

Dimethylformamide (CAS 68-12-2)

The following document analyzes the implications of designating dimethylformamide (CAS 68-12-2) as a Higher Hazard Substance. This chemical is on the TURA Science Advisory Board (SAB) list of more hazardous substances and has been recommended for HHS designation by the SAB.

With this designation, the reporting threshold for this chemical would be lowered from 10,000/25,000 lb/year to 1,000 lb/year for companies in TURA-covered industry sectors with ten or more employees. New companies entering the program under the lower reporting threshold would be required to file annual toxics use reports, pay annual toxics use fees, and develop a toxics use reduction plan every two years.

This policy analysis summarizes key scientific information on this chemical, estimates the number of facilities that are likely to enter the program as a result of the lower reporting threshold, notes opportunities and challenges that new filers are likely to face, and discusses the implications of this policy measure for the TURA program. Based on this analysis, the Toxics Use Reduction Institute supports the SAB's recommendation that dimethylformamide be designated as a Higher Hazard Substance.

1. State of the Science

Dimethylformamide (DMF) is an organic solvent produced in large quantities throughout the world. It is used in the chemical industry as a solvent, an intermediate & an additive. The main routes of exposure to DMF are inhalation or dermal exposure in occupational settings. DMF is rapidly absorbed via oral, inhalation and dermal routes with poor warning properties, and passes through the placenta to the developing fetus. Systemic effects primarily focus on the liver, but also include kidney, cardiac, blood, and gastrointestinal effects. DMF is a teratogen in animal studies, and has an EU harmonized classification of Repr 1B – may damage the unborn child.

2. Number of facilities affected

To develop an estimate of the number and type of companies likely to be affected by a 1,000 lb reporting threshold, the Institute consulted sources including the TURA data, facilities reporting under EPCRA Tier II requirements, and past experience with other HHS designations.

Uses of DMF reported under TURA include coated fabrics, chemical manufacturing, and chemical distribution, among others. A total of 31 facilities have reported DMF use under TURA at some point. In 2012, the most recent year for which data are available, eight companies reported the use of DMF under TURA, 3 in the coated fabrics SIC code, 1 in paints and allied products, 1 in adhesives and sealants, and 3 in chemical distribution. In addition to the types of facilities listed above, DMF is

a common laboratory solvent. As well as use as a solvent, it can also be used for organic synthesis. Most laboratory uses are not covered under TURA. For those that are (in facilities that manufacture products) there could be up to 5 new facilities.

We estimate that approximately 2-7 new filers would be brought in by the HHS designation; one of these would be a facility that already files under TURA for other chemicals, and a few would be new to TURA.

3. Opportunities for New Filers

- Practical alternatives to DMF are available for many applications, but there is also a significant need for additional research and development to identify and test safer alternatives.
- DMF use reported under TURA has increased since reporting began in 1995, while releases have decreased significantly. Use increased from 4,527,373 lb in 1995 to 7,174,590 lb in 2007, down to 5,567,168 lb in 2012. Releases have declined 88%, from 115,743 lb in 1995 to 13,856 lb in 2012 (figures not adjusted for changes in production levels).
- Uses as an Industrial Solvent: Alternatives include DMSO, among other alternative solvents.
- Pharmaceutical preparations & research labs: Potential alternatives for DMF in laboratory applications include benzotrifluoride, ethanol, 2-methyl tetrahydrofuran, diethoxymethane, and dibasic esters, depending on the chemistry.

4. Regulatory Context

- Due to its toxicity, DMF is subject to a number of regulations. At the federal level, it is reportable under TRI, and regulated as a Hazardous Air Pollutant under the Clean Air Act, among other regulations. DMF waste is not regulated under RCRA.
- Internationally, DMF is included on the candidate list of SVHC (Substances of Very High Concern) by the European Chemicals Agency (ECHA) due to its reproductive toxicity, and is in the February 2014 recommendation of substances to be subject to authorization. DMF was prioritized among the SVHC candidates for authorization due to high volume of use, wide dispersiveness of use (used at many industrial facilities) and potential for exposure.

