BUDESONIDE

MATERIAL SAFETY DATA SHEET

In accordance with Regulation (CE) 1907/2006, (CE) 1272/2008 and (EU) 453/2010 (Annex I)

Revision no. 4 - Revision date: April 5, 2012

SECTION 1.
IDENTIFICATION OF THE SUBSTANCE AND OF THE COMPANY

1.1. Substance identifier

Substance name:	**BUDESONIDE**
Other names (if available): Name in Annex VI-CLP: Name reported in the inventory of harmonized classification and labelling:	16-α,17-[(1RS)-Butylidene (oxy)]-11-β,21-dihydroxypregna-1,4-diene-3,20-dione unlisted not available
CAS number	51333-22-3
REACH registration number	Exempt of registration

1.2. Relevant identified uses of the substance and uses advised against

Relevant use(s)	Sybthetic hormone - API (Active Pharmaceutical Ingredient)
Uses advised against	none

1.3. Details of the supplier of the safety data sheet

Manufacturer/Distributor:
Company name: **STERLING S.r.l**
Address : **Via della Carboneria, 30 Solomeo**
06073 Corciano (PG) – Italy
Phone number : 075/5294001
Fax number: 075/5294000

Competent person responsible for the safety data sheet:
Aragona Anna Alessandra
e-mail: aragona@sterling.it

1.4. Emergency telephone number

02 66101029 (Centro Antiveleni Niguarda Ca' Granda – Milano)

SECTION 2
HAZARDS IDENTIFICATION

2.1 Classification of the substance

- **Classification of the substance in accordance with Regulation (CE) n. 1272/2008:**

Hazard class	Class code and hazard category	Hazard statement	Hazard warning
Aquatic environment	**Aquatic chronic 3**	**H412**	**Harmful to aquatic life with long lasting effects.**

- **Classification in accordance with Directive 67/548/CEE :**

Classification	Risk phrases	
R52/53	**R52/53**	**Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment**

Main adverse effects

Physico-chemical effects — No adverse effects known.

Health effects — Therapeutic use of corticosteroids may cause adverse effects due to the mineralocorticoid or glucocorticoid actions or from inhibition of the hypothalamic-pituitary-adrenal axis. The incidence of adverse effects increases with dose and duration of exposure; effects are rare with administration of less than three weeks.
Symptoms from chronic exposure may include acne; pain in hips, shoulders, back, ribs, arms, or legs; filling or rounding out of face; increased hair growth; menstrual irregularities; muscle weakness, cramps, or pain; reddish-purple lines on skin; bruising; weight gain or loss; change in appetite; swelling of feet or lower legs; changes in vision; eye pain; irregular heartbeat; unusual tiredness or weakness; headache; insomnia; abdominal or stomach pain; nausea; vomiting; bloody or black, tarry stools; mood or mental changes; and increased susceptibility to infection. Inhalation may cause dry mouth, hoarseness, sore throat, creamy white patches in mouth or throat, and difficulty swallowing. Possible allergic reaction to material if inhaled, ingested or in contact with skin.

Environmental effects — Harmful to aquatic life with long lasting effects.

See also sections from 9 to 12

2.2 Label elements

- **Labelling in accordance with regulation n. 1272/2008/EC**

Warning	**None**
Signal Word	**None**
Hazard indication (H))[1]	**H412 - Harmful to aquatic life with long lasting effects.**
Safety statements (P)[1]	
- Prevention	**P273**
- Reaction	**-**
- Storage	**-**
- Disposal	**P501**

[1] For the explanation of H and P statements: see Section 16

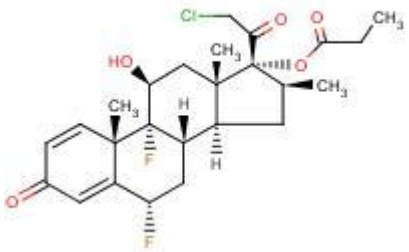
2.3 Other hazards (which do not results in the classification)

The substance satisfies the PBT criteria	YES	NO
- PBT		X
- vPvB		X

- Health hazards	May be harmful if ingested, inhaled or in contact with skin. May be irritant or sensitizer. The incidence of adverse effects increases with dose and duration of exposure; effects are rare with administration of less than three weeks.
- Environmental hazards	Other not known
- Physico-chemical hazards	none
- Specific effects	unknown

