

**IDENTIFICATION OF THE PRODUCT AND OF THE COMPANY**

**Identification of the product**

Product Name: **COATEST™ APC™ Resistance**

Product Number: **00082264363**

Use of the product: For in vitro diagnostic use

**Company identification:**

MANUFACTURER:  
Instrumentation Laboratory Co.  
180 Hartwell Road,  
Bedford, MA 01730-2443 (USA)  
Tel. +1 800 678 0710  
Fax +1 781 863 9928

DISTRIBUTOR EU:  
Via Leonardo da Vinci, 36  
20877 Roncello (MB), Italy

DISTRIBUTOR US/CANADA:  
DiaPharma Group, Inc.  
8948 Beckett Rd.  
West Chester, OH 45069 (USA)

E-mail address of the competent person: [infosds@mail.ilww.it](mailto:infosds@mail.ilww.it)

Emergency phone: +44 (0) 3700 492 795  
+1 215 207 0061 (USA and Canada)

**INFORMATION ON COMPOSITION/HAZARD OF THE PRODUCT**

| P/N       | Mixture name          | Mixture classification<br>According to<br>Hazard Communication Standard,<br>29 CFR 1910.1200 (HCS)<br>Hazardous Product Regulation HPR (WHMIS 2015) | Mixture classification<br>According to<br>1272/2008/EC Regulation | Kit<br>configuration |
|-----------|-----------------------|---|---|----------------------|
| 000H00527 | CaCl <sub>2</sub>     | Not classified  | Not classified  | 1 x 8 ml             |
| 000H01176 | APTT Reagent          | Not classified  | Not classified  | 1 x 16 ml            |
| 000H01422 | APC/CaCl <sub>2</sub> | Sensitization-Respiratory, cat. 1   | Not classified  | 4 x 2 ml             |

**Disclaimer**

This document is intended only as a guide to appropriate precautionary handling of this product by a trained person, or supervised by a person trained in chemical handling. The product shall not be used for purposes different from those indicated in section 1, unless having received suitable written instructions on how to handle the material. Use the product in accordance with the Good Laboratory Practice. This document cannot describe all potential dangers of use or interaction with other chemicals or materials. It is the user's responsibility for the product's safe use, the product's suitability for the intended use and the product's safe disposal. No representation or warranties, either expressed or implied, of merchantability, fitness for a particular purpose or of any other nature are made hereunder with respect to the information set forth herein or to the product to which the information refers. The contained information in this SDS are in accordance with Annex II of the Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) and its subsequent amendments, in accordance with Hazard Communication Standard (HCS), 29 CFR 1910.1200 (HazCom 2012) as recommended by US OSHA, and in accordance with Hazardous Product Regulation HPR (WHMIS 2015) as recommended by Health Canada (HC).

Prepared by: Chemsafe Srl

**SECTION 1. IDENTIFICATION OF THE MIXTURE AND OF THE COMPANY**

**1.1 Identification of the mixture**

Product Name: **CaCl<sub>2</sub>**  
Product Number: **000H00527**

**1.2 Use of the mixture:**

Relevant use: For in vitro diagnostic use.  
Uses advised against: There are no specific uses advised against.

**1.3 Company identification:**

MANUFACTURER:  
Instrumentation Laboratory Co.  
180 Hartwell Road,  
Bedford, MA 01730-2443 (USA)  
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**1.4 Emergency phone:** +44 (0) 3700 492 795  
+1 215 207 0061 (USA and Canada)

**SECTION 2. HAZARDS IDENTIFICATION**

**2.1 Classification of the mixture:**

This product is not hazardous according to Regulations (EC) No 1272/2008, OSHA 29 CFR 1910.1200 and Hazardous Product Regulation HPR (WHMIS 2015).

Any additional information concerning the risks for health and/or the environment are given in sections 11 and 12 of this sheet.

**According to Regulation (EC) No 1272/2008, according to Hazard Communication Standard, 29 CFR 1910.1200 (HCS), and according to Hazardous Product Regulation HPR (WHMIS 2015):**

| <i>Hazard class</i>                  | <i>Hazard category</i> | <i>Hazard statement</i> |
|--------------------------------------|------------------------|-------------------------|
| <b>Not classified</b>                |                        |                         |
| <i>For exposure limits see Ch. 8</i> |                        |                         |

**Potential adverse physicochemical, human health and environmental effects** *(see also Ch. 9-12)*

Under normal conditions of use, the mixture does not cause adverse effects to humans and to the environment.

**2.2 Label elements, according to Regulation (EC) No 1272/2008, according to Hazard Communication Standard, 29 CFR 1910.1200 (HCS), and according to Hazardous Product Regulation HPR (WHMIS 2015):**

|                                    |      |
|------------------------------------|------|
| <b>Hazard pictogram(s):</b>        | None |
| <b>Signal word(s):</b>             | None |
| <b>Hazard statement(s):</b>        | None |
| <b>Precautionary statement(s):</b> | None |
| <b>Other labeling details:</b>     | None |

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

The mixture does not meet the criteria for PBT or vPvB.

**Warning:**

The product contains bovine material. All donor animals were sourced from BSE-free herds. The cattle received ante- and post mortem health inspection by a veterinarian, and they were apparently free from infectious and contagious material. However, the material should be treated as potentially infectious.

Bovine serum albumin (BSA) might cause allergic skin reaction and/or allergy or asthma symptoms or breathing difficulties if inhaled.

**SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS**

**Composition:** Liquid containing organic and inorganic components, bovine source material.

**3.1 Hazardous components:**

| Name   | EINECS/<br>ELINCS n°                               | CAS n°   | Conc. %<br>w/w* | Classification<br>29 CFR 1910.1200 (HCS)<br>HPR (WHMIS 2015)   | Classification<br>1272/2008/EC  |
|--|--|--|-----------------|--|---|
| Calcium chloride dihydrate<br><i>Index N. (Annex VI of CLP Reg.):<br/>017-013-00-2</i> | 233-140-8<br>(as Calcium<br>chloride<br>anhydrous) | 10035-04-8<br>(10043-52-4<br>as Calcium<br>chloride anhydr.) | 0.3-0.6%        | Eye damage/irritation, cat. 2  | Eye Irrit.2, H319   |
| Tris Hydrochloride   | 214-684-5  | 1185-53-1  | 0.1-0.2%        | Skin Corrosion/Irritation, cat. 2<br>Eye damage/Eye Irritation, cat 2B   | Skin Irrit. 2, H315<br>Eye Irrit. 2, H319   |
| Tris-Hydroxymethyl aminomethane<br>(Tris Amino)  | 201-064-4  | 77-86-1  | 0.03-<br>0.05%  | Skin Corrosion/Irritation, cat. 2  | Skin Irrit. 2, H315   |
| 1,2-dibromo-2,4-dicyanobutane<br>(MDBGN)   | 252-681-0  | 35691-65-7   | 0.01-<br>0.02%  | Acute Tox. – Oral, cat. 4<br>Skin Corrosion/Irritation, cat. 2<br>Eye damage/irritation, cat. 1<br>Sensitization – Skin, cat.1<br>Aquatic Acute, cat 1** | Acute Tox. 4, H302<br>Skin Irrit. 2, H315<br>Eye Dam. 1, H318<br>Skin Sens. 1, H317<br>Aquatic Acute 1, H400<br>(M=1) |

*For exposure limits see Ch. 8, for hazard statements text see Ch. 16.  
\* A range may be indicated, considering batch-to batch variation.  
\*\*Environmental classification according to Reg. N. 1272/2008 (EC) and subsequent amendments.*

The mixture contains one substance listed in the Hazardous Substance Lists and/or evaluated for carcinogenicity by IARC, NTP, OSHA: 1,2-dibromo-2,4-dicyanobutane. See Section 11 and 15.

**SECTION 4. FIRST AID MEASURES****4.1 Description of first aid measures**

|                      |  |
|----------------------|--|
| Ingestion:           | If swallowed rinse mouth with plenty of water provided person is conscious. Do not induce vomiting. Get medical advice if adverse symptoms appear.   |
| Inhalation exposure: | If inhaled, move person to fresh air. If breathing is difficult, oxygen should be administered. Get medical advice if adverse symptoms appear.   |
| Contact with skin:   | Remove contaminated clothes and shoes. Wash immediately affected area with soap or mild detergent and plenty of water until the removal of the mixture (15-20 minutes). Get medical advice if adverse symptoms appear. |
| Contact with eyes:   | Wash immediately with plenty of water or normal saline for at least 15 minutes. Keep eyelid open with the finger. Get medical advice if adverse symptoms appear.   |

**4.2 Most important symptoms and effects (acute and delayed)**

|          |   |
|----------|---|
| Acute:   | Inhalation: May cause irritation to the mucous membranes and upper respiratory tract.<br>Skin: May be irritant for skin.<br>Eyes: May cause irritation.<br>Ingestion: may cause irritation to the gastrointestinal mucous membranes.<br>Contains Bovine serum albumin (BSA), might cause allergic skin reaction and/or allergy or asthma symptoms or breathing difficulties if inhaled. |
| Delayed: | Delayed symptoms and effects are not known.   |

**4.3 Indication of any immediate medical attention and special treatment needed**

|                      |               |
|----------------------|---------------|
| Medical monitoring:  | Not foreseen. |
| Antidotes, if known: | Not known.    |

**SECTION 5. FIRE-FIGHTING MEASURES****5.1 Extinguishing media**

|                                 |  |
|---------------------------------|--|
| Suitable extinguishing media:   | Water spray or regular foam, CO <sub>2</sub> , dry powder. |
| Unsuitable extinguishing media: | Not known.   |

**5.2 Special hazards arising from the substance or mixture**

Hazardous combustion products: Thermal decomposition or combustion may generate toxic and hazardous fumes of CO<sub>x</sub>, HCl, HF, HBr, NO<sub>x</sub>.

**5.3 Advice for firefighters**

Protective actions: Water jets can be used successfully to cool containers exposed to the fire and disperse fumes.

Equipment for self-protection: Self-contained breathing apparatus, flame and chemical resistant clothing, boots and gloves. Equipment must be conformed with the national/international standards 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:** Remove the ignition and heat sources, provide sufficient ventilation and evacuate the area. Respiratory protection: is not required. Where risk assessment shows air-purifying respirators are appropriate, use masks with approved filter. Suitable protective clothing, rubber or polythene gloves, rubber shoes, safety glasses.

**For emergency responders:** Wear appropriate protective equipment (see Section 8) to minimize exposure to the product.

**6.2 Environmental precautions** Do not let the product enter drainage system, surface and ground-water or soil. Contact local authorities in case of environmental release. Do not empty into drains.

**6.3 Methods and material for containment and cleaning up** Soak up with inert absorbent material, and clean with plenty of water. Collect spilled material in containers. Send to the storage waiting for disposal procedures.

**6.4 Reference to other sections** See also section 8 and 13.

**SECTION 7. HANDLING AND STORAGE**

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

**7.2 Conditions for safe storage, incompatibilities** Recommended temperature: store at 2-8°C. Avoid light exposure and keep away from heat sources. Room ventilation: well ventilated workplace. Keep containers tightly closed and labelled with the name of the product. Avoid environmental release. Keep away from food and drinks.

**7.3 Specific end use** CaCl<sub>2</sub> is intended for in vitro diagnostic use. The material contains bovine material, and it should be treated as potentially infectious. Bovine serum albumin (BSA) might cause allergic skin reaction and/or allergy or asthma symptoms or breathing difficulties if inhaled. Use the product in accordance with the Good Laboratory Practice.

**SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION**

**8.1 Control parameters**

**Community/National occupational exposure limit values:**

**Calcium chloride** <sup>(1)</sup>

Canada – Ontario: Occupational exposure limit (OEL) for calcium chloride of 5 mg/m<sup>3</sup> has been established by the Ministry of Labor

**Community/National biological exposure limit values:** Not established.

**DNEL values (components):**

| Component                               | Route of exposure   | Workers       |          |                 |          | Consumers     |          |                 |          |
|---|---|---------------|----------|-----------------|----------|---------------|----------|-----------------|----------|
|   |   | Acute effects |          | Chronic effects |          | Acute effects |          | Chronic effects |          |
|   |   | local         | systemic | local           | systemic | local         | systemic | local           | systemic |
| Calcium chloride anhydr. <sup>(3)</sup> | Oral (mg/(mg/kg bw/day)<br>Dermal (mg/kg bw/day)<br>Inhalation (mg/m <sup>3</sup> ) | 10            |          | 5               |          | 5             |          | 2.5             |          |

The measurement of substances at the workplace must be carried out with standardized methods or, failing that, with appropriate methods.

**8.2 Exposure controls**

**8. 2. 1. Appropriate engineering controls**

Appropriate risk management measures, that must be adopted at the workplace, have to be selected and applied, following the risks assessment carried out by the employer, in connection with his working activity. If the results of this evaluation show that the general and collective prevention measures are not sufficient to reduce the risk, and if you cannot prevent exposure to the mixture by other means, adequate personal protective equipment must be adopted, complying with the relevant technical national/international standards.

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

|                           |  |
|---------------------------|--|
| Respiratory protection:   | Respiratory protection is not required. Where risk assessment shows air-purifying respirators are appropriate, use masks with approved filter.<br>Use only devices approved by the Competent Authorities such as NIOSH (USA) and CEN (EU). |
| Skin protection:          | Protective clothing, rubber gloves.  |
| Eye protection:           | Safety glasses.  |
| Hand protection:          | Protective gloves.   |
| Other protective systems: | Personal protective equipment (PPE) useful for reducing individual exposure.   |

**8.2.3. Environmental exposure controls**

Avoid any release into the environment.

**SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES**
**9.1 Information on basic physical and chemical properties**

|                       | Value  | Related to |
|-----------------------|--|------------|
| Appearance:           | Liquid   |            |
| Odor:                 | Not available                                  |            |
| Color:                | Not available                                  |            |
| pH:                   | not available                                  |            |
| Flammability:         | Aqueous solution, not expected to be flammable |            |
| Explosive properties: | Aqueous solution, not expected to be explosive |            |
| Oxidizing properties: | Aqueous solution, not expected to be oxidant   |            |
| Density:              | Not available                                  |            |
| Solubility:           | not available                                  |            |
| Water Solubility:     | Miscible                                       | Mixture    |
| Melting point/range:  | Liquid, not applicable                         |            |

**9.2 Other information**

|             |          |
|-------------|----------|
| Miscibility | miscible |
|-------------|----------|

**SECTION 10. STABILITY AND REACTIVITY**

|  |   |
|--|---|
| <b>10.1 Reactivity</b>                         | This mixture is considered not reactive under the normal conditions of the usage.   |
| <b>10.2 Chemical stability</b>                 | The product is stable until the expiration date shown on the box and on the labels when stored at 2 – 8 °C.                     |
| <b>10.3 Possibility of hazardous reactions</b> | Not foreseen.   |
| <b>10.4 Conditions to avoid:</b>               | Keep away from heat and light.  |
| <b>10.5 Incompatible materials</b>             | Strong oxidising agents.  |
| <b>10.6 Hazardous decomposition products:</b>  | Thermal decomposition or combustion may generate toxic and hazardous fumes of CO <sub>x</sub> , HF, HBr, HCl, NO <sub>x</sub> . |

**SECTION 11. TOXICOLOGICAL INFORMATION**

The health effects of the product have not been thoroughly investigated. Data on toxicological effects of the hazardous ingredients are provided bellow.

**11.1 Information on toxicological effects**
**Symptoms and effects for each route of exposure:**

|         |                            |
|---------|----------------------------|
| Dermal: | May cause skin irritation. |
|---------|----------------------------|

**Ingestion:** Ingestion may cause irritation to the gastrointestinal mucous membranes.

**Inhalation:** May cause irritation to the mucous membranes and upper respiratory tract.

**Contact with eyes:** May cause eye irritation.

**Other:** Contains Bovine serum albumin (BSA), might cause allergic skin reaction and/or allergy or asthma symptoms or breathing difficulties if inhaled.

