Annex XV dossier

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE AS A CMR CAT 1A OR 1B, PBT, vPvB OR A SUBSTANCE OF AN EQUIVALENT LEVEL OF CONCERN

Substance Name(s): Formamide

EC Number(s): 200-842-0

CAS Number(s): 75-12-7

Submitted by: **Federal Institute for Occupational Safety and Health**
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PUBLIC VERSION: This report does not include the confidential annexe referred to in the document.

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Substance Name(s): Formamide

EC Number(s): 200-842-0

CAS number(s):75-12-7

- The substance is proposed to be identified as substance meeting the criteria of Article 57 (c) of Regulation (EC) 1907/2006 (REACH) owing to its classification as toxic for reproduction category 1B[1] which corresponds to classification as toxic for reproduction category 2[2].

Summary of how the substance meets the CMR (1A or 1B) criteria

Formamide is listed by Index number 616-052-00-8 of Regulation (EC) No 1272/2008 in Annex VI, Part 3, Table 3.1 (list of harmonised classification and labelling of hazardous substances) as toxic for reproduction, Repr. 1B (H360D: "May damage the unborn child."). The corresponding classification in Annex VI, part 3, Table 3.2 (the list of harmonised classification and labelling of hazardous substances from Annex I to Directive 67/548/EEC) of Regulation (EC) No 1272/2008 is toxic for reproduction, Repr. Cat. 2 (R61;" May cause harm to the unborn child").

Therefore, this classification of the substance in Regulation (EC) No 1272/2008 shows that it meets the criteria for classification as toxic for reproduction in accordance with Article 57 (c) of REACH.

Registration dossiers submitted for the substance? Yes

1 Classification in accordance with Regulation (EC) No 1272/2008 Annex VI, part 3, Table 3.1 List of harmonised classification and labelling of hazardous substances.

2 Classification in accordance with Regulation (EC) No 1272/2008, Annex VI, part 3, Table 3.2 List of harmonised classification and labelling of hazardous substances (from Annex I to Council Directive 67/548/EEC).

PART I

JUSTIFICATION

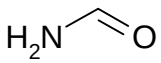
1 IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

1.1 Name and other identifiers of the substance

Table 1: Substance identity

EC number:	200-842-0
EC name:	Formamide
CAS number (in the EC inventory):	75-12-7
CAS number:	-
CAS name:	Formamide
IUPAC name:	Formamide
Index number in Annex VI of the CLP Regulation	616-052-00-8
Molecular formula:	CH_3NO
Molecular weight range:	45.0406 g/mol
Synonyms:	

Structural formula:



1.2 Composition of the substance

Name: Formamide

Description: mono constituent substance

Degree of purity: >= 99.5%[3] (w/w)

[3] Based on the minimum typical content indicated in the registration dossiers (downloaded on 28/02/2010)

Further details on the composition of the substance are confidential and can be found in the technical dossier and the confidential annex.

Table 2: Constituents

Constituents	Typical concentration	Concentration range	Remarks
Formamide, EC number: 200-842-0	**>= 99.5%[3] (w/w)**		

Table 3: Impurities

Impurities	Typical concentration	Concentration range	Remarks
See confidential annex			

Table 4: Additives

Additives	Typical concentration	Concentration range	Remarks
See confidential annex			

1.3 Physico-chemical properties

The physico-chemical properties were taken from the lead registration dossier for formamide (as available on 28/02/2010).

Table 5: Overview of physicochemical properties

Property	Value	Remarks	Reference
Physical state at 20°C and 101.3 kPa	Slightly viscous colourless and odourless liquid		*Kirk-Othmer, 1994, Encylopedia of Chemical Technology, 4th edition, Vol. 11., John Wiley & Sons, New York, USA*
Melting/freezing point	2.6°C (275.6 K)		*US EPA 2005, EPISuite (v3.12) data assessment, Estimation Programs Interface Suite,™. for Microsoft® Windows, v 3.12. United States Environmental Protection Agency, Washington, DC, USA.*
Boiling point	218.3 °C, 1013.3hPa (decomposition starts above 140 °C)	*Extrapolated, (decomposition starts above 140 °C)*	*Körösi G and Kováts E sz. 1981, Density and Surface Tension of 83 Organic Liquids, J. Chem. Eng. Data 26, 323-332*
Vapour pressure	0.06 hPa at 20 °C		*BASF AG, 1984, BASF AG, ZET/FC, Study-No.: 184.0631.1*
Water solubility	1E06 mg/L at 25 °C	*EPISuite v3.12 (WSKOW v1.41)*	*US EPA 2005, EPISuite (v3.12) data assessment, Estimation Programs Interface Suite,™. for Microsoft® Windows, v 3.12. United States Environmental Protection Agency, Washington, DC, USA.*
Partition coefficient n-octanol/water (log value)	-0.82 at 25°C		*BASF AG, 1984, Determination of Log Pow from Formamid in 1-octanol/water at roomtemperature (25°C), Department of Analytical Chemistry, Report No.: 130365/02*
Dissociation constant	pK_a at 20/25°C: -0.48		*Kirk-Othmer, 1994, Encylopedia of Chemical Technology, 4th edition, Vol. 11., John Wiley & Sons, New York, USA*
Surface tension	57.46 mN/m at 20°C Based on the chemical structure, no surface activity is expected.	*The value is given in the registration dossier for pure Formamide. Furthermore the endpoint can be waived.*	*Körösi G and Kováts E sz. 1981, Density and Surface Tension of 83 Organic Liquids, J. Chem. Eng. Data 26, 323-332*
Viscosity	3.764 mPa s at 20 °C		*Kirk-Othmer, 1994, Encylopedia of Chemical*