SECTION 3
COMPOSITION/INFORMATION ON INGREDIENTS

Description: Active Pharmaceutical Principle; anti-inflammatory corticosteroid

Name of the component	Budesonide
Concentration	Pure substance
Structural formula	
Chemical formula	$C_{25}H_{34}O_6$
Molecular weight	430.5 g/mol
Substance with Community OEL	No
CAS name	Pregna-1,4-diene-3,20-dione, 16,17-[butylidenebis(oxy)]-11,21-dihydroxy-, (11.beta.,16.alpha.)-
CAS number	51333-22-3
IUPAC name	11β,21-dihydroxy-16α,17α-(butane-1,1-diyldioxy)pregna-1,4-diene-3,20-dione
EC number	257-139-7
Index number	not assigned
Impurity/ies (if classified)	-
Additive/ies (if classified)	-

SECTION 4
FIRST AID MEASURES

4.1 Description of the first aid measures

- Eye contact	Wash immediately with large amounts of water or normal saline. Keep eyelid open during the washing. Get medical advice if adverse symptoms will appear.
- Skin contact	Remove contaminated clothes (eventually shoes). Wash affected area with soap or mild detergent and large amount of water until no evidence of substance remains. Get medical advice if adverse symptoms will appear.
- Ingestion	If swallowed wash mouth with large amounts of water provided person is conscious. If victim is conscious and alert, give milk or water. Get medical advice if adverse symptoms will appear.
- Inhalation	Remove the person from the exposed area to fresh air immediately. If breathing has stopped perform artificial respiration, keep person warm and at rest. Get medical advice if the exposure was significant in terms of quantity or time.

4.2 Most important symptoms and effects (acute and delayed)

- Acute effects	Possible eye, skin, gastrointestinal, and/or respiratory tract irritation.
- Delayed effects:	Symptoms from chronic exposure may include acne; pain in hips, shoulders, back, ribs, arms, or legs; filling or rounding out of face; increased hair growth; menstrual irregularities; muscle weakness, cramps, or pain; reddish-purple lines on skin; bruising; weight gain or loss; change in appetite; swelling of feet or lower legs; changes in vision; eye pain; irregular heartbeat; unusual tiredness or weakness; headache; insomnia; abdominal or stomach pain; nausea; vomiting; bloody or black, tarry stools; mood or mental changes; and increased susceptibility to infection. Inhalation may cause dry mouth, hoarseness, sore throat, creamy white patches in mouth or throat, and difficulty swallowing. Possible allergic reaction to material if inhaled, ingested or in contact with skin.

4.3 Indication of any immediate medical attention and special treatment needed

Medical monitoring:	none
- Antidotes, if known	unknow
- Contraindications	unknow
- Immediate treatment at workplace	not known

SECTION 5
FIREFIGHTING MEASURES

5.1 Extinguishing media

- Suitable estinguishing media	Water spray or chemical foam, dry foam, CO_2.
- Unsuitable estinguishing media	not known

5.2 Special hazards arising from the substance

- Hazardous combustion products	May generate toxic fumes of Cox.
- Other special hazards	not known

5.3 Advice fo firefighters

- *Technical actions for protection*	Keep containers cool with water.
- *Special protective equipment for firefighters*	Wear boots, overalls, gloves, eye and face protection and breathing apparatus. Equipment must be conformed with EN criteria and used in highest condition of protection on the basis of the information reported in the previous sub-sections

SECTION 6
ACCIDENTAL RELEASE MEASURES

6.1 Personal precautions, protective equipment and emergency procedures

- For non-emergency personnel
Wear appropriate protective equipment (see Section 8) to prevent contamination of the skin, eyes and personal clothing.
In case of fire and/or and explosions avoid breathing fumes and vapors. Use a self-contained breathing apparatus (SCBA) and appropriate protective clothing. The fumes can be eliminated by spraying with water.
See also section 8

- **For emergency responders**
See section 8.

6.2 Environmental precautions

In case of accidental release in the environment avoid that the substance can reach drains, surface water and ground water. Contact local authorities in case of environmental release.

6.3 Methods and material for containment and clearing up

- *Containment procedures:*	Coverage of the discharges
- *Cleaning up procedures:*	Recover the substance for suction or other mechanical means and wash the area with plenty of water and detergents. Store the material into a company that specializes pending disposal. Containers must be cleaned up and disposed of as waste remediation above.

