SAFETY DATA SHEET
COAMATIC® HEPARIN

Doc. ID: SDS00082339363_EN
Revision: 02
CO: 459601
Edited on: 10/28/2015

IDENTIFICATION OF THE PRODUCT AND OF THE COMPANY

Identification of the product

Product Name: **COAMATIC® HEPARIN**

Product Number: **82339363**

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:
Instrumentation Laboratory Co.
526 Route 303
Orangeburg, New York 10962 (USA)

E-mail address of the competent person: 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 According to Hazard Communication Standard, 29 CFR 1910.1200 (HCS) Hazardous Product Regulation HPR (WHMIS 2015)	Mixture classification According to 1272/2008/EC Regulation	Kit configuration
000H01391F	**S-2732**	**Not classified**	**Not classified**	**2 x 15mg**
000H01382F	**FACTOR Xa**	**Not classified**	**Not classified**	**2 x 35 nkat**

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: **S-2732**

Product Number: **000H01391F**

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:
Instrumentation Laboratory Co.
526 Route 303
Orangeburg, New York 10962 (USA)

E-mail address of the competent person: 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 Regulation (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):

Hazard class	*Hazard category*	*Hazard statement*
Not classified		
		For exposure limits see section 8.

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):

Hazard pictogram(s):	None
Signal word(s):	None
Hazard statement(s):	None
Precautionary statement(s):	None
Other labeling details:	**≈ 2% 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.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Composition: solid containing organic components.

3.1 Hazardous components:

Name	EINECS/ ELINCS n°	CAS n°	Conc. % w/w*	Classification 29 CFR 1910.1200 (HCS) HPR (WHMIS 2015)	Classification 1272/2008/EC
p-nitroaniline*** *Index N. (Annex VI of CLP Reg.): 612-012-00-9*	202-810-1	100-01-6	< 0.0001 %***	Acute Toxicity – Oral, cat. 3 Acute Toxicity – Dermal, cat. 3 Acute Toxicity – Inhalation, cat. 3 Aquatic Chronic, cat. 3**	Acute Tox. 3, H331 Acute Tox. 3, H311 Acute Tox. 3, H301 STOT RE 2, H373 Aquatic Chronic 3, H412

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.***

*****p-nitroaniline, including the proportion of p-nitroaniline from Succinyl-isoleucyl-glutamyl(Υ-piperidide)-glycyl-arginine-p-nitroanilide hydrochloride.Succinyl-isoleucyl-glutamyl($_{Y}$-piperidide)-glycyl-arginine-p-nitroanilide is readily split by specific enzymes and releases p-nitroaniline.**

The mixture contains one substance listed in the Hazardous Substance Lists and/or evaluated for carcinogenicity by IARC, NTP, OSHA: p-Nitroaniline. 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 respiratory ways.
Skin : May be irritant for skin.
Eyes: May cause irritation.
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_2, 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 COx, NOx.

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	*S-2732* is intended for in vitro diagnostic use. 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:

p-Nitroaniline [(1)]	***Limit value – 8 hours***	***Limit value – short term***
Austria	1 ppm; 6 mg/m^3	
Belgium	3 mg/m^3	
Denmark	0.5 ppm; 3 mg/m^3	1 ppm; 6 mg/m^3
Finland	1 ppm; 5.7 mg/m^3	3 ppm; 17 mg/m^3 - 15 minutes average value
France	3 mg/m^3	
Hungary	6 mg/m^3	
Ireland	3 mg/m^3	
Latvia	0.1 mg/m^3	
Poland	3 mg/m^3	10 mg/m^3
Spain	3 mg/m^3 - skin	
Switzerland	0.5 ppm; 3 mg/m^3	
United Kingdom	[6 mg/m^3]	

The UK Advisory Committee on Toxic Substances has expressed concern that, for the OELs shown in parentheses [..], health may not be adequately protected because of doubts that the limit was not soundly-based. These OELs were included in the published UK 2002 list and its 2003 supplement, but are omitted from the published 2005 list.

