

# SAFETY DATA SHEET

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## SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/ UNDERTAKING

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### Contact information

#### General



Kindred Biosciences, Inc.  
1555 Bayshore Highway - Suite 200, Burlingame, CA 94010  
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#### Emergency telephone number

+1 888-608-2542 *Availability: 24 hours/7 days*

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<b>Product identifier</b>	Zimeta (dipyron injection)
<b>Synonyms</b>	Dipyron, dipyron sodium, dipyron sodium monohydrate, metamizole, metamizole sodium monohydrate
<b>Trade names</b>	Zimeta
<b>Chemical family</b>	Mixture - contains a pyrazolone derivative
<b>Relevant identified uses of the substance or mixture and uses advised against</b>	Bulk formulated pharmaceutical mixture for research and development purposes only; dipyron is indicated for the treatment of fever in horses.
<b>Note</b>	The physical, chemical, toxicological and ecological properties of this mixture have not been fully characterized. This SDS will be revisited as more data become available.

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## SECTION 2 - HAZARDS IDENTIFICATION

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### Classification of the substance or mixture

**Globally Harmonized System [GHS]** Skin sensitizer - Category 1B. Respiratory sensitizer - Category 1B.

### Label elements

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**SECTION 2 - HAZARDS IDENTIFICATION** ...continued

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**GHS hazard pictogram****GHS signal word**

Danger

**GHS hazard statements**

H317 - May cause allergic skin reaction. H334 - May cause allergy or asthma symptoms or breathing difficulties if inhaled.

**GHS precautionary statements**

P261 - Avoid breathing dust/mist/vapors/spray.  
P280 - Wear eye/face protection.  
P284 - Use respiratory protection.  
P304 + P340 - IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing.  
P321 - Specific treatment (see First Aid information on product label and/or Section 4 of the SDS).  
P333 + P313 - If skin irritation or rash occurs: Get medical advice/attention.  
P342 + P311 - If experiencing respiratory symptoms: Call a POISON CENTER or doctor/physician.  
P501 - Dispose of contents/container to location in accordance with local/regional/national/international regulations.  
P272 - Contaminated work clothing should not be allowed out of the workplace.  
P302 + P352 - IF ON SKIN: Wash with plenty of soap and water.

**Other hazards**

Zimeta contains dipyron, a non-steroidal anti-inflammatory drug (NSAID) that inhibits cyclooxygenase. It has formerly been used in humans for severe pain and fever, and is indicated for veterinary use to treat fever. It is associated with agranulocytosis in humans and may cause allergic reaction. In humans, skin sensitization and respiratory sensitization have been reported with low frequency.

**Note**

This mixture is classified as hazardous under GHS as implemented by Regulation EC No 1272/2008 (EU CLP) and Hazard Communication Standard No. 1910.1200 (US OSHA).

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

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<u>Ingredient</u>	<u>CAS #</u>	<u>EINECS/ ELINCS#</u>	<u>Amount</u>	<u>GHS Classification</u>
Dipyron sodium monohydrate	5907-38-0	N/A	35-55%	SS1B: H317; RS1B: H334
Benzyl alcohol (BnOH)	100-51-6	202-859-9	5-20%	ATO4: H302; ATD4: H312; ATI3: H331

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

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**Note** The ingredient(s) listed above are considered hazardous. The remaining components are non-hazardous and/or present at amounts below reportable limits. See Section 16 for full text of GHS classifications.

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**SECTION 4 - FIRST AID MEASURES**

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**Description of first aid measures**

<b>Immediate Medical Attention Needed</b>	Yes
<b>Eye Contact</b>	If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and/or supervisor.
<b>Skin Contact</b>	Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and/or supervisor.
<b>Inhalation</b>	Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and/or supervisor.
<b>Ingestion</b>	Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and/or supervisor.
<b>Protection of first aid responders</b>	See Section 8 for Exposure Controls/Personal Protection recommendations.
<b>Most important symptoms and effects, both acute and delayed</b>	See Sections 2 and 11.
<b>Indication of immediate medical attention and special treatment needed, if necessary</b>	Medical conditions aggravated by exposure: None reported. Treat symptomatically and supportively.

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**SECTION 5 - FIREFIGHTING MEASURES**

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<b>Extinguishing media</b>	Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.
<b>Specific hazards arising from the substance or mixture</b>	No information identified. May emit carbon monoxide, carbon dioxide, nitrogen-, sulfur-, and sodium-containing compounds.
<b>Flammability/Explosivity</b>	No explosivity or flammability data identified. As product is an aqueous solution, it is not expected to be flammable or explosive.