			Technology, 4th edition, Vol. 11., John Wiley & Sons, New York, USA
Density	1.13 g/cm³ at 20 °C		*Körösi G and Kováts E sz. 1981, Density and Surface Tension of 83 Organic Liquids, J. Chem. Eng. Data 26, 323-332*
Flash point	152 °C at 1013 hPa		*BASF AG, 2007, Determination of the flashpoint of formamide, GCT/S -Safety Engineering, Report No. SIK-No. 07/1202*
Auto flammability	> 500 °C		*Kirk-Othmer, 1994, Encylopedia of Chemical Technology, 4th edition, Vol. 11., John Wiley & Sons, New York, USA*
Flammability	Not flammable; based on the molecular structure and experience in use formamide has no pyrophoric properties; it does not react with water under f ormation of flammable gases.		
Explosiveness:	Not oxidising; due to the structural composition of the substance it is not considered to be oxidising.		
Stability in organic solvents and identity of relevant degradation products:	In accordance with column 1 of Annex IX, the study does not need to be conducted if the stability of the substance is considered to be critical. Formamide is not considered as critical.		

2 HARMONISED CLASSIFICATION AND LABELLING

Formamide is listed by Index number 616-052-00-8 of Regulation (EC) No 1272/2008 in Annex VI, Part 3, Table 3.1 (list of harmonised classification and labelling of hazardous substances) as follows:

Table 6: Classification according to Annex VI, Part 3, Table 3.1 (list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008

Index No	International Chemical Identification	Classification		Labelling		
		Hazard Class and Category Code	Hazard statement Code	Pictogram, Signal Word Code	Hazard statement Code	Suppl. Hazard statement Code(s)
616-052-00-8	formamide	Repr. 1B	H360D***	GHS08 **Dgr**	H360D***	

Hazard statement code: H360D[§§]: May damage the unborn child.

Formamide is covered by Index number 616-052-00-8 of Regulation (EC) No 1272/2008 in Annex VI, Part 3, Table 3.2 (list of harmonised classification and labelling of hazardous substances from Annex I to Directive 67/548/EEC) as follows:

Table 7: Classification according to Annex VI, Part 3, Table 3.2 (list of harmonised classification and labelling of hazardous substances from Annex I to Directive 67/548/EEC) of Regulation (EC) No 1272/2008

Index No	Chemical name	Classification	Labelling
616-052-00-8	formamide	Repr.Cat. 2; R61	T R: 61 S: 53-45

[§§] *Hazard statements H360 and H361 indicate a general concern for effects on both fertility and development: 'May damage/Suspected of damaging fertility or the unborn child'. According to the criteria, the general hazard statement can be replaced by the hazard statement indicating only the property of concern, where either fertility or developmental effects are proven to be not relevant.*

In order not to lose information from the harmonised classifications for fertility and developmental effects under Directive 67/548/EEC, the classifications have been translated only for those effects classified under that Directive.

3 ENVIRONMENTAL FATE PROPERTIES

Not relevant.

4 HUMAN HEALTH HAZARD ASSESSMENT

See section 2 on Harmonised Classification and Labelling.

5 ENVIRONMENTAL HAZARD ASSESSMENT

Not relevant.

6 CONCLUSIONS ON THE SVHC PROPERTIES

6.1 PBT, vPvB assessment

Not relevant.

6.2 CMR assessment

Formamide is covered by Index number 616-052-00-8 of Regulation (EC) No 1272/2008 and classified in Annex VI, Part 3, Table 3.1 (list of harmonised classification and labelling of hazardous substances) as toxic for reproduction, Repr. 1B (H360D: “May damage the unborn child.”). The corresponding classification in Annex VI, part 3, Table 3.2 (the list of harmonised classification and labelling of hazardous substances from Annex I to Directive 67/548/EEC) of Regulation (EC) No 1272/2008 is toxic for reproduction, Repr. Cat. 2 (R61;” May cause harm to the unborn child”).