5. Implications for the TURA program

- *General.* Designating DMF as a Higher Hazard Substance would help to fulfill the intent of the 2006 amendments to TURA, providing important guidance and incentives to Massachusetts businesses to help them move away from the most hazardous chemicals and toward safer alternatives. A focus on DMF in Massachusetts would also be consistent with efforts to address this chemical in other states and nationally.
- *Avoiding adverse substitutions.* Designating DMF as a Higher Hazard Substance in 2014 would also help avoid facilities switching from other Higher Hazard solvents such as methylene chloride to DMF.
- *Other considerations: trends among existing filers.* Use of DMF by existing TURA filers has increased over time. In this respect, DMF differs from many of the chemicals that have been designated as HHS to date.
- *Costs to businesses of reporting, planning, and fees.* Assuming 2-7 new DMF filers and assuming that three of them are completely new to TURA, the total additional cost in fees to filers (and revenue to the program) could be approximately \$7,750-19,550.



*Toxics Use Reduction Institute
Policy Analysis
Aug 12, 2014
Higher Hazard Substance Designation Recommendation:*

Dimethylformamide (CAS 68-12-2)

The following document analyzes the implications of designating dimethylformamide (CAS 68-12-2) as a Higher Hazard Substance. This chemical is on the TURA Science Advisory Board (SAB) list of more hazardous substances and has been recommended for HHS designation by the SAB.

With this designation, the reporting threshold for this chemical would be lowered from 10,000/25,000 lb/year to 1,000 lb/year for companies in TURA-covered industry sectors with ten or more employees. New companies entering the program under the lower reporting threshold would be required to file annual toxics use reports, pay annual toxics use fees, and develop a toxics use reduction plan every two years.

This policy analysis summarizes key scientific information on this chemical, estimates the number of facilities that are likely to enter the program as a result of the lower reporting threshold, notes opportunities and challenges that new filers are likely to face, and discusses the implications of this policy measure for the TURA program. Based on this analysis, the Toxics Use Reduction Institute supports the SAB's recommendation that dimethylformamide be designated as a Higher Hazard Substance.



Toxics Use Reduction Institute

Policy Analysis

Aug 12, 2014

Higher Hazard Substance Designation Recommendation:

Dimethylformamide (CAS 68-12-2)

Dimethylformamide (DMF)

1. State of the Science

Dimethylformamide (DMF) is an organic solvent produced in large quantities throughout the world. It is used in the chemical industry as a solvent, an intermediate & an additive.¹ The main routes of exposure to DMF are inhalation or dermal exposure in occupational settings. DMF is rapidly absorbed via oral, inhalation and dermal routes with poor warning properties, and passes through the placenta to the developing fetus. Systemic effects primarily focus on the liver, but also include kidney, cardiac, blood, and gastrointestinal effects. DMF is a teratogen in animal studies.²

Acute toxicity

- Liver function may be disturbed, and blood pressure changes, tachycardia and ECG abnormalities have been reported.³
- Toxic amounts of DMF may be absorbed by inhalation and through the skin.⁴
- Acute exposure to DMF causes abdominal pain, nausea, vomiting, jaundice, alcohol intolerance, and rashes.

Chronic toxicity

- Chronic exposure by inhalation can cause liver and digestive disturbances
- DMF shows reproductive and developmental toxicity in many studies⁵ and has a harmonized classification under the EU Globally Harmonized System (GHS) as a reproductive toxin, Repro 1B, H360D (May damage/Suspected of damaging fertility or the unborn child)

Role of uncertainty

DMF has been identified as a high priority chemical primarily based on its reproductive and liver effects on human health, and the ease with which it is absorbed into the body via inhalation and dermal exposure. Uncertainty does not play a significant role in the development of our recommendations for this substance.