Canada - Ontario	3 mg/m^3
Canada - Quebec	3 mg/m^3
New Zealand	3 mg/m^3
USA - NIOSH	3 mg/m^3
USA - OSHA	1 ppm; 6 mg/m^3
Australia	3 mg/m^3

ACGIH (1992)[(2)]: TLV/TWA: 3 mg/m^3 (skin). Notation: A4: not classifiable as a human carcinogen.

IDLH[(3)]: 300 mg/m^3

Community/National biological exposure limit values:
P-Nitroaniline [(2)]: Methemoglobin inducers: *Determinant*: methemoglobin in blood; *BEI* = 1.5% of hemoglobin. *Sampling time*: during or end of shift.

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*
P-Nitroaniline [(4)]	*Oral (mg/(mg/kg bw/day*								0.201
	Dermal (mg/kg bw/day)				0.1763				0.04347
	Inhalation (mg/m^3)				0.201				0.05

PNEC values (components): **P-Nitroaniline [(4)]**

PNEC aqua freshwater = 0.024 mg/l

PNEC aqua marine water = 0.0024 mg/l

PNEC aqua intermittent release = 0.24 mg/l

PNEC STP = 1 mg/l

PNEC sediment freshwater = 64.247424 mg/kg sediment dw

PNEC sediment marine water = 64.247424 mg/kg sediment dw

PNEC soil = 25.961088 mg/kg soil dw

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:	Solid	
Odor:	Not available	
Color:	White to off white	
pH:	Not available	
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 not available

SECTION 10. STABILITY AND REACTIVITY

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

10.2 Chemical stability The product is stable until the expiration date shown on the box and on the labels when stored at 2 – 8°C.

10.3 Possibility of hazardous reactions Not foreseen.

10.4 Conditions to avoid: Keep out from heat and light.

10.5 Incompatible materials Strong oxidizing agents.

10.6 Hazardous decomposition products: Thermal decomposition or combustion may include toxic and hazardous fumes of COx, NOx.

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:	Prolonged or repeated skin contact may cause irritation.
Ingestion:	Ingestion may cause irritation to the gastrointestinal mucous membranes.
Inhalation:	Inhalation of the product may cause irritation to respiratory ways.
Contact with eyes:	May cause irritation.

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

4-Nitroaniline : is readily absorbed orally, by inhalation and dermally and is eliminated in the form of numerous metabolites essentially via the kidneys. 4-Nitroaniline is rapidly distributed into all tissues. [5]

Acute toxicity	Value	m.u.	Effects		Related to
Oral:	LD50 (wild bird) = 75	mg/Kg		[4]	p-nitroaniline
	LD50 (rat) = 750 – 3,250	mg/Kg		[4][5]	p-nitroaniline
Dermal:	LD50 (rat) > 500 LD50 (guinea pig) > 500	mg/Kg		[4] [6]	p-nitroaniline
Inhalation:	LC50 (rat) = 2.53	mg/l/4h	Read across from 2-nitroaniline	[7]	p-nitroaniline

Other data: *p-Nitroaniline* causes the formation of MetHb. Due to the formation of methemoglobin (MetHb), is capable of significantly disturbing the oxygen supply in organs and tissues. This can induce hypoxic effects. [5][6]

Corrosion/Irritation

Skin Corrosion/Irritation — *p-Nitroaniline*: When applied to rabbits' skin (test according to OECD guideline 404), there were slight erythema and yellow discoloration short-term. Both effects were reversible within 24 hours. (6) According to Aggregated Computational Toxicology Resource (ACToR) database; 4-nitroaniline was not found to be irritating to the skin of rabbit. (4)

Serious eye damage/ irritation — *p-Nitroaniline*: application to rabbits' eyes (test according to OECD guideline 405) led to only short-term reddening of the conjunctiva and the effects were reversible within 24 hours.(6)

