

SECTION-1: Identification of the substance / mixture and the company / undertaking

Catalogue Number	CS-T-34153
Product Name	2-Methyl-4-isothiazolin-3-one
CAS No.	2682-20-4
Category	Pesticide Standards
Synonyms	Methylisothiazolinone
Brand	Clearsynth Labs Ltd.
Identified uses	Laboratory Chemicals
Uses advised against	Not available
Company	Clearsynth Labs Ltd. Mumbai, India
Emergency Phone #	+91-22-245045900
REACH No.	Not available

SECTION 2: Hazards identification

Disclaimer: This is sample MSDS. Please email sales@clearsynth.com for more details.

2.1 Classification of the substance or mixture-Regulation (EC) No 1272/2008:

Acute toxicity (Category 4)

2.2 Label Elements

Signal Word: Warning



Hazard Statement(s)

Code	Statement
H301	Not available
H311	Not available
H314	Not available
H317	May cause an allergic skin reaction.

H318	Causes serious eye damage.
H330	Not available
H400	Not available
H410	Not available
H301+H311	Not available
H302	Harmful if swallowed.
H331	Not available
H335	Not available
H370	Not available

Precautionary Statement(s)

Code	Statement
P260	Not available
P261	Avoid breathing dust/fume/gas/mist/vapours/spray.
P262	Not available
P264	Wash hands thoroughly after handling.
P264+P265	Not available
P270	Not available
P271	Use only outdoors or in a well-ventilated area.
P272	Not available
P273	Not available
P280	Wear protective gloves/protective clothing/eye protection/face protection.
P284	Not available
P301+P316	Not available
P301+P330+P331	Not available
P302+P352	IF ON SKIN: Wash with plenty of water and soap.
P302+P361+P354	Not available
P304+P340	IF INHALED: Remove person to fresh air and keep comfortable for breathing.
P305+P354+P338	Not available
P316	Not available

P317	Not available
P320	Not available
P321	Specific treatment (see ... on this label).
P330	Not available
P333+P317	Not available
P361+P364	Not available
P362+P364	Take off contaminated clothing and wash it before reuse.
P363	Not available
P391	Not available
P403+P233	Store in a well-ventilated place. Keep container tightly closed.
P405	Store locked up.
P501	Dispose of contents/container in accordance with local/regional/national/international regulation
P301+P317	Not available
P319	Get medical help if you feel unwell.
P308+P316	Not available

SECTION 3: Composition / information on ingredients

3.1 Substance

Component : 2-Methyl-4-isothiazolin-3-one

CAS Number : 2682-20-4

Molecular Formula : C₄H₅NOS

Molecular Weight : 115.15

Parent Chemical : .

Synonyms : Methylothiazolinone

Concentration : Not available

SECTION 4: First aid measures

Not available

SECTION 5: Firefighting measures

Not available

SECTION 6: Accidental release measures

Not available

SECTION-7: Handling and storage

Not available

SECTION 8: Exposure controls / personal protection

Not available

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

Test	Result
Appearance	No data available
IR spectrum	No data available
pH	No data available
Solubility	No data available

Property	Value
a) Physical State	No data available
b) Color	No data available
c) Odor	No data available
d) pH	No data available
e) Vapour Pressure	No data available
f) Viscosity	No data available
g) Initial Boiling Point and boiling range	No data available
h) Melting Point / Freezing Point	No data available
i) Auto Ignition Temperature	No data available
j) Flash Point	No data available
k) Explosion Limit, Lower	No data available
l) Explosion Limit, Upper	No data available

Property	Value
m) Decomposition Temperature	No data available
n) Loss on Drying	No data available
o) Relative Density	No data available
p) Solubility (in DMSO)	No data available
q) Oxidizing Properties	No data available