**Toxicokinetic effects (Absorption, Distribution, Metabolism, Excretion):**

*Calcium chloride* : is easily dissociated into calcium and chloride ions in water. The absorption, the distribution and the excretion of the ions in animals are regulated separately. Both ions are essential constituents of the body of all animals. <sup>(1)</sup>

*Tris amino*: is not metabolized appreciably and is eliminated by the kidneys. Ionized tromethamine is excreted by kidney, so the effect is that of excretion of hydrogen ions. Elimination of drug from body is entirely by renal excretion. It is not known whether tromethamine is distributed into human milk. <sup>(4)</sup>

*1,2-dibromo-2,4-dicyanobutane (MDBGN)* is readily absorbed following oral and dermal administration. Once inside the body, is rapidly metabolized to 2-MGN before eventually being eliminated from the body, mostly via urine. Debromination of MDBGN occurs prior to systemic distribution; therefore, tissue exposure to parent chemical is expected to be low. <sup>(10)</sup>

| Acute toxicity         | Value                     | m.u.  | Effects  | Related to                                    |
|------------------------|---------------------------|---|--|---|
| <u>Oral:</u>           | LD50 (rat) > 3,000        | mg/kg   |  | <sup>(5)</sup> Tris Amino                     |
|                        | LD50 (rat) =3,798 - 4,179 | mg/Kg   | The acute oral toxicity is attributed to the severe irritating property of the original substance or its high-concentration solutions to the gastrointestinal tract. | <sup>(1)</sup> Calcium chloride               |
|                        | LD50 (rabbit)=500 – 1,000 |   |  |   |
| LD50 (rat) = 515 - 770 | mg/Kg                     | <sup>(11)</sup> 1,2-dibromo-2,4-dicyanobutane |  |   |
| <u>Dermal:</u>         | LD50 (rat) > 5,000        | mg/kg   |  | <sup>(6)</sup> Tris Amino                     |
|                        | LD50 (rabbit) > 5,000     | mg/Kg   |  | <sup>(1)</sup> Calcium chloride               |
|                        | LD50 (rabbit) > 5,000     | mg/Kg   |  | <sup>(11)</sup> 1,2-dibromo-2,4-dicyanobutane |
| <u>Inhalation:</u>     | LC50 (rat) > 40           | mg/m <sup>3</sup> /4h                         |  | <sup>(1)</sup> Calcium chloride               |
|                        | LC50 (rat) > 5,09         | mg/l/4h                                       |  | <sup>(12)</sup> 1,2-dibromo-2,4-dicyanobutane |
|                        | LC50 (rat) > 13           |   |  | <sup>(13)</sup> 1,2-dibromo-2,4-dicyanobutane |

**Corrosion/Irritation**

**Skin Corrosion/Irritation** *Tris Amino*: Tromethamine was a mild irritant to rabbits at 25% with a pH of 10.8. At 40%, tromethamine was not irritating. Intradermal injections of tromethamine were severely irritating to rabbits at pH 10.4 but were only mildly irritating at pH 7.4. The supporting substance 2-Amino-2-methyl-1-Propanol (AMP) was found to be irritating to rabbits, with burrowing lesions noted when applied to abraded skin sites; there was mild irritation noted when applied to unabraded skin. <sup>(5)</sup>

*Tris Hydrochloride*: irritant to skin (read across from Tris Amino).

*Calcium chloride* is not irritating for the skin. <sup>(1)</sup>

*1,2-dibromo-2,4-dicyanobutane* (Technical 98%) was severe irritant to rabbit skin. <sup>(14)</sup>

**Serious eye damage/ irritation** *Tris Amino (100%)* was not an ocular irritant when administered to rabbits. <sup>(5)</sup>

*Tris Hydrochloride* : mild eye irritant in rabbits. <sup>(17)</sup>

*Calcium chloride* is irritating for the eyes. <sup>(1)</sup>

*1,2-dibromo-2,4-dicyanobutane* : In pure form (98%) is a severe eye irritant. Instillation of 1,2-dibromo-2,4-dicyanobutane powder into the rabbit eye resulted in severe irritation, which persisted for at least 21 days post-instillation. <sup>(10)</sup>

**Sensitization:**

Skin sensitization: *Tris Amino*: The supporting chemical AMP is not sensitizing to guinea pig skin. <sup>(5)</sup>

*Tris Hydrochloride*: Not a sensitizer in experimental animals. <sup>(8)</sup>

*Calcium chloride*: Due to lack of data the classification is not possible.

*1,2-dibromo-2,4-dicyanobutane* : is a skin sensitizer agent, based on in vivo and in vitro animal data, and based on human data. <sup>(10)(15)</sup>

*Bovine serum albumin (BSA)*, which is present in bovine plasma, could develop allergic skin reactions in laboratory workers after dealing with BSA powder. Based on the available data, the criteria for classification are not satisfied.

Respiratory sensitization:

*Bovine serum albumin (BSA)*, which is present in bovine plasma, could develop allergic reactions in laboratory workers after dealing with BSA powder. It is reported a case of occupational asthma and rhinitis in a laboratory worker caused by the inhalation of 100% BSA powder. The patient had a high serum-specific IgE level to BSA, and experienced severe systemic reactions, including eye itching, conjunctivitis, rhinorrhea, nasal obstruction, sneezing, shortness of breath, bronchospasm and decreased blood pressure. It was suggested an IgE-mediated response as the pathogenic mechanism.<sup>(17)</sup> Based on the available data, the criteria for classification are not satisfied.

**CMR effects**

Germ cell mutagenicity:

*Tris Amino*: The supporting chemical, AMP, was not mutagenic to bacteria and mammalian cells in vitro, and did not induce micronuclei in mice in vivo.

*Tris Hydrochloride*: Ames test negative.<sup>(9)</sup>

*Calcium chloride*: Genetic toxicity of calcium chloride was negative in the bacterial mutation tests and the mammalian chromosome aberration test.<sup>(1)</sup>

*1,2-dibromo-2,4-dicyanobutane*: did not show evidence of mutagenic activity in a variety of in vitro and in vivo assays, except for one assay where increased frequencies of chromosomal aberrations in CHO cells were observed in an in vitro chromosomal aberration test<sup>(10)(16)</sup>

Reproductive toxicity:

*Tris Amino*: In an oral gavage combined reproductive/developmental toxicity screening test in rats no effects on reproductive or developmental parameters were observed at the doses tested; the NOAEL for reproductive and developmental toxicity is 1000 mg/kg-day, the highest dose tested.<sup>(5)</sup>

*Calcium chloride*: No reproductive toxicity study has been reported. A developmental toxicity study equivalent to an OECD Guideline Study reveals no toxic effects on dams or fetuses at doses up to 189 mg/kg bw/day (mice), 176 mg/kg bw/day (rats) and 169 mg/kg bw/day (rabbits).<sup>(1)</sup>

*1,2-dibromo-2,4-dicyanobutane*. In a study in rats exposed to 1,2-dibromo-2,4-dicyanobutane, a NOAEL for developmental toxicity was determined to be 175 mg/kg bw. Available information suggests that the substance is neither a reproductive nor a developmental toxin at doses that are not associated with maternal toxicity.<sup>(1)(12)(16)</sup>

Carcinogenesis:

Substances listed in the National Toxicology Program (NTP) Report on Carcinogens, in the International Agency for Research on Cancer (IARC) Monographs or found to be potential carcinogen by OSHA:

| Substance           | OSHA | IARC | NTP |
|---------------------|------|------|-----|
| No component listed |      |      |     |

*Tris Amino*: based on the available data, the substance is not carcinogenic.<sup>(7)</sup>

*1,2-dibromo-2,4-dicyanobutane*. Under the conditions of 2-year dermal studies there was no evidence of carcinogenic activity of 1,2-dibromo-2,4-dicyanobutane in male or female rats administered 2, 6, or 18 mg/kg.<sup>(10)(16)</sup>

**STOT –single exposure**

Not available.

**STOT – repeated exposure**

There are no documented long-term effects of *TRIS AMINO* treatment, and no serious side-effects on record that are directly attributed to treatment with the compound.<sup>(6)</sup>

*Calcium chloride*: A study for repeated dose oral toxicity in rats shows no adverse effect of calcium chloride on rats fed 20 mg CaCl<sub>2</sub>/g diet (comparable to 1000 mg/kg bw/day or more) for 12 months.<sup>(1)</sup>

*1,2-dibromo-2,4-dicyanobutane* : In long-term repeat feeding studies in animals, the observed effects were thyroid follicular cell hypertrophy, thyroid hyperplasia, increased pigmentation of the liver and spleen and increased extramedullary haematopoiesis when administered at high doses (4000 ppm) in dogs. Follow-up studies found no significant changes in levels of thyroid hormones. Repeated dermal application of 1,2-dibromo-2,4-dicyanobutane was associated with moderate to severe erythema and slight to moderate oedema.<sup>(10)(16)</sup>

**Aspiration hazards**

Not available.

**Other information:**

Not available.

**Reasons for the lack of classification:**

Where the mixture resulted in a non-classification, this may be due to the availability of data which does not impose a classification for that specific end-point, or due to lack of data, or due to availability of inconclusive data or data which are not sufficient to get a classification as for the criteria adopted in Regulations mentioned in this data sheet.



**SECTION 12. ECOLOGICAL INFORMATION**

The environmental effects of the product have not been thoroughly investigated. Data on toxicological effects of the hazardous ingredients are provided below.

| <b>12.1 Toxicity</b>                            | <b>species, media, units, test duration and test conditions.</b>   | <b>Related to</b>                        |
|---|--|--|
| Acute toxicity with fish:                       | LC50 <i>Leuciscus idus</i> > 10,000 mg/L/ 96-h   | (5) Tris Amino                           |
|   | LC50 <i>Pimephales promelas</i> = 4,630 mg/l/96 hours  | (1) Calcium chloride                     |
|   | LC50 <i>Salmo gairdneri</i> = 1.75 mg/l/96 hour  | (12) 1,2-dibromo-2,4-dicyanobutane       |
| Chronic toxicity with fish:                     | Not available  |  |
| Acute toxicity with crustaceans:                | Water fleas ( <i>Daphnia magna</i> ) were exposed to AMP at unspecified concentrations for 48 hours. LC50 = 193 mg/L/48 h.   | (4) Tris Amino                           |
|   | EC50 daphnia > 100 mg/l/48h  | (9) Tris HCl                             |
|   | EC50 <i>Daphnia magna</i> = 1062 mg/L/48 hr  | (1) Calcium chloride                     |
|   | EC50 <i>Daphnia magna</i> = 6.16 mg/L/48 hr  | (12) 1,2-dibromo-2,4-dicyanobutane       |
| Chronic toxicity with crustaceans:              | The chronic toxicity study with <i>Daphnia magna</i> shows that a 16% impairment of reproduction (EC16) is caused at the concentration of 320 mg/L.  | (1) Calcium chloride                     |
| Acute toxicity with algae:                      | EC50 <i>Selenastrum capricornutum</i> >100 mg/L/ 96 h  | (5) Tris Amino                           |
|   | EC <sub>50</sub> <i>Selenastrum capricornutum</i> = 2900 mg/L/72 hours (biomass)   | (1) Calcium chloride                     |
|   | EC50 <i>Selenastrum capricornutum</i> =0.15 mg/L/72 hours  | (12) 1,2-dibromo-2,4-dicyanobutane       |
| Chronic toxicity with algae:                    | Not available.   |  |
| Toxicity data on soil micro- and macroorganisms | Not available.   |  |
| Toxicity data on birds, bees and plants:        | LD50 <i>Mallard Duck</i> = 1064 mg/kg  | (14) 1,2-dibromo-2,4-dicyanobutane (98%) |
| <b>12.2 Persistency and degradability:</b>      | <i>Tris Amino</i> is not readily biodegradable is expected to have moderate persistence. (4)   |  |
|   | <i>Tris Hydrochloride</i> : readily biodegradable. (9)   |  |
|   | <i>1,2-dibromo-2,4-dicyanobutane</i> is expected to degrade rapidly in aquatic environments. (14)  |  |
|   | Once emitted into the environment, calcium chloride which has a high water solubility, will dissociate into the calcium and the chloride anion. The calcium ion may bind to soil particulate or may form stable inorganic salts with sulphate and carbonate ions |  |
| <b>12.3 Bioaccumulation potential:</b>          | <i>Tris-Hydroxymethyl aminomethane</i> is expected to have low bioaccumulation potential. (4)  |  |
|   | Considering its dissociation properties, <i>Calcium chloride</i> per se is not expected to accumulate in living organisms.   |  |
| <b>12.4 Mobility in soil:</b>                   | <i>Tris Amino</i> is expected to have high mobility in soil. (5)   |  |
|   | <i>1, 2-dibromo-2, 4-dicyanobutane</i> is expected to be very mobile and non-persistent in aquatic and soil environments. (14)   |  |
|   | The chloride ion is mobile in soil and eventually drains into surface water because it is readily dissolved in water.  |  |
| <b>12.5 Results of PBT and vPvB assessment</b>  | Not performed.   |  |
| <b>12.6 Other toxic effects:</b>                | Not available.   |  |

**SECTION 13. DISPOSAL CONSIDERATION**

National laws on disposal must be considered, local and UE requirements for wastes recycling must be respected.

**13.1 Waste treatment methods**

Used waste product, surplus product or spillage products shall be disposed of in accordance with national, state and local laws.



**SECTION 14. TRANSPORT INFORMATION**

Not classified in accordance with ADR/RID, IMDG, IATA and DOT regulations.

**SECTION 15. REGULATORY INFORMATION**
**15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture**
**EU Regulations**

- \* 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 (Official Journal L 183 , 29/06/1989 P. 0001 – 0008) 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.
- \* Council Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices.
- \* Commission Regulation (EU) 2015/830 of 28 May 2015 amending Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH).
- \* Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December on classification, labelling and packaging of substances and mixtures 2008 (and subsequent amendments and supplements).

Restriction of use: none

Substance(s) under authorization: none

**US Federal Regulations:**

| State         | Components listed             | Note    |
|---------------|-------------------------------|---------|
| Massachusetts | No component listed           |         |
| New York      | No component listed           |         |
| New Jersey    | 1,2-dibromo-2,4-dicyanobutane | No note |
| Pennsylvania  | No component listed           |         |

**California Prop. 65**

| Ingredient name     | Cancer | Reproductive | NSRL or MADL (µg/day) |
|---------------------|--------|--------------|-----------------------|
| No component listed |        |              |                       |

|  |                     |
|--|---------------------|
| Clean Water Act (CWA) 307                                    | No component listed |
| Clean Air Act Section 112(b) Hazardous Air Pollutants (HAPs) | No component listed |
| Clean Air Act Section 602 Class I Substances                 | No component listed |
| Clean Air Act Section 602 Class II Substances                | No component listed |
| DEA List I Chemicals (Precursor Chemicals)                   | No component listed |
| DEA List II Chemicals (Essential Chemicals)                  | No component listed |

**EPA List of Lists**

| Regulatory Name               | CAS No./SARA/313 Category Code <sup>i</sup> | SARA/EPCRA 302 EHS TPQ <sup>ii</sup> | SARA/EPCRA 304 EHS RQ <sup>iii</sup> | CERCLA RQ <sup>iv</sup> | SARA/EPCRA 313 TRI <sup>v</sup> | RCRA Code <sup>vi</sup> | CAA 112(r) RMP TQ <sup>vii</sup> |
|-------------------------------|---|--------------------------------------|--------------------------------------|-------------------------|---------------------------------|-------------------------|----------------------------------|
| 1,2-dibromo-2,4-dicyanobutane | 35691-65-7                                  | -                                    | -                                    | -                       | 313                             | -                       | -                                |

<sup>i</sup>SARA/313 Category Code: Emergency Planning and Community Right-to Know Act Section 313 Category Code

<sup>ii</sup>SARA/EPCRA 302 EHS TPQ: Extremely Hazardous Substance Threshold Planning Quantity (Emergency Planning and Community Right-to Know Act Section 302 Category Code)

<sup>iii</sup>SARA/EPCRA 304 EHS RQ: Extremely Hazardous Substance Reportable Quantity (Emergency Planning and Community Right-to Know Act Section 304 Category Code)

<sup>iv</sup>CERCLA RQ: Reportable Quantity (Comprehensive Environmental Response, Compensation, and Liability Act)

<sup>v</sup>SARA/EPCRA 313 TRI: Toxics Release Inventory (Emergency Planning and Community Right-to Know Act Section 313 Category Code)

<sup>vi</sup>RCRA Code: Resource Conservation and Recovery Act Code

<sup>vii</sup>CAA 112(r) RMP TQ: Risk Management Plan Threshold Quantity (Clean Air Act Section 112(r))

**United States Inventory (TSCA 8b):** All components are listed or exempted.

**Canada Domestic Substances List (DSL):** All components are listed.

**15.2 Chemical safety assessment:** A chemical safety assessment has not been carried out for the mixture by the supplier.

