulation. However, it can be assumed that succinic acid in contact with the mucous membranes of the respiratory tract hydrates to the corresponding acid resulting in an irritation/corrosion of the respiratory tract.

In the current CLH-Dossier succinic anhydride is proposed to be classified as corrosive.

According to the CLP-Guidance it is a reasonable assumption that corrosive substances may also cause respiratory tract irritation when inhaled at exposure concentrations below those causing frank respiratory tract corrosion. If there is evidence from animal studies or from human experience to support this then Category 3 may be appropriate. In general, a classification for corrosivity is considered to implicitly cover the potential to cause RTI and so the additional Category 3 is considered to be superfluous, although it can be assigned at the discretion of the classifier. The Category 3 classification would occur only when more severe effects in the respiratory system are not observed.

It is presumed that corrosive substances will cause toxicity by inhalation exposure. In cases where no acute inhalation test has been performed special consideration should be given to the need to communicate this potential hazard (CLP guidance). According to Section 1.2.6 of Annex II to the CLP Regulation, the Hazard statement EUH071 must also be applied to inhaled substances or mixtures classified for skin corrosion and not tested for acute inhalation toxicity.

Based on the available data and the arguments above withdrawal of the classification for respiratory irritation (STOT SE3) is proposed. The hazard statement EUH071 (corrosive to the respiratory tract) shall be applied to be aware of the potential hazard.

RAC's response

EUH071:RAC concur with the response provided by the DS.
STOT SE3: In general RAC concur with the comment by the MS as well as the response given by the DS. However the current classification in STOT SE 3 could be considered superfluous if succinic anhydride will be classified for respiratory sensitisation.