SECTION 10: Stability and reactivity

Not available

SECTION 11: Toxicological information

11.1 Information on toxicological effects

- Acute toxicity: IDENTIFICATION AND USE: Methylisothiazolinone (MIT) forms colorless prisms. It is used as preservative in personal care and cosmetics products such as leave-on products, namely hand and body lotions and moisturizers, sun tanning lotions and some rinse-off products like shampoos, surfactants and conditioners. In addition, MIT is an antimicrobial used to control slime-forming bacteria, fungi, and algae in cooling water systems, fuel storage tanks, pulp and paper mill water systems, oil extraction systems, and other industrial settings. It is also used to control the growth of mold, mildew, and sapstain on wood products. It is registered for use in the USA but approved pesticide uses may change periodically and so federal, state and local authorities must be consulted for currently approved uses. It is often used in a combination products with 5-chloro-2-methyl-4-isothiazolin-3-one. HUMAN EXPOSURE AND TOXICITY: In vitro studies show that a brief exposure to MIT is highly toxic to cultured neurons but not to glia. The toxic actions of this biocide are zinc-dependent and require the activation of p44/42 extracellular signal-regulated kinase (ERK) via a 12-lipoxygenase-mediated pathway. The cell death process also involves activation of NADPH oxidase, generation of reactive oxygen species, DNA damage, and overactivation of poly(ADP-ribose) polymerase, all occurring downstream from ERK phosphorylation. The Cosmetic Ingredient Review Expert Panel noted the in vitro evidence of neurotoxicity but concluded that the absence of any neurotoxicity findings in the many in vivo studies, including subchronic, chronic, and reproductive and developmental animal studies, suggests that MIT would not be neurotoxic as used in cosmetics. Although recognizing that MIT was a sensitizer in both animal and human studies, the panel concluded that there is a threshold dose response and that cosmetic products formulated to contain concentrations of MIT at 100 ppm (0.01%) or less would not be expected to pose a sensitization risk. Accordingly, MIT may be safely used as a preservative in cosmetics up to that concentration. ANIMAL STUDIES: The exposure of rats to MIT at dose levels up to 2.64 mg/cu m via inhalation for 90 days resulted in decreased body weight in the high-dose males and decreased body-weight gains in both sexes at the high-dose level. There were no treatment-related deaths, and no effects were observed in the hematology, clinical chemistry, ophthalmoscopic, and gross pathology parameters that could be attributed to treatment. Similar observations were made when rats were exposed to this chemical (up to 225 ppm) in drinking water for 3 months. In the carcinogenicity study in rats there was no treatment-related increase in the incidence of any tumor in either sex. MIT was not found to be fetotoxic, embryotoxic, or teratogenic in rats. MIT was positive in the Ames assay in TA100 at concentrations as low as 0.0005 uL/plate without metabolic activation. TA100 with activation and all other strains with and without metabolic activation were negative. MIT was positive in the mouse lymphoma gene mutation assay at dose levels as low as 1 nL/mL without metabolic activation and at 1.22 nL/mL with metabolic activation. Negative

results were observed in the *Drosophila* sex-linked recessive lethal assay. MIT did not cause a significant increase in the frequency of structural chromosome aberrations in mouse bone marrow cells *in vivo*, and did not induce unscheduled DNA synthesis in primary rat hepatocytes *in vitro*. However, *in vitro* study in rat cortical neurons found that MIT induced a dramatic inhibition of neurite outgrowth, and concluded that prolonged exposure to low levels of MIT and related compounds may have damaging consequences to the developing nervous system. For more Human Toxicity Excerpts (Complete) data for Methylisothiazolinone (35 total), please visit the HSDB record page.

- Skin corrosion/irritation: /LABORATORY ANIMALS: Acute Exposure/ 2-Methyl-4-isothiazolin-3-one was applied undiluted by a single application of 0.5 mL to the shaved intact skin of 7 New Zealand White rabbits. Contact time was 3 minutes for 5 animals, 1- hr (and 3 min.) for one animal, 4-hr for one animal. The application sites were semi-occluded. After removal of the patch, the animals were observed for 14 days for signs of irritation. No mortality of clinical sign of systemic toxicity were observed during the study. On the 4 and 1 hr sites, skin irritation indicative of corrosivity was observed on day 14 and 7, respectively. On the 3 min. site, very slight to well defined erythema was noted through day 7 and slight edema was noted at 1 hr. The 5 animals exposed during 3 min., very slight to well defined erythema was noted through 48 hr in most rabbits. Very slight to moderate edema was noted at 1 and 24 hr. Very slight to slight edema was noted in one rabbit at 48 and 72 hr. 2-Methyl-4-isothiazolin-3-one is corrosive to the skin when applied undiluted.

