

Justification Document for the Selection of a CoRAP Substance

Substance Name (public name): N-methylaniline

EC Number: 202-870-9

CAS Number: 100-61-8

Authority: Bureau for Chemical Substances,
Poland

Date: 19/03/2019

Cover Note

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

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1 IDENTITY OF THE SUBSTANCE

1.1 Other identifiers of the substance

Table: Other Substance identifiers

EC name (public):	N-methylaniline
IUPAC name (public):	Benzenamine, N-methyl- N-Methylaniline N-methyl-N-phenylamine N-methylaniline
Index number in Annex VI of the CLP Regulation:	612-015-00-5
Molecular formula:	C ₇ H ₉ N
Molecular weight or molecular weight range:	107.15
Synonyms:	(Methylamino)benzene Benzenamine, N-methyl- methylaniline-n Methylphenylamine MONOMETHYLANILINE

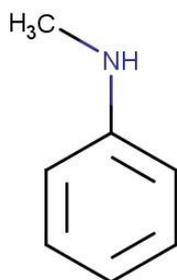
Type of substance

Mono-constituent

Multi-constituent

UVCB

Structural formula:



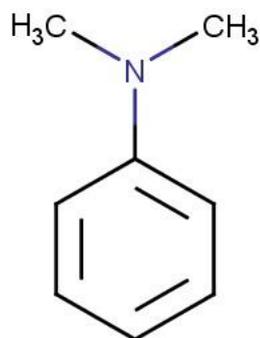
1.2 Similar substances/grouping possibilities

- **N,N-dimethylaniline**

EC: 204-493-5

CAS: 121-69-7

Mol. formula: C₈H₁₁N

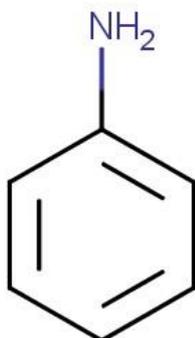


- **Aniline**

EC no.: 200-539-3

CAS no.: 62-53-3

Mol. formula: C₆H₇N



2 OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Table: Completed or ongoing processes

RMOA	<input type="checkbox"/> Risk Management Option Analysis (RMOA)	
REACH Processes	Evaluation	<input type="checkbox"/> Compliance check
		<input checked="" type="checkbox"/> Testing proposal
		<input type="checkbox"/> CoRAP and Substance Evaluation
	Authorisation	<input type="checkbox"/> Candidate List
		<input type="checkbox"/> Annex XIV
Restriction	<input type="checkbox"/> Annex XVII ¹	
CLH	<input type="checkbox"/> Annex VI (CLP) (see section 3.1)	
Processes under other EU legislation	<input type="checkbox"/> Plant Protection Products Regulation Regulation (EC) No 1107/2009	
	<input type="checkbox"/> Biocidal Product Regulation Regulation (EU) 528/2012 and amendments	
Previous legislation	<input type="checkbox"/> Dangerous substances Directive 67/548/EEC (NONS)	
	<input type="checkbox"/> Existing Substances Regulation 793/93/EEC (RAR/RRS)	
(UNEP) Stockholm convention (POPs Protocol)	<input type="checkbox"/> Assessment	
	<input type="checkbox"/> In relevant Annex	
Other processes/ EU legislation	<input type="checkbox"/> Other (provide further details below)	
Further details		

¹ Please specify the relevant entry.

3 HAZARD INFORMATION (INCLUDING CLASSIFICATION)

3.1 Classification

3.1.1 Harmonised Classification in Annex VI of the CLP

Index number: 612-015-00-5

- Acute Tox. 3 *, H301
- Acute Tox. 3 *, H311
- Acute Tox. 3 *, H331
- STOT RE 2 *, H373
- Aquatic Acute 1, H400
- Aquatic Chronic 1, H410

3.1.2 Self classification

The following hazard classes are in addition notified among the aggregated self classifications in the C&L Inventory:

- Acute Tox. 3, H301
- Acute Tox. 3, H311
- Acute Tox. 3, H331
- Skin Irrit. 2, H316
- Eye Irrit. 2, H319, H320
- Muta. 2, H341
- Carc. 2, H351
- STOT RE 2, H373 (affected organs: target: spleen, liver and bone marrow; route of exposure: oral and Inhalation)
- Aquatic Acute 1, H400
- Aquatic Chronic 1, H410

