

DMSO - DIMETHYL SULFOXIDE

A polar aprotic solvent with virtually no toxicity constraints

→ Looking for a polar aprotic solvent to substitute toxic solvents?

- Not a reproduction toxin (R61) like NMP, DMF, DMAc
- Maximum available information on toxicity and ecotoxicity
- Readily available at low cost
- Very low regulation constraints.

→ Arkema DMSO, the safe and competitive alternative

- Well-known solvent manufactured by Arkema for more than 40 years
- Extensive and available toxicological and eco-toxicological study data
- Not classified as flammable, irritating, or harmful*
- Available for delivery around the globe

*According to European Directive 67/548/CE modified by European Directive 2001/59/CE.

→ DMSO the worker and environmentally friendly high performance solvent

1. Not classified	1. Easy to handle and store, requires no specific governmental authorizations for use.
2. EMEA Class 3	2. Up to 50 mg/day of residual solvent would be acceptable in your API without justification.
3. Biodegradable	3. Easily treated in a biological wastewater treatment unit.
4. Recycling	4. Easily recycled, low solvent consumption.

→ According to the European directive 67/548/EEC, DMSO is not classified as dangerous.

DMSO is one of the most popular polar aprotic solvent with similar applications as dimethyl acetamide, dimethyl formamide and N-methyl pyrrolidone.

DMSO is the only polar aprotic industrial solvent without labeling restrictions.

Labeling

DMSO	NMP *	DMF	DMAc
none	Xi (R36/37/38)	Xi (R36)	
		Xn (R20/21)	Xn (R20/21)
	T (R61 cat.2)	T (R61 cat.2)	T (R61 cat.2)

* Proposal adopted by the EU classification and labeling committee.

Xi: Irritant

R36: Irritating to eyes

R36/37/38: Irritating to eyes, respiratory system and skin

Xn: Harmful

R20/21: Harmful by inhalation and in contact with skin

T: Toxic

R61: May cause harm to the unborn child (reprotoxic category 2)

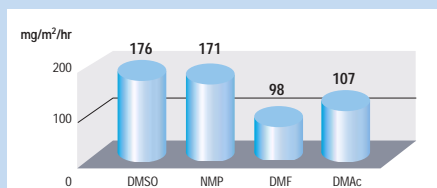
Over the last 40 years, Arkema or independent laboratories have performed numerous (eco)toxicity studies on DMSO. In this page, Arkema presents a summary on the facts of DMSO properties.

→ PHARMACOKINETICS

As with many organic solvents, DMSO is readily absorbed by all routes of administration.

After rapid skin absorption, DMSO is widely and evenly distributed to the tissues, then rapidly metabolized and excreted.

Permeability through skin



Some of the DMSO is reduced to dimethyl sulfide (DMS) which is exhaled (garlic-like breath). Any DMS that is not eliminated via the lungs is reoxidized back to DMSO. Some DMSO is also oxidized to DMSO₂ (dimethyl sulfone). Both DMSO and DMSO₂ are fully excreted in the urine.

→ LOCAL EFFECTS

DMSO induced only a slight irritation after dermal or ocular application in rabbits. This effect was rapidly reversible and all symptoms cleared after 48 hr. No skin sensitisation was observed in guinea pig.

In humans, skin contact, especially with the undiluted substance, results in perceptible hyperthermia because of the heat of solution of DMSO in water and local vasodilatation. Repeated skin contact may lead to erythema, oedema, pruritis, and hardening of the skin and scale formation.

In animal studies, a slight irritation was observed after occlusive application up to 24 hours. The degree of eye injury described in human and animal studies would not result in DMSO being considered as an eye irritant. Allergic-like reactions have occasionally been described in human, but animal studies were consistently negative for skin sensitisation.

→ ACUTE TOXICITY

DMSO is of very low acute toxicity by oral, inhalation and dermal routes.

In rats, LD(LC)₅₀'s are higher than 15 g/kg and 40 g/kg by the oral and dermal routes, and higher than 5 mg/l by inhalation.

→ REPEATED DOSE TOXICITY

Even with repeated oral, dermal or inhalation exposures, DMSO toxicity remains low.

According to the results of a 13-week inhalation toxicity study, designed to comply with OECD/US-EPA guidelines and GLP regulations, the no adverse effects concentration could be established at 1 mg/l for respiratory tract irritation and 2.8 mg/l for systemic toxicity.

Limited data generated with several species and routes of administration (oral, dermal) have shown that DMSO produces only slight systemic toxicity. Typical findings in experimental animals include increase diuresis, and damage to liver and kidney. Prolonged treatment of animals with high dose levels of DMSO leads to changes of the refractive power of the lens. Species in which such lens alterations readily develop include the dog and small laboratory rodents; primates are less sensitive. Excluding the ocular toxicity seems not to be relevant, as it has never been observed in humans treated with DMSO, it is possible to estimate that the dose level without toxic effects would be higher than 1000 mg/kg/day.

→ GENOTOXICITY

Overall, DMSO does not act as a primary genotoxin.

DMSO is used world wide as a solvent for poorly water-soluble substances in the genotoxicity tests.

→ REPRODUCTIVE TOXICITY - TERATOGENICITY

No toxicity to the reproductive organs and no harmful effects to the embryo or to the fetus were observed in carefully controlled studies.

No effect was observed on the reproductive organs of male and female rats after a 90-day inhalation exposure to DMSO concentrations up to 2.8 mg/l. Oral administration of DMSO to pregnant female rats or rabbits during the period of organogenesis was not teratogenic. The no observed effect levels (NOEL) for maternal toxicity were 1 000 and 300 mg/kg/day in rats and rabbits, respectively, and the NOEL's for embryo/feto-toxicity were 1 000 mg/kg/day in both species.

→ ECOTOXICITY

DMSO is readily biodegradable and has very low acute toxicity for the aquatic organisms.

Biodegradability (OECD guideline 310D)	94% after 27 days
Fish LC ₅₀ (96H)	35 200 - 50 600 mg/l
Daphnia EC ₁₀ (l)50, (24h)	16 250 mg/l
Bacteria (EC ₁₀ , 16H)	7 100 mg/l
Algae IC ₅₀ (10-14d)	3 900 - 40 200 mg/l

The data presented herein represents a summary of our most current understanding of the toxicological information. If any of these data or conclusions were to significantly change, Arkema will inform all customers.

The information contained in this document is based on trials carried out by our Research Centres and data selected from the literature, but shall in no event be held to constitute or imply any warranty, undertaking, express or implied commitment from our part. Our formal specifications define the limit of our commitment.

No liability whatsoever can be accepted by Arkema with regard to the handling, processing or use of the product or products concerned which must in all cases be employed in accordance with all relevant laws and/or regulations in force in the country or countries concerned.



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