- Serious eye damage/eye irritation: /LABORATORY ANIMALS: Acute Exposure/ Neolone 950 [9.5% active ingredient in water] was applied to the conjunctival sac of a group of six New Zealand White rabbits, as a 100 ppm aqueous solution (0.1 mL). Eye irritation was evaluated according to Draize criteria at approximately 1, 24, 48, and 72 hours. After the 24 hour observation, each eye (treated and control) was irrigated with 0.9% saline for approximately 60 seconds. No mortality or clinical signs of systemic toxicity were observed. No corneal, conjunctival or iridial effects were observed during the study.

- Respiratory or skin sensitization: IDENTIFICATION AND USE: Methylisothiazolinone (MIT) forms colorless prisms. It is used as preservative in personal care and cosmetics products such as leave-on products, namely hand and body lotions and moisturizers, sun tanning lotions and some rinse-off products like shampoos, surfactants and conditioners. In addition, MIT is an antimicrobial used to control slime-forming bacteria, fungi, and algae in cooling water systems, fuel storage tanks, pulp and paper mill water systems, oil extraction systems, and other industrial settings. It is also used to control the growth of mold, mildew, and sapstain on wood products. It is registered for use in the USA but approved pesticide uses may change periodically and so federal, state and local authorities must be consulted for currently approved uses. It is often used in a combination products with 5-chloro-2-methyl-4-isothiazolin-3-one. HUMAN EXPOSURE AND TOXICITY: *In vitro* studies show that a brief exposure to MIT is highly toxic to cultured neurons but not to glia. The toxic actions of this biocide are zinc-dependent and require the activation of p44/42 extracellular signal-regulated kinase (ERK) via a 12-lipoxygenase-mediated pathway. The cell death process also involves activation of NADPH oxidase, generation of reactive oxygen species, DNA damage, and overactivation of poly(ADP-ribose) polymerase, all occurring downstream from ERK phosphorylation. The Cosmetic Ingredient Review Expert Panel noted the *in vitro* evidence of neurotoxicity but concluded that the absence of any neurotoxicity findings in the many *in vivo* studies, including subchronic, chronic, and reproductive and developmental animal studies, suggests that MIT would not be neurotoxic as used in cosmetics. Although recognizing that MIT was a sensitizer in both animal and human studies, the panel concluded that there is a threshold dose response and that cosmetic products formulated to contain concentrations of MIT at 100 ppm (0.01%) or less would not be expected to pose a sensitization risk. Accordingly, MIT may be safely used as a preservative in cosmetics up to that concentration. ANIMAL STUDIES: The exposure of rats to MIT at dose levels up to 2.64 mg/cu m via inhalation for 90 days resulted in decreased body weight in the high-dose males and decreased body-weight gains in both sexes at the high-dose level. There were no treatment-related deaths, and no effects were observed in the hematology, clinical chemistry, ophthalmoscopic, and gross pathology parameters that could be attributed to treatment. Similar observations were made when rats were exposed to this

chemical (up to 225 ppm) in drinking water for 3 months. In the carcinogenicity study in rats there was no treatment-related increase in the incidence of any tumor in either sex. MIT was not found to be fetotoxic, embryotoxic, or teratogenic in rats. MIT was positive in the Ames assay in TA100 at concentrations as low as 0.0005 uL/plate without metabolic activation. TA100 with activation and all other strains with and without metabolic activation were negative. MIT was positive in the mouse lymphoma gene mutation assay at dose levels as low as 1 nL/mL without metabolic activation and at 1.22 nL/mL with metabolic activation. Negative results were observed in the Drosophila sex-linked recessive lethal assay. MIT did not cause a significant increase in the frequency of structural chromosome aberrations in mouse bone marrow cells in vivo, and did not induce unscheduled DNA synthesis in primary rat hepatocytes in vitro. However, in vitro study in rat cortical neurons found that MIT induced a dramatic inhibition of neurite outgrowth, and concluded that prolonged exposure to low levels of MIT and related compounds may have damaging consequences to the developing nervous system. /HUMAN EXPOSURE STUDIES/ Ninety-eight [98] adult volunteers were enrolled into an intensified Shelanski and Shelanski Repeated Insult Patch Test with Kordek™ 50C (Methyl-4-isothiazolin-3-one; MI), 0.15 mL of a 100 ppm aqueous solution, which was applied to a webriol pad to the back of the volunteers under occlusion. Patches were applied four times a week for three weeks [induction phase]. After a week of dosing, the subjects were challenged on a fresh site with MI, 0.15 mL of a 100 ppm aqueous solution applied to a webriol pad. One of the 98 subjects showed a positive response [grade 4] on the fifth day of the induction phase. This subject was judged to be pre-sensitized. Of the remaining 97 subjects, none reacted to challenge [elicitation] with 100 ppm aqueous MI. Under the conditions of this test, 100 ppm Methyl-4-isothiazolin-3-one did not induce skin sensitization in human volunteers.