4 INFORMATION ON (AGGREGATED) TONNAGE AND USES²

4.1 Tonnage and registration status

Table: Tonnage and registration status

From ECHA dissemination site *		
<input checked="" type="checkbox"/> Full registration(s) (Art. 10)	<input type="checkbox"/> Intermediate registration(s) (Art. 17 and/or 18)	
Tonnage band (as per dissemination site)		
<input type="checkbox"/> 1 - 10 tpa	<input type="checkbox"/> 10 - 100 tpa	<input checked="" type="checkbox"/> 100 - 1000 tpa
<input type="checkbox"/> 1000 - 10,000 tpa	<input type="checkbox"/> 10,000 - 100,000 tpa	<input type="checkbox"/> 100,000 - 1,000,000 tpa
<input type="checkbox"/> 1,000,000 - 10,000,000 tpa	<input type="checkbox"/> 10,000,000 - 100,000,000 tpa	<input type="checkbox"/> > 100,000,000 tpa
<input type="checkbox"/> <1 >+ tpa (e.g. 10+ ; 100+ ; 10,000+ tpa)		<input type="checkbox"/> Confidential
This substance has 7 active registrations under REACH, 2 Joint Submission(s) and 2 Individual Submission(s).		

*the total tonnage band has been calculated by excluding the intermediate uses, for details see the Manual for Dissemination and Confidentiality under REACH Regulation (section 2.6.11): https://echa.europa.eu/documents/10162/22308542/manual_dissemination_en.pdf/7e0b87c2-2681-4380-8389-cd655569d9f0

4.2 Overview of uses

This substance is used by consumers, by professional workers (widespread uses), in formulation or re-packing, at industrial sites and in manufacturing.

Table: Uses

Part 1:

<input checked="" type="checkbox"/> Manufacture	<input checked="" type="checkbox"/> Formulation	<input checked="" type="checkbox"/> Industrial use	<input checked="" type="checkbox"/> Professional use	<input checked="" type="checkbox"/> Consumer use	<input type="checkbox"/> Article service life	<input checked="" type="checkbox"/> Closed system
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Part 2:

	Use(s)
Uses as intermediate	Manufacture of bulk, large scale chemicals (including petroleum products in an industrial process)
Formulation	Formulation of mixtures (including the application as additive in fuel)
Uses at industrial sites	Additive in fuels. Manufacturing of another substance (use of intermediates) .
Uses by professional workers	Cooling liquids in refrigerators, oil-based electric heaters, hydraulic liquids in automotive suspension, lubricants in motor oil and break fluids, fuels.
Consumer Uses	Fuels, cooling liquids in refrigerators, oil-based electric heaters, hydraulic liquids in automotive suspension, lubricants in motor oil and break fluids.
Article service life	-

² The dissemination site was accessed August 2018.

5. JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

5.1. Legal basis for the proposal

- Article 44(2) (refined prioritisation criteria for substance evaluation)
- Article 45(5) (Member State priority)

5.2. Selection criteria met (why the substance qualifies for being in CoRAP)

- Fulfils criteria as CMR/ Suspected CMR
- Fulfils criteria as Sensitiser/ Suspected sensitiser
- Fulfils criteria as potential endocrine disrupter
- Fulfils criteria as PBT/vPvB / Suspected PBT/vPvB
- Fulfils criteria high (aggregated) tonnage (*tpa* > 1000)
- Fulfils exposure criteria
- Fulfils MS's (national) priorities

5.3. Initial grounds for concern to be clarified under Substance Evaluation

Hazard based concerns		
CMR <input type="checkbox"/> C <input type="checkbox"/> M <input type="checkbox"/> R	Suspected CMR ¹ <input checked="" type="checkbox"/> C <input checked="" type="checkbox"/> M <input type="checkbox"/> R	<input type="checkbox"/> Potential endocrine disruptor
<input type="checkbox"/> Sensitiser	<input type="checkbox"/> Suspected Sensitiser ³	
<input type="checkbox"/> PBT/vPvB	<input type="checkbox"/> Suspected PBT/vPvB ¹	<input type="checkbox"/> Other (please specify below)
Exposure/risk based concerns		
<input checked="" type="checkbox"/> Wide dispersive use	<input type="checkbox"/> Consumer use	<input type="checkbox"/> Exposure of sensitive populations
<input type="checkbox"/> Exposure of environment	<input checked="" type="checkbox"/> Exposure of workers	<input checked="" type="checkbox"/> Cumulative exposure
<input checked="" type="checkbox"/> High RCR	<input type="checkbox"/> High (aggregated) tonnage	<input type="checkbox"/> Other (please specify below)
Mutagenicity Data from the registration dossier: All studies on in-vitro gene mutation in bacteria with N-Methylaniline show negative results. A comet assay and a chromosomal aberration test with mammalian cells are also available, but these assays give a negative and positive result, respectively. However, the publication of the comet assay refers to earlier publications, which indicate N-methylaniline as mutagenic and carcinogenic. In addition, aniline and N, N-		

dimethylaniline, present as impurities above 1%, are both classified as carcinogenic (Carc. 2). Hence, N-methylaniline is considered to be potentially genotoxic.