6.4 Reference to other sections

See also section 8 and 13.

SECTION 7
HANDLING AND STORAGE

7.1. Precautions for safe handling

- *Recommandation for handling:*	Handle away from sparkles and flames - sources of ignition Handle in a well ventilated place Avoid contact with incompatible materials Wear suitable Personal Protection Equipment (see section 8) Keep the substance away from drains, surface or ground waters
- *Recommandation for personal hygiene:*	Do not eat, drink and smoke in the working areas Wash hands after handling the substance Remove contaminated clothing and protective equipment before entering eating areas

7.2. Condition for safe storage including any incompatibilities

The substance is not classified for any physical and chemical properties and no risk management is foreseen.

Other advice

	Store at controlled room temperature
	Store in the original package
- *Ventilation requirements*	Use in a well ventilated place at room temperature
- *Containers*	Keep containers tightly closed and correctly labelled
- *Specific design of storage rooms*	Not requested on the base of the classification
- *Quantity limits for storage*	Not requested on the base of the classification
- *Packaging compatibilities*	See also section 10.5

7.3. Specific end use(s)

- Recommendation for specific final use(s): Active Pharmaceutical Principle

	YES	NO
- Exposure scenario attached		X
- Chemical Safety Assessment (CSA) attached		X
- Industry or sector specific guidance available and attached		X

SECTION 8
EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control parameters

- National/European Occupational Exposure Limits	unknow
- Other National/European Occupational Exposure Limits	unknow
- Recommended monitoring procedures	The measurement of substances in the workplace must be carried out with standardized methods (eg EN 689:1997: Workplace atmospheres - Guide for assessment of exposure by inhalation to chemical agents for comparison with limit values and measurement strategy; UNI EN 482:2006: atmospheres in the workplace - General requirements for the provision of procedures for the measurement of chemical agents) or, failing that, with appropriate methods.
- DNEL values (components)	unknow
- PNEC values (components)	unknow

8.2. Exposure controls

	YES	NO
- Exposure scenario attached		X
- Chemical Safety Assessment (CSA) attached		X

8.2.1. Appropriate engineering controls

The adoption of the most appropriate technical controls is also based on the local Risk Assessment done by the employer in its workplace conditions (use of the substance) when a unique and standardized exposure scenario described in a dossier registered REACH is not available.

8.2.2. Individual protection measures, such as Personal Protective Equipment (PPE)

a) Eye and Face protection	Safety goggles as for EN 166; facial shield
b) Skin protection	
- *hands protection*	Wear protective gloves. Gloves resistant to chemical agents as for the EN 374, parts 1, 2 e 3 and the European Directive 89/89/CEE. The glove material has to be made of rubber or polyethylene impermeable and resistant to the substance. Make the choice of the glove material on consideration of the penetration times, rates of diffusion and degradation. The selection of suitable gloves not only depends on the material, but also on further marks of quality and varies from manufacturer to manufacturer.
- *other, body protection*	Select the suitable protective equipment based on the activity of use and possible exposure. Wear gauntlets, boots, bodysuit and other devices in accordance with EN 13982.
c) Respiratory protection	Dust mask with approved dust filter. Use only devices approved by the Competent Authorities such as NIOSH (USA) and CEN (EU) In the case of brief exposure or minimal exposure use respiratory filter; in case of intensive and sustained exposition wear self-contained breathing. Where risk assessment shows air-purifying respirators are appropriate use a dust mask type P3 (EN 143) respirator
d) Thermal hazards	Not foreseen in the standard use. Assess possible Personal Protection Equipment on the basis of specific uses of the substance.

8.2.3 Environmental exposure controls

	YES	NO
- Exposure scenario attached		X
- Chemical Safety Assessment (CSA) attached		X

SECTION 9
PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on basic physical and chemical properties

Appearance:	white or whitish solid (powder)
Odor:	-
Odour threshold:	-
pH:	Data not available in the literature search carried out
Melting point:	220 °C (1)
Boiling point:	599.7 °C (predicted) (2)
Flash point:	201.8 °C (predicted) (2)
Auto-ignition temperature:	Data not available in the literature search carried out
Surface tension:	55.2 dyne/cm (predicted) (2)
Vapour pressure:	6.94x 10^{-17} mmHg at 25°C (predicted) (2)
Density:	1,27 g/cm³ (predicted) (2)
Water solubility:	Insoluble; 0.7874 (predicted) (2)
Organic solvent solubility:	Soluble in dichloromethane and sparingly soluble in ethanol.
Partition coefficient Octonol/water	