2. Number of facilities affected

To develop an estimate of the number and type of companies likely to be affected by a 1,000 lb reporting threshold, the Institute consulted sources including the TURA data, facilities reporting under EPCRA Tier II requirements, and past experience with other HHS designations.

Uses of DMF reported under TURA include coated fabrics, chemical manufacturing, and chemical distribution, among others.

a. Historical data on sectors using Dimethylformamide in Massachusetts

A total of 31 facilities have reported DMF use under TURA at some point. These facilities have been in the following sectors:

2269	Finishing plants, nec
2295	Coated fabrics, not rubberized
2752	Commercial printing, lithographic
2821	Plastics materials and resins
2851	Paints and allied products
2865	Cyclic crudes and intermediates
2869	Industrial organic chemicals, nec
2891	Adhesives and sealants
2899	Chemical preparations, nec
3471	Plating and polishing
3569	General industrial machinery, nec
3679	Electronic components, nec
3821	Laboratory apparatus and furniture
3861	Photographic equipment and supplies
5169	Chemicals and allied products

Source: TURA Data

b. Current TURA data on DMF use in Massachusetts

In 2012, the most recent year for which data are available, eight companies reported the use of DMF under TURA.

SIC Code		No. of 2012 Filers	Type of Use
2295	coated fabrics, not rubberized	3	(1 processed, 3 otherwise used)
2851	paints and allied products	1	Processed

2891	adhesives and sealants	1	Otherwise used
5169	chemicals and allied products	3	Processed

Source: TURA Data

c. Storage & hazardous waste reporting data

Reports filed under EPCRA Tier II indicate current or recent DMF use by additional facilities. The EPCRA Tier II data show that 16 facilities reported storing DMF in 2012. DMF is not a RCRA listed hazardous waste, so there are no data available.

Storage of at least 500 lb onsite was used as a basis for estimating the number of facilities that may be using at least 1,000 lb/year of DMF. Based on the maximum amounts reported under Tier II for 2012, 10 facilities have reported at least 500 lb of DMF stored onsite and have at least 10 FTEs. Sectors represented in this data set include resin facilities, laminating facilities, chemical manufacturing and distributors, among others. Nine of these are past or current TURA filers.

In addition to the types of facilities listed above, DMF is a common laboratory solvent. As well as use as a solvent, it can also be used for organic synthesis. Most laboratory uses are not covered under TURA. For those that are (in facilities that manufacture products) there could be up to 5 new facilities.

d. Past experience with HHS designations

Experience since 2006 indicates that in general, an HHS designation brings in a number of new filers in the first couple of years of the designation, and this number falls in subsequent years as filers move to safer substitutes. Each sector is different, but this pattern may be indicative of future trends as well. For the six HHS for which data are currently available, the number of new filers in the first year the designation was effective ranged from 5 to 19.

e. Estimated number of companies that would be affected by a lower reporting threshold

We estimate that approximately 2-7 new filers would be brought in by the HHS designation; one of these would be a facility that already files under TURA for other chemicals, and a few would be new to TURA.

3. Opportunities for New Filers

In this section, we briefly review trends in DMF use among existing TURA filers, and summarize basic information on DMF alternatives in selected applications.

a. Trends in dimethylformamide use

DMF use reported under TURA has increased since reporting began in 1995, while releases have decreased significantly. Use increased from 4,527,373 lb in 1995 to 7,174,590 lb in 2007, down to 5,567,168 lb in 2012. Releases have declined 88%, from 115,743 lb in 1995 to 13,856 lb in 2012 (figures not adjusted for changes in production levels).

