

Milbemycin oxime

sc-362030



The Power to Question

Material Safety Data Sheet

Hazard Alert Code
Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

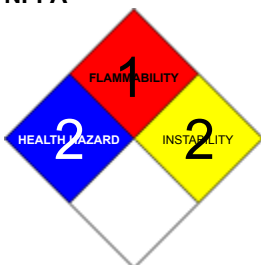
PRODUCT NAME

Milbemycin oxime

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

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EMERGENCY

ChemWatch

Within the US & Canada: 877-715-9305

Outside the US & Canada: +800 2436 2255

(1-800-CHEMCALL) or call +613 9573 3112

SYNONYMS

CGA-179246, Interceptor, Milbemax, "macrolide antibiotic/ antiparasite/ insecticide/ acaricide"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

		Min	Max
Flammability	1		
Toxicity	2		
Body Contact	0		
Reactivity	2		
Chronic	2		

Min/Nil=0
Low=1
Moderate=2
High=3
Extreme=4



CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

May form explosive peroxides.
Very toxic to aquatic organisms.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

- Accidental ingestion of the material may be damaging to the health of the individual.
- There have been several reports of acute human exposure incidents with abamectin containing formulations. Abamectin is a mixture of avermectins. Clinical symptoms of severe abamectin intoxication include mydriasis, sedation, emesis, tremors, convulsions, coma and death. One successful suicide attempt was reported (estimated lethal doses 3.6 to 4.5 grams of abamectin).

Systemic reactions in humans may include fever, rash and lymph-node pain or swelling. Ocular reactions have been minimal.

In monkeys, emesis occurred following a single oral dosage of 2 mg/kg; mydriasis was seen at 24 mg/kg indicating a dose-response curve is flatter in monkeys than in rodents.

- Macrolides comprise a large group of antibiotics derived from *Streptomyces* spp. having in common a macrocyclic lactone ring to which one or more sugars are attached. They are all weak bases.

EYE

- Although the material is not thought to be an irritant, direct contact with the eye may cause transient discomfort characterized by tearing or conjunctival redness (as with windburn). Slight abrasive damage may also result.

SKIN

- The material is not thought to produce adverse health effects or skin irritation following contact (as classified using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.

- In rats and rabbits, dermal exposure to abamectin, under occluded conditions for 24 hours, at a dosage of 300 and 2000 mg/kg, respectively, produced tremors, ataxia, decreased activity, weight loss and death.

Dermal penetration of abamectin in monkeys was determined to be less than 1% Abamectin did not show potential to produce skin sensitisation in the guinea pig maximisation test.

- Open cuts, abraded or irritated skin should not be exposed to this material.

- Entry into the blood-stream, through, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects. Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

INHALED

- The material is not thought to produce respiratory irritation (as classified using animal models). Nevertheless inhalation of dusts, or fume, especially for prolonged periods, may produce respiratory discomfort and occasionally, distress.

- Inhalation of dusts, generated by the material during the course of normal handling, may be damaging to the health of the individual.

- Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled.

- There were no deaths recorded in rats inhaling 5.73 mg/l abamectin (avermectins); the animals also exhibited normal behaviour and there were no changes in body weights.

CHRONIC HEALTH EFFECTS

- Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.

Prolonged or repeated use of antibiotics, at therapeutic doses, may produce bacterial resistance for some types of bacteria. Prolonged use may result in the overgrowth of non-susceptible organisms (i.e.

Long term exposure to high dust concentrations may cause changes in lung function i.e. pneumoconiosis; caused by particles less than 0.5 micron penetrating and remaining in the lung.

There are generally two types of oximes ketoximes derived from ketones and aldoximes derived from aldehydes. Several ketoximes (p-quinone dioxime, acetoxime and methyl ethyl ketoxime) have elicited carcinogenic effects on chronic exposure. Few substantive studies have been performed with aldoximes. The fact that aldoximes can be metabolised to cyanide via a pathway not applicable to ketoximes distinguishes the type of response which might be anticipated. Dehydration of aldoximes to produce nitriles has been shown to be catalysed in vitro by cytochrome P450; dehydration of ketoximes produces amides, rather than nitriles, via a Beckmann rearrangement but this apparently has no analogue in biological systems.