(Log Kow):	3.14 (predicted by ACS/Lab); 3.98 (predicted by EPISuite) [2]
Explosive properties:	Data not available in the literature search carried out
Oxidising properties:	Data not available in the literature search carried out

9.2. Other information

Henrys Law Constant (25 °C) :	6.56 x10^{-13} atm-m^3/mole (predicted) [2]
Atmospheric OH Rate Constant (25 °C):	1.28 x10^{-10} cm^3/molecule-sec [1]

SECTION 10
STABILITY AND REACTIVITY

10.1. Reactivity

Stable in normal conditions of storage.

10.2. Chemical stability

The substance is stable at the normal condition of temperature and pressure and if stored in closed containers in well ventilated and cool place.

	NO	YES	Used stabiliser
- Stabilisers:	X	-	
- Change in physical appearance	X	-	

10.3. Possibility of hazardous reactions

	NO	YES
- Possibility of an exothermic reaction:	X	-
- Possibility of a reaction releasing excessive pressure	X	-
- Possible degradation with instable product formation	X	-

10.4. Condition to avoid

Keep protected from light, humidity and high temperatures.

10.5. Incompatible materials

Strong oxidizing agents

10.6. hazardous decomposition products

If heated at high temperatures, decomposes re leasing fumes and toxic gases of Cox.

SECTION 11
INFORMATION ON TOXICOLOGICAL EFFECTS

- **Exposure routes:**	YES	NO
- Inhalation:	X	
- Ingestion:	X	
- Skin contact:	X	
- Eye contact:	X	

- Effects (acute, delayed, chronic) following the exposure (short and/or prolonged):

- *Inhalation:* May be harmful or sensitizing by inhalation
- *Ingestion:* May be harmful if swallowed
- *Skin contact:* May be irritant or sensitizing.
- *Eye contact:* May be irritant

-Toxico-kinetics information (ADME=Adsorption,**D**istribution,**M**etabolism,**E**xcretion**):** (3)

Adsorption: total absolute bioavailability following administration of inhalation suspension was approx. 6% of the labeled dose. Peak plasma concentration of 2.6 nmol/L was obtained approximately 20 minutes after nebulization of a 1 mg dose.

Distribution: the volume of distribution at steady-state was 3 L/kg. Budesonide is 85 to 90% bound to plasma protein. The substance showed little or no binding to corticosteroid-binding globulin. Budesonide rapidly equilibrated with red blood cells in a concentration independent manner with a blood/plasma ratio of about 0.8.

Metabolism: budesonide is rapidly and extensively metabolized. Two major metabolites are 16 α -hydroxyprednisolone and 6β -hydroxybudesonide. The corticosteroid activity of each of these two metabolites is less than 1% of that of the parent compound.

Excretion: Budesonide is primarily cleared by the liver and is excreted in urine and feces in the form of metabolites. In adults, approximately 60% of an intravenous radiolabeled dose was recovered in the urine. No unchanged budesonide was detected in the urine.

- Acute toxicity effects:

- *Oral:* DL50 Orale - ratto > 3200 ml/kg (4)
  Effects: Nutrition and metabolism - weight loss or weight gain reduced
  DL50 Orale - topo 4750 ml/kg (4)
  Effects: Behavioral - altered sleep time (including change in righting reflex). Somnolence (general depressed activity)
- *Dermal:* Data not available in the literature search carried out
- *Inhalation:* Data not available in the literature search carried out
- *Other effects:* (4) DL50 subcutaneous rat 58,4 mg/kg Effects: Behavioral - altered sleep time (including change in righting reflex). Blood - changes in spleen
  LD50 subcutaneous mouse 53.6 mg/kg Effects: Behavioral - altered sleep time (including change in righting reflex). Somnolence (general depressed activity)
  DL50 Intraperitoneal rat 138 mg/kg Effects: Behavioral - altered sleep time (including change in righting reflex). Blood - changes in spleen
  DL50 Intraperitoneal mouse 179 mg/kg Effects: Behavioral - altered sleep time (including change in righting reflex). Somnolence (general depressed activity)
  DL50 Intraverous rat 98.9 mg/kg Effects: Behavioral - altered sleep time (including change in righting reflex); convulsions or effect on seizure threshold
  DL50 Intraverous mouse 124 mg/kg Effects: Behavioral - altered sleep time (including change in righting reflex); convulsions or effect on seizure threshold.