- Germ cell mutagenicity: IDENTIFICATION AND USE: Methylisothiazolinone (MIT) forms colorless prisms. It is used as preservative in personal care and cosmetics products such as leave-on products, namely hand and body lotions and moisturizers, sun tanning lotions and some rinse-off products like shampoos, surfactants and conditioners. In addition, MIT is an antimicrobial used to control slime-forming bacteria, fungi, and algae in cooling water systems, fuel storage tanks, pulp and paper mill water systems, oil extraction systems, and other industrial settings. It is also used to control the growth of mold, mildew, and sapstain on wood products. It is registered for use in the USA but approved pesticide uses may change periodically and so federal, state and local authorities must be consulted for currently approved uses. It is often used in a combination products with 5-chloro-2-methyl-4-isothiazolin-3-one. HUMAN EXPOSURE AND TOXICITY: In vitro studies show that a brief exposure to MIT is highly toxic to cultured neurons but not to glia. The toxic actions of this biocide are zinc-dependent and require the activation of p44/42 extracellular signal-regulated kinase (ERK) via a 12-lipoxygenase-mediated pathway. The cell death process also involves activation of NADPH oxidase, generation of reactive oxygen species, DNA damage, and overactivation of poly(ADP-ribose) polymerase, all occurring downstream from ERK phosphorylation. The Cosmetic Ingredient Review Expert Panel noted the in vitro evidence of neurotoxicity but concluded that the absence of any neurotoxicity findings in the many in vivo studies, including subchronic, chronic, and reproductive and developmental animal studies, suggests that MIT would not be neurotoxic as used in cosmetics. Although recognizing that MIT was a sensitizer in both animal and human studies, the panel concluded that there is a threshold dose response and that cosmetic products formulated to contain concentrations of MIT at 100 ppm (0.01%) or less would not be expected to pose a sensitization risk. Accordingly, MIT may be safely used as a preservative in cosmetics up to that concentration. ANIMAL STUDIES: The exposure of rats to MIT at dose levels up to 2.64 mg/cu m via inhalation for 90 days resulted in decreased body weight in the high-dose males and decreased body-weight gains in both sexes at the high-dose level. There were no treatment-related deaths, and no effects were observed in the hematology, clinical chemistry, ophthalmoscopic, and gross pathology parameters that could be attributed to treatment. Similar observations were made when rats were exposed to this chemical (up to 225 ppm) in drinking water for 3 months. In the carcinogenicity study in rats there was no treatment-related increase in the incidence of any tumor in either sex. MIT was not found to be fetotoxic, embryotoxic, or teratogenic in rats. MIT was positive in the Ames assay in TA100 at concentrations as low as 0.0005

uL/plate without metabolic activation. TA100 with activation and all other strains with and without metabolic activation were negative. MIT was positive in the mouse lymphoma gene mutation assay at dose levels as low as 1 nL/mL without metabolic activation and at 1.22 nL/mL with metabolic activation. Negative results were observed in the *Drosophila* sex-linked recessive lethal assay. MIT did not cause a significant increase in the frequency of structural chromosome aberrations in mouse bone marrow cells in vivo, and did not induce unscheduled DNA synthesis in primary rat hepatocytes in vitro. However, in vitro study in rat cortical neurons found that MIT induced a dramatic inhibition of neurite outgrowth, and concluded that prolonged exposure to low levels of MIT and related compounds may have damaging consequences to the developing nervous system.

