

**6 February 2014**

## **Background document for N,N-Dimethylformamide (DMF)**

### **Document developed in the context of ECHA's fifth Recommendation for the inclusion of substances in Annex XIV**

*Information comprising confidential comments submitted during public consultation, or relating to content of Registration dossiers which is of such nature that it may potentially harm the commercial interest of companies if it was disclosed, is provided in a confidential annex to this document.*

## **1. Identity of the substance**

Chemical name:	N,N-Dimethylformamide (DMF)
EC Number:	200-679-5
CAS Number:	68-12-2
IUPAC Name:	N,N-Dimethylformamide

## **2. Background information**

### **2.1. Intrinsic properties**

N,N-Dimethylformamide (DMF) was identified as a Substance of Very High Concern (SVHC) according to Article 57 (c) as it is classified in Annex VI, part 3, Table 3.1 (the list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008 as toxic for reproduction, Repr. 1B, H360D ("May damage the unborn child")<sup>1</sup>, and was therefore included in the Candidate List for authorisation on 19 December 2012, following ECHA's decision ED/169/2012.

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<sup>1</sup> This corresponds to a classification as toxic for reproduction category 2 (R61: May cause harm to the unborn child) 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) N° 1272/2008

## 2.2. Imports, exports, manufacture and uses

### 2.2.1. Volume(s), imports/exports

The amount of DMF manufactured and/or imported into the EU is, according to registration data, in the range of 10,000 – 100,000 t/y. No information on exports is provided.

Most of the amount in the EU seems to be used in applications in the scope of authorisation, except limited uses such as intermediate in synthesis and uses in scientific research and development.

### 2.2.2. Manufacture and uses

#### 2.2.2.1. Manufacture and releases from manufacture

The manufacturing process described in registration dossiers comprises confidential information.

According to open literature, dimethylformamide is produced either via catalysed reaction of dimethylamine and carbon monoxide in methanol or via the reaction of methyl formate with dimethylamine. It may also be prepared on a laboratory scale by reacting dimethylamine with formic acid (Annex XV report, 2012).

Within the EU, DMF is manufactured in high integrity contained systems where little potential for exposure exists (PROC 1) (ECHA, 2013).

#### 2.2.2.2. Uses and releases from uses

### Uses

According to registration information complemented by information from industry consultation performed in 2011 (Annex XV report, 2012), as well as from public consultations in 2012 and 2013 (RCOM, 2012; RCOM 2014), the substance is used mainly:

- as solvent<sup>2</sup> in synthesis of chemicals, e.g. of Active Pharmaceutical ingredients (API) and crop protection ingredients (~ 50%),
- as solvent in the production of polyurethane coated textiles such as artificial leather, rain and protection wear, footwear, medical mattress covers, surgical incise films etc. (~25%)
- as solvent in the production of synthetic fibres (~10%),
- in other applications such as in the electronic industry, in formulation of mixtures, as gas stabiliser in acetylene cylinders, in the production of medical devices (e.g. In Vitro Diagnostic Devices (IVD)), as cleaning solvent, as intermediate, as laboratory chemical etc.

Tonnages used as intermediate in synthesis and in scientific research and development appear to be limited (RCOM, 2012).

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<sup>2</sup> Use as solvent e.g. in purification, crystallisation, extraction operations or as reagent, catalyst or cross-linking agent.

Types of mixtures mentioned in the Annex XV report (2012) (here only considered information from 2010 onwards) and in the RCOM (2012) include paints, coatings, adhesives, mastics, sealants, binding agents, finishes and compounds. The use of DMF at industrial sites in solvent-based corrosion inhibitor product(s) has been confirmed in recent registration dossier(s) (ECHA, 2013). Furthermore, the substance may be used by aerospace industry (at least in the USA; in EU not confirmed) in strippers and in epoxy inks (RCOM, 2012)<sup>3</sup>. Use of such mixtures is of potential relevance for industrial workers and possibly for professional workers. However, no use of DMF by professionals has been registered except as laboratory chemical, therefore these uses by professionals should not occur in the EU and are not considered in the context of this recommendation.

The majority of the uses take place at industrial settings.