The mechanism and toxicity of oximes to erythrocytes is recognised and might be attributed to hydroxylamine, a product of hydrolysis. Hydroxylamine produces haematologic effects such as methaemoglobinaemia and splenomegaly in mice similar to those observed after exposure to oximes such as butanal oxime. Studies demonstrated the formation of haeme-associated free radicals in erythrocytes exposed to hydroxylamine, leading ultimately to peroxidation of membrane lipids. Lipid peroxidation in cellular membranes may produce several morphological alterations resulting, for example, in membrane aggregation, deformation or breakage. This may result in the release of hydrolytic enzymes which in turn may degrade functional macromolecules and cause secondary damage. In addition membrane-bound enzyme systems may be disrupted. Levels of hydroxylamine produced as a result of hydrolysis are thought to be too low to produce another sign of hydroxylamine toxicity, namely the formation of Heinz bodies

Oximes are not easily oxidised at near neutral conditions and hydrolysis by liver microsomes or S9 is hypothesised (however this conclusion was based on the formation of a ketone rather than hydroxylamine). Another possibility is that oximes are oxidatively metabolised to yield a ketone or aldehyde and some yet to be determined nitrogen-containing species. Cytochrome P450 appears to provide a source of superoxide and hydrogen peroxide which catalyses oxidation in the presence of iron. At least part of the nitrogen in the oxime is converted to nitric oxide which complexes with haeme to give a nitrosylhaemoglobin complex.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
milbemycin oxime	129496-10-2	>98
being a mixture of milbemycin oximes:		
milbemycin A4 5-oxime		
(C32-H45-N-O7)		
milbemycin A3 5-oxime		
(C31-H43-N-O7)		

Section 4 - FIRST AID MEASURES

SWALLOWED

- If swallowed do NOT induce vomiting.
- If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.

EYE

If this product comes in contact with the eyes

- Wash out immediately with fresh running water.
- Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.

SKIN

If skin or hair contact occurs

- Flush skin and hair with running water (and soap if available).
- Seek medical attention in event of irritation.

INHALED

- If fumes or combustion products are inhaled remove from contaminated area.
- Lay patient down. Keep warm and rested.

NOTES TO PHYSICIAN

- Treat symptomatically.

For abamectin (avermectins)

Toxicity following accidental ingestion may be minimised by emesis-induction within one half hour of exposure. Since abamectin is thought to bind to glutamate-gated chloride ion channels, it is probably wise to avoid drugs that also interact with other ligand-gated chloride channels, including those that enhance GABA activity in patients with potentially toxic abamectin exposure

Avoid drugs that enhance GABA activity (barbiturate, benzodiazepines, valproic acid, etc.).
for poisons (where specific treatment regime is absent)

BASIC TREATMENT

- Establish a patent airway with suction where necessary.
- Watch for signs of respiratory insufficiency and assist ventilation as necessary.

Section 5 - FIRE FIGHTING MEASURES

Vapour Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not available.
Specific Gravity (water=1)	Not available
Lower Explosive Limit (%)	Not available

EXTINGUISHING MEDIA

- Foam.
- Dry chemical powder.

FIRE FIGHTING

- Alert Emergency Responders and tell them location and nature of hazard.
- Wear full body protective clothing with breathing apparatus.

When any large container (including road and rail tankers) is involved in a fire, consider evacuation by 800 metres in all directions.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

- Combustible solid which burns but propagates flame with difficulty.
- Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion. Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust may burn rapidly and fiercely if ignited.

Combustion products include carbon monoxide (CO), carbon dioxide (CO₂), other pyrolysis products typical of burning organic material.

May emit poisonous fumes.

FIRE INCOMPATIBILITY

Avoid contamination with oxidizing agents i.e. nitrates, oxidizing acids, chlorine bleaches, pool chlorine etc. as ignition may result.

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

- Clean up waste regularly and abnormal spills immediately.
- Avoid breathing dust and contact with skin and eyes.
- Wear protective clothing, gloves, safety glasses and dust respirator.
- Use dry clean up procedures and avoid generating dust.
- Vacuum up or sweep up. NOTE Vacuum cleaner must be fitted with an exhaust micro filter (HEPA type) (consider explosion-proof machines designed to be grounded during storage and use).
- Dampen with water to prevent dusting before sweeping.
- Place in suitable containers for disposal.