- Carcinogenicity: IDENTIFICATION AND USE: Methylisothiazolinone (MIT) forms colorless prisms. It is used as preservative in personal care and cosmetics products such as leave-on products, namely hand and body lotions and moisturizers, sun tanning lotions and some rinse-off products like shampoos, surfactants and conditioners. In addition, MIT is an antimicrobial used to control slime-forming bacteria, fungi, and algae in cooling water systems, fuel storage tanks, pulp and paper mill water systems, oil extraction systems, and other industrial settings. It is also used to control the growth of mold, mildew, and sapstain on wood products. It is registered for use in the USA but approved pesticide uses may change periodically and so federal, state and local authorities must be consulted for currently approved uses. It is often used in a combination products with 5-chloro-2-methyl-4-isothiazolin-3-one.

HUMAN EXPOSURE AND TOXICITY: In vitro studies show that a brief exposure to MIT is highly toxic to cultured neurons but not to glia. The toxic actions of this biocide are zinc-dependent and require the activation of p44/42 extracellular signal-regulated kinase (ERK) via a 12-lipoxygenase-mediated pathway. The cell death process also involves activation of NADPH oxidase, generation of reactive oxygen species, DNA damage, and overactivation of poly(ADP-ribose) polymerase, all occurring downstream from ERK phosphorylation. The Cosmetic Ingredient Review Expert Panel noted the in vitro evidence of neurotoxicity but concluded that the absence of any neurotoxicity findings in the many in vivo studies, including subchronic, chronic, and reproductive and developmental animal studies, suggests that MIT would not be neurotoxic as used in cosmetics. Although recognizing that MIT was a sensitizer in both animal and human studies, the panel concluded that there is a threshold dose response and that cosmetic products formulated to contain concentrations of MIT at 100 ppm (0.01%) or less would not be expected to pose a sensitization risk. Accordingly, MIT may be safely used as a preservative in cosmetics up to that concentration. ANIMAL STUDIES: The exposure of rats to MIT at dose levels up to 2.64 mg/cu m via inhalation for 90 days resulted in decreased body weight in the high-dose males and decreased body-weight gains in both sexes at the high-dose level. There were no treatment-related deaths, and no effects were observed in the hematology, clinical chemistry, ophthalmoscopic, and gross pathology parameters that could be attributed to treatment. Similar observations were made when rats were exposed to this chemical (up to 225 ppm) in drinking water for 3 months. In the carcinogenicity study in rats there was no treatment-related increase in the incidence of any tumor in either sex. MIT was not found to be fetotoxic, embryotoxic, or teratogenic in rats. MIT was positive in the Ames assay in TA100 at concentrations as low as 0.0005 uL/plate without metabolic activation. TA100 with activation and all other strains with and without metabolic activation were negative. MIT was positive in the mouse lymphoma gene mutation assay at dose levels as low as 1 nL/mL without metabolic activation and at 1.22 nL/mL with metabolic activation. Negative results were observed in the *Drosophila* sex-linked recessive lethal assay. MIT did not cause a significant increase in the frequency of structural chromosome aberrations in mouse bone marrow cells in vivo, and did not induce unscheduled DNA synthesis in primary rat hepatocytes in vitro. However, in vitro study in rat cortical neurons found that MIT induced a dramatic inhibition of neurite outgrowth, and concluded that prolonged exposure to low levels of MIT and related compounds may have damaging consequences to the developing nervous system.

- Reproductive toxicity: IDENTIFICATION AND USE: Methylisothiazolinone (MIT) forms colorless prisms. It is used as preservative in personal care and cosmetics products such as leave-on products, namely hand and body lotions and moisturizers, sun tanning lotions and some rinse-off products like shampoos, surfactants and conditioners. In addition, MIT is an antimicrobial used to control slime-forming bacteria, fungi, and algae in cooling water systems,