Various Ames tests on multiple strains show that N-Methylaniline does not induce genetic toxicity in bacterial in-vitro tests. However two different mammalian in-vitro tests show contra-dictionary results. The doubts described above need to be clarified. According to the CLP regulation 1272/2008, classification of N-methylaniline (pure) does not include mutagenicity. However, N-methylaniline is suspected as being genotoxic based on the reported positive result in a chromosomal aberration test with mamalian cells.

Other available data:

A mutagenic effect was observed in an Ames test with Salmonella typhimurium strain TA98 and, to a lesser extent, with TA100 in the presence of metabolic activation (Recommendation from the Scientific Committee on Occupational Exposure Limits for N-Methylaniline, SCOEL/SUM/178, 2012).

N-Methylaniline induced chromosomal aberrations in cultured Chinese hamster lung (CHL/IU) cells after 6 hours of exposure with metabolic activation or 24 hours of exposure without metabolic activation. Aniline did not induce chromosomal aberrations in a different strain of Chinese hamster lung (Don) cells. In other studies, aniline showed positive genotoxic responses such as increasing the frequency of sister chromatid exchanges in human and hamster cells, increasing DNA damage in cultured mouse lymphoma cells, and transforming mouse Balb/3T3 cells. In in vivo studies, aniline increased the frequencies of micronucleus formation in bone marrow of rats and mice, and sister chromatid exchanges in bone marrow of mice, but not rats (Provisional Peer Reviewed Toxicity Values for N-Methylaniline, EPA/690/R-05/017F Final 8-03-2005).

Carcinogenicity

Data from the registration dossier:

According to the CLP regulation 1272/2008, classification of N-methylaniline (pure) does not include carcinogenicity. However, according to the same regulation, the test substance presented in this dossier should be classified as potential carcinogen based on its impurities (as stated on the ECHA dissemination site). In addition, this classification is further justified by the high similarity between N-methylaniline and these two impurities, aniline and N,N-dimethylaniline, together with the reported positive result in a chromosomal aberration test with mamalian cells.

Aniline and N,N-dimethylaniline, although negative in Salmonella tests, were clastogenic in cultured mammalian cells (Abdo, 1989). The clastogenic response with N,N-dimethylaniline increases in the presence of S9 and is observed at lower doses than with aniline. These observations are consistent with the hypothesis that a DNA-reactive arene oxide intermediate may be involved in the clastogenic activity of N,N-dimethylaniline. Further evaluation of existing data is needed.

Exposure of workers

³ CMR/Sensitiser: known carcinogenic and/or mutagenic and/or reprotoxic properties/known sensitising properties (according to CLP harmonized or registrant self-classification or CLP Inventory)

Suspected CMR/Suspected sensitiser: suspected carcinogenic and/or mutagenic and/or reprotoxic properties/suspected sensitising properties (not classified according to CLP harmonized or registrant self-classification)

Suspected PBT: Potentially Persistent, Bioaccumulative and Toxic

The combinations of exposure scenarios results in cumulative exposure of humans consist of the exposure as worker via inhalation and dermalexposure routes, exposure via the environment and exposure as a consumer. The values for the summed RCR including contribution of exposure via the environment are often above 1, indicating a significant risk. It is clear that the exposure of workers at the industrial sites is the main contributing factor.

Potential concerns for mutagenicity and carcinogenicity exist in all workplace scenarios, as the main impurities are identified as a non-threshold carcinogens.

Additional information

Two testing proposal on vertebrate animals were submitted by registrant:

- Repeated dose toxicity by dermal route (Sub-chronic toxicity (90 day): dermal, OECD 408) and

- Toxicity to reproduction (extended one-generation reproductive toxicity study OECD 443).

ECHA has held a third-party consultation (lasted on 23/04/2018-23/04/2018), to call for available information on above testing proposals.

5.4. Preliminary indication of information that may need to be requested to clarify the concern

<input checked="" type="checkbox"/> Information on toxicological properties	<input type="checkbox"/> Information on physico-chemical properties
<input type="checkbox"/> Information on fate and behaviour	<input checked="" type="checkbox"/> Information on exposure
<input type="checkbox"/> Information on ecotoxicological properties	<input checked="" type="checkbox"/> Information on uses
<input type="checkbox"/> Information ED potential	<input type="checkbox"/> Other (provide further details below)
<i>Please provide further details/explanation. The information here should be consistent with concerns given in 5.3.</i>	

5.5. Potential follow-up and link to risk management

<input type="checkbox"/> Harmonised C&L	<input type="checkbox"/> Restriction	<input type="checkbox"/> Authorisation	<input checked="" type="checkbox"/> Other (provide further details)
Depends on the substance evaluation results.			