The supply of DMF to general public as a substance or in mixtures above the classification threshold is banned in accordance with entry 30 of Annex XVII. Moreover no subsequent "article service-life" is declared for the intended industrial uses: DMF is not supposed to be a component of the final articles resulting from processes where it is used as solvent (e.g. artificial leather articles), although some residues may remain (Annex XV report, 2012). According to the available information from public consultation (RCOM, 2012) there is some evidence that in many cases the concentration in articles produced within the EU is very low (below 0.2%). Some concerns exist with regard to imported articles (RCOM, 2012; RCOM, 2014). So far<sup>4</sup> ECHA has not received any substance in articles notification for DMF according to Art. 7(2) of REACH via REACH-IT. The deadline for notifying DMF in articles to ECHA was mid-June 2013.

## Releases

Registration data indicate that the substance is used at industrial sites in closed systems with no or only occasional opportunity for exposure (PROC 1, PROC 2, PROC 3) but also in systems where potential for significant exposure arises (e.g. PROC 4, PROC 5, PROC 8a). According to these use descriptors and taking into account additional information provided in the registration dossiers and during the public consultations potential for exposure is associated with various steps which could be generally described as control, transfer/loading, mixing (potentially in open or semi-open systems), maintenance and cleaning operations (ECHA, 2013; RCOM, 2012; RCOM, 2014). The frequency of such operations is apparently sector and company specific but, taken into account also the diversity of sectors/uses and the high number of sites at which DMF is used, it appears not to be justified to regard the frequency and therefore the exposure as negligible.

It is noted that DMF is a water soluble organic solvent that is readily absorbed via all exposure routes. In industrial settings, the primary routes of exposure to DMF are skin contact and inhalation.

Annex XV report (2012) describes studies performed in the synthetic fibres industry indicating worker exposure. These studies refer to 1998 and 2005.

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<sup>3</sup> Multiple uses of DMF, mainly as solvent at industrial sites, have been confirmed by the Aeronautics, Space, Security and Defence sector (RCOM, 2014) without further specification.

<sup>4</sup> Last check: 25 October 2013

Comments (including some measurement data) provided by individual companies and industrial associations from the chemical, pharmaceutical, agrochemical, textiles and gas sectors during public consultations (RCOM, 2012; RCOM, 2014) include information to describe measures implemented in order to control workplace exposure.

No substantial information is available with respect to process descriptions / operational conditions or potential for exposure for further confirmed uses of DMF (e.g. use in electronic industry, formulation, use in mixtures).

Potential for exposure can not be excluded for confirmed use of DMF in mixtures such as sealants and finishes and, to the extent they occur in the EU market also in paints, adhesives, mastics and strippers

### 2.2.2.3. Geographical distribution and conclusions in terms of (organisation and communication in) supply chain

Based on the available information, it appears that the supply chains of DMF contain a medium number of EU manufacturers and importers, and a high number of industrial end-users spread across several industrial sectors. The number of formulators is unknown.

Comments received during public consultations (RCOM, 2012; RCOM, 2014) reflect a high number of companies (among which many SMEs) using DMF in the artificial leather and technical coating sector, in the pharmaceutical and biopharmaceutical sectors, in the in-vitro diagnostic (IVD) medical device sector and in various industrial sectors as part of acetylene cylinders. Moreover, the uses of DMF in different mixtures such as sealants, coatings and finishes serve to further confirm that the substance is used throughout the EU at hundreds of use sites.

## 2.3. Availability of information on alternatives<sup>5</sup>

DMF is one of a class of solvents designated as polar aprotics. According to the information received during the public consultation from industry stakeholders of the chemical, pharmaceutical and textiles sectors<sup>6</sup> (RCOM, 2012), as well as from the gas sector association (RCOM, 2014), research for alternative solvents and/or technologies has not provided conclusive results. Potential alternatives identified so far for DMF in some sectors mentioned above are other similar polar aprotic solvents such as N-methylpyrrolidone (NMP), 1-ethylpyrrolidin-2-one (NEP), N,N-dimethylacetamide (DMAC), N-methylformamide, N-methylacetamide, formamide. These solvents are to some extent interchangeable. However they all have essentially the same intrinsic properties with regards to reproductive toxicity, some of these substances being already on the Candidate List.

Dimethylsulfoxide (DMSO) could be seen as a safer alternative but is not considered as a viable substitute in many instances: DMSO has a solvating capability comparable to DMF; nevertheless it is affected by important limits such as corrosivity and a melting point at 18°C. Possible substitution of DMF by DMSO

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<sup>5</sup> Please note that this information was not used for prioritisation.

<sup>6</sup> These sectors count for ~85% of the tonnage of DMF used within EU

would require a radical modification in all the productive chains (RCOM, 2012). According to the DMSO producers association although corrosivity and high melting point are issues to be taken into consideration when designing a DMSO based chemical processing plant, DMSO is already an established industrial solvent in the chemical, pharmaceutical and textile industries (RCOM, 2014).