Therefore, this classification of the substance in Regulation (EC) No 1272/2008 shows that it meets the criteria for classification as toxic for reproduction in accordance with Article 57 (c) of REACH.

6.3 Substances of equivalent level of concern assessment.

Not relevant.

PART II

INFORMATION ON USE, EXPOSURE, ALTERNATIVES AND RISKS

1 INFORMATION ON MANUFACTURE, IMPORT/EXPORT AND USES – CONCLUSIONS ON EXPOSURE

1.1 Information on Manufacture, Import/Export and Uses

Formamide has been registered with a total volume of 10000-50000 t/y. No information could be identified on current annual EU import/export volumes. Formamide is used for the manufacture of pharmaceuticals, as intermediate, solvent, and laboratory chemical by professional workers and by workers in industrial settings.

Formamide can be used in the agrochemical and pharmaceutical industries, in the production of vitamins and pyrimidines, in hydrogen cyanide production, as an intermediate for paper finishing and as a solvent for example in the production of synthetic leather and inks. Formamide is a building block used to make triazoles as starting materials for crop protection products (BASF 2011).

1.2 Information on Occupational Exposure

No current data on worker exposure levels have been found in the publicly available literature and no worker exposure assessment has been provided in the registration dossiers due to low tonnage band or a registration as intermediate.

The occupational exposure limit (OEL) for formamide in Switzerland is 18 mg/m^3 (SUVA, 2012) and France established an 8 h-OEL of 30 mg/m^3 (ANSES, 2011). Sweden has a binding 8 h-OEL (established 1993) for formamide of 10 ppm (20 mg/m^3) with a short term limit value (15 min) of 15 ppm (30 mg/m^3) and a “skin notation”, so possible dermal exposure of formamide may have high impact on the risk (AFS, 2005). For the United Kingdom a Workplace Exposure Limit (WEL) of 20 ppm (37 mg/m^3) is reported (Gestis, 2012). The following table gives an overview of the current OELs in Europe.

The use as an intermediate does not give cause for concern if strictly controlled conditions are observed. According to the registration dossiers, formamide is also used as a laboratory reagent, solvent and in the production of other chemicals. In the use as laboratory chemical, in formulation, transfer and maintenance operations at least limited exposure is likely to occur, however no exposure levels can be given at this point due to the lack of data. There is currently no evidence that would suggest that worker exposure levels to formamide present an unacceptable risk.

***Table** 8: European Limit Values of Formamide (Gestis, 2012)*

	Limit Value (8 hours)		**Limit Value (Short Term)**	
	ppm	**mg/m^3**	**ppm**	**mg/m^3**
Austria	9	16	18	32
Belgium	10	18		
Denmark	10	18	20	36
France	20	30		
Poland		23		
Spain*	10	19		
Sweden	10	20	15	30
Switzerland	10	18		
United Kingdom	20	37	30	56

* Skin annotation

1.3 Information on Consumer Uses and Consumer Exposure

Although formamide is not registered for consumer use it was measured in toys like wooden toys (Danish EPA, 2005) and foam puzzle mats as well as in fitness and exercise mats which are made of ethylene vinyl acetate (EVA). The results obtained by the Belgian authorities did not give clarification on the formamide concentrations present in the puzzle mats, it was only noted that they were above 150 ppm. The Belgian report has provided values for formamide emissions from puzzle mats which ranged from 1.7 to 8590 µg/m^3 (EC 2011). A comprehensive report on the uses of formamide in consumer goods and health risks related to formamide in children's foam puzzle mats was published in July 2011 by ANSES (2011).

The report states, that it was not possible to characterise the origin for its presence in foam puzzle mats. It is assumed that formamide is associated with a blowing agent used in the creation of foam and other consumer products, particularly those produced from EVA foam, that contain formamide, too. The TÜV Rheinland LGA Beteiligungs GmbH and the INVITRO-CONNECT GmbH indicate clearly the blowing agent as source of formamide (LGA 2009, Invitro 2012). During processing of foam formamide is formed as a by-product at higher temperatures. Especially tosylsemicarbazide and azodicarbonamide are responsible for the presence of formamide in EVA-consumer products (BfR personal communication, Invitro 2012).

The ANSES-report summarises the results of concentration and emission of the Belgian (analysis of 36), Danish (analysis of 7), and Swiss (analysis of 13 puzzle mats) studies. In most of the toys formamide was detected.

