Justification for the selection of a candidate CoRAP substance

Substance Name (Public Name):	Maleic Anhydride
Chemical Group:	
EC Number:	203-571-6
CAS Number:	108-31-6
Submitted by:	Environment Agency Austria on behalf of the Austrian Competent Authority (Austrian Federal Ministry of Agriculture, Forestry, Environment and Water Management)
Published:	20/03/2013

Note

This document has been prepared by the evaluating Member State given in the CoRAP update.

Contents

1 IDENTITY OF THE SUBSTANCE

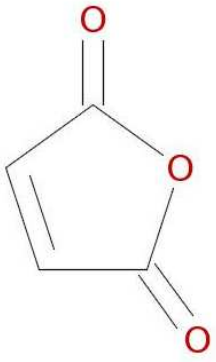
1.1 Name and other identifiers of the substance

Table 1: Substance identity

Public Name:	Maleic anhydride
EC number:	203-571-6
EC name:	Maleic anhydride
CAS number (in the EC inventory):	108-31-6
CAS number:	108-31-6
CAS name:	2,5-Furandione
IUPAC name:	Furan-2,5-dione
Index number in Annex VI of the CLP Regulation	607-096-00-9
Molecular formula:	C4H2O3
Molecular weight or molecular weight range:	98.0569
Synonyms:	---

Type of substance ☒ Mono-constituent ☐ Multi-constituent ☐ UVCB

Structural formula:



2 CLASSIFICATION AND LABELLING

2.1 Harmonised Classification in Annex VI of the CLP

Table 2: Classification according to part 3 of Annex VI, Table 3.1 (list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008

Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling		
				Hazard Class and Category Code(s)	Hazard statement code(s)	Pictogram, Signal Word Code(s	Hazard statement code(s)	Suppl. Hazard statement code(s)
607-096-00-9	maleic anhydride	203-571-6	108-31-6	Acute Tox. 4 * Skin Corr. 1B Resp. Sens. 1 Skin Sens. 1	H302 H314 H334 H317	GHS08 GHS05 GHS07 Dgr	H302 H314 H334 H317	

H302 Harmful if swallowed; H314Causes severe skin burns and eye damage;
H334 May cause allergy or asthma symptoms or breathing difficulties if inhaled;
H317 May cause an allergic skin reaction

Table 3: Classification according to part 3 of Annex VI, Table 3.2 (list of harmonized classification and labelling of hazardous substances from Annex I of Council Directive 67/548/EEC) of Regulation (EC) No 1272/2008

Index No	International Chemical Identification	EC No	CAS No	Classification	Labelling
607-096-00-9	maleic anhydride	203-571-6	108-31-6	Xn; R22 C; R34 R42/43	C R: 22-34-42/43 S: (2-)22-26-36/37/39-45

2.2 Proposal for Harmonised Classification in Annex VI of the CLP

None

2.3 Self classification

In addition to the harmonized classification, the following classifications are notified to the C&L inventory:

Flam. Liq. 3	H226 Flammable liquid and vapour
Eye Irrit. 2	H319 Causes serious eye irritation
Eye Dam. 1	H318 Causes serious eye damage
Acute Tox 1	H330 Fatal if inhaled
Acute Tox3	H311 Toxic in contact with skin
STOT SE1	H370 Causes damage to organs
STOT SE2	H371 May cause damage to organs
STOT RE1	H372 Causes damage to organs
STOT RE2	H373 May cause damage to organs
Aquatic Chronic 3	H412 Harmful to aquatic life with long lasting effects

No specific concentrations limits are given for any endpoint listed.