Sensitization:

Skin sensitization: — *p-Nitroaniline*: No significant skin sensitization potential by 4-nitroaniline can be derived, either from the few results with humans described in literature, or from the results of animal studies. (5)

Respiratory sensitization: — *p-Nitroaniline*: No significant respiratory sensitization potential by 4-nitroaniline can be derived, either from the few results with humans described in literature, or from the results of animal studies. (5)

CMR effects

Germ cell mutagenicity; — *p-Nitroaniline*: Various tests with the substance in microorganisms and mammalian cells produced positive but sometimes inconsistent results. p-Nitroaniline was ascribed to have a genotoxic potential in vitro but two in-vivo tests had negative results. Summarizing, the data pool available is insufficient to assess the mutagenic potential of N. (6)

Reproductive toxicity: — *p-Nitroaniline*: produced no evidence of adverse reproductive performance, including mating, fertility and pregnancy, littering or pup survival and development, in a two-generation rat reproduction study using a dosage which produced significant maternal toxicity (increased spleen weight, anemia, elevated blood methemoglobin levels) related to methemoglobinia following chronic dosing. p-Nitroaniline is not considered to cause a primary effect on fetal development. (8)

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			

p-Nitroaniline: In a two-year study, the administration of p-Nitroaniline to mice by gavage showed inconclusive evidence of carcinogenic activity in male mice, based to increased incidence of hemangiomas of the liver and haemangiosarcomas or haemangiosarcomas (combined) in other locations. In female mice is not observed evidence of carcinogenic activity. (9)(6)

STOT –single exposure — Not available.

STOT – repeated exposure — *p-Nitroaniline:* The repeated exposure to p-Nitroaniline can cause methemoglobinemia and hemolysis, anemia and jaundice, liver damage. (9)(6)

Aspiration hazards — Not available.

Other information:

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 bellow.

12.1 Toxicity	**species, media, units, test duration and test conditions.**		**Related to**
Acute toxicity with fish:	LC_{50} *Brachydanio rerio* = 87.6 mg/l/96 hours	(4)	p-nitroaniline
Chronic toxicity with fish:	Not available		
Acute toxicity with crustaceans:	EC50 crustaceans = 24 mg/l/48hours	(4)	p-nitroaniline
Chronic toxicity with crustaceans:	Not available		
Acute toxicity with algae:	EC50 = 68 mg/l/24 h	(4)	p-nitroaniline
Chronic toxicity with algae:	Not available		
Toxicity data on soil micro- and macroorganisms	Not available		

	Toxicity data on birds, bees and plants:	Not available
12.2	**Persistency and degradability:**	p-nitroaniline is not biodegradable and is expected to have moderate persistence potential.(7)
12.3	**Bioaccumulation potential:**	p-nitroaniline is are expected to have low bioaccumulation potential. (7)
12.4	**Mobility in soil:**	*p-Nitroaniline:* If released to soil, is expected to have high mobility, based upon Koc values of 54-87.(10)
12.5	**Results of PBT and vPvB assessment**	Not available.
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	p-Nitroaniline	-
New York	p-Nitroaniline	-
New Jersey	p-Nitroaniline	Mutagen Reactive* - Second Degree
Pennsylvania	p-Nitroaniline	Environmental Hazard

* "Reactive" is used interchangeably with the NFPA term "instability."

