Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

formic acid … %

EC Number: 200-579-1
CAS Number: 64-18-6

CLH-O-0000007128-73-01/F

Adopted

2 June 2022

P.O. Box 400, FI-00121 Helsinki, Finland | Tel. +358 9 686180 | Fax +358 9 68618210 | echa.europa.eu

2 June 2022

CLH-O-0000007128-73-01/F

OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT EU LEVEL

In accordance with Article 37 (4) of Regulation (EC) No 1272/2008, the Classification, Labelling and Packaging (CLP) Regulation, the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling (CLH) of:

Chemical name: **formic acid ... %**

EC Number: **200-579-1**

CAS Number: **64-18-6**

The proposal was submitted by **Belgium** and received by RAC on **29 July 2021.**

In this opinion, all classification and labelling elements are given in accordance with the CLP Regulation.

PROCESS FOR ADOPTION OF THE OPINION

Belgium has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at ***http://echa.europa.eu/harmonised-classification-and-labelling-consultation/*** on **23 August 2021**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **22 October 2021**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: **Michal Martínek**

The opinion takes into account the comments provided by MSCAs and concerned parties in accordance with Article 37(4) of the CLP Regulation and the comments received are compiled in Annex 2.

The RAC opinion on the proposed harmonised classification and labelling was adopted on **2 June 2022** by **consensus.**

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	Chemical name	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	607-001-00-0	formic acid ... %	200-579-1	64-18-6	Skin Corr. 1A	H314	GHS05 Dgr	H314		Skin Corr. 1A; H314: C ≥ 90% Skin Corr. 1B; H314: 10% ≤ C < 90% Skin Irrit. 2; H315: 2% ≤ C < 10% Eye Irrit. 2; H319: 2% ≤ C < 10%	B
Dossier submitters proposal	607-001-00-0	formic acid ... %	200-579-1	64-18-6	**Add** Flam. Liq. 3 Met. Corr. 1 Acute Tox. 4 Acute Tox. 3 Eye Dam. 1	**Add** H226 H290 H302 H331 H318	**Add** GHS02 GHS06	**Add** H226 H290 H302 H331	**Add** EUH071	**Add** Flam. Liq. 3; H226: C ≥ 99% Met. Corr. 1; H290: C ≥ 85% Eye Dam. 1; H318: C ≥ 10%	
RAC opinion	607-001-00-0	formic acid ... %	200-579-1	64-18-6	**Add** Flam. Liq. 3 Met. Corr. 1 Acute Tox. 4 Acute Tox. 3 Eye Dam. 1	**Add** H226 H290 H302 H331 H318	**Add** GHS02 GHS06	**Add** H226 H290 H302 H331	**Add** EUH071	**Add** Flam. Liq. 3; H226: C > 85% oral: ATE = 500 mg/kg bw inhalation: ATE = 7.4 mg/l (vapours) Eye Dam. 1; H318: C ≥ 10%	
Resulting Annex VI entry if agreed by COM	607-001-00-0	formic acid ... %	200-579-1	64-18-6	Flam. Liq. 3 Met. Corr. 1 Acute Tox. 4 Acute Tox. 3 Skin Corr. 1A Eye Dam. 1	H226 H290 H302 H331 H314 H318	GHS02 GHS05 GHS06 Dgr	H226 H290 H302 H331 H314	EUH071	Flam. Liq. 3; H226: C > 85% oral: ATE = 500 mg/kg bw inhalation: ATE = 7.4 mg/l (vapours) Skin Corr. 1A; H314: C ≥ 90% Skin Corr. 1B; 314: 10% ≤ C < 90% Skin Irrit. 2; H315: 2% ≤ C < 10% Eye Dam. 1; H318: C ≥ 10% Eye Irrit. 2; H319: 2% ≤ C < 10%	B

GROUNDS FOR ADOPTION OF THE OPINION

RAC general comment

Formic acid is a colourless, volatile liquid with a pungent odour. The main uses include silaging, feed additive, leather and textile industry and chemical synthesis. Formic acid also occurs in nature (e.g. insect venoms, plants, mammalian body). It is miscible with water and the name of the Annex VI entry, 'formic acid … %', reflects the fact that the substance is placed on the market as aqueous solution.