MAJOR SPILLS

- Clear area of personnel and move upwind.

- Alert Emergency Responders and tell them location and nature of hazard.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

- Avoid all personal contact, including inhalation.
- Wear protective clothing when risk of exposure occurs.

Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.

- Do NOT cut, drill, grind or weld such containers.
- In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.

RECOMMENDED STORAGE METHODS

Glass container.

- Lined metal can, Lined metal pail/drum
- Plastic pail

For low viscosity materials

- Drums and jerricans must be of the non-removable head type.
- Where a can is to be used as an inner package, the can must have a screwed enclosure.

STORAGE REQUIREMENTS

- Store in original containers.
- Keep containers securely sealed.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

- milbemycin oxime CAS129496-10-2

PERSONAL PROTECTION



RESPIRATOR

- Particulate. (AS/NZS 1716 & 1715, EN 1432000 & 1492001, ANSI Z88 or national equivalent)

EYE

For laboratory, larger scale or bulk handling or where regular exposure in an occupational setting occurs

- Chemical goggles
- Face shield. Full face shield may be required for supplementary but never for primary protection of eyes
- Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59], [AS/NZS 1336 or national equivalent]

HANDS/FEET

Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include

- frequency and duration of contact,

- chemical resistance of glove material,
- glove thickness and
- dexterity

Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739, AS/NZS 2161.1 or national equivalent).

- When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374, AS/NZS 2161.10.1 or national equivalent) is recommended.
- When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374, AS/NZS 2161.10.1 or national equivalent) is recommended.
- Contaminated gloves should be replaced.

Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.

- Rubber gloves (nitrile or low-protein, powder-free latex). Employees allergic to latex gloves should use nitrile gloves in preference.
- Double gloving should be considered.
- PVC gloves.
- Protective shoe covers. [AS/NZS 2210]
- Head covering.

OTHER

- For quantities up to 500 grams a laboratory coat may be suitable.
- For quantities up to 1 kilogram a disposable laboratory coat or coverall of low permeability is recommended. Coveralls should be buttoned at collar and cuffs.
- For quantities over 1 kilogram and manufacturing operations, wear disposable coverall of low permeability and disposable shoe covers.
- For manufacturing operations, air-supplied full body suits may be required for the provision of advanced respiratory protection.
- Eye wash unit.
- Ensure there is ready access to an emergency shower.
- For Emergencies Vinyl suit

ENGINEERING CONTROLS

Enclosed local exhaust ventilation is required at points of dust, fume or vapor generation.

HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapors.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.

Does not mix with water.

State	Divided solid	Molecular Weight	541.7 (A3), 555.7 (A4)
Melting Range (°F)	336.6- 351.4	Viscosity	Not Applicable
Boiling Range (°F)	Not available	Solubility in water (g/L)	Partly miscible
Flash Point (°F)	Not available	pH (1% solution)	6.3
Decomposition Temp (°F)	Not Available	pH (as supplied)	Not applicable
Autoignition Temp (°F)	Not available	Vapour Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not available.	Specific Gravity (water=1)	Not available
Lower Explosive Limit (%)	Not available	Relative Vapor Density (air=1)	Not Applicable
Volatile Component (%vol)	Negligible	Evaporation Rate	Not applicable

APPEARANCE

Practically odourless to powder; does not mix well with water.

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

- Presence of incompatible materials.
- Product is considered stable.

STORAGE INCOMPATIBILITY

- Explosion or violent decomposition during distillation of aldoximes has been attributed to the presence of peroxides arising from autooxidation.
- Peroxides may form on the $-C=NOH$ system (both aldehydes and hydroxylamine peroxides) or perhaps arise from unreacted aldehyde.
- Explosion hazards are inherent to ketoximes and many of their derivatives. Such hazard has been attributed to the inadvertent occurrence of acidic conditions leading to the highly exothermic Beckmann rearrangement accompanied by potentially catastrophic gas evolution.
- The presence of acidic salts (iron(III) chloride), or the ketoxime hydrochloride markedly lowers decomposition temperatures.
- A range of exothermic decomposition energies for oximes is given as 170-230 kJ/mol. The relationship between energy of decomposition and processing hazards has been the subject of discussion; it is suggested that values of energy released per unit of mass, rather than on a molar basis (J/g) be used in the assessment. For example, in "open vessel processes" (with man-hole size openings, in an industrial setting), substances with exothermic decomposition energies below 500 J/g are unlikely to present a danger, whilst those in "closed vessel processes" (opening is a safety valve or bursting disk) present some danger where the decomposition energy exceeds 150 J/g.