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* [I]	*SARA/ EPCRA 302 EHS TPQ* [II]	*SARA/ EPCRA 304EHS RQ* [III]	*CERCLA RQ* [IV]	*SARA/EPCRA 313 TRI* [V]	*RCRA Code* [VI]	*CAA 112(r) RMP TQ* [VII]
p-Nitroaniline	100-01-6	-	-	5000	313	P077	-

[I] **SARA/313 Category Code:** Emergency Planning and Community Right-to Know Act Section 313 Category Code
[II] **SARA/EPCRA 302 EHS TPQ:** Extremely Hazardous Substance Threshold Planning Quantity (Emergency Planning and Community Right-to Know Act Section 302 Category Code)
[III] **SARA/EPCRA 304 EHS RQ:** Extremely Hazardous Substance Reportable Quantity (Emergency Planning and Community Right-to Know Act Section 304 Category Code)
[IV] **CERCLA RQ:** Reportable Quantity (Comprehensive Environmental Response, Compensation, and Liability Act)
[V] **SARA/EPCRA 313 TRI:** Toxics Release Inventory (Emergency Planning and Community Right-to Know Act Section 313 Category Code)
[VI] **RCRA Code:** Resource Conservation and Recovery Act Code
[VII] **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 11/05/2010
- Revision n. 01, dated 03/22/2011
- Revision n. 02, dated 10/28/2015. 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 Esposure 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, Bioaccumulative 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 Bioaccumulative
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): H318: Causes serious eye damage.
H331: Toxic if inhaled.
H311: Toxic in contact with skin.
H301: Toxic in contact with skin.
H373: May cause damage to organs through prolonged or repeated exposure.
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) :

Classification:	*Classification procedure*
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) GESTIS International Limit Values, available on http://limitvalue.ifa.dguv.de/WebForm_ueliste.aspx

(2) ACGIH, TLVs and BEIs based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices, 2012

(3) OSHA Occupational Chemical Database, https://www.osha.gov/chemicaldata/chemResult.html?recNo=2

(4) 4-nitroaniline, Registration dossier on ECHA, available at http://apps.echa.europa.eu/registered/data/dossiers/DISS-d018ef27-b601-3c5c-e044-00144f67d249/AGGR-7af23cd1-289d-4962-8eda-cbf579986b83_DISS-d018ef27-b601-3c5c-e044-00144f67d249.html#AGGR-7af23cd1-289d-4962-8eda-cbf579986b83

(5) The MAK Collection for Occupational Health and Safety Published Online: 14 AUG 2014, available at http://onlinelibrary.wiley.com/doi/10.1002/3527600418.mb10001e3014/pdf

(6) GESTIS Substance database, 4-Nitroaniline, ZVG 17030

(7) U.S. Environmental Protection Agency September, 2009 Hazard Characterization Document, SCREENING-LEVEL HAZARD CHARACTERIZATION Mononitroanilines Category , 2-Nitrobenzenamine (CASRN 88-74-4) , 4-Nitrobenzenamine (CASRN 100-01-6)

(8) High Productio Volume Chemical Challenge program, test Plan for the Mononitroaniline category, Solutia Inc.

(9) http://www.salute.gov.it/sicurezzaChimica, MSDS for p-nitroaniline, Code RE 1623

(10) Hazardous Substances Data Bank (HSDB), p-Nitroaniline, HSN: 1156

SECTION 1. IDENTIFICATION OF THE MIXTURE AND OF THE COMPANY

1.1 Identification of the mixture

Product Name: **FACTOR Xa**

Product Number: **000H01382F**

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:
Instrumentation Laboratory Co.
526 Route 303
Orangeburg, New York 10962 (USA)

E-mail address of the competent person: 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 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):

Hazard class	*Hazard category*	*Hazard statement*
RESPIRATORY OR SKIN SENSITISATION	**cat. 1**	**May cause allergy or asthma symptoms or breathing difficulties if inhaled.** (H334)
SKIN CORROSION/IRRITATION	**Cat 2**	**Causes skin irritation.** (H315)
SERIOUS EYE DAMAGE/EYE IRRITATION	**Cat 2**	**Causes serious eye irritation.** (H319)
		For exposure limits see ch. 8

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

The product may cause allergy or asthma symptoms or breathing difficulties if inhaled. Causes skin irritation and serious eye irritation.
Under normal conditions of use, the mixture does not cause 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):