fuel storage tanks, pulp and paper mill water systems, oil extraction systems, and other industrial settings. It is also used to control the growth of mold, mildew, and sapstain on wood products. It is registered for use in the USA but approved pesticide uses may change periodically and so federal, state and local authorities must be consulted for currently approved uses. It is often used in a combination products with 5-chloro-2-methyl-4-isothiazolin-3-one. **HUMAN EXPOSURE AND TOXICITY:** In vitro studies show that a brief exposure to MIT is highly toxic to cultured neurons but not to glia. The toxic actions of this biocide are zinc-dependent and require the activation of p44/42 extracellular signal-regulated kinase (ERK) via a 12-lipoxygenase-mediated pathway. The cell death process also involves activation of NADPH oxidase, generation of reactive oxygen species, DNA damage, and overactivation of poly(ADP-ribose) polymerase, all occurring downstream from ERK phosphorylation. The Cosmetic Ingredient Review Expert Panel noted the in vitro evidence of neurotoxicity but concluded that the absence of any neurotoxicity findings in the many in vivo studies, including subchronic, chronic, and reproductive and developmental animal studies, suggests that MIT would not be neurotoxic as used in cosmetics. Although recognizing that MIT was a sensitizer in both animal and human studies, the panel concluded that there is a threshold dose response and that cosmetic products formulated to contain concentrations of MIT at 100 ppm (0.01%) or less would not be expected to pose a sensitization risk. Accordingly, MIT may be safely used as a preservative in cosmetics up to that concentration. **ANIMAL STUDIES:** The exposure of rats to MIT at dose levels up to 2.64 mg/cu m via inhalation for 90 days resulted in decreased body weight in the high-dose males and decreased body-weight gains in both sexes at the high-dose level. There were no treatment-related deaths, and no effects were observed in the hematology, clinical chemistry, ophthalmoscopic, and gross pathology parameters that could be attributed to treatment. Similar observations were made when rats were exposed to this chemical (up to 225 ppm) in drinking water for 3 months. In the carcinogenicity study in rats there was no treatment-related increase in the incidence of any tumor in either sex. MIT was not found to be fetotoxic, embryotoxic, or teratogenic in rats. MIT was positive in the Ames assay in TA100 at concentrations as low as 0.0005 uL/plate without metabolic activation. TA100 with activation and all other strains with and without metabolic activation were negative. MIT was positive in the mouse lymphoma gene mutation assay at dose levels as low as 1 nL/mL without metabolic activation and at 1.22 nL/mL with metabolic activation. Negative results were observed in the Drosophila sex-linked recessive lethal assay. MIT did not cause a significant increase in the frequency of structural chromosome aberrations in mouse bone marrow cells in vivo, and did not induce unscheduled DNA synthesis in primary rat hepatocytes in vitro. However, in vitro study in rat cortical neurons found that MIT induced a dramatic inhibition of neurite outgrowth, and concluded that prolonged exposure to low levels of MIT and related compounds may have damaging consequences to the developing nervous system.

- STOT-single exposure: No data available.

- STOT-repeated exposure: **IDENTIFICATION AND USE:** Methylisothiazolinone (MIT) forms colorless prisms. It is used as preservative in personal care and cosmetics products such as leave-on products, namely hand and body lotions and moisturizers, sun tanning lotions and some rinse-off products like shampoos, surfactants and conditioners. In addition, MIT is an antimicrobial used to control slime-forming bacteria, fungi, and algae in cooling water systems, fuel storage tanks, pulp and paper mill water systems, oil extraction systems, and other industrial settings. It is also used to control the growth of mold, mildew, and sapstain on wood products. It is registered for use in the USA but approved pesticide uses may change periodically and so federal, state and local authorities must be consulted for currently approved uses. It is often used in a combination products with 5-chloro-2-methyl-4-isothiazolin-3-one. **HUMAN EXPOSURE AND TOXICITY:** In vitro studies show that a brief exposure to MIT is highly toxic to cultured neurons but not to glia. The toxic actions of this biocide are zinc-dependent and require the activation of p44/42 extracellular signal-regulated kinase (ERK) via a 12-lipoxygenase-mediated pathway. The cell death process also involves activation of NADPH oxidase, generation of reactive oxygen species, DNA damage, and overactivation of poly(ADP-ribose) polymerase, all occurring downstream from ERK phosphorylation. The Cosmetic Ingredient Review Expert Panel noted the in vitro evidence of neurotoxicity but concluded that the absence of any neurotoxicity findings in the many in vivo studies, including

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- Aspiration hazard: No data available.