**SECTION 16. OTHER INFORMATION**

**Revisions:**

- Edition n. 01, dated 02/28/2011.
- Revision n. 01, dated 11/24/2015. Main changes are in sections 2 to 16, adapting the SDS format and contents to Hazard Communication Standard (HCS), 29 CFR 1910.1200 (HazCom 2012), Hazardous Product Regulation HPR (WHMIS 2015), and Regulation (EU) 2015/830 of 28 May 2015.

**Acronyms:**

ACGIH: American Conference of Governmental Industrial Hygienists  
 AIHA: American Industrial Hygiene Association  
 ADR: Agreement concerning the carriage of dangerous goods by Road  
 BCF: Bioaccumulative factor  
 BEI : Biological Exposure Indices  
 CAS: Chemical Abstract Service (division of the American Chemical Society)  
 CLP: Classification, Labeling and Packaging  
 DNEL: Derived No-Effect Levels  
 EC50: the effect concentration associated with 50% response.  
 EINECS: European Inventory of Existing Commercial Substances  
 EPA: US Environmental Protection Agency  
 IARC: International Agency for Research on Cancer  
 IATA: International Air Transport Association Code  
 IMDG: International Maritime Dangerous Goods Code  
 LC50: Lethal Concentration to 50 % of a test population  
 LD50: Lethal Dose to 50% of a test population (Median Lethal Dose)  
 LOEL: Lowest Observed Effect Level  
 MADL: Maximum Allowable Daily (or Dose) Level  
 NOAEL: No Observed Adverse Effect Level  
 NOEC: no observed effect concentration, means the test concentration immediately below the lowest tested concentration with statistically significant adverse effect.  
 NSRL: National Science Research Laboratory  
 NTP: National Toxicology Program  
 OEL: Occupational Exposure Limit  
 OSHA: Occupational Safety and Health Administration  
 PPE : Personal protective Equipment  
 PBT: Persistent, Bio accumulative and Toxic substances  
 PNEC: Predicted No Effect Concentration  
 RID: Regulation concerning the International carriage of Dangerous goods by rail  
 TLV/TWA: Threshold Limit Value/Threshold Weighted Average  
 vPvB: very Persistent, very Bio accumulative  
 WEEL: Workplace Environmental Exposure Level (air concentration of agents in a healthy worker's breathing zone)

**Information related to the Regulation EC/1272/2008:**

**Hazard statement(s):**

- H315: Causes skin irritation.
- H319: Causes serious eye irritation.
- H302: Harmful if swallowed.
- H317: May cause an allergic skin reaction.
- H318: Causes serious eye damage.
- H400: Very toxic to aquatic life.

**Information on workers training:** Follow National requirements to ensure protection of human health and the environment.

**Classification and procedure used to derive the classification for mixtures according to Regulation (EC) 1272/2008, according to Hazard Communication Standard, 29 CFR 1910.1200 (HCS), and according to HPR (WHMIS 2015) :**

| <i>Classification:</i> | <i>Classification procedure</i> |
|------------------------|---------------------------------|
| Not classified         | -                               |

The contained information in this SDS are in accordance with Annex II of the COMMISSION REGULATION (EU) No 1907/2006 (REACH) and its subsequent amendments, in accordance with Hazard Communication Standard (HCS), 29 CFR 1910.1200 (HazCom 2012) as recommended by US OSHA, and in accordance with Hazardous Product Regulation HPR (WHMIS 2015) as recommended by Health Canada (HC).

**Bibliographic references:**

- 
- (1) Calcium Chloride, SIDS Initial Assessment Report For SIAM 15 Boston, USA 22-25th October 2002
  - (2) ChemIDplus Lite, full records for CAS 302-95-4.
  - (3) Calcium chloride anh., Registration dossier, available at: [http://apps.echa.europa.eu/registered/data/dossiers/DISS-9eb43f6f-23a1-5205-e044-00144f67d031/AGGR-dc2ba8fd-c7fc-402e-906e-b6cd0864ad5e\\_DISS-9eb43f6f-23a1-5205-e044-00144f67d031.html#AGGR-dc2ba8fd-c7fc-402e-906e-b6cd0864ad5e](http://apps.echa.europa.eu/registered/data/dossiers/DISS-9eb43f6f-23a1-5205-e044-00144f67d031/AGGR-dc2ba8fd-c7fc-402e-906e-b6cd0864ad5e_DISS-9eb43f6f-23a1-5205-e044-00144f67d031.html#AGGR-dc2ba8fd-c7fc-402e-906e-b6cd0864ad5e)
  - (4) HSDB Hazardous Substances Databank, Tromethamine
  - (5) Screening-Level Hazard Characterization, Sponsored chemical 2-Amino-2-hydroxymethyl-1,3-propanediol (TRIS AMINO) CASRN 77-86-1, U.S. Environmental Protection Agency, Hazard Characterization Document, September, 2014
  - (6) ECHA, Registration Dossier, Tromethamine, [http://apps.echa.europa.eu/registered/data/dossiers/DISS-d7f60455-0965-1602-e044-00144f67d031/AGGR-932e53a4-4218-4161-b380-2c99a562941f\\_DISS-d7f60455-0965-1602-e044-00144f67d031.html#AGGR-932e53a4-4218-4161-b380-2c99a562941f](http://apps.echa.europa.eu/registered/data/dossiers/DISS-d7f60455-0965-1602-e044-00144f67d031/AGGR-932e53a4-4218-4161-b380-2c99a562941f_DISS-d7f60455-0965-1602-e044-00144f67d031.html#AGGR-932e53a4-4218-4161-b380-2c99a562941f)
  - (7) TEST PLAN For Tris(hydroxymethyl)aminomethane (77-86-1) Submitted to the U.S. Environmental Protection Agency Under the High Production Volume (HPV) Chemicals Challenge Program The Dow Chemical Company Midland, Michigan, 48674
  - (8) Haz-Map, Tromethamine hydrochloride, available at <http://hazmap.nlm.nih.gov/category-details?table=copytblagents&id=18456>
  - (9) Sigma Aldrich, SDS for Tromethamine Hydrochloride, Version 5.0, revision date 17.10.2013
  - (10) Australian Government, Department of Health and Ageing, NICNAS Existing Chemicals Information Sheet, Methylidibromo Glutaronitrile, June 2009
  - (11) NTP Nomination History and Review, 1,2-dibromo-2,4-dicyanobutane, CAS No. 35691-65-7
  - (12) LANXESS, Material Safety Data Sheet for Tektamer 38LV
  - (13) Gestis Substance database, 1,2-Dibromo-2,4-dicyanobutane, ZVG 139996
  - (14) EPA R.E.D. Facts, DIBROMODICYANOBUTANE
  - (15) SCIENTIFIC COMMITTEE ON CONSUMER PRODUCTS, SCCP, Opinion on Methylidibromo glutaronitrile (sensitization only), COLIPA n° P77, Adopted by the SCCP during the 3rd plenary meeting of 15 March 2005
  - (16) HSDB: 1,2-DIBROMO-2,4-DICYANOBUTANE, available at <http://toxnet.nlm.nih.gov/cgi-bin/sis/search2/?./temp/~tRCfcl:1>
  - (17) <http://e-aair.org> - Allergy, Asthma and Immunology Research (AAIR) 2009, October, Occupational asthma caused by inhalation of bovine serum albumin powder, Case report

**SECTION 1. IDENTIFICATION OF THE MIXTURE AND OF THE COMPANY**

**1.1 Identification of the mixture**

Product Name: **APTT REAGENT**

Product Number: **000H01176**

**1.2 Use of the mixture:**

Relevant use: For in vitro diagnostic use.

Uses advised against: There are no specific uses advised against.

**1.3 Company identification:**

MANUFACTURER:  
Instrumentation Laboratory Co.  
180 Hartwell Road,  
Bedford, MA 01730-2443 (USA)  
Tel. +1 800 678 0710  
Fax +1 781 863 9928

DISTRIBUTOR EU:  
Via Leonardo da Vinci, 36  
20877 Roncello (MB), Italy

DISTRIBUTOR US/CANADA:  
DiaPharma Group, Inc.  
8948 Beckett Rd.  
West Chester, OH 45069 (USA)

E-mail address of the competent person: [infosds@mail.ilww.it](mailto:infosds@mail.ilww.it)

**1.4 Emergency phone:** +44 (0) 3700 492 795  
+1 215 207 0061 (USA and Canada)

**SECTION 2. HAZARDS IDENTIFICATION**

**2.1 Classification of the mixture:**

This product is not hazardous according to Regulations (EC) No 1272/2008, OSHA 29 CFR 1910.1200 and Hazardous Product Regulation HPR (WHMIS 2015).

Any additional information concerning the risks for health and/or the environment are given in sections 11 and 12 of this sheet.

**According to Regulation (EC) No 1272/2008, according to Hazard Communication Standard, 29 CFR 1910.1200 (HCS), and according to Hazardous Product Regulation HPR (WHMIS 2015):**

| <i>Hazard class</i>                  | <i>Hazard category</i> | <i>Hazard statement</i> |
|--------------------------------------|------------------------|-------------------------|
| <b>Not classified</b>                |                        |                         |
| <i>For exposure limits see Ch. 8</i> |                        |                         |

**Potential adverse physicochemical, human health and environmental effects** *(see also Ch. 9-12)*

Contains 1,2-benzisothiazolin-3-one. May produce an allergic reaction in already sensitized individuals.

Under normal conditions of use, the mixture does not cause other adverse effects to humans or adverse effects to the environment.

**2.2 Label elements, according to Regulation (EC) No 1272/2008, according to Hazard Communication Standard, 29 CFR 1910.1200 (HCS), and according to Hazardous Product Regulation HPR (WHMIS 2015):**

|                                    |   |
|------------------------------------|---|
| <b>Hazard pictogram(s):</b>        | None  |
| <b>Signal word(s):</b>             | None  |
| <b>Hazard statement(s):</b>        | None  |
| <b>Precautionary statement(s):</b> | None  |
| <b>Other labeling details:</b>     | Contains 1,2-benzisothiazolin-3-one. May produce an allergic reaction. (EUH208)<br>Up to 20.85% of the mixture consists of component of unknown acute toxicity (oral, dermal, inhalation) for the human health and for the aquatic environment. |

**Safety precautions:** Use the product in accordance with the Good Laboratory Practice.  
Wear suitable protective clothing, gloves and eye/face protection.  
Do not let the product enter drainage system, surface and ground-water or soil. Do not empty into drains.

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

The mixture does not meet the criteria for PBT or vPvB.

**SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS**

**Composition:** liquid containing organic and inorganic components.

**3.1 Hazardous components:**

| Name   | EINECS/<br>ELINCS n° | CAS n°     | Conc. %<br>w/w*  | Classification<br>29 CFR 1910.1200 (HCS)<br>HPR (WHMIS 2015)  | Classification<br>1272/2008/EC  |
|--|----------------------|------------|------------------|---|---|
| Tris Hydrochloride   | 214-684-5            | 1185-53-1  | 0.2-0.3%         | Skin Corrosion/Irritation, cat 2<br>Eye damage/Eye Irritation, cat. 2B  | Skin Irrit. 2, H315<br>Eye Irrit. 2, H319   |
| Tris-Hydroxymethyl<br>aminomethane (Tris Amino)  | 201-064-4            | 77-86-1    | 0.02-<br>0.03%   | Skin Corrosion/Irritation, cat. 2   | Skin Irrit. 2, H315   |
| Oxydipropanol<br>(Dipropylene glycol)  | 246-770-3            | 25265-71-8 | 0.02-<br>0.03%   | Not classified  | Not classified  |
| 1,2-benzisothiazolin-3-one (BIT)<br><i>Index N. (Annex VI of CLP Reg.):<br/>613-088-00-6</i> | 220-120-9            | 2634-33-5  | 0.007<br>0.008%  | Acute Toxicity – Oral, cat. 4<br>Skin Corrosion/Irritation, cat. 2<br>Eye damage/irritation, cat. 1<br>Sensitization – Skin, cat.1<br>Aquatic Acute, cat 1**<br>Aquatic Chronic 3** | Acute Tox. 4, H302<br>Skin Irrit. 2, H315<br>Eye Dam. 1, H318<br>Skin Sens. 1, H317<br>Aquatic Acute 1, H400 (M = 1)<br>Aquatic Chronic 3, H412<br><u>Specific Conc. Limits</u><br>Skin Sens. 1; H317: C ≥ 0,05 % |
| Sodium hydroxide<br><i>Index N. (Annex VI of CLP Reg.):<br/>011-002-00-6</i>                 | 215-185-5            | 1310-73-2  | 0.001-<br>0.003% | Skin Corrosion/Irritation, cat. 1A  | Skin Corr. 1A, H314<br><u>Specific Conc. Limits</u><br>Skin Corr. 1A,H314: C ≥5%<br>Skin Corr. 1B; H314: 2 % ≤ C < 5 %<br>Skin Irrit. 2; H315: 0,5 % ≤ C < 2 %<br>Eye Irrit. 2; H319: 0.5 % ≤ C < 2 %             |

*For exposure limits see Ch. 8, for hazard statements text see Ch. 16.  
\* A range may be indicated, considering batch-to batch variation.  
\*\*Environmental classification according to Reg. N. 1272/2008 (EC) and subsequent amendments.*

The mixture contains substances listed in the Hazardous Substance Lists and/or evaluated for carcinogenicity by IARC, NTP, OSHA: Sodium hydroxide, Dipropylene glycol. See Section 11 and 15.

**SECTION 4. FIRST AID MEASURES**
**4.1 Description of first aid measures**

|                      |  |
|----------------------|--|
| Ingestion:           | If swallowed rinse mouth with plenty of water provided person is conscious. Do not induce vomiting. Get medical advice if adverse symptoms appear.   |
| Inhalation exposure: | If inhaled, move person to fresh air. If breathing is difficult, oxygen should be administered. Get medical advice if adverse symptoms appear.   |
| Contact with skin:   | Remove contaminated clothes and shoes. Wash immediately affected area with soap or mild detergent and plenty of water until the removal of the mixture (15-20 minutes). Get medical advice if adverse symptoms appear. |
| Contact with eyes:   | Wash immediately with plenty of water or normal saline for at least 15 minutes. Keep eyelid open with the finger. Get medical advice if adverse symptoms appear.   |

**4.2 Most important symptoms and effects (acute and delayed)**

|          |  |
|----------|--|
| Acute:   | Skin : May be irritant for skin. Contains 1,2-benzisothiazolin-3-one. May produce an allergic reaction in already sensitised individuals.<br>Eyes: May cause irritation.<br>Inhalation: May cause irritation to the mucous membranes and upper respiratory tract.<br>Ingestion: may cause irritation to the gastrointestinal mucous membranes. |
| Delayed: | Delayed symptoms and effects are not known.  |

**4.3 Indication of any immediate medical attention and special treatment needed**

|                      |               |
|----------------------|---------------|
| Medical monitoring:  | Not foreseen. |
| Antidotes, if known: | Not known.    |

## SECTION 5. FIRE-FIGHTING MEASURES

### 5.1 Extinguishing media

Suitable extinguishing media: Water spray or regular foam, CO<sub>2</sub>, dry powder.

Unsuitable extinguishing media: Not known.