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## SECTION 5 - FIREFIGHTING MEASURES ...continued

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**Advice for firefighters**      Wear full protective clothing and a self-contained breathing apparatus with a full facepiece operated in the pressure demand or other positive pressure mode. Decontaminate all equipment after use.

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## SECTION 6 - ACCIDENTAL RELEASE MEASURES

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**Personal precautions, protective equipment and emergency procedures**      If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated. Do not breathe mist/vapors/spray.

**Environmental precautions**      Do not empty into drains. Avoid release to the environment.

**Methods and material for containment and cleaning up**      DO NOT CAUSE MATERIAL TO BECOME AIRBORNE. For small spills, soak up material with absorbent, e.g., paper towels. For large spills, cordon off spill area and minimize the spreading of spilled material. Soak up material with absorbent. Collect spilled material, absorbent, and rinse water into suitable containers for proper disposal in accordance with applicable waste disposal regulations (see Section 13). Decontaminate the area twice with an appropriate solvent (see Section 9).

**Reference to other sections**      See Sections 8 and 13 for more information.

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## SECTION 7 - HANDLING AND STORAGE

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**Precautions for safe handling**      Follow recommendations for handling potent pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Avoid breathing vapor/mist/spray. Wash thoroughly after handling.

**Conditions for safe storage including any incompatibilities**      Store at Controlled Room Temperature 20°C to 25°C (68°F to 77°F); with excursions permitted between 15°C and 30°C (59°F and 86°F). Protect from light.

**Specific end use(s)**      No information identified.

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## SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

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**Note**      Dispose of broken vials in a sharps container.

**Control Parameters/  
Occupational Exposure  
Limit Values**

<u>Compound</u>	<u>Issuer</u>	<u>Type</u>	<u>OEL</u>
Benzyl alcohol (BnOH)	AIHA	TWA 8-hour	10 ppm

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

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<b>Exposure/Engineering controls</b>	If vials are crushed/broken and/or if handling bulk liquid: Control exposures to below the OEL (for the active ingredient(s) if available). Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Solutions can be handled outside a containment system or without local exhaust ventilation (LEV). Use engineered LEV and/or enclosure for high-energy operations such as spraying. All containers for solutions and slurries must be covered while being transferred.
<b>Respiratory protection</b>	If vials are crushed/broken and/or if handling bulk liquid: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. Respirators are generally not required. At minimum, a tight-fitting full-face respirator with HEPA filters is required for spill cleanup.
<b>Hand protection</b>	Wear nitrile or other impervious gloves if skin contact is possible.
<b>Skin protection</b>	Wear appropriate work uniform or lab coat. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use. Protective garments are not to be worn in common areas (e.g., cafeterias) or outdoors.
<b>Eye/face protection</b>	Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.
<b>Environmental Exposure Controls</b>	Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedures to prevent release or spread of contamination and to prevent inadvertent contact by personnel.
<b>Other protective measures</b>	Wash hands in the event of contact with this substance, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-doors).

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**SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES**

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**Information on basic physical and chemical properties**

<b>Appearance</b>	Liquid
<b>Color</b>	Light yellow to yellow
<b>Odor</b>	No information identified.
<b>Odor threshold</b>	No information identified.
<b>pH</b>	No information identified.

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**SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES** ...continued

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<b>Melting point/ freezing point</b>	No information identified.
<b>Initial boiling point and boiling range</b>	No information identified.
<b>Flash point</b>	No information identified.
<b>Evaporation rate</b>	No information identified.
<b>Flammability (solid, gas)</b>	No information identified.
<b>Upper/lower flammability or explosive limits</b>	No information identified.
<b>Vapor pressure</b>	No information identified.
<b>Vapor density</b>	No information identified.
<b>Relative density</b>	1.16 g/mL
<b>Water solubility</b>	No information identified.
<b>Solvent solubility</b>	No information identified.
<b>Partition coefficient (<i>n</i>-octanol/water)</b>	No information identified.
<b>Auto-ignition temperature</b>	No information identified.
<b>Decomposition temperature</b>	No information identified.
<b>Viscosity</b>	No information identified.
<b>Explosive properties</b>	No information identified.
<b>Oxidizing properties</b>	No information identified.
<b>Other information</b>	
<b>Molecular formula</b>	Not applicable (Mixture)
<b>Molecular weight</b>	Not applicable (Mixture)

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**SECTION 10 - STABILITY AND REACTIVITY**

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<b>Reactivity</b>	No information identified.
<b>Chemical stability</b>	Stable under normal temperatures.