Formic acid has a harmonised classification as Skin Corr. 1A with specific concentration limits. During the assessment of the substance under the Biocidal Products Regulation it was concluded that the harmonised classification should be updated. The current CLH proposal covers selected hazard classes: flammability, corrosion to metals, acute toxicity (oral, inhalation) and eye damage/irritation.

RAC evaluation of physical hazards

Summary of the Dossier Submitter's proposal

Flammable liquids

The dossier submitter (DS) presented a study with 99.4% formic acid reporting a flash point of 49.5 °C (Bitterlich, 2007). The criterion for classification is a flash point of ≤ 60 °C. The DS proposed classification as Flam. Liq. 3 with a specific concentration limit of ≥ 99%.

Corrosive to metals

85% formic acid was positive and 99.4% formic acid was negative in 7-day corrosion tests according to the UN method C.1. Initially (in the CLH report) the DS proposed classification as Met. Corr. with a specific concentration limit of ≥ 85%.

Comments received during consultation

Comments on flammable liquids were received from two member-state competent authorities (MSCAs). One of them stated that the usual flash point of formic acid is 69-71 °C. The other MSCA questioned the proposed specific concentration limit of ≥ 99% and provided a set of flash point data for various concentrations of formic acid that had been used as a basis for the current concentration limit of > 85% in the UN Recommendations on the Transport of Dangerous Goods, Model Regulations.

Comments on corrosivity to metals were received from 1 MSCA and 1 manufacturer. The industry commenter requested no classification for formic acid at ≥ 99% due to the negative result at 99.4%; they proposed the classification to apply only at 85% ≤ C < 99%. The DS disagreed, explaining that although 99.4% formic acid does not meet the criteria, the corrosion hazard may appear after a relatively small addition of water.

The commenting MCSA pointed out that corrosivity of solutions containing less than 85% formic acid was not investigated and therefore a concentration limit cannot be established without further testing. The DS agreed and did not anymore support the originally proposed specific concentration limit of 85%.

Assessment and comparison with the classification criteria

Flammable liquids

Liquid substances are classified in Category 3 if their flash point is ≥ 23 °C and ≤ 60 °C. With a flash point of 48 °C pure formic acid (100%; Germany, 2004) meets the CLP criteria for Flam. Liq. 3.

The flash point of aqueous solutions of formic acid increases with decreasing concentration. The threshold for classification (flash point 60 °C) lies between 85% and 90% (Germany, 2004). This information served as a basis for the concentration limit for flammability of formic acid of > 85% in the UN Model Regulations (entries 1779 and 3412).

RAC proposes a classification as **Flam. Liq. 3; H226** with a concentration limit of **> 85%** in line with the UN Recommendations on the Transport of Dangerous Goods, Model Regulations.

Corrosive to metals

The results of the two available C.1 tests are summarised below. The criteria for a positive result in a 7-day test are mass loss of ≥ 13.5% or localised corrosion with an intrusion depth of ≥ 120 µm. Both criteria were fulfilled for steel in the test with 85% formic acid (Henke, 2016). The criteria were not met by 99.4% formic acid (Krebs, 2017) presumably due to the low content of water leading to suppressed dissociation.

UN C.1 tests (exposure duration 7 days)					
Reference	**Concentration**	**Steel**		**Aluminium**	
		mass loss	**intrusion depth**	**mass loss**	**intrusion depth**
Henke (2016)	85%	28.2%	>120 µm	4.8%	none
Krebs (2017)	99.4%	2.0%	none	0.0%	none

RAC considers that classification is clearly warranted. Nevertheless, as pointed out in the third-party consultation, the available data do not allow setting of a lower specific concentration limit. The corrosivity classification in Model Regulations has a limit of ≥ 5% (see the "Additional key elements" section in the BD and Germany, 2004) but the data behind this value are not available to RAC.

Singh and Gupta (1996) investigated corrosion rate of mild steel in formic acid at different concentrations (5% to 80%), temperatures (25 to 45 °C) and immersion periods (6 to 72 h). They found that the corrosion rates were highest at formic acid concentrations around 20%, and that the corrosion rates at 5% were higher than at 80%. Although this investigative study did not follow the UN C.1 protocol, the results indicate that the specific concentration limit of 5% from the UN Model Regulations should not be adopted under CLP without further verification.