### 5.2 Special hazards arising from the substance or mixture

Hazardous combustion products: Thermal decomposition or combustion may generate toxic and hazardous fumes of CO<sub>x</sub>, NO<sub>x</sub>, Na<sub>2</sub>O, SO<sub>x</sub>, HCl, HF, P<sub>x</sub>O<sub>y</sub>.

### 5.3 Advice for firefighters

Protective actions: Water jets can be used successfully to cool containers exposed to the fire and disperse fumes.

Equipment for self-protection: Self-contained breathing apparatus, flame and chemical resistant clothing, boots and gloves. Equipment must be conformed with the national/international standards 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:** Remove the ignition and heat sources, provide sufficient ventilation and evacuate the area. Respiratory protection: is not required. Where risk assessment shows air-purifying respirators are appropriate, use masks with approved filter. Suitable protective clothing, rubber or polythene gloves, rubber shoes, safety glasses.

**For emergency responders:** Wear appropriate protective equipment (see Section 8) to minimize exposure to the product.

**6.2 Environmental precautions** Do not let the product enter drainage system, surface and ground-water or soil. Contact local authorities in case of environmental release. Do not empty into drains.

**6.3 Methods and material for containment and cleaning up** Soak up with inert absorbent material, and clean with plenty of water. collect spilled material in containers. Send to the storage waiting for disposal procedures.

**6.4 Reference to other sections** See also section 8 and 13.

## SECTION 7. HANDLING AND STORAGE

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

**7.2 Conditions for safe storage, incompatibilities** Recommended temperature: store at 2-8°C. Avoid light exposure and keep away from heat sources. Room ventilation: well ventilated workplace. Keep containers tightly closed and labelled with the name of the product. Avoid environmental release. Keep away from food and drinks.

**7.3 Specific end use** *APTT Reagent* is intended for in vitro diagnostic use. Contains 1,2-benzisothiazolin-3-one. May produce an allergic reaction in already sensitised individuals. Use the product in accordance with the Good Laboratory Practice.

## SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

### 8.1 Control parameters

Community/National occupational exposure limit values:

| Sodium hydroxide <sup>(7)(8)</sup> | Limit value – 8 hours                   | Limit value – short term                |
|------------------------------------|---|---|
| Austria                            | 2 mg/m <sup>3</sup> - inhalable aerosol | 4 mg/m <sup>3</sup> - inhalable aerosol |
| Belgium                            | 2 mg/m <sup>3</sup>                     | -                                       |
| Denmark                            | 2 mg/m <sup>3</sup>                     | 2 mg/m <sup>3</sup>                     |
| France                             | 2 mg/m <sup>3</sup>                     |   |
| Hungary                            | 2 mg/m <sup>3</sup>                     | 2 mg/m <sup>3</sup>                     |

|   |   |   |
|---|---|---|
| New Zealand                                     |   | 2 mg/m <sup>3</sup> - ceiling value                 |
| Poland  | 0.5 mg/m <sup>3</sup>                   | 1 mg/m <sup>3</sup>                                 |
| Spain   | 2 mg/m <sup>3</sup>                     | -   |
| Sweden  | 1 mg/m <sup>3</sup>                     | 2 mg/m <sup>3</sup> - inhalable dust; ceiling value |
| Switzerland                                     | 2 mg/m <sup>3</sup> - inhalable aerosol | 2 mg/m <sup>3</sup> - inhalable aerosol             |
| United Kingdom                                  | -                                       | 2 mg/m <sup>3</sup>                                 |
| Canada – Québec                                 | -                                       | 2 mg/m <sup>3</sup> - ceiling value                 |
| Canada – Ontario                                | -                                       | 2 mg/m <sup>3</sup> - ceiling value                 |
| USA – NIOSH                                     | -                                       | 2 mg/m <sup>3</sup> - ceiling value (15 min)        |
| USA – OSHA                                      | 2 mg/m <sup>3</sup>                     | -   |
| ACGIH: STEL 2 mg/m <sup>3</sup> - ceiling value |   |   |
| NIOSH IDLH: 10 mg/m <sup>3</sup> for NaOH       |   |   |

**Community/National biological exposure limit values:** Not established.

**DNEL values (components):**

| Component                        | Route of exposure   | Workers       |          |                 |          | Consumers     |          |                 |          |
|----------------------------------|---|---------------|----------|-----------------|----------|---------------|----------|-----------------|----------|
|                                  |   | Acute effects |          | Chronic effects |          | Acute effects |          | Chronic effects |          |
|                                  |   | local         | systemic | local           | systemic | local         | systemic | local           | systemic |
| Sodium hydroxide <sup>(16)</sup> | Oral (mg/(mg/kg bw/day)<br>Dermal (mg/kg bw/day)<br>Inhalation (mg/m <sup>3</sup> ) |               |          | 1               |          |               |          | 1               |          |

**PNEC values (components):** *NaOH*: Because the buffer capacity, the pH and the fluctuation of the pH are very specific for a certain ecosystem it is not considered useful to derive a PNEC.<sup>(14)</sup>

The measurement of substances at the workplace must be carried out with standardized methods or, failing that, with appropriate methods.

## 8.2 Exposure controls

### 8.2.1. Appropriate engineering controls

Appropriate risk management measures, that must be adopted at the workplace, have to be selected and applied, following the risks assessment carried out by the employer, in connection with his working activity. If the results of this evaluation show that the general and collective prevention measures are not sufficient to reduce the risk, and if you cannot prevent exposure to the mixture by other means, adequate personal protective equipment must be adopted, complying with the relevant technical national/international standards.

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

**Respiratory protection:** Respiratory protection is not required. Where risk assessment shows air-purifying respirators are appropriate, use masks with approved filter.  
Use only devices approved by the Competent Authorities such as NIOSH (USA) and CEN (EU).

**Skin protection:** Protective clothing, rubber gloves.

**Eye protection:** Safety glasses.

**Hand protection:** Protective gloves.

**Other protective systems:** Personal protective equipment (PPE) useful for reducing individual exposure.

### 8.2.3. Environmental exposure controls

Avoid any release into the environment.

## SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

### 9.1 Information on basic physical and chemical properties

|             | Value         | Related to |
|-------------|---------------|------------|
| Appearance: | Liquid        |            |
| Odor:       | not available |            |
| Color:      | not available |            |
| pH:         | not available |            |



|                       |  |         |
|-----------------------|--|---------|
| Flammability:         | Aqueous solution, not expected to be flammable |         |
| Explosive properties: | Aqueous solution, not expected to be explosive |         |
| Oxidizing properties: | Aqueous solution, not expected to be oxidant   |         |
| Density:              | Not available                                  |         |
| Solubility:           | not available                                  |         |
| Water Solubility:     | Miscible                                       | Mixture |
| Melting point/range:  | Liquid, not applicable                         |         |

## 9.2 Other information

|             |          |
|-------------|----------|
| Miscibility | miscible |
|-------------|----------|

## SECTION 10. STABILITY AND REACTIVITY

|  |   |
|--|---|
| <b>10.1 Reactivity</b>                         | This mixture is considered not reactive under the normal conditions of the usage.                                 |
| <b>10.2 Chemical stability</b>                 | The product is stable until the expiration date shown on the box and on the labels when stored at 2 – 8 °C.       |
| <b>10.3 Possibility of hazardous reactions</b> | Not foreseen.   |
| <b>10.4 Conditions to avoid:</b>               | Keep away from heat and light.  |
| <b>10.5 Incompatible materials</b>             | Oxidising agents. Sodium hydroxide is corrosive to most metals.   |
| <b>10.6 Hazardous decomposition products:</b>  | Thermal decomposition or combustion may generate toxic and hazardous fumes of COx, NOx, Na2O, SOx, HCl, HF, PxOy. |

## SECTION 11. TOXICOLOGICAL INFORMATION

The health effects of the product have not been thoroughly investigated. Data on toxicological effects of the hazardous ingredients are provided below.

### 11.1 Information on toxicological effects

#### Symptoms and effects for each route of exposure:

|                    |  |
|--------------------|--|
| Dermal:            | May cause skin irritation. Contains 1,2-benzisothiazolin-3-one. May produce an allergic reaction in already sensitized individuals |
| Ingestion:         | Ingestion may cause irritation to the gastrointestinal mucous membranes.   |
| Inhalation:        | May cause irritation to the mucous membranes and upper respiratory tract.  |
| Contact with eyes: | May cause eye irritation.  |

#### Toxicokinetic effects (Absorption, Distribution, Metabolism, Excretion):

*Tris amino:* is not metabolized appreciably and is eliminated by the kidneys. Ionized tromethamine is excreted by kidney, so the effect is that of excretion of hydrogen ions. Elimination of drug from body is entirely by renal excretion. It is not known whether tromethamine is distributed into human milk. <sup>(1)</sup>

*1,2-benzisothiazolin-3-one (BIT):* in animals is rapidly and completely metabolized. Neither the substance nor its metabolites do not accumulate in the liver and adipose tissue. The major metabolites are o-(methylsulfinyl)-benzamide and o-(methylsulphonyl)-benzamide. Elimination is within 24 hours and almost entirely through the urine. <sup>(9)</sup>

*Sodium hydroxide:* Alkalis penetrate skin slowly and act at the site of contact. Sodium is a normal constituent of the blood. Exposure to NaOH could potentially increase the pH of the blood. An excess of sodium is avoided through increased elimination which is directed by homeostatic mechanisms. The main excretion route of NaOH is via urine, small amounts were found in feces, sweat, tears, nasal mucous, saliva, and vaginal and urethral discharges. NaOH is not expected to be systemically available in the body under normal handling and use conditions. <sup>(13)(14)(15)</sup>

| Acute toxicity     | Value   | m.u.  | Effects | Related to                |
|--------------------|---|-------|---------|---------------------------|
| <u>Oral:</u>       | LD50 (rat) > 3,000  | mg/kg |         | <sup>(2)</sup> Tris Amino |
|                    | LD50 (rat) = 670-1,200  | mg/Kg |         | <sup>(9)</sup> BIT        |
| <u>Dermal:</u>     | LD50 (rat) > 5,000  | mg/kg |         | <sup>(3)</sup> Tris Amino |
|                    | LD50 (rabbit) > 2,000   | mg/Kg |         | <sup>(9)</sup> BIT        |
| <u>Inhalation:</u> | not available   |       |         |                           |
| <u>Other data:</u> | <i>NaOH:</i> The existing animal and human data on acute toxicity show that NaOH has a local effect and that systemic effects are not to be expected. <sup>(15)</sup> |       |         |                           |

**Corrosion/Irritation**

Skin Corrosion/Irritation

*Tris Amino*: Tromethamine was a mild irritant to rabbits at 25% with a pH of 10.8. At 40%, tromethamine was not irritating. Intradermal injections of tromethamine were severely irritating to rabbits at pH 10.4 but were only mildly irritating at pH 7.4. The supporting substance 2-Amino-2-methyl-1-Propanol (AMP) was found to be irritating to rabbits, with burrowing lesions noted when applied to abraded skin sites; there was mild irritation noted when applied to unabraded skin.<sup>(2)</sup>

*Tris Hydrochloride*: irritant to skin (read across from Tris Amino).

*1,2-benzisothiazolin-3-one* : According to a study conducted in rabbits BIT can be classified as a moderate irritant to skin.<sup>(10)</sup>

*NaOH* is highly irritating and highly corrosive for the skin.<sup>(14)</sup>

Serious eye damage/ irritation

*Tris Amino (100%)* was not an ocular irritant when administered to rabbits.<sup>(2)</sup>

*Tris Hydrochloride* : mild eye irritant in rabbits.<sup>(5)</sup>

*1,2-benzisothiazolin-3-one* : A study in rabbits classified the compound as a severe eye irritant.<sup>(10)</sup>

*NaOH*: even strongly diluted solutions still cause irritation and chemical burns. The available animal data on eye irritation revealed small differences in eye irritation levels. The non-irritant level was 0.2-1.0%, while the corrosive concentration was 1.2% or higher than 2%. There is a danger of blindness.<sup>(15)</sup>

**Sensitization:**

Skin sensitization:

*Tris Amino*: The supporting chemical AMP is not sensitizing to guinea pig skin.<sup>(2)</sup>

*Tris Hydrochloride*: Not a sensitizer in experimental animals.<sup>(5)</sup>

*1, 2-benzisothiazolin-3-one* : A guinea pig maximization test classified BIT as a moderate contact sensitizer whilst the Buehler test classifies BIT as non-sensitizing. Literature data for the local lymph node assay support a classification of BIT as a moderate dermal sensitizer (EC3 2.3%). (In the context of occupational uses, benzisothiazolinone (BIT) is a well-documented contact allergen.<sup>(10)</sup>

*NaOH* is not considered to be a skin sensitizer.<sup>(14)</sup>

Respiratory sensitization:

**CMR effects**

Germ cell mutagenicity:

*Tris Amino*: The supporting chemical, AMP, was not mutagenic to bacteria and mammalian cells in vitro, and did not induce micronuclei in mice in vivo.

*Tris Hydrochloride*: Ames test negative.<sup>(6)</sup>

*1, 2-benzisothiazolin-3-one*: The compound has been found to be clastogenic in mammalian cells treated *in vitro*, non-mutagenic *in vitro*, non clastogenic and DNA damaging *in vivo*.<sup>(10)</sup>

*NaOH*: Both the in vitro and the in vivo genetic toxicity test indicate no evidence for a mutagenic activity.<sup>(14)</sup>

Reproductive toxicity:

*Tris Amino*: In an oral gavage combined reproductive/developmental toxicity screening test in rats no effects on reproductive or developmental parameters were observed at the doses tested; the NOAEL for reproductive and developmental toxicity is 1000 mg/kg-day, the highest dose tested.<sup>(2)</sup>

*1,2-benzisothiazolin-3-one* : Studies on rats carried out to date did not indicate a reproductive toxic potential (fetal toxicity and teratogenicity) in the maternal-toxic dosage range.<sup>(9)</sup>

*NaOH* is not expected to be systemically available in the body under normal handling and use conditions and for this reason it can be stated that the substance will not reach the fetus nor reach male and female reproductive organs.<sup>(14)</sup>

Carcinogenesis:

Substances listed in the National Toxicology Program (NTP) Report on Carcinogens, in the International Agency for Research on Cancer (IARC) Monographs or found to be potential carcinogen by OSHA:

| Substance           | OSHA | IARC | NTP |
|---------------------|------|------|-----|
| No component listed |      |      |     |

*Tris Amino*: based on the available data, the substance is not carcinogenic.<sup>(4)</sup>

*1,2-benzisothiazolin-3-one* : Based on its characteristics, BIT is unlikely to demonstrate a carcinogenic potential.<sup>(11)</sup>

*NaOH*: Following chemical burns due to alkalis, the incidence of the occurrence of esophageal tumors is increased by a factor between 1000 and 3000. However, the tumor formation is a consequence of massive tissue destruction and the regenerative processes which subsequently start and is not the result of a direct carcinogenic effect. If irritation is avoided, the formation of tumors is not to be expected.<sup>(15)</sup>

**STOT –single exposure** *1,2-benzisothiazolin-3-one*: At room temperature, exposure to vapor is minimal due to low volatility. A single exposure is unlikely to be hazardous. Mist may cause severe irritation to the upper respiratory tract (nose and throat) and lungs. <sup>(11)</sup>

*NaOH* in the atmosphere causes irritation to the airways (in particular in the nose and throat). A concentration of 2 mg/m<sup>3</sup> was reported to have produced distinct but not excessive irritation.

**STOT – repeated exposure** There are no documented long-term effects of *TRIS AMINO* treatment, and no serious side-effects on record that are directly attributed to treatment with the compound. <sup>(3)</sup>

*1, 2-benzisothiazolin-3-one*: A 90-day study on dogs that were administered gelatine capsules with different BIT levels (corresponding to 5; 20 or 50 mg of B per kg of body weight per day) revealed irritations in the gastrointestinal tract (vomiting, diarrhea), slight functional changes of the liver and slightly increased liver weights, but no pathological organ changes. The LOAEL was stated to be 50, and the NOAEL 5, mg per kg of body weight per day. <sup>(9)</sup>

*NaOH*: In studies in workplaces, irritation to the eyes, nose and throat as well as skin was reported. Animal experimental results also indicate possible chronic damage to the airways. <sup>(15)</sup>

**Aspiration hazards** Not available.

**Other information:** Not available.

**Reasons for the lack of classification:**

Where the mixture resulted in a non-classification, this may be due to the availability of data which does not impose a classification for that specific end-point, or due to lack of data, or due to availability of inconclusive data or data which are not sufficient to get a classification as for the criteria adopted in Regulations mentioned in this data sheet.