BREITHERICK Handbook of Reactive Chemical Hazards, 4th Edition.
Avoid reaction with oxidizing agents.

For incompatible materials - refer to Section 7 - Handling and Storage.

Section 11 - TOXICOLOGICAL INFORMATION

milbemycin oxime

TOXICITY AND IRRITATION

MILBEMYCIN OXIME

unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.

No significant acute toxicological data identified in literature search.

For avermectins

Technical avermectin exhibits high mammalian acute toxicity. It is not considered to be mutagenic and does not sensitise skin. It is not readily absorbed by mammals and the majority of the residue is excreted in the faeces within 2 days. The 24-month rat chronic feeding/ oncogenicity study and 94-week mouse chronic toxicity oncogenicity study were negative for oncogenic potential. The results of a series of developmental toxicity studies (rat, rabbit, mouse) have been evaluated and showed that avermectin B1 produces developmental toxicity (cleft palate) in the CF1 mouse. Toxicology data were also evaluated for the delta-8,9-isomer of avermectin B1 which is a plant photodegradate that can range between 5 and 20 percent of the residue on/in cottonseed. This isomer possesses avermectin-like toxicological activity. It was concluded that the delta 8,9-isomer also produces developmental toxicity (cleft palate) in mice, but not in rats. In addition to avermectin and its delta 8,9-isomer, toxicology data were also evaluated for the "polar degradates" of avermectin, which constitute a large percentage (up to 70%) of the total residue on cottonseed. Review of the toxicology data indicated that these polar degradates do not possess avermectin-like toxicological activity and for this reason need not be included in the tolerance expression for residues in/on cottonseed.

Abamectin (a mixture of avermectin isomers) is a reproductive toxin in laboratory animals at doses which are acutely toxic to the mother. In development toxicity studies with abamectin, cleft palates were seen in mice and rabbits and clubbing of the forepaws was seen in rabbits. The no-observed-adverse-effect-level (NOAEL) for maternal and developmental toxicity in rabbits was 1 mg/kg/day. In CF-1 mice, a strain recognised to be particularly sensitive to avermectins, the NOAEL for maternal toxicity was 0.05 mg/kg/day and the NOAEL for malformations was 0.2 mg/kg/day. Studies show that the sensitivity of a subpopulation of CF-1 mice to avermectins is due to the absence of a transmembrane P-glycoprotein, a significant component of the blood-brain

interface that normally acts as a non-selective protective barrier in a wide range of species including humans. CF-1 mice are therefore an unlikely candidate for assessing human risk. No evidence of developmental toxicity was seen in oral studies in rats in the absence of maternal toxicity (NOAEL = 1.6 mg/kg/day). In a rat multigenerational reproduction study, pup toxicity and deaths were seen at 0.4 mg/kg/day (NOAEL = 0.12 mg/kg/day). Neonatal rats are not an appropriate model for assessing human risk in humans because (a) rat milk has a greater fat

content than human breast milk and abamectin concentrates in fat; (b) on a weight basis, the neonatal rat consumes significantly greater quantities of milk than the newborn human and (c) the blood brain barrier in rodents is formed post-natally (as evidenced by low P-glycoprotein levels) while in humans this membrane is formed pre-natally.

Ivermectin, a close structural analogue, has been used extensively in the treatment of human onchocerciasis at an oral therapeutic dose of 0.2 mg/kg, without serious drug-related effects. Despite its wide usage in animals and humans, ivermectin does not appear to produce birth defects.

Abamectin is non-mutagenic in the Ames test and the micronucleus test.