Hazard pictogram(s):	
Signal word(s):	**Danger**
Hazard statement(s):	**May cause allergy or asthma symptoms or breathing difficulties if inhaled.** (H334) **Causes skin irritation.** (H315) **Causes serious eye irritation.** (H319)

Precautionary statement(s):	**Avoid breathing dust/fume.** (P261) **Wear protective gloves/protective clothing/eye protection/face protection.** (P280) **IF INHALED: Remove person to fresh air and keep comfortable for breathing.** (P304 + P340) **If experiencing respiratory symptoms: Call a POISON CENTER/doctor.** (P342 + P311) **IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.** (P305 + P351 + P338) **If eye irritation persists: Get medical advice/ attention.** (P337 + P313) **IF ON SKIN: Wash with plenty of water.** (P302+P352) **If skin irritation or rash occurs: Get medical advice/attention.** (P333+P313)
Other labeling details:	**Contains Factor Xa.**
	Up to 6% of the mixture consists of component of unknown acute toxicity (oral, dermal, inhalation) for the human health and for the aquatic environment.

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

3.1 Hazardous components:

Name	EINECS/ ELINCS n°	CAS n°	Conc. % w/w*	Classification 29 CFR 1910.1200 (HCS) HPR (WHMIS 2015)	Classification 1272/2008/EC
Factor Xa *Index N. (Annex VI of CLP Reg.): 647-014-00-9 - proteases with the exception of those specified elsewhere in this Annex*	Not available	Not available	< 5.6%	Skin Corrosion/Irritation, cat. 2 Eye damage/Eye Irritation, cat. 2A Specific target organ Toxicity – Single Exposure, cat. 3 Sensitization-Respiratory, cat. 1	Skin Irrit. 2, H315 Eye Irrit. 2, H319 STOT SE 3, H335 Resp. Sens. 1, H334
Tris Hydrochloride	214-684-5	1185-53-1	< 4%	Skin Corrosion/Irritation, cat. 2 Eye damage/Eye Irritation, cat. 2B	Skin Irrit. 2, H315 Eye Irrit. 2, H319
Tris-Hydroxymethyl aminomethane (Tris Amino)	201-064-4	77-86-1	< 2%	Skin Corrosion/Irritation, cat. 2	Skin Irrit. 2, H315
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 allergy or asthma symptoms or breathing difficulties if inhaled. Skin : May be irritant for skin. Eyes: May cause irritation. 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:	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_2, 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 COx, NOx, SOx, 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

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	*Factor Xa* is intended for in vitro diagnostic use. The material contains bovine albumin and Factor Xa, may cause allergy or asthma symptoms or breathing difficulties if inhaled. It should be treated as potentially infectious. 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: Not established.

Community/National biological exposure limit values: Not established.

DNEL values (components): Not established.

PNEC values (components): Not established.

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:	Solid	
Odor:	Not available	
Color:	White to off white	
pH:	7.9 to 8.1	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 Not available

SECTION 10. STABILITY AND REACTIVITY

10.1 Reactivity	This mixture is considered not reactive under the normal conditions of the usage.
10.2 Chemical stability	The product is stable until the expiration date shown on the box and on the labels when stored at 2 – 8 °C.
10.3 Possibility of hazardous reactions	Not foreseen.
10.4 Conditions to avoid:	Keep away from heat, water, humidity and light.

10.5 Incompatible materials Strong oxidising agents.

10.6 Hazardous decomposition products: Thermal decomposition or combustion may generate toxic and hazardous fumes of COx, NOx, SOx, HCl.

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: Causes skin irritation.

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

Inhalation: The product may cause allergy or asthma symptoms or breathing difficulties if inhaled.