**SECTION 12. ECOLOGICAL INFORMATION**

The environmental effects of the product have not been thoroughly investigated. Data on toxicological effects of the hazardous ingredients are provided below.

| 12.1 Toxicity                                   | species, media, units, test duration and test conditions.  | Related to                                 |
|---|--|--|
| Acute toxicity with fish:                       | LC50 <i>Leuciscus idus</i> > 10,000 mg/L/ 96-h   | <sup>(2)</sup> Tris Amino                  |
|   | LC50 <i>Oncorhynchus mykiss</i> = 1.9 mg a.i./L/96 h   | <sup>(12)</sup> 1,2-benzisothiazolin-3-one |
|   | LC50 <i>Gambusia affinis</i> = 125 mg/l/96 hours   | <sup>(14)</sup> NaOH                       |
| Chronic toxicity with fish:                     | MATC* (growth) <i>Pimephales promelas</i> = 0.41 mg a.i./L/33-day  | <sup>(12)</sup> 1,2-benzisothiazolin-3-one |
| Acute toxicity with crustaceans:                | Water fleas ( <i>Daphnia magna</i> ) were exposed to AMP at unspecified concentrations for 48 hours. LC50 = 193 mg/L/48 h.   | <sup>(1)</sup> Tris Amino                  |
|   | EC50 <i>daphnia</i> > 100 mg/l/48h   | <sup>(6)</sup> Tris HCl                    |
|   | EC50 <i>Daphnia</i> = 3.7 mg a.i./L/48h  | <sup>(12)</sup> 1,2-benzisothiazolin-3-one |
|   | LC50 <i>Ceriodaphnia cf dubia</i> = 40 mg/l/48 hours. The toxicity threshold concentration for <i>Daphnia magna</i> was reported to range from 40 to 240 mg/l.   | <sup>(14)</sup> NaOH                       |
| Chronic toxicity with crustaceans:              | EC50 <i>Daphnia magna</i> = 3.8 mg a.i./L/ 21-day Flow-Through Life-Cycle  | <sup>(12)</sup> 1,2-benzisothiazolin-3-one |
| Acute toxicity with algae:                      | EC50 <i>Selenastrum capricornutum</i> >100 mg/L/ 96 h  | <sup>(2)</sup> Tris Amino                  |
|   | EC50 <i>Pseudokirchneriella subcapitata</i> = 0.38-0.98 mg a.i./L/96 h   | <sup>(12)</sup> 1,2-benzisothiazolin-3-one |
| Chronic toxicity with algae:                    | Not available.   |  |
| Toxicity data on soil micro- and macroorganisms | LC50 <i>Eisenia foetida</i> = 278 mg a.i./L  | <sup>(12)</sup> 1,2-benzisothiazolin-3-one |
|   | EC50 <i>Photobacterium phosphoreum</i> = 22 mg/l/15 minutes  | <sup>(14)</sup> NaOH                       |
| Toxicity data on birds, bees and plants:        | Six Terrestrial Plant Species: EC50s = 18.4-166 mg a.i./L/21-day   | <sup>(12)</sup> 1,2-benzisothiazolin-3-one |
| <b>12.2 Persistence and degradability:</b>      | <i>Tris Amino</i> is not readily biodegradable is expected to have moderate persistence. <sup>(1)</sup>  |  |
|   | <i>Tris Hydrochloride</i> : readily biodegradable. <sup>(6)</sup>  |  |
|   | <i>1,2-benzisothiazolin-3-one</i> : has a low volatility and is slightly soluble in water. Once introduced into the aquatic environment, BIT will have a tendency to remain in water. BIT is considered degradable and will not persist in the environment. Although the product is hydrolytically stable in water, it is susceptible to photodegradation in aquatic environments. <sup>(11)</sup> |  |

*NaOH* : It is highly soluble in water and dissociates to sodium and hydroxide ions, with the effect of increasing pH and alkalinity. Na<sup>+</sup> and OH<sup>-</sup> persist indefinitely in the environment with equilibrium between various forms of complexes and precipitates. <sup>(17)</sup>

**12.3 Bioaccumulation potential:** *Tris-Hydroxymethyl aminomethane* is expected to have low bioaccumulation potential. <sup>(1)</sup>

*1, 2-Benzisothiazolin-3-one*: based on a Kow value of 20 at 25°C is unlikely to bio accumulate in aquatic organisms. <sup>(12)</sup>

Considering its high water solubility, *NaOH* is not expected to bio concentrate in organisms.

**12.4 Mobility in soil:** *Tris Amino* is expected to have high mobility in soil. <sup>(2)</sup>

*1,2-Benzisothiazolin-3-one* shows moderate to strong binding to soil sand it is not likely to migrate into the ground and there is low potential for ground water contamination. <sup>(12)</sup>

*NaOH* is very soluble and mobile in water. In soil, mobility depends directly on the importance of the liquid phase of the soil and the possibility to form metal hydroxo-complexes with metal solid species. <sup>(13)</sup>

**12.5 Results of PBT and vPvB assessment** Not performed.

**12.6 Other toxic effects:** Not available.

\* **Maximum Acceptable Toxicant Concentrations (MATC)** – An estimated value that represents the highest “no-effect” concentration of a specific substance within the range including the NOEC and LOEC.

## SECTION 13. DISPOSAL CONSIDERATION

National laws on disposal must be considered, local and UE requirements for wastes recycling must be respected.

### 13.1 Waste treatment methods

Used waste product, surplus product or spillage products shall be disposed of in accordance with national, state and local laws.

## SECTION 14. TRANSPORT INFORMATION

Not classified in accordance with ADR/RID, IMDG, IATA and DOT regulations.

## SECTION 15. REGULATORY INFORMATION

### 15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture

#### EU Regulations

\* 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 (Official Journal L 183 , 29/06/1989 P. 0001 – 0008) 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.

\* Council Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices.

\* Commission Regulation (EU) 2015/830 of 28 May 2015 amending Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH).

\* Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December on classification, labelling and packaging of substances and mixtures 2008 (and subsequent amendments and supplements).

**Restriction of use:** none

**Substance(s) under authorization:** none

#### US Federal Regulations:

| State         | Components listed  | Note  |
|---------------|--------------------|---|
| Massachusetts | Sodium hydroxide   | -   |
| New York      | Sodium hydroxide   | -   |
| New Jersey    | Sodium hydroxide   | Corrosive   |
| Pennsylvania  | Sodium hydroxide   | E - Substance is on the Environmental Hazard List |
|               | Dipropylene glycol | PROPANOL, OXYBIS                                  |

#### California Prop. 65

| Ingredient name     | Cancer | Reproductive | NSRL or MADL (µg/day) |
|---------------------|--------|--------------|-----------------------|
| No component listed |        |              |                       |

|  |                     |
|--|---------------------|
| Clean Water Act (CWA) 307                                    | No component listed |
| Clean Air Act Section 112(b) Hazardous Air Pollutants (HAPs) | No component listed |
| Clean Air Act Section 602 Class I Substances                 | No component listed |
| Clean Air Act Section 602 Class II Substances                | No component listed |
| DEA List I Chemicals (Precursor Chemicals)                   | No component listed |
| DEA List II Chemicals (Essential Chemicals)                  | No component listed |

**EPA List of Lists**

| Regulatory Name  | CAS No./SARA/<br>313 Category<br>Code <sup>i</sup> | SARA/<br>EPCRA 302<br>EHS TPQ <sup>ii</sup> | SARA/<br>EPCRA 304<br>EHS RQ <sup>iii</sup> | CERCLA<br>RQ <sup>iv</sup> | SARA/EPCRA<br>313 TRI <sup>v</sup> | RCRA<br>Code <sup>vi</sup> | CAA 112(r)<br>RMP TQ <sup>vii</sup> |
|------------------|--|---|---|----------------------------|------------------------------------|----------------------------|-------------------------------------|
| Sodium Hydroxide | 1310-73-2  | -   | -   | 1,000                      | -                                  | -                          | -                                   |

<sup>i</sup>SARA/313 Category Code: Emergency Planning and Community Right-to Know Act Section 313 Category Code

<sup>ii</sup>SARA/EPCRA 302 EHS TPQ: Extremely Hazardous Substance Threshold Planning Quantity (Emergency Planning and Community Right-to Know Act Section 302 Category Code)

<sup>iii</sup>SARA/EPCRA 304 EHS RQ: Extremely Hazardous Substance Reportable Quantity (Emergency Planning and Community Right-to Know Act Section 304 Category Code)

<sup>iv</sup>CERCLA RQ: Reportable Quantity (Comprehensive Environmental Response, Compensation, and Liability Act)

<sup>v</sup>SARA/EPCRA 313 TRI: Toxics Release Inventory (Emergency Planning and Community Right-to Know Act Section 313 Category Code)

<sup>vi</sup>RCRA Code: Resource Conservation and Recovery Act Code

<sup>vii</sup>CAA 112(r) RMP TQ: Risk Management Plan Threshold Quantity (Clean Air Act Section 112(r))

**United States Inventory (TSCA 8b):** All components are listed or exempted.

**Canada Domestic Substances List (DSL):** All components are listed.

15.2 **Chemical safety assessment:** A chemical safety assessment has not been carried out for the mixture by the supplier.

**SECTION 16. OTHER INFORMATION**

- Revisions:**
- Edition n. 01, dated 02/28/2011.
  - Revision n. 01, dated 11/24/2015. Main changes are in sections 2 to 16, adapting the SDS format and contents to Hazard Communication Standard (HCS), 29 CFR 1910.1200 (HazCom 2012), Hazardous Product Regulation HPR (WHMIS 2015), and Regulation (EU) 2015/830 of 28 May 2015.
- Acronyms:**
- ACGIH: American Conference of Governmental Industrial Hygienists
  - AIHA: American Industrial Hygiene Association
  - ADR: Agreement concerning the carriage of dangerous goods by Road
  - BCF: Bioaccumulative factor
  - BEI : Biological Exposure Indices
  - CAS: Chemical Abstract Service (division of the American Chemical Society)
  - CLP: Classification, Labeling and Packaging
  - DNEL: Derived No-Effect Levels
  - EC50: the effect concentration associated with 50% response.
  - EINECS: European Inventory of Existing Commercial Substances
  - EPA: US Environmental Protection Agency
  - IARC: International Agency for Research on Cancer
  - IATA: International Air Transport Association Code
  - IMDG: International Maritime Dangerous Goods Code
  - LC50: Lethal Concentration to 50 % of a test population
  - LD50: Lethal Dose to 50% of a test population (Median Lethal Dose)
  - LOEL: Lowest Observed Effect Level
  - MADL: Maximum Allowable Daily (or Dose) Level
  - NOAEL: No Observed Adverse Effect Level)
  - NOEC: no observed effect concentration, means the test concentration immediately below the lowest tested concentration with statistically significant adverse effect.
  - NSRL: National Science Research Laboratory
  - NTP: National Toxicology Program
  - OEL: Occupational Exposure Limit
  - OSHA: Occupational Safety and Health Administration

PPE : Personal protective Equipment  
 PBT: Persistent, Bio accumulative and Toxic substances  
 PNEC: Predicted No Effect Concentration  
 RID: Regulation concerning the International carriage of Dangerous goods by rail  
 TLV/TWA: Threshold Limit Value/Threshold Weighted Average  
 vPvB: very Persistent, very Bio accumulative  
 WEEL: Workplace Environmental Exposure Level (air concentration of agents in a healthy worker's breathing zone)

**Information related to the Regulation EC/1272/2008:**

Hazard statement(s): H315: Causes skin irritation.  
 H319: Causes serious eye irritation.  
 H302: Harmful if swallowed.  
 H318: Causes serious eye damage  
 H317: May cause an allergic skin reaction.  
 H314: Causes severe skin burns and eye damage.  
 H400: Very toxic to aquatic life.  
 H412: Harmful to aquatic life with long lasting effects.

**Information on workers training:** Follow National requirements to ensure protection of human health and the environment.

**Classification and procedure used to derive the classification for mixtures according to Regulation (EC) 1272/2008, according to Hazard Communication Standard, 29 CFR 1910.1200 (HCS), and according to HPR (WHMIS 2015) :**

| <i>Classification:</i> | <i>Classification procedure</i> |
|------------------------|---------------------------------|
| Not classified         | -                               |

The contained information in this SDS are in accordance with Annex II of the COMMISSION REGULATION (EU) No 1907/2006 (REACH) and its subsequent amendments, in accordance with Hazard Communication Standard (HCS), 29 CFR 1910.1200 (HazCom 2012) as recommended by US OSHA, and in accordance with Hazardous Product Regulation HPR (WHMIS 2015) as recommended by Health Canada (HC).

**Bibliographic references:**

- (1) HSDB Hazardous Substances Databank, Tromethamine
- (2) Screening-Level Hazard Characterization, Sponsored chemical 2-Amino-2-hydroxymethyl-1,3-propanediol (TRIS AMINO) CASRN 77-86-1, U.S. Environmental Protection Agency, Hazard Characterization Document, September, 2014
- (3) ECHA, Registration Dossier, Tromethamine, [http://apps.echa.europa.eu/registered/data/dossiers/DISS-d7f60455-0965-1602-e044-00144f67d031/AGGR-932e53a4-4218-4161-b380-2c99a562941f\\_DISS-d7f60455-0965-1602-e044-00144f67d031.html#AGGR-932e53a4-4218-4161-b380-2c99a562941f](http://apps.echa.europa.eu/registered/data/dossiers/DISS-d7f60455-0965-1602-e044-00144f67d031/AGGR-932e53a4-4218-4161-b380-2c99a562941f_DISS-d7f60455-0965-1602-e044-00144f67d031.html#AGGR-932e53a4-4218-4161-b380-2c99a562941f)
- (4) TEST PLAN For Tris(hydroxymethyl)aminomethane (77-86-1) Submitted to the U.S. Environmental Protection Agency Under the High Production Volume (HPV) Chemicals Challenge Program The Dow Chemical Company Midland, Michigan, 48674
- (5) Haz-Map, Tromethamine hydrochloride, available at <http://hazmap.nlm.nih.gov/category-details?table=copytblagents&id=18456>
- (6) Sigma Aldrich, SDS for Tromethamine Hydrochloride, Version 5.0, revision date 17.10.2013
- (7) GESTIS International Limit Values, available on [http://limitvalue.ifa.dguv.de/WebForm\\_ueliste.aspx](http://limitvalue.ifa.dguv.de/WebForm_ueliste.aspx)
- (8) ACGIH, TLVs and BEIs based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices, 2012
- (9) [Gestis Substance database](#), 1,2-Benzisothiazol-3(2H)-one, ZVG 35240
- (10) SCCS (Scientific Committee on Consumer Safety), Opinion on benzisothiazolinone, 26-27 June 2012
- (11) Product Safety Assessment: 1,2-Benzisothiazol-3(2H)-one (BIT) The Dow Chemical Company, Created: December 4, 2012
- (12) Environmental Assessment, FCN 001108, July 26, 2011, <http://www.fda.gov/downloads/Food/FoodIngredientsPackaging/EnvironmentalDecisions/UCM287533.pdf>
- (13) IUCLID data set for Sodium hydroxide, 18-feb-2000.
- (14) Sodium hydroxide, SIDS Initial Assessment Report For SIAM 14 Paris, 26-28 March 2002
- (15) Sodium hydroxide, IFA, GESTIS Substance database , ZVG n. 1270
- (16) Sodium hydroxide, ECHA, Registration dossier, available at [http://echa.europa.eu/it/information-on-chemicals/registered-substances?p\\_p\\_id=registeredsubstances\\_WAR\\_regsportlet&registeredsubstances\\_WAR\\_regsportlet\\_name=sc=&registeredsubstances\\_WAR\\_regsportlet\\_ec-number-sc=1310-73-2&registeredsubstances\\_WAR\\_regsportlet\\_cas-number-sc=1310-73-2&registeredsubstances\\_WAR\\_regsportlet\\_sc=true&registeredsubstances\\_WAR\\_regsportlet\\_do-search=](http://echa.europa.eu/it/information-on-chemicals/registered-substances?p_p_id=registeredsubstances_WAR_regsportlet&registeredsubstances_WAR_regsportlet_name=sc=&registeredsubstances_WAR_regsportlet_ec-number-sc=1310-73-2&registeredsubstances_WAR_regsportlet_cas-number-sc=1310-73-2&registeredsubstances_WAR_regsportlet_sc=true&registeredsubstances_WAR_regsportlet_do-search=)
- (17) Environmental and Health Assessment of Substances in Household Detergents and Cosmetic Detergent Products, available at <http://eng.mst.dk/>

**SECTION 1. IDENTIFICATION OF THE MIXTURE AND OF THE COMPANY**

**1.1 Identification of the mixture**

Product Name: **APC/CaCl<sub>2</sub>**  
Product Number: **000H01422**

**1.2 Use of the mixture:**

Relevant use: For in vitro diagnostic use.  
Uses advised against: There are no specific uses advised against.