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**SECTION 10 - STABILITY AND REACTIVITY ...continued**

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<b>Possibility of hazardous reactions</b>	No information identified.
<b>Conditions to avoid</b>	No information identified.
<b>Incompatible materials</b>	No information identified.
<b>Hazardous decomposition products</b>	No information identified.

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**SECTION 11 - TOXICOLOGICAL INFORMATION**

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**Note** No data for this mixture were identified. The following data describe the active ingredient and/or the individual ingredients where applicable.

**Information on toxicological effects**

**Route of entry** May be absorbed by inhalation, skin contact and ingestion.

**Acute toxicity**

<u>Compound</u>	<u>Type</u>	<u>Route</u>	<u>Species</u>	<u>Dose</u>
Dipyron sodium monohydrate	LD <sub>50</sub>	Oral	Rat	3127 mg/kg
Benzyl alcohol (BnOH)	LC <sub>50</sub>	Inhalation (4 hour)	Rat	8.8 mg/L
	LD <sub>50</sub>	Oral	Rat	1230 mg/kg
	LD <sub>50</sub>	Dermal	Rabbit	2000 mg/kg

**Irritation/Corrosion** No studies were identified.

**Sensitization** No studies were identified.

**STOT-single exposure** Mice administered oral doses of dipyron sodium demonstrated depressed respiration and sedation at  $\geq 100$  mg/kg. The NOEL was 10 mg/kg.

**STOT-repeated exposure/Repeat-dose toxicity** In a 26-week rat study, increased reticulocytes and changes in red blood cells (Heinz bodies) were observed at 900 mg/kg/day IV dipyron. A NOAEL was not identified in this study. Similar effects were observed in a 4-week rat study. The NOEL was 150 mg/kg/day.

In a 26-week dog study, oral doses of  $\geq 300$  mg/kg/day dipyron resulted in increased red blood cell counts and changes to red blood cells (Heinz bodies), changes in serum chemistry, and increased liver and spleen weights in the presence of microscopic effects. The NOAEL was 30 mg/kg/day.

**Reproductive toxicity** No adverse effects on fertility were observed in rats following oral doses of dipyron up to 625 mg/kg/day starting 2 weeks prior to mating and throughout pregnancy and lactation in the presence of severe maternal toxicity.

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**SECTION 11 - TOXICOLOGICAL INFORMATION ...continued**

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<b>Developmental toxicity</b>	In a study in rats administered $\geq 250$ mg/kg/day dipyrone orally starting from 2 weeks prior to mating through pregnancy and lactation, reduced pup survival was noted. Significant reductions in the number of pups born per dam were noted at 625 mg/kg/day. The NOEL was 100 mg/kg/day. In a teratology study in rats, no evidence of teratogenicity was observed at oral doses up to 800 mg/kg/day dipyrone in the presence of maternal toxicity. Increased incidence of resorptions with corresponding reductions in the total number of fetuses and numbers of fetuses per dam were observed in rats and rabbits in the presence of maternal toxicity following oral doses of 800 and $\geq 100$ mg/kg/day, respectively. Fetal weight reductions were observed in rabbits at 400 mg/kg/day. The NOELs were 400 and 25 mg/kg/day in rats and rabbits, respectively.
<b>Genotoxicity</b>	Dipyrone was negative in one Ames assay, and positive in a number of others reported with limited details. It was also reported to be positive in poorly reported <i>in vitro</i> assays in human lymphocytes and in sister chromatid exchange assays in Chinese hamster cells. It was reported to be negative in two <i>in vivo</i> mouse micronucleus assays, but positive in a one <i>in vivo</i> micronucleus assay with limited reported detail. It was negative in two high quality studies: an <i>in vitro</i> HPRT and an <i>in vivo</i> mouse micronucleus assay. Overall, when accounting for the quality of the studies and weight of evidence, dipyrone is not expected to be genotoxic.
<b>Carcinogenicity</b>	An increased incidence of benign liver tumors was observed in mice administered $\geq 0.125\%$ dipyrone in water for 78 weeks and in a second study in mice administered 0.75% dipyrone in water for 18 months, but was negative in a third study in mice at 2500 mg/kg/ day in feed for 104 months. No evidence of carcinogenicity was observed in two rat studies at doses up to 145-193 mg/kg/day in feed (for 24 months) or 0.125% in drinking water (no further details identified). Overall, dipyrone is not expected to be carcinogenic. None of the components of the product present at levels greater than or equal to 0.1% are listed by NTP, IARC, ACGIH or OSHA as a carcinogen.
<b>Aspiration hazard</b>	No data available.
<b>Human health data</b>	See "Section 2 - Other Hazards"

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**SECTION 12 - ECOLOGICAL INFORMATION**