Contact with eyes: Causes serious 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. [3]

Acute toxicity	**Value**	**m.u.**	**Effects**		**Related to**
Oral:	LD50 (rat) > 3,000	mg/kg		[4]	Tris Amino
Dermal:	LD50 (rat) > 5,000	mg/kg		[18]	Tris Amino
Inhalation:	Not available				
Other data:	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.[4]

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

Serious eye damage/ irritation: *Tris Amino (100%)* was not an ocular irritant when administered to rabbits. [4]

Tris Hydrochloride : mild eye irritant in rabbits. [17]

Sensitization:

Skin sensitization: *Tris Amino:* The supporting chemical AMP is not sensitizing to guinea pig skin. [4]

Tris Hydrochloride: Not a sensitizer in experimental animals. [4]

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-spercific 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. [5] 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.[5]

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. [4]

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. (2)

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. (1)

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 bellow.

12.1 Toxicity	**species, media, units, test duration and test conditions.**		**Related to**
Acute toxicity with fish:	LC50 *Leuciscus idus* > 10,000 mg/L/ 96-h	(4)	Tris Amino
Chronic toxicity with fish:	Not available		
Acute toxicity with crustaceans:	Water fleas (Daphnia magna) 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	(18)	Tris HCl
Chronic toxicity with crustaceans:	Not available		
Acute toxicity with algae:	EC50 *Selenastrum capricornutum* >100 mg/L/ 96 h	(4)	Tris Amino
Chronic toxicity with algae:	Not available		
Toxicity data on soil micro- and macroorganisms	Not available		
Toxicity data on birds, bees and plants:	Not available		

12.2 Persistency and degradability: *Tris Amino* is not readily biodegradable is expected to have moderate persistence. (4)
Tris Hydrochloride: readily biodegradable. (5)

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

12.4 Mobility in soil: *Tris Amino* is expected to have high mobility in soil. (4)

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* [I]	*SARA/ EPCRA 302 EHS TPQ* [II]	*SARA/ EPCRA 304 EHS RQ* [III]	*CERCLA RQ* [IV]	*SARA/EPCRA 313 TRI* [V]	*RCRA Code* [VI]	*CAA 112(r) RMP TQ* [VII]
No component listed							

[I] **SARA/313 Category Code:** Emergency Planning and Community Right-to Know Act Section 313 Category Code
[II] **SARA/EPCRA 302 EHS TPQ:** Extremely Hazardous Substance Threshold Planning Quantity (Emergency Planning and Community Right-to Know Act Section 302 Category Code)
[III] **SARA/EPCRA 304 EHS RQ:** Extremely Hazardous Substance Reportable Quantity (Emergency Planning and Community Right-to Know Act Section 304 Category Code)
[IV] **CERCLA RQ:** Reportable Quantity (Comprehensive Environmental Response, Compensation, and Liability Act)
[V] **SARA/EPCRA 313 TRI:** Toxics Release Inventory (Emergency Planning and Community Right-to Know Act Section 313 Category Code)
[VI] **RCRA Code:** Resource Conservation and Recovery Act Code
[VII] 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 11/05/2010
- Revision n. 01, dated 03/22/2011
- Revision n. 02, dated 10/28/2015. 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 Esposure 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, Bioaccumulative 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 Bioaccumulative
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.
H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled.
H335: May cause respiratory irritation.

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) :

Classification:	*Classification procedure*
May cause allergy or asthma symptoms or breathing difficulties if inhaled. (H334)	**Cut-off method**
Causes skin irritation. (H315)	**Calculation method**
Causes serious eye irritation. (H319)	**Calculation method**

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) 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

(2) TEST PLAN For Tris(hydroxymethy1)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

(3) HSDB Hazardous Substances Databank, Tromethamine

(4) Haz-Map, Tromethamine hydrochloride, available at http://hazmap.nlm.nih.gov/category-details?table=copytblagents&id=18456

(5) Sigma Aldrich, SDS for Tromethamine Hydrochloride, Version 5.0, revision date 17.10.2013

(4) 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

(5) http://e-aair.org - Allergy, Asthma and Immunology Research (AAIR) 2009, October, Occupational asthma caused by inhalation of bovine serum albumin powder, Case report