As to the upper limit of 99% proposed by industry, RAC agrees with the DS that such a limit would not be appropriate as the corrosion hazard will appear on dilution.

In conclusion, RAC agrees with the revised DS's proposal of **Met. Corr. 1; H290**. The available data do not allow setting a specific concentration limit.

HUMAN HEALTH HAZARD EVALUATION

RAC evaluation of acute toxicity

Summary of the Dossier Submitter's proposal

Acute oral toxicity

The DS presented animal and human data. They proposed classification as Acute Tox. 4 based on an LD_{50} of 730 mg/kg bw from an acute oral toxicity study in rats.

Acute inhalation toxicity

The DS proposed classification as Acute Tox. 3 based on a 4-hour LC_{50} of 7.4 mg/l (vapours) from an acute inhalation toxicity study in rats. They additionally proposed labelling with EUH071 as the toxicity of formic acid was considered to be caused by its corrosive properties.

Comments received during consultation

Two MSCAs supported the DS's proposal. One of them recommended adding the respective ATE values.

A manufacturer (BASF) asked to raise the LC_{50} value of the key acute inhalation toxicity study from 7.4 mg/l to 7.85 mg/l based on an amendment of the study report (see the "Additional key elements" section in the BD). The DS disagreed.

One individual proposed H300 and H330 due to the experience of formic acid causing serious skin burns.

Assessment and comparison with the classification criteria

Acute oral toxicity

The key information consists of a guideline-compliant acute oral toxicity study in rats (1985) and human case reports. The CLH report further mentions an LD_{50} of 1100 mg/kg bw from a poorly reported mouse study (1969).

Acute oral toxicity study in rats (1985)

Wistar rats (5/sex/group) were dosed with undiluted formic acid (purity 99%) via gavage at dose levels of 501, 631, 794 and 1000 mg/kg bw. Post-exposure observation period was 14 days.

LD_{50} was 863 mg/kg bw for males, 618 mg/kg bw for females and 730 mg/kg bw for combined sexes. Mortality rates are presented in the following table. Females appear slightly more sensitive than males.

Mortality in the acute oral toxicity study (1985)

Dose (mg/kg bw)	Mortality	
	males	females
501	0/5	1/5
631	2/5	2/5
794	1/5	5/5
1000	4/5	4/5

Clinical signs included hunched posture, dyspnea, sedation, convulsions, blood in urine, hypothermia, body weight loss and pale limbs. Gross pathology of decedents showed hyperemia of the stomach and intestines.

Human case reports

Table 11 of the CLH report summarises several case reports and reviews. Of particular relevance for classification are well-described fatal cases where the ingested amount was known at least approximately; these are listed in the table below. All four cases in the table had a fatal outcome despite intense treatment (e.g. ventilation, transfusion, dialysis). The estimated dose ranged between 200 and 1700 mg/kg bw.

Human case reports		
Reference	**Subject;** **ingested material, amount;** **dose of formic acid** (estimated by RAC)	**Brief description of the case** (in all cases medical treatment, not described in the table)
Verstraete *et al.* (1989)	39-year old female Approx. 200 ml of a descaling product (pH 1.97) containing 50% formic acid Ca. 1700 mg/kg bw	Main findings: pain, vomiting of blood, shock, severe metabolic acidosis, hemolysis, severe lesions of the esophagus and stomach, severe gastrointestinal bleeding, pneumonia, acute tubular necrosis, respiratory distress syndrome, peritonitis, sepsis Died 6 weeks after admission in multiorgan failure Pre-existing conditions: Cushing syndrome with hypertension and diabetes
Naik *et al.* (1980), case 1	35-year old female 3 mouthfuls of a 40% formic acid solution (bath stain remover) Ca. 500 mg/kg bw	Main findings: vomiting of blood, massive bleeding per rectum, abdominal pain, clotting defect, hemolysis, profound metabolic acidosis, anuria, pulmonary complications, ulceration throughout the esophagus and stomach, acute tubular necrosis Died on day 14 after shock and massive vomiting of blood (blood-filled stomach and small bowel)
Naik *et al.* (1980), case 2	66-year old female 50-100 ml of kettle descaler containing 55% formic acid Ca. 500-1000 mg/kg bw	Main findings: vomiting, shock, tachycardia, ulceration of mouth and pharynx, profound metabolic acidosis, aspiration pneumonia, cardiac and respiratory arrest, pulmonary edema, hemolysis, gross clotting defect, hematuria, acute renal failure and anuria, hypotension, extensive erosion of the esophagus, stomach and duodenum Died 5 days after admission Pre-existing conditions: ischemic heart disease, brain stem vascular insufficiency
Naik *et al.* (1980), case 3	56-year old male A mouthful of kettle descaler containing 55% formic acid Ca. 200 mg/kg bw	Main findings: pain, vomiting, tachycardia, hypotension, cyanosis, anuria, sloughing of the mucosa of the soft palate and oropharynx, acute respiratory distress, intravascular coagulation, tubular necrosis Died on day 11 due to circulatory failure Pre-existing conditions: asbestosis, duodenal ulceration