Massachusetts TURA DMF Use and Release Data: 1995 and 2012 (figures not adjusted for production)				
	Year		Change In lbs	% Change
	1995	2012		
DMF used (lbs)	4,527,373	5,567,168	1,039,795	+23%
DMF released (lbs)	115,743	13,856	-101,887	-88%

Source: TURA Data

b. Opportunities to reduce DMF use

i. Uses as an Industrial Solvent

DMF is used as a solvent in a variety of applications, such as resins and laminating. Alternatives to DMF can include a variety of substitute solvents. The Substitution Support Portal (Subsport), an NGO project designed to compile information on alternatives to a variety of chemicals, includes information on DMF alternatives for solvent uses. Subsport notes that dimethyl sulfoxide (DMSO) is an efficient solvent for polar or polarizable organic compounds, and also for many acids, alkalis and mineral salts. For those processes for which there is no feasible alternative, solvent recovery systems can help reduce DMF use. For resin manufacturing, the use of alternative resins may eliminate the need for DMF.

ii. Pharmaceutical preparations & Research labs

DMF is a common reaction and extraction solvent in research labs and pharmaceutical preparations, used for its polar aprotic properties. Potential alternatives for DMF in laboratory applications include benzotrifluoride, ethanol, 2-methyl tetrahydrofuran, diethoxymethane, and dibasic esters, depending on the chemistry.⁶ Of these, some are clearly safer (e.g. ethanol), while others present health and environmental concerns as well. Ethyl acetate, dimethyl sulfoxide (DMSO), and acetone are other alternative solvents with polar aprotic properties. Ethyl acetate and acetone are TURA reportable substances; both are categorized as relatively less hazardous chemicals by the Science Advisory Board, compared with other chemicals on the TURA list.

These changes may involve reformulation and processing changes. In some cases they may require FDA approval and certification/ recertification of products.

4. Regulatory context and exposure limits

Due to its toxicity, DMF is subject to a number of regulations. Selected federal regulations are shown in the table below. Note that DMF waste is not regulated under RCRA.

EPCRA	<ul style="list-style-type: none"> • Reportable under TRI⁷ • Subject to US EPA Tier II reporting requirements⁸
CAA	<ul style="list-style-type: none"> • Regulated as a Hazardous Air Pollutant (HAP) – Section 112B (68-12-2)⁹ • Clean Air Act Section 111 Standards of Performance for New Stationary Sources of Air Pollutants¹⁰
SARA	<ul style="list-style-type: none"> • Section 110 – Priority List of Hazardous Substances¹¹
CERCLA	<ul style="list-style-type: none"> • Reportable quantity: 100 lb.¹²
OSHA PEL	<ul style="list-style-type: none"> • OSHA PEL: 10 ppm, skin designation.¹³
IDLH	<ul style="list-style-type: none"> • Immediately Dangerous to Life or Health: 500 ppm¹⁴
NIOSH REL	<ul style="list-style-type: none"> • NIOSH REL: 10-hr TWA, 10ppm, skin¹⁵
ACGIH TLV (TWA)	10 ppm (Skin)
Note: The ACGIH recommended TLV value noted above is based liver damage.	

Other international regulations

- DMF is found on the second Priority Substance List (PSL2) of the Canadian Environmental Protection Act (CEPA) – published in December, 1995¹⁶.
- Included in the candidate list of SVHC (Substances of Very High Concern) by the European Chemicals Agency (ECHA) and in the February 2014 recommendation of substances to be subject to authorization.¹⁷ DMF was prioritized among the SVHC candidates for authorization due to high volume of use, wide dispersiveness of use (used at many industrial facilities) and potential for exposure.¹⁸ If this recommendation from ECHA is approved, DMF will be subject to authorization in the EU.

Harmonized Classification and Labeling

Harmonised Classification of DMF according to part 3 of Annex VI, Table 3.1 (list of harmonised classification and labeling of hazardous substances) of Regulation (EC) No 1272/2008.¹⁹

Chemical Identification	EC No.	CAS No.	Classification	
			Hazard Class and Category	Hazard Statement
N,N-dimethylformamide; dimethyl formamide	200-679-5	68-12-2	Repr. 1B*	H360D: May damage the unborn child
			Acute Tox 4**	H332: Harmful if inhaled
			Acute Tox 4**	H312: Harmful in contact with skin
			Eye Irrit. 2	H319: Causes serious eye irritation

*) Repr. Category 1B is a “Presumed human reproductive toxicant” based largely on clear evidence from animal studies.