All other readily available solvents like toluene, tetrahydrofuran (THF), Methyl ethyl ketone (MEK), Methyl Isobutyl Ketone (MIBK), ethylacetate, hexane, heptane, isopropanol have in most applications too limited dissolving power.

In the textile sector, alternative technologies have been considered for processing DMF-free polyurethane (e.g. water-based PU coatings) but the performance of such systems has not been able to match the demanding technical specification required (RCOM, 2012).

No substantial information on alternatives for other confirmed uses has been made available, except for the use of DMF in sealants in the aerospace industry. Alternative solutions may soon be available for this use (RCOM, 2012).

#### **2.4. Existing specific Community legislation relevant for possible exemption**

There seems to be no specific Community legislation in force that would allow consideration of exemption(s) of (categories of) uses from the authorisation requirement on the basis of Article 58(2) of the REACH Regulation.

#### **2.5. Any other relevant information (e.g. for priority setting)**

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### 3. Conclusions and justification

#### 3.1. Prioritisation

The substance is used in very high volumes in the scope of authorisation. The substance is expected to be used at a high number of sites. For some operations significant potential for workers exposure cannot be excluded.

*Verbal-argumentative approach*

On the basis of the prioritisation criteria, N,N-dimethylformamide (DMF) gets high priority for inclusion in Annex XIV.

*Scoring approach*

Score			Total Score (= IP + V + WDU)
Inherent properties (IP)	Volume (V)	Uses - wide dispersiveness (WDU)	
Score: 0 Toxic for reproduction 1B.	Score: 9 (Very high volume in the scope of authorisation)	Overall score: $3 * 3 = 9$ Site-#: 3 (Uses in industrial settings at a high number of sites)  Release: 3 (Significant potential for worker exposure from uses within the scope of authorisation)	18

*Conclusion, taking regulatory effectiveness considerations into account*

On the basis of the prioritisation criteria, N,N-dimethylformamide (DMF) gets high priority.

Therefore, it is proposed to prioritise N,N-dimethylformamide (DMF) for inclusion in Annex XIV.

## 4. References

Annex XV report (2012): N,N-dimethylformamide. Proposal for identification of a substance as a CMR Cat 1A or 1B, PBT, vPvB or a substance of an equivalent level of concern. N,N-dimethylformamide. Submitted by Sweden, August 2012.

<http://www.echa.europa.eu/documents/10162/5d7b909d-ef93-4fb3-8ca0-60e4e799e0e6>

ECHA (2013): N,N-dimethylformamide. ECHA's dissemination website on registered substances.

[http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances?p\\_p\\_id=registeredsubstances\\_WAR\\_regsubsportlet&registeredsubstances\\_WAR\\_regsubsportlet\\_name-sc=&registeredsubstances\\_WAR\\_regsubsportlet\\_ec-number-sc=200-679-5&registeredsubstances\\_WAR\\_regsubsportlet\\_cas-number-sc=&registeredsubstances\\_WAR\\_regsubsportlet\\_sc=true&registeredsubstances\\_WAR\\_regsubsportlet\\_do-search=](http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances?p_p_id=registeredsubstances_WAR_regsubsportlet&registeredsubstances_WAR_regsubsportlet_name-sc=&registeredsubstances_WAR_regsubsportlet_ec-number-sc=200-679-5&registeredsubstances_WAR_regsubsportlet_cas-number-sc=&registeredsubstances_WAR_regsubsportlet_sc=true&registeredsubstances_WAR_regsubsportlet_do-search=)

RCOM (2012): "Responses to comments" document compiled by Sweden from the commenting period 03/09/2012 – 18/10/2012 on the proposal to identify the substance N,N-Dimethylformamide (DMF) as a Substance of Very High Concern.

<http://echa.europa.eu/candidate-list-table/-/substance/2443/search/+/term>

RCOM (2014): "Responses to comments" document for DMF. Document compiling comments and respective answers from commenting period 24/06/2013 – 23/09/2013 on ECHA's 5th draft recommendation of priority substances for inclusion in the list of substances subject to authorisation (Annex XIV).

[http://echa.europa.eu/documents/10162/13640/axiv\\_5th\\_recommendation\\_dmf\\_rcom\\_en.pdf](http://echa.europa.eu/documents/10162/13640/axiv_5th_recommendation_dmf_rcom_en.pdf)