

24 June 2013

Draft 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")¹, and was therefore included in the Candidate List for authorisation on 19 December 2012, following ECHA's decision ED/169/2012.

¹ 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 EU, DMF is manufactured within 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 consultations performed in 2011 and 2012 (Annex XV report, 2012; RCOM, 2012), the substance is used mainly:

- as solvent² in synthesis of chemicals (e.g. Active Pharmaceutical ingredients (API), 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, 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).

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

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

compounds. The use of DMF at industrial sites in solvent-based corrosion inhibitor product(s) has been confirmed in recent registration dossier(s) (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). 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.

The majority of the uses take place at industrial settings.

There is no registered use for consumers. Moreover no subsequent "service-life" is declared for the intended 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 EU is below 0.2%. Some concerns exist with regard to imported articles (RCOM, 2012). So far 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 is mid-June 2013.

Releases

DMF is a water soluble organic solvent that is readily absorbed via all exposure routes. DMF has a relatively low vapour pressure (0.377kPa at 20°C). In industrial settings, the primary routes of exposure to DMF are skin contact and inhalation.

Registration data indicates 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 dossier and during the public consultation for SVHC identification, the most significant potential for exposure seems to be associated with transfer (e.g. manual discharge), mixing (potentially in open or semi-open systems) and industrial cleaning operations (ECHA, 2013; RCOM, 2012).

Annex XV report describes studies performed in the synthetic fibres industry indicating worker exposure. However, these studies are for 1998 and 2005 and not repeated here.

Comments and measurement data provided by individual companies and industrial associations from the chemical, pharmaceutical, and textiles sectors during public consultation (RCOM, 2012) include information to demonstrate that management measures are implemented in order to control workplace exposure, and occupational controls are carried out. Such information could be used by applicants at a later stage of the process to demonstrate adequate control of / estimate residual risks.

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).

According to registration dossiers (ECHA, 2013), professional workers may only be exposed while using DMF as laboratory chemical (no other use by professional

workers has been registered). However, to the extent uses of mixtures such as sealants, strippers, paints, coatings, mastics or glue containing DMF take place in the EU, potential for significant exposure cannot be excluded.

Conclusion

The uses as described in the registration dossiers entail potential for significant workers exposure at some stages of the industrial processes. According to comments received from industry stakeholders during public consultation, risk management measures are applied in many instances, however evidence is lacking that such risk management measures are consistently applied across all uses and at all sites at which DMF is used. Therefore, potential for significant exposure cannot be excluded.

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 consultation (RCOM, 2012) 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, and in the in-vitro diagnostic (IVD) medical device industry. Moreover, the uses of DMF in mixtures such as coatings serve to confirm that the substance is used throughout the EU at hundreds of use sites.

2.3. Availability of information on alternatives³

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 sectors⁴ (RCOM, 2012), research for alternative solvents and/or technologies has not provided conclusive results. Potential alternatives identified so far for DMF 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 carry essentially the same intrinsic properties with regards to reproductive toxicity, some of these substances being already on the Candidate List.

Dimethylsulfoxide (DMSO) could be considered 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 high melting point at 18°C. Possible substitution of DMF by DMSO would require a radical modification in all the productive chain.

³ Please note that this information was not used for prioritisation.

⁴ These sectors count for ~85% of the tonnage of DMF used within EU

All other readily available solvents like toluene, tetrahydrofuran (THF), MEK, MIBK, ethylacetate, hexane, heptane, isopropanol, IPA etc. have a too limited dissolving power.

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

No substantial information on alternatives for other confirmed uses has been made available, except for the use of DMF in sealant in the aerospace industry. This use appears not to be critical as alternative solutions are potentially available soon (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
Inherent properties (IP)	Volume (V)	Uses - wide dispersiveness (WDU)	(= IP + V + 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): 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®isteredsubstances_WAR_regsubsportlet_name-sc=®isteredsubstances_WAR_regsubsportlet_ec-number-sc=200-679-5®isteredsubstances_WAR_regsubsportlet_cas-number-sc=®isteredsubstances_WAR_regsubsportlet_sc=true®isteredsubstances_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>