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- Corrosion/Irritation effects: Data not available in the literature search carried out

- Severe ocular lesion *:* Data not available in the literature search carried out

- Sensitisation: Data not available in the literature search carried out

- **Repeated dose toxicity** (experimental.): Data not available in the literature search carried out

- CMR effects:

- **Germinal cell mutagenicity** [3]: Budesonide was not mutagenic or clastogenic in six different test systems: Ames Salmonella/microsome plate test, mouse micronucleus test, mouse lymphoma test, chromosome aberration test in human lymphocytes, sexlinked recessive lethal test in Drosophila melanogaster , and DNA repair analysis in rat hepatocyte culture.

- **Carcinogenicity** [3]:
In a two-year study in Sprague-Dawley rats, budesonide caused a statistically significant increase in the incidence of gliomas in male rats at an oral dose of 50 mcg/kg. No tumorigenicity was seen in male and female rats at respective oral doses up to 25 and 50 mcg/kg. In two additional two-year studies in male Fischer and Sprague-Dawley rats, budesonide caused no gliomas at an oral dose of 50 mcg/kg. However, in the male Sprague-Dawley rats, budesonide caused a statistically significant increase in the incidence of hepatocellular tumors at an oral dose of 50 mcg/kg.
In a 91-week study in mice, budesonide caused no treatment-related carcinogenicity at oral doses up to 200 mcg/kg.
- **Reproductive toxicity** [3],[7]:
Budesonide caused birth defects and fetal death in rabbits and rats at high and low doses:
.
TDLo - Lowest published toxic dose, Subcutaneous. Rat = 220 µg/kg
female 7-17 day(s) after conception
Note: Reproductive – Fertility – litter size (e.g. # fetuses per litter; measured before birth).
- Effects on Embryo or Fetus - fetotoxicity (except death, e.g., stunted fetus).
– Specific developmental abnormalities – musculoskeletal system.

TDLo - Lowest published toxic dose, Subcutaneous. Rat = 540 µg/kg
female 17 - 22 day(s) after conception. Lactating female 21 days post-birth
Note: Reproductive – effects on Newborn – sex ratio, physical.

TDLo - Lowest published toxic dose, Subcutaneous. Rat = 21600 ng/kg
female 17 - 22 day(s) after conception. Lactating female 21 days post-birth
Note: Reproductive – fertility – litter size (e.g. # fetuses per litter; measured before birth)
– effects on embryio or fetus – fetotoxicity (except death, e.g., stunted fetus)

TDLo - Lowest published toxic dose, Subcutaneous. Rabbit = 1625 µg/kg
female 6-18 day(s) after conception
Note: Reproductive – Fertility – abortion.

Experience with oral corticosteroids since their introduction in pharmacologic, as opposed to physiologic, doses
suggests that rodents are more prone to teratogenic effects from corticosteroids than humans.
Studies in pregnant women who received budesonide by inhalation during pregnancy did not show an increased risk of abnormalities
PregnancyTeratogenic EffectsPregnancy category B – animal studies have shown an adverse effect, but adeguate and well-controlled studies in pregnant women have failed to demonstrate a risk to fetus in any trimester

- Specific Target Organ Toxicity (STOT)-single exposure: Data not available in the literature search carried out

- Specific Target Organ Toxicity (STOT)- repeated exposure : Data not available in the literature search carried out

- Aspiration hazards: Data not available in the literature search carried out

- Epidemiological information: [5]
Budesonide, like other corticosteroids, is secreted in human milk. The amounts of inhaled budesonide excreted into breastmilk are minute and infant exposure is negligible.

Controlled clinical studies have shown that inhaled corticosteroids may cause a reduction in growth velocity in pediatric patients.