3 JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

3.1 Legal basis for the proposal

☒ Article 44(1) (refined prioritisation criteria for substance evaluation)

☐ Article 45(5) (Member State priority)

3.2 Grounds for concern

☐ (Suspected) CMR	☐ Wide dispersive use	☐ Cumulative exposure
☒ (Suspected) Sensitiser	☐ Consumer use	☒ High RCR
☐ (Suspected) PBT	☐ Exposure of sensitive populations	☒ Aggregated tonnage
☐ Suspected endocrine disruptor	☐ Other (provide further details below)	

The substance Maleic Anhydride (MA) was screened by experts of the German CA. The following grounds for concern are based on the findings of the German CA, extended by findings of the Austrian CA:

The main use of MA is as intermediate in the preparation of other chemicals. Therefore, human exposure is limited to workers at industrial sites. Based on the information on intended uses derived from the registration dossier it can be assumed that there exist processes/tasks processes/tasks where MA is used in ways that higher exposure levels may occur, which might result in unacceptable risk.

Specific concerns related to the dossier information of the lead dossier of the joint submission

Hazard:

MA has a harmonized classification for skin and respiratory sensitisation, skin corrosion and acute toxic category 4 (oral).

a) Derived No Effect Levels

The following DNELs were derived for the worker population, but not for the general population:

- DNEL long term, inhalation, local & systemic: 0,4 mg/m^3

The DNEL long term, inhalation, local was based on the German MAK value which was derived from a 6 months inhalation study in rats, hamsters and rhesus monkeys.

General systemic toxic effects can be expected to be covered by this DNEL.

Two case reports of occupational respiratory sensitisation with unclear exposure (MA 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 MA concentrations which can be related to sensitisation or elicitation.

Therefore, the sensitising effects of MA are not covered by this DNEL.

The applied assessment factors (AFs) in the registration data are not in line with the REACH guidance. If AFs are reduced from the default this has to be justified adequately. This justification is missing.

- DNEL acute, inhalation, local & systemic: 0,8 mg/m^3

MA is classified in category I by the MAK commission. This allows applying a factor of 2 for acute peak exposures. However, it is not guaranteed that this value is protective against respiratory sensitisation. Sensitisation can result from a single contact.

AFs: see above.

- DNEL long term, dermal, local & systemic: 40 µg/cm^2

The registrants stated based on the corrosivity, and skin & respiratory sensitising properties (it is stated that dermal contact may also induce respiratory sensitisation) of MA dermal contact has to be excluded completely. This recommendation would be in line with the REACH guidance on CSA & IR. The registrant states that this is, however, hard to achieve – therefore the DNEL of 40 µg/cm^2 is used to cover local & systemic as well as acute & chronic dermal effects.

This value is derived from an EC_3 value from a LLNA. The information presented in the registration dossiers is insufficient to conclude whether this value was derived correctly. An EC_3 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 EC_3 values. Not a single assessment factor (AF) was applied to derive this DNEL, and no justification was provided.

It also has to be checked whether the available human data (including information from workplace as well as patch tests) might result in a different value.

The registrant applied the above DNELs in the risk characterisation. As the resulting RCRs are below 1 (though quite close to 1 in some cases) the registrants concluded that the applied RMMs and PPEs are sufficient to guarantee safe use conditions. However, it seems that the sensitising properties of MA are not adequately covered by this approach.

b) Carcinogenicity:

One rat carcinogenicity study is available which has several deficiencies. Therefore IARC put the substance in group 3, i.e. insufficient data to evaluate carcinogenic potential (Carcinogenicity study in rats is inadequate). It has to be checked whether this endpoint is sufficiently evaluated in the registration dossier.

c) Reproductive toxicity:

The presented information is insufficient to evaluate the available studies.

Exposure:

- ECETOC TRA was applied for quantitatively estimating the exposure of workers:

The substance was characterized as solid particles revealing a low dustiness (inhalative exposure to particles) for all of the calculations. Based on these parameters only, inhalation exposure is estimated to be comparatively low and no LEV is required referring to the calculations and the corresponding RCRs.

As the pure substance has a high volatility at room temperature (33 Pa at 25°C) and some uses are performed at elevated temperatures above the melting point of the substance (substance is liquid and not solid), gaseous releases of the substance have to be taken into account in addition to potential exposure to particles in air. Therefore, a higher degree of risk management measures than recommended in the exposure scenarios seems to be required (closed systems, LEV, etc.).