Dietary carcinogenicity studies in mice and rats showed negative results. In a 14-week oral study in monkeys no effects were seen at 0.2, 0.5 or 1.0 mg/kg/day; emesis was seen at 2.0 mg/kg/day; delayed pupillary obstruction at 6 and 8 mg/kg/day and mydriasis at 12 mg/kg/day.

In chronic oral toxicity, abamectin produced decreased body weight gain in mice (no-observed-adverse-effect-level (NOAEL) = 1.5 mg/kg/day); tremors in rats (NOAEL = 1.5 mg/kg/day), weight loss, tremors, mydriasis, liver and gall bladder changes and death in dogs (NOAEL = 0.25 mg/kg/day); and emesis, mydriasis and sedation in monkeys (NOAL = 1 mg/kg/day).

Section 12 - ECOLOGICAL INFORMATION

Very toxic to aquatic organisms.

This material and its container must be disposed of as hazardous waste.

Avoid release to the environment.

Refer to special instructions/ safety data sheets.

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

All waste must be handled in accordance with local, state and federal regulations.

! Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area. In some areas, certain wastes must be tracked.

A Hierarchy of Controls seems to be common - the user should investigate:

- Reduction
- Reuse
- Recycling
- Disposal (if all else fails)

This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. Shelf life considerations should also be applied in making decisions of this type. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate.

DO NOT allow wash water from cleaning equipment to enter drains. Collect all wash water for treatment before disposal.

- Recycle wherever possible.
- Consult manufacturer for recycling options or consult Waste Management Authority for disposal if no suitable treatment or disposal facility can be identified.

Section 14 - TRANSPORTATION INFORMATION



DOT:

Symbols:	None	Hazard class or Division:	6.1
Identification Numbers:	UN2588	PG:	III
Label Codes:	6.1	Special provisions:	IB8, IP3, T1, TP33
Packaging: Exceptions:	153	Packaging: Non-bulk:	213
Packaging: Exceptions:	153	Quantity limitations: Passenger aircraft/rail:	100 kg
Quantity Limitations: Cargo aircraft only:	200 kg	Vessel stowage: Location:	A
Vessel stowage: Other:	40		

Hazardous materials descriptions and proper shipping names:

Pesticides, solid, toxic, n.o.s.

Air Transport IATA:

ICAO/IATA Class:	6.1	ICAO/IATA Subrisk:	None
UN/ID Number:	2588	Packing Group:	III
Special provisions:	A3		

Cargo Only

Packing Instructions:	677	Maximum Qty/Pack:	200 kg
Passenger and Cargo		Passenger and Cargo	
Packing Instructions:	670	Maximum Qty/Pack:	100 kg
Passenger and Cargo Limited Quantity		Passenger and Cargo Limited Quantity	
Packing Instructions:	Y645	Maximum Qty/Pack:	10 kg

Shipping Name: PESTICIDE, SOLID, TOXIC, N.O.S. *(CONTAINS MILBEMYCIN OXIME)

Maritime Transport IMDG:

IMDG Class:	6.1	IMDG Subrisk:	None
UN Number:	2588	Packing Group:	III
EMS Number:	F-A,S-A	Special provisions:	61 223 274
Limited Quantities:	5 kg	Marine Pollutant:	Yes

Shipping Name: PESTICIDE, SOLID, TOXIC, N.O.S.(contains milbemycin oxime)

Section 15 - REGULATORY INFORMATION

No data for milbemycin oxime (CAS: , 129496-10-2)

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

■ Inhalation and/or ingestion may produce health damage*.

■ Cumulative effects may result following exposure*.

* (limited evidence).

Reasonable care has been taken in the preparation of this information, but the author makes no warranty of merchantability or any other warranty, expressed or implied, with respect to this information. The author makes no representations and assumes no liability for any direct, incidental or consequential damages resulting from its use. For additional technical information please call our toxicology department on +800 CHEMCALL.

■ Classification of the preparation and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references.

A list of reference resources used to assist the committee may be found at:

www.chemwatch.net/references.

■ The (M)SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings. Risks may be determined by reference to Exposures Scenarios. Scale of use, frequency of use and current or available engineering controls must be considered.

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www.chemwatch.net

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