In addition, Jefferys and Wiseman (1980) briefly reviewed 45 cases of formic acid poisoning from ingestion of descaling agents (formic acid content 44-60%). Ingestion of 5 to 30 g of formic acid produced no deaths, and the majority of subjects developed minor burns only. Ingestion of 30-45

g produced more serious effects; of the 6 patients recorded, one died, and the rest developed serious conditions such as acute renal failure, hematemesis, intravascular conditions and oesophageal strictures. Ingestion of 45 to 200 g of formic acid was recorded from 16 patients, of whom 14 died, the majority from corrosive perforations of the abdominal viscera, gastrointestinal haemorrhage or acute renal failure. The consumption of 60 g or more of formic acid (approx. 100 ml of the descaling fluid) produced death in all cases. 45 g of formic acid corresponds to ca. 700 mg/kg bw if assuming a body weight of 65 kg.

The available human information indicates that doses around 500 mg/kg bw may be lethal in humans despite treatment.

Conclusion

Both animal and human data are consistent with Category 4 (300 mg/kg bw < ATE ≤ 2000 mg/kg bw). The lowest animal LD_{50} is 620 mg/kg bw (rounded-off) from females in the rat study, mortality started at 500 mg/kg bw/d. Human data indicate a similar threshold for mortality but a somewhat higher sensitivity cannot be excluded as all the cases underwent intense medical treatment (such as intravascular bicarbonate, dialysis, ventilation). Due to this uncertainty about human sensitivity, RAC prefers the somewhat lower converted ATE of 500 mg/kg bw (CLP, Annex I, Table 3.1.2).

In conclusion, RAC proposes classification as **Acute Tox. 4; H302** with an **ATE** of **500 mg/kg bw**.

Acute inhalation toxicity

The key study is a guideline-compliant acute inhalation toxicity study in rats (1980). The DS further presented non-guideline acute studies, repeated dose studies and human data.

Acute inhalation toxicity study in rats (1980)

Sprague-Dawley rats (10/sex/group) were exposed (whole body) to vapours of formic acid for 4 hours at concentrations of 2.8, 6.6, 8.1, 10.6 and 14.7 mg/l. Post-exposure observation period was 14 days.

RAC notes the Amendment no. 1 to the study report, issued in 2014, changing the exposure concentrations and the LC_{50}. However, after examination of the documentation RAC concluded that this amendment is unjustified and should not be accepted (for details see the "Additional key elements" section in the BD). The original study report from 1980 remains valid.

LC_{50} was 7.3 mg/l for males, 7.5 mg/l for females and 7.4 mg/l for combined sexes. Mortality rates are presented in the following table. Since there was no significant difference in susceptibility between sexes, the combined LC_{50} of 7.4 mg/l is considered to represent an appropriate overall ATE from this study.

Mortality in the acute inhalation toxicity study (1980)		
Concentration (mg/l)	**Mortality**	
	males	**females**
2.8	0/10	0/10
6.6	2/10	1/10
8.1	8/10	8/10
10.6	10/10	10/10
14.7	10/10	10/10

Clinical signs included discharge from nose and eye, corneal opacity, loss of pain reflex, dyspnea, respiration sounds, hunched posture and unsteady gait. Pathology of decedents showed corneal opacity, corrosion of the dorsal nose, inflated lungs and dilated hearts.