**) For certain hazard classes, including acute toxicity and STOT repeated exposure, the classification according to the criteria in Directive 67/548/EEC does not correspond directly to the classification in a hazard class and category under this Regulation. In these cases the classification in this Annex shall be considered as a minimum classification.

5. Implications for the TURA program

Designating DMF as a Higher Hazard Substance would help to fulfill the intent of the 2006 amendments to TURA, providing important guidance and incentives to Massachusetts businesses to help them move away from the most hazardous chemicals and toward safer alternatives.

Avoiding adverse substitutions

Designating DMF as a Higher Hazard Substance would discourage the adoption of DMF as a substitute for other solvents that have been designated, or are in the process of being designated, as Higher Hazard Substances (methylene chloride, TCE, PCE, and nPB).

Consistency with EU regulations

The Advisory Committee recommended that in prioritizing chemicals for action in 2014, the TURA program consider chemicals that have been prioritized under REACH regulation, in order to ensure that Massachusetts regulations are up to date and consistent with regulations in other jurisdictions. This goal was flagged by business representatives as particularly important. DMF meets the criterion of having been prioritized under REACH, and its use in the EU will likely be subject to authorization in the near future.

The TURA program’s work with chemicals prioritized in the EU can help Massachusetts businesses to stay ahead of the regulatory curve internationally and, in some cases, has helped businesses to retain or expand market share. This is relevant if the chemical in question is used in a final product that may be sold in the EU.

Prioritization of a chemical in the EU also means that additional informational resources from the EU may be available to the TURA program as it provides training and technical assistance to Massachusetts businesses.

Costs to businesses of reporting, planning, and fees

There would be some additional cost to companies that would begin reporting DMF based on a lower reporting threshold, including preparing annual toxics use reports and biennial toxics use reduction plans, and paying toxics use fees.

Based on the Tier II data and program staff members' knowledge of use in research labs, we estimate new reporting by 2-7 facilities. Current Tier II facilities are primarily in the 10-50 or 50-100 employee range.

One of these filers would not be new to the program and already pays a base fee, but would begin to pay a per-chemical fee of \$1,100.

Companies that want to have their own in-house TUR planner can qualify either by relying on past work experience in toxics use reduction or by having a staff member take the TUR Planners' training course. Those companies with experienced staff can become certified for as little as \$100. For those that want staff to take a course the cost is \$650. Companies with in-house toxics use reduction planners are likely to reap ancillary benefits from having an employee who is knowledgeable about methods for reducing the costs and liabilities of toxics use. Additionally, through the process of planning and reducing or eliminating DMF use, companies may be able to expand markets, improve compliance with other regulations, and achieve financial savings through process improvements.

Assuming 2-7 new DMF filers with the size distribution listed above, assuming that three of them are completely new to TURA, the total additional cost in fees to filers (and revenue to the program) could be approximately \$7,750-19,550.

¹Hazardous Substances Data Bank (HSDB). 2012. "*N,N-Dimethylformamide*." Available from. <http://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~oY3cUc:1>. Viewed July 21, 2014.

²Chemicals Evaluation and Research Institute (CERI), Japan. 2005, English version May 2007. "*CERI-NITE Hazard Assessment for N,N-Dimethylformamide CAS No. 68-12-2*."

³Hazardous Substances Data Bank (HSDB). 2012. "*N,N-Dimethylformamide*." Available from. <http://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~oY3cUc:1>. Viewed July 21, 2014.

⁴Hazardous Substances Data Bank (HSDB). 2012. "*N,N-Dimethylformamide*." Available from. <http://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~oY3cUc:1>. Viewed July 21, 2014.

⁵Hazard Assessment Report, N, N-Dimethylformamide, Chemicals Evaluation and Research Institute, Japan.

⁶Green Chemistry in Practice. Cannon.