The content of formamide in 32 puzzle mats and 8 other foam toys was measured on behalf of ANSES and the concentrations vary between 31 and 1266 mg/kg. Five puzzle mats contain more than 1000 mg/kg, respectively more than 0.1 % formamide. Nearly all toys are coming from Asia. Furthermore the emission of three puzzle mats was detected over time up to 28 days. The air concentrations amount to 124-189 µg/m^3 from beginning up to 20-31 µg/m^3 after 28 days. In

comparison the Danish study reported values in the range of 1.5-305 µg/m^3, the Belgian study values in the range of 1.7-8590 µg/m^3 (see above). Time dependant migration measurements were carried out with three samples in artificial saliva: migration for 30 minutes on one day and for 60 minutes on seven days. At the beginning no significant difference between 30 and 60 minutes (approximately 60 µg/kg) can be observed. Continuous detection shows a clear decrease of migration during the first three days which was stabilised afterwards (approximately 5 µg/kg).

Exposure could occur via inhalation, dermal contact and orally due to sucking and/or chewing on toys which was observed as a special behaviour pattern by little children. Probabilistic short-term and long-term exposure estimates for all exposure routes were carried out for little children in the age of 0-1, 1-2 and 2-3 years and for pregnant women (for detailed information refer to ANSES report).

The ANSES-report concludes, that the exposure to formamide in puzzle mats is considered to be less probable. However, formamide which is classified as toxic to reproduction, Repr. 1B, was found in consumer products above 0.1 %. Other sources can be assumed, with less information available.

The new Toy Safety Directive 2009/48 introduces, as from July 2013, a general restriction on CMR substances in toys to their generic or specific concentration limits as laid down in EU regulation 1272/2008, but fitness and exercise mats have also been proven to contain formamide in partly high concentrations being emitted to the air when in use (LGA 2009). Observed contents of formamide are between 500 and several thousand mg/kg. As formamide is a comparably volatile substance exposure of consumers being in contact with the material can not be excluded (Invitro 2012).

Furthermore, formamide is used as a solvent and plasticizer in consumer products. It can be an ingredient as softener for paper, animal glues (which is mainly used for gluing wood), water soluble glues and wood stains (HSDB 2012) which may explain the positive results of migration measurements of the Danish EPA (2005). No information about the formamide concentrations in the mixtures is available. Ma et al. (2004) reported that a combination of urea and formamide might be a better plasticizer for thermoplastic starch. The SPIN database (2011) indicates a probable exposure of “one or several uses” due to their recorded use categories cleaning/washing agents, construction materials, food/feedstuff flavourings and nutrients and solvents. The Swedish total quantities in mixtures are between 0.5 to 1.5 tpa (The Swedish Products register, export included, 2004-2009). There were 8 products on the Swedish market 2009 (SE, personal communication). The Use Index in SPIN indicates highest potential exposure in Danish mixtures (mainly waste water and consumers, 2009).

In conclusion, due to occurrence of formamide in consumer products and indications of exposure from some uses, consumer exposure from these as well as unknown sources might be possible.

2 CURRENT KNOWLEDGE ON ALTERNATIVES

For the main applications of formamide alternatives are currently not known. In chemical synthesis established processes are in use and for substitution research and development would be necessary. For the application as solvent formamide might be replaced by other solvents like dipropylene glycol (CAS No. 25265-71-8) as both have similar physicochemical properties (CATSUB 2003). Potential alternatives as *N*,*N*-dimethylformamide (CAS No. 68-12-2), *N*-methylformamide (CAS No. 123-39-7) or ethylene glycol ethers are not considered to be adequate substitutes due their similar toxicity to reproduction (ECHA 2011). The origin of formamide in consumer articles must be clarified, especially by investigating the hypotheses that it is used either as plasticiser or as a

substance associated with a blowing agent. If the blowing agent is responsible for formamide other processing should be taken into account.

3 RISK-RELATED INFORMATION

No Chemical Safety Report has been provided for formamide because it is not required for the registration. As formamide was measured in consumer products and probable exposure is indicated, consumers might be at risk.

REFERENCES

References to Part I

REACH Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC.
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=oj:l:2006:396:0001:0849:en:pdf

EU 2008: Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:353:0001:1355:en:PDF

References to Part II

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ANSES 2011: Opinion of the French Agency for Food, Environmental and Occupational Health & Safety on the uses of formamide in consumer goods and health risks related to formamide in children's foam puzzle mats (Formamide. Usages dans les produits de consommation et évaluation des risques sanitaires liés aux jouets en mousse « tapis puzzle » Avis de l'Anses Rapport d'expertise collective) http://www.anses.fr/Documents/CHIM2010sa0302Ra-2EN.pdf

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CATSUB 2003: http://www.catsub.eu/sog.aspx?sogeord=formamid

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http://echa.europa.eu/doc/consultations/svhc/svhc_axvrep_austria_belgium_poland_cmr_diglyme_20110829.pdf

Gestis 2012:
http://limitvalue.ifa.dguv.de/WebForm_ueliste.aspx

HSDB 2012: Hazardous Substances Data Bank:
http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

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