Other information

In two non-standard acute studies (registration dossier, studies dated 1981 and 1982) rats were exposed to a saturated atmosphere of formic acid (concentration presumably in the range of 80 mg/l) for 3 to 116 min. All animals exposed for ≥ 10 minutes died. These studies do not provide information useful for classification mainly because they used a single very high and poorly defined concentration.

In a set of NTP studies (Thompson, 1992) rats and mice were exposed for formic acid vapours for 2 or 13 weeks (6 hours/day, 5 days/week). The top concentration in the 2-week studies was 500 ppm (0.94 mg/l), at this concentration all 10 mice died within the first week and 4 out of 10 rats died on day 10. Clinical signs included nasal discharge, laboured breathing and corneal opacity. Histopathological examination of the respiratory tract revealed necrosis of the nasal epithelium in most of the top concentration animals of both species, mice additionally showed changes in the larynx, pharynx and trachea. The top concentration in the 13-week studies was 128 ppm (0.24 mg/l), histopathological changes were minimal and limited to the nasal cavity. Overall, these studies showed (mainly upper) respiratory tract irritation after repeated exposure.

The DS further summarised several reports of suicidal attempts where the subjects mixed formic acid and sulphuric acid to generate toxic carbon monoxide. The involvement of CO and lack of exposure quantification precludes their use for classification. Nevertheless, the respiratory tract injuries (including lack of the respiratory epithelium of the trachea, pulmonary edema) in the case described by Bakovic *et al.* (2015) were attributed to formic acid and could be used as supporting evidence for EUH071.

Conclusion

The 4-hour LC_{50} of 7.4 mg/l from a guideline-compliant rat study corresponds to Category 3 (2.0 mg/l < ATE ≤ 10.0 mg/l). RAC agrees with the DS's proposal of **Acute Tox. 3; H331** with an **ATE** of **7.4 mg/l (vapours)** based on the guideline-compliant acute inhalation toxicity study.

The substance is classified as corrosive to the skin. While the available animal data indicate irritation of the respiratory tract after inhalation of formic acid vapours, it is not clear whether the deaths were mainly due to local effects. Still, formic acid can also be inhaled in the form of aerosol, which would most likely lead to serious respiratory tract corrosion. Therefore, RAC agrees to add **EUH071**.

RAC evaluation of serious eye damage/irritation

Summary of the Dossier Submitter's proposal

No test data are presented in the CLH report. The substance has a harmonised classification as corrosive to the skin with an SCL of ≥ 10% (more specifically, Skin Corr. 1A at C ≥ 90%, Skin Corr. 1B at 10% ≤ C < 90%). According to the CLP (Annex I, 3.3.2.2.2), skin corrosive substances shall be considered as leading to serious eye damage (Category 1). Therefore, the DS proposes to add a classification as Eye Dam. 1 with an SCL of ≥ 10%.

Comments received during consultation

One MSCA supported the DS's proposal.

Assessment and comparison with the classification criteria

Classification as Eye Irrit. 2 is already part of the Annex VI entry with SCLs identical to those for Skin Irrit. 2, that is 2% ≤ C < 10%. Only a skin corrosion classification is included in the current entry with an SCL of ≥ 10%, obviously because in the past, when a substance was classified as corrosive, the eye hazard was considered to be implicit. According to the current interpretation of the CLP regulation (Annex I, 3.3.2.2.2), Eye Dam. 1 should be part of the classification in addition to the classification for skin corrosion, but H318 is omitted from the labelling (CLP, Annex III).

In conclusion, RAC agrees with the DS's proposal to add **Eye Dam. 1; H318** with an **SCL** of **≥ 10%**.

Additional references

Germany (2004) Proposal to add new UN numbers for formic acid (UN 1779) and propionic acid (UN 1848). Transmitted by the expert from Germany. ST/SG/AC.10/C.3/2004/12. 31 March 2004. Online: https://digitallibrary.un.org/record/520952

Singh and Gupta (1996) Corrosion behaviour of mild steel in formic acid solutions. Material Chemistry and Physics 46:15-22

ANNEXES:

Annex 1 The Background Document (BD) gives the detailed scientific grounds for the opinion. The BD is based on the CLH report prepared by the Dossier Submitter; the evaluation performed by RAC is contained in 'RAC boxes'.

Annex 2 Comments received on the CLH report, response to comments provided by the Dossier Submitter and RAC (excluding confidential information).