**1.3 Company identification:**

MANUFACTURER:  
Instrumentation Laboratory Co.  
180 Hartwell Road,  
Bedford, MA 01730-2443 (USA)  
Tel. +1 800 678 0710  
Fax +1 781 863 9928

DISTRIBUTOR EU:  
Via Leonardo da Vinci, 36  
20877 Roncello (MB), Italy

DISTRIBUTOR US/CANADA:  
DiaPharma Group, Inc.  
8948 Beckett Rd.  
West Chester, OH 45069 (USA)

E-mail address of the competent person: [infosds@mail.ilww.it](mailto:infosds@mail.ilww.it)

**1.4 Emergency phone:** +44 (0) 3700 492 795  
+1 215 207 0061 (USA and Canada)

**SECTION 2. HAZARDS IDENTIFICATION**

**2.1 Classification of the mixture:**

This product is not classified as hazardous according to Regulation (EC) No 1272/2008.  
Classified as hazardous according to OSHA 29 CFR 1910.1200 and Hazardous Product Regulation HPR (WHMIS 2015).  
Any additional information concerning the risks for health and/or the environment are given in sections 11 and 12 of this sheet.

**According to Regulation (EC) No 1272/2008:**

| <i>Hazard class</i>                       | <i>Hazard category</i> | <i>Hazard statement</i> |
|---|------------------------|-------------------------|
| <b>Not classified</b>                     |                        |                         |
| <i>For exposure limits see section 8.</i> |                        |                         |

**According to Hazard Communication Standard, 29 CFR 1910.1200 (HCS), and according to Hazardous Product Regulation HPR (WHMIS 2015):**

| <i>Hazard class</i>                       | <i>Hazard category</i> | <i>Hazard statement</i>   |
|---|------------------------|---|
| <b>Sensitization-Respiratory</b>          | <b>Cat.1</b>           | <b>May cause allergy or asthma symptoms or breathing difficulties if inhaled.</b> |
| <i>For exposure limits see section 8.</i> |                        |   |

**Potential adverse physicochemical, human health and environmental effects** *(see also Ch. 9-12)*

Contains APC (Activated Protein C). May cause allergy or asthma symptoms or breathing difficulties if inhaled.  
Under normal conditions of use, the mixture does not cause other adverse effects to human health or adverse effects to the environment.


**2.2 Label elements:**

**According to Regulation (EC) No 1272/2008**

|                                    |   |
|------------------------------------|---|
| <b>Hazard pictogram(s):</b>        | None  |
| <b>Signal word(s):</b>             | None  |
| <b>Hazard statement(s):</b>        | None  |
| <b>Precautionary statement(s):</b> | None  |
| <b>Other labeling details:</b>     | Contains APC (Activated Protein C). May produce an allergic reaction. (EUH208)  |
|                                    | Safety data sheet available on request. (EUH210)  |
|                                    | Up to 3.97% of the mixture consists of component of unknown acute toxicity (dermal, inhalation) for the human health and for the aquatic environment. |



According to Hazard Communication Standard, 29 CFR 1910.1200 (HCS), and to Hazardous Product Regulation HPR (WHMIS 2015):

|                                    |  |
|------------------------------------|--|
| <b>Hazard pictogram(s):</b>        |   |
| <b>Signal word(s):</b>             | Danger   |
| <b>Hazard statement(s):</b>        | May cause allergy or asthma symptoms or breathing difficulties if inhaled.   |
| <b>Precautionary statement(s):</b> | Avoid breathing dust/fume.<br>If inhaled: If breathing is difficult, remove person to fresh air and keep comfortable for breathing.<br>If experiencing respiratory symptoms: Call a poison center/doctor.<br>Dispose of contents container in accordance with local/regional/national/international regulations. |
| <b>Other labeling details:</b>     | Up to 3.97% of the mixture consists of component of unknown acute toxicity (dermal, inhalation) for the human health and unknown hazard to the aquatic environment.  |

**Safety precautions:** Use the product in accordance with the Good Laboratory Practice.  
Wear suitable protective clothing, gloves and eye/face protection.  
Do not let the product enter drainage system, surface and ground-water or soil. Do not empty into drains.

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

The mixture does not meet the criteria for PBT or vPvB.

**Warning:**

The product contains bovine material. All donor animals were sourced from BSE-free herds. The cattle received ante- and post mortem health inspection by a veterinarian, and they were apparently free from infectious and contagious material. However, the material should be treated as potentially infectious.

Bovine serum albumin (BSA) might cause allergic skin reaction and/or allergy or asthma symptoms or breathing difficulties if inhaled.

This product contains human source material that tested non-reactive for HIV antibody, Hepatitis B Surface Antigen and Anti-HCV at the donor stage. This product, as with all human based specimens, should be handled with proper laboratory safety procedures to minimize the risk of transmission of infectious disease.

## SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

**Composition:** solid containing organic and inorganic components, bovine and human source material.

### 3.1 Hazardous components:

| Name  | EINECS/<br>ELINCS n°                               | CAS n°  | Conc. %<br>w/w* | Classification<br>29 CFR 1910.1200 (HCS)<br>HPR (WHMIS 2015)  | Classification<br>1272/2008/EC  |
|---|--|---|-----------------|---|---|
| Calcium chloride dihydrate<br><i>Index N. (Annex VI of CLP Reg.):<br/>017-013-00-2</i>  | 233-140-8<br>(as Calcium<br>chloride<br>anhydrous) | 10035-04-8<br>(10043-52-4<br>as Calcium<br>chloride<br>anhydr.) | 0.3-0.4%        | Eye damage/Irritation, cat. 2   | Eye Irrit.2, H319   |
| APC (Activated Protein C)<br><i>Index N. (Annex VI of CLP Reg.):<br/>647-014-00-9 - proteases with the<br/>exception of those specified<br/>elsewhere in this Annex</i> | Not available                                      | Not available   | 0.3-0.4%        | Skin Corrosion/Irritation, cat. 2<br>Eye damage/Eye Irritation, cat. 2A<br>Specific target organ Toxicity –<br>Single Exposure, cat. 3<br>Sensitization-Respiratory, cat. 1 | Skin Irrit. 2, H315<br>Eye Irrit. 2, H319<br>STOT SE 3, H335<br>Resp. Sens. 1, H334 |
| Tris Hydrochloride  | 214-684-5  | 1185-53-1   | 0.1-0.2%        | Skin Corrosion/Irritation, cat. 2<br>Eye damage/Eye Irritation, cat. 2B   | Skin Irrit. 2, H315<br>Eye Irrit. 2, H319   |
| Tris-Hydroxymethyl<br>aminomethane (Tris Amino)   | 201-064-4  | 77-86-1   | 0.02-<br>0.03%  | Skin Corrosion/Irritation, cat. 2   | Skin Irrit. 2, H315   |
| Manganese Chloride<br>Tetrahydrate  | 603-826-5  | 13446-34-9<br>(7773-01-5 as<br>manganese<br>chloride anh)       | 0.01-<br>0.02%  | Acute Tox. 4 – Oral, cat. 4<br>Eye damage/Eye Irritation, cat. 1<br>Specific target organ Toxicity –<br>Repeated Exposure, cat. 2<br>Aquatic Chronic, cat. 2**              | Acute Tox. 4, H302<br>Eye Dam.1, H318<br>STOT RE 2, H373<br>Aquatic Chronic 2 H411  |

*For exposure limits see Ch. 8, for hazard statements text see Ch. 16.  
\* A range may be indicated, considering batch-to batch variation.  
\*\*Environmental classification according to Reg. N. 1272/2008 (EC) and subsequent amendments.*

The mixture does not contain substances listed in the Hazardous Substance Lists and/or evaluated for carcinogenicity by IARC, NTP, OSHA. See Section 11 and 15.

## SECTION 4. FIRST AID MEASURES

### 4.1 Description of first aid measures

|                      |  |
|----------------------|--|
| Ingestion:           | If swallowed rinse mouth with plenty of water provided person is conscious. Do not induce vomiting. Get medical advice if adverse symptoms appear.   |
| Inhalation exposure: | If inhaled, move person to fresh air. If breathing is difficult, oxygen should be administered. Get medical advice immediately (show the SDS or the label were possible).  |
| Contact with skin:   | Remove contaminated clothes and shoes. Wash immediately affected area with soap or mild detergent and plenty of water until the removal of the mixture (15-20 minutes). Get medical advice if adverse symptoms appear. |
| Contact with eyes:   | Wash immediately with plenty of water or normal saline for at least 15 minutes. Keep eyelid open with the finger. Get medical advice if adverse symptoms appear.   |

### 4.2 Most important symptoms and effects (acute and delayed)

|          |   |
|----------|---|
| Acute:   | Inhalation: May cause irritation to the mucous membranes and upper respiratory tract.<br>Skin : May be irritant for skin.<br>Eyes: May cause irritation.<br>Ingestion: may cause irritation to the gastrointestinal mucous membranes.<br>Contains APC (Activated Protein C). May cause allergy or asthma symptoms or breathing difficulties if inhaled. The product contains bovine albumin that might cause allergic skin reaction and/or allergy or asthma symptoms or breathing difficulties if inhaled. |
| Delayed: | Delayed symptoms and effects are not known.   |

### 4.3 Indication of any immediate medical attention and special treatment needed

|                      |  |
|----------------------|--|
| Medical monitoring:  | Based on the assessment of risk of hazardous chemical agents, the competent person will settle the appropriate medical surveillance protocol, in accordance with the national/Community legislation, in order to protect the health status of the workers. |
| Antidotes, if known: | Not known.   |

## SECTION 5. FIRE-FIGHTING MEASURES

### 5.1 Extinguishing media

|                                 |  |
|---------------------------------|--|
| Suitable extinguishing media:   | Water spray or regular foam, CO <sub>2</sub> , dry powder. |
| Unsuitable extinguishing media: | Not known.   |

### 5.2 Special hazards arising from the substance or mixture

|                                |  |
|--------------------------------|--|
| Hazardous combustion products: | Thermal decomposition or combustion may generate toxic and hazardous fumes of CO <sub>x</sub> , NO <sub>x</sub> , HCl. |
|--------------------------------|--|

### 5.3 Advice for firefighters

|                                |   |
|--------------------------------|---|
| Protective actions:            | Water jets can be used successfully to cool containers exposed to the fire and disperse fumes.  |
| Equipment for self-protection: | Self-contained breathing apparatus, flame and chemical resistant clothing, boots and gloves. Equipment must be conformed with the national/international standards 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

|                                     |   |
|-------------------------------------|---|
| <b>For non-emergency personnel:</b> | Remove the ignition and heat sources, provide sufficient ventilation and evacuate the area. Respiratory protection: is not required. Where risk assessment shows air-purifying respirators are appropriate, use masks with approved filter. Suitable protective clothing, rubber or polythene gloves, rubber shoes, safety glasses. |
| <b>For emergency responders:</b>    | Wear appropriate protective equipment (see Section 8) to minimize exposure to the product.  |

- 6.2 Environmental precautions** Do not let the product enter drainage system, surface and ground-water or soil. Contact local authorities in case of environmental release. Do not empty into drains.
- 6.3 Methods and material for containment and cleaning up** Soak up with inert absorbent material, and clean with plenty of water. Collect spilled material in containers. Send to the storage waiting for disposal procedures.
- 6.4 Reference to other sections** See also section 8 and 13.

## SECTION 7. HANDLING AND STORAGE

- 7.1 Precautions for safe handling** Handle in a well ventilated place, and away from sparks and flames - sources of ignition. Keep the mixture away from drains, surface or ground waters. Avoid contact with incompatible materials. Wear suitable Personal Protection Equipment (see section 8). Do not eat, drink and smoke in the working areas. Wash hands with soap and water after handling the mixture. Remove contaminated clothing and protective equipment before entering eating areas.
- 7.2 Conditions for safe storage, incompatibilities** Recommended temperature: store at 2-8°C. Avoid light exposure and keep away from heat sources. Room ventilation: well ventilated workplace. Keep containers tightly closed and labeled with the name of the product. Avoid environmental release. Keep away from food and drinks.
- 7.3 Specific end use** *APC/CaCl<sub>2</sub>* is intended for in vitro diagnostic use. Contains APC (Activated Protein C). May cause allergy or asthma symptoms or breathing difficulties if inhaled. The material contains also human and bovine material, and should be treated as potentially infectious. Bovine serum albumin (BSA) might cause allergic skin reaction and/or allergy or asthma symptoms or breathing difficulties if inhaled. Avoid inhalation of dust/fume. Use the product in accordance with the Good Laboratory Practice.

## SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

### 8.1 Control parameters

**Community/National occupational exposure limit values:**

**Calcium chloride** <sup>(1)</sup>

Canada – Ontario: Occupational exposure limit (OEL) for calcium chloride of 5 mg/m<sup>3</sup> has been established by the Ministry of Labor

**Manganese and inorganic compounds (as Mn)** <sup>(20)</sup>

|                  | <i>Limit value – 8 hours</i>   | <i>Limit value – short term</i>  |
|------------------|--|--|
| Austria          | 0,5 mg/m <sup>3</sup> - inhalable aerosol  | 2 mg/m <sup>3</sup> - inhalable aerosol  |
| Belgium          | 0,2 mg/m <sup>3</sup>  |  |
| Denmark          | 0,2 mg/m <sup>3</sup>  | 0,4 mg/m <sup>3</sup>  |
| Finland          | 0,2 mg/m <sup>3</sup> – inhalable fraction<br>0.02 mg/m <sup>3</sup> - respirable fraction |  |
| Germany (AGS)    | 0,5 mg/m <sup>3</sup> - inhalable aerosol  |  |
| Germany (DFG)    | 0.02 mg/m <sup>3</sup> - respirable aerosol<br>0,2 mg/m <sup>3</sup> - inhalable aerosol   | 0.16 mg/m <sup>3</sup> - respirable aerosol <sup>(a)/(c)</sup><br>1.6 mg/m <sup>3</sup> - inhalable aerosol <sup>(b)/(c)</sup> |
| Hungary          | 5 mg/m <sup>3</sup>  | 20 mg/m <sup>3</sup>   |
| Ireland          | 0,2 mg/m <sup>3</sup> – manganese fume   | 3 mg/m <sup>3</sup> – manganese fume <sup>(c)</sup>  |
| Latvia           | 0.1 mg/m <sup>3</sup> – welding aerosol  |  |
| Poland           | 0.3 mg/m <sup>3</sup>  |  |
| Spain            | 0.2 mg/m <sup>3</sup>  |  |
| Sweden           | 0.2 mg/m <sup>3</sup> - total aerosol<br>0.1 – respirable fraction                         |  |
| Switzerland      | 0,5 mg/m <sup>3</sup> - inhalable aerosol  |  |
| United Kingdom   | 0,5 mg/m <sup>3</sup>  |  |
| Canada - Ontario | 0.2 mg/m <sup>3</sup>  |  |
| Canada- Quebec   | 5 mg/m <sup>3</sup>  |  |
| USA - NIOSH      | 1 mg/m <sup>3</sup>  | 3 mg/m <sup>3</sup> <sup>(c)</sup>   |
| USA - OSHA       |  | 5 mg/m <sup>3</sup>  |

SCOEL: 8 hour TWA: 0.200 mg/m<sup>3</sup> (inhalable fraction); 0.050 mg/m<sup>3</sup> (respirable fraction) <sup>(14)</sup>

**Manganous chloride, anhydr.** Finland  
(20)

0,2 mg/m<sup>3</sup> – inhalable fraction, calculated as Mn  
0.02 mg/m<sup>3</sup> - respirable fraction, calculated as Mn

<sup>(a)</sup> permanganates: STV 0,02 mg/m<sup>3</sup>; <sup>(b)</sup> permanganates: STV 0,2 mg/m<sup>3</sup>; <sup>(c)</sup> 15 minutes average value; <sup>(d)</sup> Manganese and compounds as Mn.