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**Toxicity**

<u>Compound</u>	<u>Type</u>	<u>Species</u>	<u>Concentration</u>
Benzyl alcohol (BnOH)	LC <sub>50</sub> (48h)	<i>Leuciscus idus</i> (freshwater fish)	646 mg/L
	LC <sub>50</sub> (96 hr)	<i>Pimephales promelas</i> (freshwater fish)	460 mg/L
	EC <sub>50</sub> (48 hr)	<i>Daphnia magna</i> (crustacea)	23 mg/L
	EC <sub>50</sub> (48hr)	<i>E. Coli</i> (bacteria)	1000 mg/L

**Additional toxicity information** No data available.



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**SECTION 12 - ECOLOGICAL INFORMATION ...continued**

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<b>Persistence and Degradability</b>	Benzyl alcohol is readily biodegradable.
<b>Bioaccumulative potential</b>	Based on a LogP of 1.1 and estimated BCF value of 1.37 L/kg, benzyl alcohol is considered to have no potential for bioaccumulation.
<b>Mobility in soil</b>	No data available.
<b>Results of PBT and vPvB assessment</b>	Not performed.
<b>Other adverse effects</b>	No data available.
<b>Note</b>	The environmental characteristics of this product have not been fully investigated. Releases to the environment should be avoided.

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**SECTION 13 - DISPOSAL CONSIDERATIONS**

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<b>Waste treatment methods</b>	Dispose of wastes in accordance to prescribed federal, state, and local guidelines, e.g., appropriately permitted chemical waste incinerator. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, e.g., appropriately permitted municipal or on-site wastewater treatment facility.
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**SECTION 14 - TRANSPORT INFORMATION**

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<b>Transport</b>	Based on the available data, this mixture is not regulated as a hazardous material under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.
<b>UN number</b>	None assigned.
<b>UN proper shipping name</b>	None assigned.
<b>Transport hazard classes and packing group</b>	None assigned.
<b>Environmental hazards</b>	Based on the available data, this mixture is not regulated as an environmental hazard or a marine pollutant.
<b>Special precautions for users</b>	No special precautions needed.
<b>Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code</b>	Not applicable.

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## SECTION 15 - REGULATORY INFORMATION

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<b>Safety, health and environmental regulations/legislation specific for the substance or mixture</b>	This SDS generally complies with the requirements listed under current guidelines in the US, EU and Canada. Consult your local or regional authorities for more information.
<b>Chemical safety assessment</b>	Not conducted.
<b>TSCA status</b>	Drugs are exempt from TSCA.
<b>SARA section 313</b>	Not listed.
<b>California proposition 65</b>	Not listed.
<b>Additional information</b>	No other information identified.

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## SECTION 16 - OTHER INFORMATION

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<b>Full text of H phrases and GHS classifications</b>	ATO4 - Acute Toxicity (Oral) Category 4. H302 - Harmful if swallowed. ATD4 - Acute Toxicity (Dermal) Category 4. H312 - Harmful in contact with skin. ATI3 - Acute Toxicity (Inhalation) Category 3. H331 - Toxic if inhaled. H317 - May cause an allergic skin reaction. SS1B - Skin sensitizer Category 1B. H334 - May cause allergic or asthmatic symptoms or breathing difficulty if inhaled. RS1B - Respiratory Sensitizer Category 1B.
<b>Sources of data</b>	Information from published literature and internal company data.
<b>Abbreviations</b>	ACGIH - American Conference of Governmental Industrial Hygienists; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AIHA - American Industrial Hygiene Association; CAS# - Chemical Abstract Services Number; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; DNEL - Derived No Effect Level; DOT - Department of Transportation; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified Chemical Substances; EU - European Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC - International Agency for Research on Cancer; IDLH - Immediately Dangerous to Life or Health; IATA - International Air Transport Association; IMDG - International Maritime Dangerous Goods; LOEL - Lowest Observed Effect Level; LOAEL - Lowest Observed Adverse Effect Level; NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STOT - Specific Target Organ Toxicity; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; WHMIS - Workplace Hazardous Materials Information System

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**SECTION 16 - OTHER INFORMATION** ...continued

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<b>Issue Date</b>	21 June 2019
<b>Revisions</b>	This is the first version of this SDS.
<b>Disclaimer</b>	<p>The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections which pertain to their particular conditions.</p> <p>No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it is a pharmaceutical product. The above information is offered in good faith and with the belief that it is accurate. As of the date of issuance, we are providing all information relevant to the foreseeable handling of the material. However, in the event of an adverse incident associated with this product, this Safety Data Sheet is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.</p>