Justification for the selection of a candidate CoRAP substance

Substance Name (Public Name):	Butyl acrylate
Chemical Group:	
EC Number:	205-480-7
CAS Number:	141-32-2
Submitted by:	Swedish Chemicals Agency
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

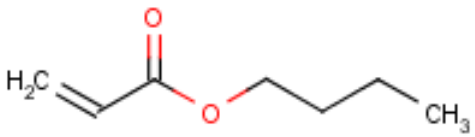
1.1 Name and other identifiers of the substance

Table 1: Substance identity

Public Name:	Butyl acrylate
EC number:	205-480-7
EC name:	Butyl acrylate
CAS number (in the EC inventory):	141-32-2
CAS number:	141-32-2
CAS name:	2-Propenoic acid, butyl ester
IUPAC name:	Butyl acrylate
Index number in Annex VI of the CLP Regulation	607-062-00-3
Molecular formula:	C7H12O2
Molecular weight or molecular weight range:	128.169
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

CLP:

Classification		
Hazard Class and Category Code(s)	**Hazard statement Code(s)**	**Hazard statements**
Flam. Liq. 3	H226	Flammable liquid and vapour
Eye Irrit. 2	H319	Causes serious eye irritation
STOT SE 3	H335	May cause respiratory irritation
Skin Irrit. 2	H315	Causes skin irritation
Skin Sens. 1	H317	May cause an allergic skin reaction

DSD:

Classification	**Risk phrases**
R10 Xi; R36/37/38 Irritant R43	Flammable Irritating to eyes, respiratory system and skin May cause sensitisation by skin contact

2.2 Proposal for Harmonised Classification in Annex VI of the CLP

No proposal at present.

2.3 Self classification

In addition to the harmonised classification in Annex VI of the CLP, the lead registrant has also included the following self-classification in the registration:

Acute Tox 4. H332: Harmful if inhaled

In addition to the classifications given by the lead registrant, the following other classifications are included in the Classification and Labelling Inventory:

Asp. Tox. 1; H304: May be fatal if swallowed and enters airways

Acute Tox. 4; H302: Harmful if swallowed

STOT SE 3; H335 – with specific concentration limit: C ≥ 10%

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)	

Three pre-natal developmental toxicity studies for n-butyl acrylate are available, but currently no studies of toxicity on fertility have been described. Merkle and Klimisch (1983) reported an increased percentage of resorptions and a reduced number of fetuses in rats exposed to n-butyl acrylate (doses 0, 25, 135, 250 ppm) via inhalation on GD 6-15. The IND argues in the CSR that the observed developmental toxicity is explained by maternal toxicity manifested as decreased weight gain at 135 ppm and 250 ppm (16% less than control, $p<0.05$ and 31% less than control, $p<0.01$ respectively). It is noted, however, that the absolute maternal weight at 135 ppm and 250 ppm at GD20 is only slightly reduced (5% and 10%, $p<0.01$, respectively) compared to control and that the reduced weight gain in exposed dams (135 ppm) compared to control dams approximately corresponds to the total weight of the reduced number of fetuses (approx. 3 fetuses á 4 g → 12 g). Therefore, the maternal toxicity (reduced weight gain) cannot explain the findings of developmental toxicity and the conclusion from the study indicates that n-butyl acrylate may induce developmental toxicity.
In a second pre-natal developmental study in rats exposed to n-butyl acrylate (does 0, 100, 200, 300 ppm) via inhalation on GD 6-20 Saillenfait et al., 1999 demonstrated reduced fetal weight (93% of control, $p<0.05$ and 74% of control, $p<0.01$ at 200 and 300 ppm respectively) in combination with significant reduced absolute maternal weight gain at all tested doses. The maternal weight at GD 21 was 96, 88, and 71% of control at 100, 200 and 300 ppm respectively. No significant effects on number of live fetuses or litters, percentage of resorption sites per litter, developmental effects or malformations were observed. Although not statistically significant and without an established dose-response relationship the percentage of resorption sites per litter was decreased in treated dams (6.8%; 4.72%; and 6.48% at 100, 200 and 300 ppm respectively) compared to control dams (10.6%). Considering the maternal toxicity at the higher doses in this study and the not very pronounced decrease in fetal weight in absence of any further clear evidence of developmental toxicity it is not possible to make a conclusion on developmental toxicity.
In a third pre-natal developmental toxicity study n-butyl acrylate (doses 100, 1000, 1500, 2000, 2500, 3000, 4000 mg/kg bw) was administered to mouse via oral gavage on GD 6-15. At doses ≥1000 mg/kg bw mortality was 3.3-6.7% and effects on maternal weight was significant at doses ≥1500 mg/kg bw (Rohm and Haas Co, 1979). Fetal body weights were also reduced from 1500 mg/kg bw. At 2500 and 3000 mg/kg bw the percentage of resorptions was significantly increased. In these dose groups, the number of fetuses with malformations was also significantly increased. The complete study report was not available and therefore the study cannot be fully evaluated.

In summary, the concern is suspected reproductive toxicity of n-butyl acrylate due to
1) Ambiguity of observed results in developmental toxicity studies
2) Lack of proper studies that address effects on fertility and reproductive function

In addition, the concern relates to the risk of high exposure in occupational settings.

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		
Please provide further details		

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

n-Butyl acrylate is manufactured as a chemical intermediate in a closed system. Its major use is in the production of homo- and co-polymers with other monomers to produce emulsion polymers.

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

☐ Compliance check final decision	☐ 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)	

For current harmonised classification included in Annex VI (CLP), please refer to section 2.1.

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)	

Based on an initial concern for reproductive toxicity of n-butyl acrylate the available data in public databases and in the registration dossier were reviewed by the Swedish Chemicals Agency. It was concluded that there are no studies on fertility for n-butyl acrylate available, neither in the published literature nor in the registration dossier. In contrast, three pre-natal developmental toxicity studies of n-butyl acrylate were available and were also presented in the registration dossier: two inhalation studies in rat and one oral (gavage) study in mouse. It was noted that the results on developmental effects of n-butyl acrylate in the three available studies were conflicting and maternal toxicity (reduced maternal weight and/or weight gain) was reported. Marked maternal toxicity is not relevant for classification purposes in certain cases, however, these dose levels could mask a potential to cause developmental toxicity. Moreover, in the study by Merkle and Klimisch (1983), the reported maternal body weight was misinterpreted (please refer to discussion above). In the registration dossier IND used the structural analogue methyl acrylate for read across purposes for reproductive effects to fulfill the data requirements of screening for reproductive/developmental toxicity and a two-generation reproduction toxicity study. The data for methyl acrylate indicated no significant effects on reproductive system or development.

In summary, the data for classification purposes to address the concern for reproductive toxicity is not sufficient and conclusive. As protective measures of human health we therefore propose to suggest n-butyl acrylate for substance evaluation to further investigate the reproductive toxicity. Specifically, a two-generation reproduction toxicity study may give insight into the effects of n-butyl acrylate on fertility and the integrity and performance of the male and female reproductive systems (lacking in the current dossier), growth and development of the offspring and in addition, developmental effects in F2 generations. These studies will also result in further data on prenatal developmental toxicity, potentially helping in the evaluation of the data in the current registration dossier.

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 evaluation of new data, a proposal for harmonised classification for reproductive toxicity may be warranted as a first step of risk management.