**Community/National biological exposure limit values:** Not established.

**DNEL values (components):**

| Component                               | Route of exposure   | Workers       |          |                 |          | Consumers     |          |                 |          |
|---|---|---------------|----------|-----------------|----------|---------------|----------|-----------------|----------|
|   |   | Acute effects |          | Chronic effects |          | Acute effects |          | Chronic effects |          |
|   |   | local         | systemic | local           | systemic | local         | systemic | local           | systemic |
| Calcium chloride anhydr. <sup>(3)</sup> | Oral (mg/(mg/kg bw/day)<br>Dermal (mg/kg bw/day)<br>Inhalation (mg/m <sup>3</sup> ) | 10            |          | 5               |          | 5             |          | 2.5             |          |

The measurement of substances at the workplace must be carried out with standardized methods or, failing that, with appropriate methods.

## 8.2 Exposure controls

### 8.2.1. Appropriate engineering controls

Appropriate risk management measures, that must be adopted at the workplace, have to be selected and applied, following the risks assessment carried out by the employer, in connection with his working activity. If the results of this evaluation show that the general and collective prevention measures are not sufficient to reduce the risk, and if you cannot prevent exposure to the mixture by other means, adequate personal protective equipment must be adopted, complying with the relevant technical national/international standards.

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

Respiratory protection: Respiratory protection is not required. Where risk assessment shows air-purifying respirators are appropriate, use masks with approved filter.  
Use only devices approved by the Competent Authorities such as NIOSH (USA) and CEN (EU).

Skin protection: Protective clothing, rubber gloves.

Eye protection: Safety glasses.

Hand protection: Protective gloves.

Other protective systems: Personal protective equipment (PPE) useful for reducing individual exposure.

### 8.2.3. Environmental exposure controls

Avoid any release into the environment.

## SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

### 9.1 Information on basic physical and chemical properties

|                       | Value              | Related to |
|-----------------------|--------------------|------------|
| Appearance:           | Lyophilized, solid |            |
| Odor:                 | not available      |            |
| Color:                | White to off white |            |
| pH:                   | 7.4 – 7.6          | Mixture    |
| Flammability:         | Not available      |            |
| Explosive properties: | Not available      |            |
| Oxidizing properties: | Not available      |            |
| Density:              | Not available      |            |
| Solubility:           | not available      |            |
| Water Solubility:     | Soluble            | Mixture    |
| Melting point/range:  | not available      |            |

### 9.2 Other information

Miscibility Not applicable

## SECTION 10. STABILITY AND REACTIVITY

### 10.1 Reactivity

This mixture is considered not reactive under the normal conditions of the usage.

|  |  |
|--|--|
| <b>10.2 Chemical stability</b>                 | The product is stable until the expiration date shown on the box and on the labels when stored at 2 – 8 °C.            |
| <b>10.3 Possibility of hazardous reactions</b> | Not foreseen.  |
| <b>10.4 Conditions to avoid:</b>               | Keep away from heat, water, humidity and light.  |
| <b>10.5 Incompatible materials</b>             | Strong oxidising agents.   |
| <b>10.6 Hazardous decomposition products:</b>  | Thermal decomposition or combustion may generate toxic and hazardous fumes of CO <sub>x</sub> , HCl, NO <sub>x</sub> . |

## SECTION 11. TOXICOLOGICAL INFORMATION

The health effects of the product have not been thoroughly investigated. Data on toxicological effects of the hazardous ingredients are provided below.

### 11.1 Information on toxicological effects

#### Symptoms and effects for each route of exposure:

|                    |   |
|--------------------|---|
| Dermal:            | Prolonged or repeated skin contact may cause irritation.  |
| Contact with eyes: | May cause irritation.   |
| Ingestion:         | Ingestion may cause irritation to the gastrointestinal mucous membranes.  |
| Inhalation:        | Inhalation of the product may cause irritation to respiratory ways.   |
| Other:             | Contains APC (Activated Protein C). May cause allergy or asthma symptoms or breathing difficulties if inhaled. The product contains bovine albumin, that might cause allergic skin reaction and/or allergy or asthma symptoms or breathing difficulties if inhaled. |

#### Toxicokinetic effects (Absorption, Distribution, Metabolism, Excretion):

*Calcium chloride* : is easily dissociated into calcium and chloride ions in water. The absorption, the distribution and the excretion of the ions in animals are regulated separately. Both ions are essential constituents of the body of all animals. <sup>(1)</sup>

*Tris amino*: is not metabolized appreciably and is eliminated by the kidneys. Ionized tromethamine is excreted by kidney, so the effect is that of excretion of hydrogen ions. Elimination of drug from body is entirely by renal excretion. It is not known whether tromethamine is distributed into human milk. <sup>(4)</sup>

*Manganese chloride* was readily absorbed after oral gavage, intraperitoneal injection, or intratracheal instillation and distributed in brain tissue to varying degrees. While rodents are able to absorb manganese via the olfactory bulb with subsequent direct accumulation in the brain, this route has not been established in humans. The major route of manganese excretion is via the bile, although some excretion occurs in urine, milk, and sweat. <sup>(12)</sup>

| Acute toxicity     | Value                     | m.u.  | Effects  | Related to                      |
|--------------------|---------------------------|---|--|---------------------------------|
| <u>Oral:</u>       | LD50 (rat) > 3,000        | mg/kg   |  | <sup>(5)</sup> Tris Amino       |
|                    | LD50 (rat) =3,798 - 4,179 | mg/Kg   | The acute oral toxicity is attributed to the severe irritating property of the original substance or its high-concentration solutions to the gastrointestinal tract. | <sup>(1)</sup> Calcium chloride |
|                    | LD50 (rabbit)=500 – 1,000 |   |  |                                 |
| LD50 (rat) = 1,484 | mg/Kg                     | <sup>(10)</sup> Manganese chloride tetrahydrate |  |                                 |
| <u>Dermal:</u>     | LD50 (rat) > 5,000        | mg/kg   |  | <sup>(6)</sup> Tris Amino       |
|                    | LD50 (rabbit) > 5,000     | mg/Kg   |  | <sup>(1)</sup> Calcium chloride |
| <u>Inhalation:</u> | LC50 (rat) > 40           | mg/m <sup>3</sup> /4h                           |  | <sup>(1)</sup> Calcium chloride |
| <u>Other data:</u> | Not available.            |   |  |                                 |

#### Corrosion/Irritation

##### Skin Corrosion/Irritation

*Tris Amino*: Tromethamine was a mild irritant to rabbits at 25% with a pH of 10.8. At 40%, tromethamine was not irritating. Intradermal injections of tromethamine were severely irritating to rabbits at pH 10.4 but were only mildly irritating at pH 7.4. The supporting substance 2-Amino-2-methyl-1-Propanol (AMP) was found to be irritating to rabbits, with burrowing lesions noted when applied to abraded skin sites; there was mild irritation noted when applied to unabraded skin. <sup>(5)</sup>

*Tris Hydrochloride*: irritant to skin (read across from Tris Amino).

| Serious eye damage/ irritation    | <p><i>Calcium chloride</i> is not irritating for the skin. <sup>(1)</sup></p> <p><i>Manganese dichloride</i> is not a dermal irritant. <sup>(11)</sup></p> <p><i>Tris Amino (100%)</i> was not an ocular irritant when administered to rabbits. <sup>(5)</sup></p> <p><i>Tris Hydrochloride</i> : mild eye irritant in rabbits.</p> <p><i>Calcium chloride</i> is irritating for the eyes. <sup>(1)</sup></p> <p><i>MnCl<sub>2</sub></i>: was a severe irritant to the rabbit eyes in an in vivo test according to OECD Guideline 405. <sup>(11)</sup></p>   |           |      |      |     |                     |  |  |  |
|-----------------------------------|--|-----------|------|------|-----|---------------------|--|--|--|
| <b>Sensitization:</b>             |  |           |      |      |     |                     |  |  |  |
| <u>Skin sensitization:</u>        | <p><i>Tris Amino</i>: The supporting chemical AMP is not sensitizing to guinea pig skin. <sup>(5)</sup></p> <p><i>Tris Hydrochloride</i>: Not a sensitizer in experimental animals. <sup>(8)</sup></p> <p><i>Calcium chloride</i>: Due to lack of data the classification is not possible.</p> <p><i>Manganese dichloride</i> is not a sensitizer. <sup>(11)</sup></p> <p><i>Bovine serum albumin (BSA)</i>, which is present in bovine plasma, could develop allergic skin reactions in laboratory workers after dealing with BSA powder. Based on the available data, the criteria for classification are not satisfied.</p>   |           |      |      |     |                     |  |  |  |
| <u>Respiratory sensitization:</u> | <p><i>Bovine serum albumin (BSA)</i>, which is present in bovine plasma, could develop allergic reactions in laboratory workers after dealing with BSA powder. It is reported a case of occupational asthma and rhinitis in a laboratory worker caused by the inhalation of 100% BSA powder. The patient had a high serum-specific IgE level to BSA, and experienced severe systemic reactions, including eye itching, conjunctivitis, rhinorrhea, nasal obstruction, sneezing, shortness of breath, bronchospasm and decreased blood pressure. It was suggested an IgE-mediated response as the pathogenic mechanism.<sup>(19)</sup> Based on the available data, the criteria for classification are not satisfied.</p>  |           |      |      |     |                     |  |  |  |
| <b>CMR effects</b>                |  |           |      |      |     |                     |  |  |  |
| <u>Germ cell mutagenicity:</u>    | <p><i>Tris Amino</i>: The supporting chemical, AMP, was not mutagenic to bacteria and mammalian cells in vitro, and did not induce micronuclei in mice in vivo.</p> <p><i>Tris Hydrochloride</i>: Ames test negative.<sup>(9)</sup></p> <p><i>Calcium chloride</i>: Genetic toxicity of calcium chloride was negative in the bacterial mutation tests and the mammalian chromosome aberration test. <sup>(1)</sup></p> <p><i>Manganese dichloride</i> : The current literature indicates that Mn may be weakly mutagenic in vitro and possibly clastogenic in vivo, with unknown genotoxic effects in humans. It seems probable that the positive results reported in several short term tests are not due to intrinsic, direct genotoxicity of manganese, but to indirect mechanisms. The genotoxicity of manganese compounds seems to be mediated by the bivalent ion Mn<sup>2+</sup> at relatively high and cytotoxic concentrations. Based on the presently available data no overall conclusion can be made on the possible genotoxic hazard to humans.<sup>(17)(18)</sup></p>  |           |      |      |     |                     |  |  |  |
| <u>Reproductive toxicity:</u>     | <p><i>Tris Amino</i>: In an oral gavage combined reproductive/developmental toxicity screening test in rats no effects on reproductive or developmental parameters were observed at the doses tested; the NOAEL for reproductive and developmental toxicity is 1000 mg/kg-day, the highest dose tested. <sup>(5)</sup></p> <p><i>Calcium chloride</i>: No reproductive toxicity study has been reported. A developmental toxicity study equivalent to an OECD Guideline Study reveals no toxic effects on dams or fetuses at doses up to 189 mg/kg bw/day (mice), 176 mg/kg bw/day (rats) and 169 mg/kg bw/day (rabbits). <sup>(1)</sup></p> <p><i>Manganese dichloride</i> : Evidence obtained in laboratory mammals indicates that exposure to high levels of manganese may adversely affect sperm quality, produce decreased testicular weights, and impair development of the male reproductive tract. Impotence and loss of libido are common symptoms in male workers afflicted with clinically identifiable signs of manganism. No direct effect of manganese toxicity has been observed on fertility in women. No information is available on developmental effects of manganese in humans. Decreased activity levels and a decrease in average pup weight have been noted in the offspring of mice exposed to manganese by inhalation.<sup>(13)</sup></p> |           |      |      |     |                     |  |  |  |
| <u>Carcinogenesis:</u>            | <p>Substances listed in the National Toxicology Program (NTP) Report on Carcinogens, in the International Agency for Research on Cancer (IARC) Monographs or found to be potential carcinogen by OSHA:</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: left;">Substance</th> <th style="text-align: left;">OSHA</th> <th style="text-align: left;">IARC</th> <th style="text-align: left;">NTP</th> </tr> </thead> <tbody> <tr> <td colspan="4" style="text-align: center;">No component listed</td> </tr> </tbody> </table> <p><i>Tris Amino</i>: based on the available data, the substance is not carcinogenic. <sup>(7)</sup></p>   | Substance | OSHA | IARC | NTP | No component listed |  |  |  |
| Substance                         | OSHA   | IARC      | NTP  |      |     |                     |  |  |  |
| No component listed               |  |           |      |      |     |                     |  |  |  |

*Manganese dichloride* : Oral human and animal studies on manganese are inadequate. Several animal studies reported an increased incidence of thyroid gland follicular cell adenomas and hyperplasia, or increased incidence of pancreatic tumors. There is insufficient evidence to indicate that inorganic Mn exposure produces cancer in animals or humans. EPA has classified manganese as a Group D, not classifiable as to carcinogenicity in humans. <sup>(13)</sup>

**STOT –single exposure** Not available.

**STOT – repeated exposure** *Tris Amino*: There are no documented long-term effects of Tris Amino treatment, and no serious side-effects on record that are directly attributed to treatment with the compound. <sup>(6)</sup>

*Calcium chloride*: A study for repeated dose oral toxicity in rats shows no adverse effect of calcium chloride on rats fed 20 mg CaCl<sub>2</sub>/g diet (comparable to 1000 mg/kg bw/day or more) for 12 months. <sup>(1)</sup>

*Manganese dichloride* : The lungs, nervous system and reproductive system are the main organs affected following inhalation exposures to manganese, although other effects have also been observed. <sup>(12)</sup> Workers chronically exposed to concentrations of manganese dust averaging 20 mg/m<sup>3</sup> showed signs of manganism. <sup>(15)</sup> Chronic exposure to concentrations averaging 210 mg/m<sup>3</sup> Mn have been associated with pneumonia.

**Aspiration hazards** Not available.

**Other information:** Not available.

**Reasons for the lack of classification:**

Where the mixture resulted in a non-classification, this may be due to the availability of data which does not impose a classification for that specific end-point, or due to lack of data, or due to availability of inconclusive data or data which are not sufficient to get a classification as for the criteria adopted in Regulations mentioned in this data sheet.