Likely routes of exposure

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the carcinogenicity study in rats there was no treatment-related increase in the incidence of any tumor in either sex. MIT was not found to be fetotoxic, embryotoxic, or teratogenic in rats. MIT was positive in the Ames assay in TA100 at concentrations as low as 0.0005 uL/plate without metabolic activation. TA100 with activation and all other strains with and without metabolic activation were negative. MIT was positive in the mouse lymphoma gene mutation assay at dose levels as low as 1 nL/mL without metabolic activation and at 1.22 nL/mL with metabolic activation. Negative results were observed in the Drosophila sex-linked recessive lethal assay. MIT did not cause a significant increase in the frequency of structural chromosome aberrations in mouse bone marrow cells in vivo, and did not induce unscheduled DNA synthesis in primary rat hepatocytes in vitro. However, in vitro study in rat cortical neurons found that MIT induced a dramatic inhibition of neurite outgrowth, and concluded that prolonged exposure to low levels of MIT and related compounds may have damaging consequences to the developing nervous system.

Symptoms related to the physical, chemical and toxicological characteristics

- IDENTIFICATION AND USE: Methylisothiazolinone (MIT) forms colorless prisms. It is used as preservative in personal care and cosmetics products such as leave-on products, namely hand and body lotions and moisturizers, sun tanning lotions and some rinse-off products like shampoos, surfactants and conditioners. In addition, MIT is an antimicrobial used to control slime-forming bacteria, fungi, and algae in cooling water systems, fuel storage tanks, pulp and paper mill water systems, oil extraction systems, and other industrial settings. It is also used to control the growth of mold, mildew, and sapstain on wood products. It is registered for use in the USA but approved pesticide uses may change periodically and so federal, state and local authorities must be consulted for currently approved uses. It is often used in a combination products with 5-chloro-2-methyl-4-isothiazolin-3-one. HUMAN EXPOSURE AND TOXICITY: In vitro studies show that a brief exposure to MIT is highly toxic to cultured neurons but not to glia. The toxic actions of this biocide are zinc-dependent and require the activation of p44/42 extracellular signal-regulated kinase (ERK) via a 12-lipoxygenase-mediated pathway. The cell death process also involves activation of NADPH oxidase, generation of reactive oxygen species, DNA damage, and overactivation of poly(ADP-ribose) polymerase, all occurring downstream from ERK phosphorylation. The Cosmetic Ingredient Review Expert Panel noted the in vitro evidence of neurotoxicity but concluded that the absence of any neurotoxicity findings in the many in vivo studies, including subchronic, chronic, and reproductive and developmental animal studies, suggests that MIT would not be neurotoxic as used in cosmetics. Although recognizing that MIT was a sensitizer in both animal and human studies, the panel concluded that there is a threshold dose response and that cosmetic products formulated to contain concentrations of MIT at 100 ppm (0.01%) or less would not be expected to pose a sensitization risk. Accordingly, MIT may be safely used as a preservative in cosmetics up to that concentration. ANIMAL STUDIES: The exposure of rats to MIT at dose levels up to 2.64 mg/cu m via inhalation for 90 days resulted in decreased body weight in the high-dose males and decreased body-weight gains in both sexes at the high-dose level. There were no treatment-related deaths, and no effects were observed in the hematology, clinical chemistry, ophthalmoscopic, and gross pathology parameters that could be attributed to treatment. Similar observations were made when rats were exposed to this chemical (up to 225 ppm) in drinking water for 3 months. In the carcinogenicity study in rats there was no treatment-related increase in the incidence of any tumor in either sex. MIT was not found to be fetotoxic, embryotoxic, or teratogenic in rats. MIT was positive in the Ames assay in TA100 at concentrations as low as 0.0005 uL/plate without metabolic activation. TA100 with activation and all other strains with and without metabolic activation were negative. MIT was positive in the mouse lymphoma gene mutation assay at dose levels as low as 1 nL/mL without metabolic activation and at 1.22 nL/mL with metabolic activation. Negative results were observed in the Drosophila sex-linked recessive lethal assay. MIT did not cause a significant increase in the frequency of structural chromosome aberrations in mouse bone marrow cells in vivo, and did not induce unscheduled DNA synthesis in primary rat hepatocytes in vitro. However, in vitro study in rat cortical neurons found that MIT induced a dramatic inhibition of neurite outgrowth, and concluded that prolonged exposure to low levels of MIT and related compounds may have damaging consequences to the developing nervous system.

SECTION 12: Ecological information

Not available

SECTION 13: Disposal considerations

Not available

SECTION 14: Transport information

Not available

SECTION 15: Regulatory information

Not available

SECTION 16: Other information

Not available

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