SECTION 12
ECOLOGICAL INFORMATION

12.1. Toxicity

LC50-96 Hour - fish : >19 mg/L [6]
EC50-48 Hour-Daphnia magna : 20 mg/L [6]
IC50-72h-Algae : >19 mg/L [6]

12.2. Persistence and degradability

Degradability : Minimally biodegradable

12.3. Bioaccumulative potential

BCF = 143.76 (predicted) [2]
Log Pow = 3.14 (predicted by ACS/Lab); .3.98 (predicted by EPISuite) [2]

12.4. Mobility in soil

Data not available in the literature search carried out

12.5. Results of PBT e vPvB assessment

Assessment is not available - in relation to the value of logPow and BCF a medium bioaccumulation potential is expected.

12.6. Other adverse effects

Not known

SECTION 13
DISPOSAL CONSIDERATION

13.1. Waste treatment methods

	Incineration	Recycling	Landfilling
- Mixture wastes:	X		
- Contaminated packaging:		X	

Should never be disposed through wastewater.
Refers to Community/National/Local requirements concerning the waste disposal.

SECTION 14
TRANSPORT INFORMATION

The substance is not classified for transport.

SECTION 15
REGULATORY INFORMATION

15.1 Safety, Health and Environmental regulation/legislation specific for the mixture or its ingredients

Council Directive 89/391/EEC of 12 June 1989 on the introduction of measures to encourage improvements in the safety and health of workers at work and following amendment and National reinforcements..

Council Directive 89/686/EEC of 21 December 1989 on the approximation of the laws of the Member States relating to the personal protective equipment

Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC) Official Journal L 131 , 05/05/1998 P. 0011 – 0023

Regulation (EC) no 689/2008 of the european parliament and of the council of 17 June 2008 concerning the export and import of dangerous chemicals.

15.2. Chemical Safety Assessment

	YES	NO
- Exposure scenario attached		X
- Chemical Safety Assessment (CSA) attached		X

SECTION 16
OTHER INFORMATION

Revisions:

- **Revision n. 03 dated** January 2011 (regarding all sections in according to Regulation no. 453/2010).

Bibliographic sources:

(1) ChemIDplus Lite data base, search for CAS no. 51333-22-3
(2) Chemspider data base, search for CAS 51333-22-3
(3) Daily Med, Current Medication Information, BUDESONIDE (budesonide) suspension
(4) Kiso to Rinsho.Clinical Report.Vol. 19, Pg. 4377, 1985.
(5) Budesonide - National Library of Medicine LactMed Database
(6) EDQM European Directorate for the Quality for Medices and Healthcare, Safety data sheet B1157300 of 9/6/2009
(7) RTECS NUMBER-TU3723000-Chemical Toxicity Database

Acronyms

- ACGIH: American Conference of Governmental Industrial Hygienists
- ADR: Agreement concerning the carriage of dangerous goods by Road
- BCF: Bioaccumulative factor
- BEI : Biological Esposure Indices (Indici di esposizione biologica)
- CAS: Chemical Abstract Service (division of the American Chemical Society

- CLP: Classification, Labelling and Packaging
- CMR: Carcinogens, Mutagens, Toxic for re production substances
- EINECS: European Inventory of existing Commercial Substances
- EPA: US Environmental Protection Agency
- GHS: Globally Harmonised System
- IARC: International Agency for Research on Cancer
- IATA: International Air Transport Association Code
- IMDG: International Maritime Dangerous Goods Code
- IUPAC: International Union of Pure and Applied Chemistry
- LOEL: Lowest Observed Effect Level
- NOAEL: No Observed Adverse Effect Level)
- NTP: National Toxicology Program
- OEL: Occupational Exposure Limit
- OSHA: Occupational Safety and Health Administration
- PPE : Personal protective Equipment
- PBT: Persistent, Bioaccumulative and Toxic substances
- RID: Regulation concerning the International carriage of Dangerous goods by rail
- TLV/TWA: Threshold Limit Value/Threshold Weighted Average
- vPvB: very Persistent, very Bioaccumulative

Information related to the regulation CE/1272/2008

List of hazards statements

H412: **Harmful to aquatic life with long lasting effects.**

List of P statements

Prevention

P273 **Avoid release to the environment.**

Reaction -

Storage -

Disposal

P501: **Dispose of contents/container in accordance with local/regional/ national/international regulation.**

Information related to the Directive 67/ 548/ CEE, Directive 1999/45/CE and Regulation (CE) n. 1907/2006

R phrases

R52/53: **Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.**

Information on workers training

Follow criteria of Directive 98/24/CE, its amendments and National reinforcements

Restriction of use : None

Substance under authorisation : no

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