- From the description of the exposure scenarios it is not clear whether LEV is mandatory or not:

LEV is only recommended and not stipulated and the required efficiency is not identified. The calculations were performed without the consideration of LEV. Omission of LEV seems to be acceptable regarding the derived DNELs, as demonstrated in the risk assessment (RCRs below 1). However, as discussed in the section on hazard (see above) it is not conclusive whether sensitisation is covered by this approach. The omission of LEV appears not acceptable at the workplace.

(Besides, there are concerns that the contribution of gaseous releases are not covered within the calculations and that these uses/ESs require higher degrees of RMM, see comment above).

- Different efficiencies for gloves are indicated for different PROCs depending on the degree and amount of expected exposure (quantitative exposure assessment).

As discussed in the hazard section it cannot be considered that the applied DNELs cover the sensitizing effects of MA. Therefore it is not recommendable to use gloves with lower efficiencies.

3.3 Information on aggregated tonnage and uses

☐ 1 – 10 tpa	☐ 10 – 100 tpa	☐ 100 – 1000 tpa
☐ 1000 – 10,000 tpa	☐ 10,000 – 100,000 tpa	
☒ 100,000 – 1000,000 tpa	☐ > 1000,000 tpa	
☐ Confidential		

☒ Industrial use	☒ Professional use	☐ Consumer use	☒ Closed System

Uses mentioned on ECHA Website:

For further information (see http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances)

Use as intermediate for the manufacture of chemical

Manufacture of substance (flakes; low dustiness)

Use as a monomer in polymer production (flakes; low dustiness)

Use as a monomer in polymer production (melting; 77°C)

Industrial use as an intermediate (melting; 77°C)

Use as a monomer in a polymer (flakes; low dustiness)

Uses by professional workers: Health care professionals

3.4 Other completed/ongoing regulatory processes that may affect suitability for substance evaluation

☐ Compliance check	☐ Dangerous substances Directive 67/548/EEC
☐ Testing proposal	☐ Existing Substances Regulation 793/93/EEC
☐ Annex VI (CLP)	☐ Plant Protection Products Regulation 91/414/EEC
☐ Annex XV (SVHC)	☐ Biocidal Products Directive 98/8/EEC
☐ Annex XIV (Authorisation)	☐ Other (provide further details below)
☐ Annex XVII (Restriction)	
Please provide further details	

3.5 Information to be requested to clarify the suspected risk

☒ Information on toxicological properties	☐ Information on physico-chemical properties
☐ Information on fate and behaviour	☒ Information on exposure
☐ Information on ecotoxicological properties	☒ Information on uses
☐ Other (provide further details below)	

It has to be checked whether carcinogenicity is sufficiently evaluated in the registration dossier. If not it might be necessary to request further data on this endpoint.

More data on human exposure of workers and the intended uses are needed. It has to be checked, if the proposed operational conditions and risk management measures in the ESs, which are targeted on the quantitative hazard assessment, also meet the required safety standard for covering the sensitising effects. In order to cover the sensitising properties exposures should be reduced to the extent possible (goal: no contact at all), if it proves correct that the available information is insufficient to derive a quantitative DNEL for skin and respiratory sensitisation. Information on common practice regarding the intended needs to be further evaluated, in order to prove if the derived ESs are safe enough for the workplace situation.

3.6 Potential follow-up and link to risk management

☒ Restriction	☐ Harmonised C&L	☒ Authorisation	☒ Other (provide further details)

Depending on the outcome of the substance evaluation the most effective Risk Management Option can be chosen.

If all questions are properly resolved and exposure is shown to be sufficiently low in order to avoid the critical effects, it may be decided that the use of MA is well controlled and presents no risks. In contrast if unacceptable risks are identified the substance evaluation may result in the preparation of an Annex XV dossier for SVHC identification under Art 57f, or a restriction dossier for the use of MA in certain products and/or applications.