**SECTION 12. ECOLOGICAL INFORMATION**

The environmental effects of the product have not been thoroughly investigated. Data on toxicological effects of the hazardous ingredients are provided below.

| 12.1 Toxicity                                   | species, media, units, test duration and test conditions.  | Related to                                      |
|---|--|---|
| Acute toxicity with fish:                       | LC50 <i>Leuciscus idus</i> > 10,000 mg/L/ 96-h   | <sup>(5)</sup> Tris Amino                       |
|   | LC50 <i>Pimephales promelas</i> = 4,630 mg/l/96 hours  | <sup>(1)</sup> Calcium chloride                 |
|   | LC50 <i>Oncorhynchus mykiss</i> = 4.8 mg/l/96 hours  | <sup>(16)</sup> Manganese                       |
| Chronic toxicity with fish:                     | 28-day LC50 (embryo-larval test) = 2.9 mg/l  | <sup>(16)</sup> MnCl <sub>2</sub>               |
| Acute toxicity with crustaceans:                | Water fleas ( <i>Daphnia magna</i> ) were exposed to AMP at unspecified concentrations for 48 hours. LC50 = 193 mg/L/48 h.   | <sup>(4)</sup> Tris Amino                       |
|   | EC50 daphnia > 100 mg/l/48h  | <sup>(9)</sup> Tris HCl                         |
|   | EC50 <i>Daphnia magna</i> = 1062 mg/L/48 hr  | <sup>(1)</sup> Calcium chloride                 |
|   | EC50 <i>Daphnia magna</i> = 4.7–56.1 mg/L/48 hr  | <sup>(16)</sup> MnCl <sub>2</sub>               |
| Chronic toxicity with crustaceans:              | The chronic toxicity study with <i>Daphnia magna</i> shows that a 16% impairment of reproduction (EC16) is caused at the concentration of 320 mg/L.                          | <sup>(1)</sup> Calcium chloride                 |
|   | 21-day EC50 = 5.7 mg/L   | <sup>(16)</sup> MnCl <sub>2</sub>               |
|   | NOEC = 0.01 mg/l/60 days   | <sup>(11)</sup> Manganese chloride tetrahydrate |
| Acute toxicity with algae:                      | EC50 <i>Selenastrum capricornutum</i> >100 mg/L/ 96 h  | <sup>(5)</sup> Tris Amino                       |
|   | EC50 <i>Selenastrum capricornutum</i> = 2900 mg/L/72 hours (biomass)   | <sup>(1)</sup> Calcium chloride                 |
|   | EC50 (growth inhibition) = 8.3 mg/L/72h  | <sup>(16)</sup> Manganese                       |
| Chronic toxicity with algae:                    | EC50 <i>Pseudokirchneriella subcapitata</i> = 3.1 mg/L /14 day (total cell volume reduction)   | <sup>(16)</sup> MnCl <sub>2</sub>               |
| Toxicity data on soil micro- and macroorganisms | Not available.   |   |
| Toxicity data on birds, bees and plants:        | Not available.   |   |
| 12.2 Persistence and degradability:             | <i>Tris Amino</i> is not readily biodegradable is expected to have moderate persistence. <sup>(4)</sup><br><i>Tris Hydrochloride</i> : readily biodegradable. <sup>(9)</sup> |   |



Once emitted into the environment, calcium chloride which has a high water solubility, will dissociate into the calcium and the chloride anion. The calcium ion may bind to soil particulate or may form stable inorganic salts with sulphate and carbonate ions.

**12.3 Bioaccumulation potential:** *Tris-Hydroxymethyl aminomethane* is expected to have low bioaccumulation potential. <sup>(4)</sup>

*Manganese* in water can be significantly bio concentrated at lower trophic levels. Bio concentration factors (BCFs) of 10000-20000 for marine and freshwater plants, 2500-6300 for phytoplankton, 300-5500 for marine algae, and 35-930 for fish have been estimated. The high reported BCFs probably reflect the essentiality of manganese for a wide variety of organisms. <sup>(12)</sup>

Considering its dissociation properties, *Calcium chloride* per se is not expected to accumulate in living organisms.

**12.4 Mobility in soil:** *Tris Amino* is expected to have high mobility in soil. <sup>(5)</sup>

Manganese is ubiquitous in the environment; it is often transported in rivers adsorbed to suspended sediments. <sup>(12)</sup>

The chloride ion is mobile in soil and eventually drains into surface water because it is readily dissolved in water.

**12.5 Results of PBT and vPvB assessment** Not performed.

**12.6 Other toxic effects:** Not available.

## SECTION 13. DISPOSAL CONSIDERATION

National laws on disposal must be considered, local and UE requirements for wastes recycling must be respected.

### 13.1 Waste treatment methods

Used waste product, surplus product or spillage products shall be disposed of in accordance with national, state and local laws.

## SECTION 14. TRANSPORT INFORMATION

Not classified in accordance with ADR/RID, IMDG, IATA and DOT regulations.

## SECTION 15. REGULATORY INFORMATION

### 15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture

#### EU Regulations

\* 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 (Official Journal L 183 , 29/06/1989 P. 0001 – 0008) 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.

\* Council Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices.

\* Commission Regulation (EU) 2015/830 of 28 May 2015 amending Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH).

\* Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December on classification, labelling and packaging of substances and mixtures 2008 (and subsequent amendments and supplements).

**Restriction of use:** none

**Substance(s) under authorization:** none

#### US Federal Regulations:

| State         | Components listed   | Note |
|---------------|---------------------|------|
| Massachusetts | No component listed |      |
| New York      | No component listed |      |
| New Jersey    | No component listed |      |
| Pennsylvania  | No component listed |      |

#### California Prop. 65

| Ingredient name     | Cancer | Reproductive | NSRL or MADL (µg/day) |
|---------------------|--------|--------------|-----------------------|
| No component listed |        |              |                       |

|  |                     |
|--|---------------------|
| Clean Water Act (CWA) 307                                    | No component listed |
| Clean Air Act Section 112(b) Hazardous Air Pollutants (HAPs) | No component listed |
| Clean Air Act Section 602 Class I Substances                 | No component listed |
| Clean Air Act Section 602 Class II Substances                | No component listed |
| DEA List I Chemicals (Precursor Chemicals)                   | No component listed |
| DEA List II Chemicals (Essential Chemicals)                  | No component listed |

**EPA List of Lists**

| Regulatory Name     | CAS No./SARA/313 Category Code <sup>I</sup> | SARA/EPCRA 302 EHS TPQ <sup>II</sup> | SARA/EPCRA 304EHS RQ <sup>III</sup> | CERCLA RQ <sup>IV</sup> | SARA/EPCRA 313 TRI <sup>V</sup> | RCRA Code <sup>VI</sup> | CAA 112(r) RMP TQ <sup>VII</sup> |
|---------------------|---|--------------------------------------|-------------------------------------|-------------------------|---------------------------------|-------------------------|----------------------------------|
| No component listed |   |                                      |                                     |                         |                                 |                         |                                  |

<sup>I</sup>SARA/313 Category Code: Emergency Planning and Community Right-to Know Act Section 313 Category Code

<sup>II</sup>SARA/EPCRA 302 EHS TPQ: Extremely Hazardous Substance Threshold Planning Quantity (Emergency Planning and Community Right-to Know Act Section 302 Category Code)

<sup>III</sup>SARA/EPCRA 304 EHS RQ: Extremely Hazardous Substance Reportable Quantity (Emergency Planning and Community Right-to Know Act Section 304 Category Code)

<sup>IV</sup>CERCLA RQ: Reportable Quantity (Comprehensive Environmental Response, Compensation, and Liability Act)

<sup>V</sup>SARA/EPCRA 313 TRI: Toxics Release Inventory (Emergency Planning and Community Right-to Know Act Section 313 Category Code)

<sup>VI</sup>RCRA Code: Resource Conservation and Recovery Act Code

<sup>VII</sup>CAA 112(r) RMP TQ: Risk Management Plan Threshold Quantity (Clean Air Act Section 112(r))

**United States Inventory (TSCA 8b):** All components are listed or exempted.

**Canada Domestic Substances List (DSL):** All components are listed.

15.2 **Chemical safety assessment:** A chemical safety assessment has not been carried out for the mixture by the supplier.

**SECTION 16. OTHER INFORMATION**

- Revisions:**
- Edition n. 01, dated 02/28/2011.
  - Revision n. 01, dated 11/24/2015. Main changes are in sections 2 to 16, adapting the SDS format and contents to Hazard Communication Standard (HCS), 29 CFR 1910.1200 (HazCom 2012), Hazardous Product Regulation HPR (WHMIS 2015), and Regulation (EU) 2015/830 of 28 May 2015.
- Acronyms:**
- ACGIH: American Conference of Governmental Industrial Hygienists
  - AIHA: American Industrial Hygiene Association
  - ADR: Agreement concerning the carriage of dangerous goods by Road
  - BCF: Bioaccumulative factor
  - BEI : Biological Exposure Indices
  - CAS: Chemical Abstract Service (division of the American Chemical Society)
  - CLP: Classification, Labeling and Packaging
  - DNEL: Derived No-Effect Levels
  - EC50: the effect concentration associated with 50% response.
  - EINECS: European Inventory of Existing Commercial Substances
  - EPA: US Environmental Protection Agency
  - IARC: International Agency for Research on Cancer
  - IATA: International Air Transport Association Code
  - IMDG: International Maritime Dangerous Goods Code
  - LC50: Lethal Concentration to 50 % of a test population
  - LD50: Lethal Dose to 50% of a test population (Median Lethal Dose)
  - LOEL: Lowest Observed Effect Level
  - MADL: Maximum Allowable Daily (or Dose) Level
  - NOAEL: No Observed Adverse Effect Level
  - NOEC: no observed effect concentration, means the test concentration immediately below the lowest tested concentration with statistically significant adverse effect.
  - NSRL: National Science Research Laboratory
  - NTP: National Toxicology Program
  - OEL: Occupational Exposure Limit
  - OSHA: Occupational Safety and Health Administration
  - PPE : Personal protective Equipment
  - PBT: Persistent, Bio accumulative and Toxic substances

PNEC: Predicted No Effect Concentration  
 RID: Regulation concerning the International carriage of Dangerous goods by rail  
 TLV/TWA: Threshold Limit Value/Threshold Weighted Average  
 vPvB: very Persistent, very Bio accumulative  
 WEEL: Workplace Environmental Exposure Level (air concentration of agents in a healthy worker's breathing zone)

**Information related to the Regulation EC/1272/2008:**

Hazard statement(s): H315: Causes skin irritation.  
 H319: Causes serious eye irritation.  
 H302: Harmful if swallowed.  
 H335: May cause respiratory irritation.  
 H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled.  
 H318: Causes serious eye damage.  
 H373: May cause damage to organs  
 H411: Toxic to aquatic life with long lasting effects.

**Information on workers training:** Follow National requirements to ensure protection of human health and the environment.

**Classification and procedure used to derive the classification for mixtures according to Regulation (EC) 1272/2008, according to Hazard Communication Standard, 29 CFR 1910.1200 (HCS), and according to HPR (WHMIS 2015) :**

| <i>Classification according to Regulation (EC) 1272/2008:</i>                      | <i>Classification procedure</i> |
|--|---------------------------------|
| <b>Not classified</b>  | -                               |
| <i>Classification according to 29 CFR 1910.1200 (HCS), and to HPR (WHMIS 2015)</i> |                                 |
| <b>May cause allergy or asthma symptoms or breathing difficulties if inhaled.</b>  | <b>Cut-off method</b>           |

The contained information in this SDS are in accordance with Annex II of the COMMISSION REGULATION (EU) No 1907/2006 (REACH) and its subsequent amendments, in accordance with Hazard Communication Standard (HCS), 29 CFR 1910.1200 (HazCom 2012) as recommended by US OSHA, and in accordance with Hazardous Product Regulation HPR (WHMIS 2015) as recommended by Health Canada (HC).

**Bibliographic references:**

- (1) Calcium Chloride, SIDS Initial Assessment Report For SIAM 15 Boston, USA 22-25th October 2002
- (2) ChemIDplus Lite, full records for CAS 302-95-4.
- (3) Calcium chloride anh., Registration dossier, available at: [http://apps.echa.europa.eu/registered/data/dossiers/DISS-9eb43f6f-23a1-5205-e044-00144f67d031/AGGR-dc2ba8fd-c7fc-402e-906e-b6cd0864ad5e\\_DISS-9eb43f6f-23a1-5205-e044-00144f67d031.html#AGGR-dc2ba8fd-c7fc-402e-906e-b6cd0864ad5e](http://apps.echa.europa.eu/registered/data/dossiers/DISS-9eb43f6f-23a1-5205-e044-00144f67d031/AGGR-dc2ba8fd-c7fc-402e-906e-b6cd0864ad5e_DISS-9eb43f6f-23a1-5205-e044-00144f67d031.html#AGGR-dc2ba8fd-c7fc-402e-906e-b6cd0864ad5e)
- (4) HSDB Hazardous Substances Databank, Tromethamine
- (5) Screening-Level Hazard Characterization, Sponsored chemical 2-Amino-2-hydroxymethyl-1,3-propanediol (TRIS AMINO) CASRN 77-86-1, U.S. Environmental Protection Agency, Hazard Characterization Document, September, 2014
- (6) ECHA, Registration Dossier, Tromethamine, [http://apps.echa.europa.eu/registered/data/dossiers/DISS-d7f60455-0965-1602-e044-00144f67d031/AGGR-932e53a4-4218-4161-b380-2c99a562941f\\_DISS-d7f60455-0965-1602-e044-00144f67d031.html#AGGR-932e53a4-4218-4161-b380-2c99a562941f](http://apps.echa.europa.eu/registered/data/dossiers/DISS-d7f60455-0965-1602-e044-00144f67d031/AGGR-932e53a4-4218-4161-b380-2c99a562941f_DISS-d7f60455-0965-1602-e044-00144f67d031.html#AGGR-932e53a4-4218-4161-b380-2c99a562941f)
- (7) TEST PLAN For Tris(hydroxymethyl)aminomethane (77-86-1) Submitted to the U.S. Environmental Protection Agency Under the High Production Volume (HPV) Chemicals Challenge Program The Dow Chemical Company Midland, Michigan, 48674
- (8) Haz-Map, Tromethamine hydrochloride, available at <http://hazmap.nlm.nih.gov/category-details?table=copytblagents&id=18456>
- (9) Sigma Aldrich, SDS for Tromethamine Hydrochloride, Version 5.0, revision date 17.10.2013
- (10) Chem IDplus Lite, Manganese chloride CAS 13446-34-9, full record.
- (11) Manganese chloride, Registration dossier on ECHA, [http://apps.echa.europa.eu/registered/data/dossiers/DISS-d0199b46-1b60-45f1-e044-00144f67d249/AGGR-2bff20de-de08-4c42-98b1-1ea417f81bab\\_DISS-d0199b46-1b60-45f1-e044-00144f67d249.html#AGGR-2bff20de-de08-4c42-98b1-1ea417f81bab](http://apps.echa.europa.eu/registered/data/dossiers/DISS-d0199b46-1b60-45f1-e044-00144f67d249/AGGR-2bff20de-de08-4c42-98b1-1ea417f81bab_DISS-d0199b46-1b60-45f1-e044-00144f67d249.html#AGGR-2bff20de-de08-4c42-98b1-1ea417f81bab)
- (12) IPCS Inchem, Concise International Chemical Assessment Document, Manganese and its compounds.
- (13) United States Environmental Protection Agency, Manganese Compounds, Hazard Summary-Created in April 1992; Revised in February 16,2010.
- (14) Recommendation from the Scientific Committee on Occupational Exposure Limits for manganese and inorganic manganese compounds, SCOEL/SUM/127, June 2011
- (15) Haz-Map: Occupational Exposure to Hazardous Agents, Manganese.
- (16) Concise International Chemical Assessment Document 63, MANGANESE AND ITS COMPOUNDS:ENVIRONMENTAL ASPECTS
- (17) The mutagenicity and carcinogenicity of inorganic manganese compounds: a synthesis of the evidence, J Toxicol Environ Health B Crit Rev. 2011;14(8):537-70. doi: 10.1080/10937404.2011.615111.
- (18) SCF/CS/NUT/UPPLEV/21 Final Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of manganese (expressed on 19 October 2000)

- <sup>(19)</sup> <http://e-aair.org> - Allergy, Asthma and Immunology Research (AAIR) 2009, October, Occupational asthma caused by inhalation of bovine serum albumin powder, Case report
- <sup>(20)</sup> GESTIS International Limit Values, available on [http://limitvalue.ifa.dguv.de/WebForm\\_ueliste.aspx](http://limitvalue.ifa.dguv.de/WebForm_ueliste.aspx)