⁷United States Environmental Protection Agency (USEPA). October 2012. "*List of Lists: Consolidated List of Chemicals Subject to the Emergency Planning and Community Right-To-Know Act (EPCRA), Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) and Section 112(r) of the Clean Air Act*." Retrieved from http://www2.epa.gov/sites/production/files/2013-08/documents/list_of_lists.pdf, viewed July 21, 2014.

⁸US EPA. 2014. "*Emergency Planning and Community Right-to-Know Act (EPCRA) Hazardous Chemical Storage Reporting Requirements*" Retrieved from http://www.epa.gov/emergencies/content/epcra/epcra_storage.htm#msds.

⁹U.S. EPA. 1990. Clean Air Act Amendments of 1990 List of Hazardous Air Pollutants. Retrieved from <http://www.epa.gov/ttn/atw/orig189.html>, viewed May 29, 2014.

-
- ¹⁰ ListEXPERT™. Expert Publishing, a division of EBSCO Publishing, Ipswich, MA <http://www.expub.com> (accessed July 22, 2014).
- ¹¹ ATSDR. 2014. “*Superfund Amendments and Reauthorization Act – Agency for Toxic Substances and Disease Registry 2013 Substance Priority List.*” Retrieved from <http://www.atsdr.cdc.gov/spl/>. Viewed July 21, 2014.
- ¹² US EPA. October 2012. “*List of Lists...*” Retrieved from http://www2.epa.gov/sites/production/files/2013-08/documents/list_of_lists.pdf , viewed July 21, 2014.
- ¹³ Hazardous Substances Data Bank. 2000. “*29 CFR 1910.1000*”, as cited in the Hazardous Substances Data Bank (HSDB), a database of the National Library of Medicine's TOXNET system, Available from <http://toxnet.nlm.nih.gov>.
- ¹⁴ US National Library of Medicine, Hazardous Substance Data Bank (HSDB). 1997. “NIOSH Pocket Guide to Chemical Hazards.” [DHHS (NIOSH) Publication No. 97-140.] Washington, D.C. U.S. Government Printing Office, p. 114.
- ¹⁵ US National Library of Medicine, Hazardous Substance Data Bank (HSDB). 1997. “NIOSH Pocket Guide to Chemical Hazards.” [DHHS (NIOSH) Publication No. 97-140.] Washington, D.C. U.S. Government Printing Office, p. 114.
- ¹⁶ ListEXPERT™. Expert Publishing, a division of EBSCO Publishing, Ipswich, MA <http://www.expub.com> (accessed July 22, 2014).
- ¹⁷ European Chemicals Agency (ECHA). 2014. “*Recommendation of the European Chemicals Agency of 6 February 2014 for the inclusion of substances in Annex XIV to REACH.*” Retrieved from http://echa.europa.eu/documents/10162/13640/5th_a_xiv_recommendation_06feb2014_en.pdf Viewed July 21, 2014.
- ¹⁸ European Chemicals Agency (ECHA). 2013. “*Draft Results of the 5th prioritization of the SVHCs on the Candidate List with the objective to recommend priority substances for inclusion in Annex XIV.*” 24 June 2013, rev. 5 July 2013. Retrieved from http://echa.europa.eu/documents/10162/13640/prioritisation_results_5th_rec_en.pdf & European Chemicals Agency (ECHA), *Recommendation of the European Chemicals Agency of 6 February 2014 for the inclusion of substances in Annex XIV to REACH.* Retrieved from http://echa.europa.eu/documents/10162/13640/5th_a_xiv_recommendation_06feb2014_en.pdf Viewed July 21, 2014.
- ¹⁹ European Chemicals Agency (ECHA). November 2012. “*Support Document for Identification of N,N-Dimethylformamide as a Substance of Very High Concern Because of its CMR Properties.*” Retrieved from <http://echa.europa.eu/documents/10162/9eb46be5-9399-49e2-a353-98a5e5091245>.