Insulin, Lispro

Effective Date: 15-Feb-2005

Eli Lilly and Company
Material Safety Data Sheet

Section 1 - Chemical Product and Company

Manufacturer:
Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285

Manufacturer's Emergency Phone:
1-317-276-2000
CHEMTREC:
1-800-424-9300 (North America)
1-703-527-3887 (International)

Common Name: Insulin, Lispro

Chemical Name: Insulin (human), 28B-L-lysine-29B-L-proline-
Chemical Name 2: Lys(B28), Pro(B29) human insulin analog
Synonym(s): Humalog Mix 25; Lispro; Lyspro; Lys-Pro-BHI; KPB-BHI; Lys-Pro Insulin; Lispro Insulin; 275585 Formulation; Insulin Lispro
Trademarks(s): Diamond Design I; Diamond Design II; Diamond Design III; Humanol; Humupro; Humulog; Liprolog; Humalog in Cyrillic Characters; Volog; Umupro; Umulog; Umalog; Prandulin; Normulin; Mix25; Humalog
Lilly Item Code(s): B01966; HP8125; HP8191; HP8193; HP8194; HP8725; HP8791; HP8793; HP8794; HP8797; HP8798; HP8799; ND1025; ND1026; ND1027; ND1037; ND1048; VL7391; VL7392; VL7393; VL7394; VL7395; VL7510; VL7511; VL7512; VL7513; VL7514; VL7515; VL7516; VL7517

See attached glossary for abbreviations.

Section 2 - Composition / Information on Ingredients

Ingredient	CAS	Concentration %
Insulin, Lispro Crystals	133107-64-9	0.35
Glycerin	56-81-5	1.4 - 1.8
Sodium Phosphate Dibasic Anhydrous	7558-79-4	0.2 - 0.42
m-Cresol	108-39-4	0.15 - 0.2
Phenol	108-95-2	0 - 0.1
Protamine Sulfate	9009-65-8	0 - 0.04
Zinc Oxide	1314-13-2	0.001 - 0.004
Water for Injection	7732-18-5	96 - 98

Exposure Guidelines:
Insulin crystals - LEG 120 micrograms/m3 TWA (respirable) for 12 hours, 600 micrograms/m3 TWA

(respirable) for 15 minutes STEG.

Glycerin (mist) - PEL 5 mg/m3 TWA (respirable) and 15 mg/m3 TWA (total). TLV 10 mg/m3 TWA.
UK - Workplace Exposure Limit 10 mg/m3 TWA.
Ireland - Occupational Exposure Limit 10 mg/m3 TWA.
Italy - Occupational Exposure Limit 10 mg/m3 TWA.
France - Occupational Exposure Limit 10 mg/m3 (VME) TWA.
Spain - Occupational Exposure Limit 10 mg/m3 (VLA-ED) TWA.

Sodium phosphate dibasic anhydrous - Exposure Guideline 1 mg/m3 TWA for 8 hours, 3 mg/m3 TWA for 15 minutes STEG (Lilly-established guideline).

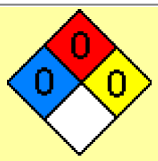
m-Cresol - PEL 5 ppm (22 mg/m3) TWA (skin). TLV 5 ppm TWA (skin).
Ireland - Occupational Exposure Limit 5 ppm (22 mg/m3) TWA (skin).
Italy - Occupational Exposure Limit 5 ppm (22 mg/m3) TWA.
France - Occupational Exposure Limit 5 ppm (22 mg/m3) (VME) TWA.
Spain - Occupational Exposure Limit 5 ppm (22 mg/m3) (VLA-ED) TWA (skin).
Germany - TRGS 900 Limit Value 5 ppm (22 mg/m3) TWA (skin), 15 minute limit not to exceed MAK (skin).

Phenol - PEL 5 ppm (19 mg/m3) TWA, TLV 5 ppm TWA (skin). BEI 250 mg total phenol per gram of creatinine in urine sampled at end of shift.
UK - Workplace Exposure Limit 2 ppm (skin).
Ireland - Occupational Exposure Limit 2 ppm (7.8 mg/m3) TWA (skin).
Italy - Occupational Exposure Limit 2 ppm (7.8 mg/m3) TWA (skin).
France - Occupational Exposure Limit 5 ppm (19 mg/m3) (VME) TWA (skin).
Spain - Occupational Exposure Limit 2 ppm (8 mg/m3) (VLA-ED) TWA (skin).
Germany - TRGS 900 Limit Value 5 ppm (19 mg/m3) TWA, 15-minute limit not to exceed MAK (skin).

Section 3 - Hazards Identification

Appearance: Clear solution
Physical State: Liquid
Odor: Odorless

Emergency Overview



Emergency Overview Effective Date: 10-Aug-1996

Lilly Laboratory Labeling Codes:
Health 0 **Fire** 0 **Reactivity** 0

Primary Physical and Health Hazards: Not Considered a Health Hazard.

Caution Statement: Insulin, Lispro is not considered to be a health hazard.

Routes of Entry: Inhalation and skin contact.

Effects of Overexposure: Dilute solutions do not pose a health hazard through typical routes of occupational exposure.

Medical Conditions Aggravated by Exposure: Hypersensitivity to insulin.

Carcinogenicity:
Insulin, lispro crystals - Not listed by IARC, NTP, ACGIH, or OSHA. One-year subcutaneous injection studies demonstrated no evidence of carcinogenicity in rats.

Glycerin - Not listed by IARC, NTP, ACGIH, or OSHA. Two-year dietary studies demonstrated no evidence of carcinogenicity in rats.

m-Cresol - Not listed by IARC, NTP, ACGIH, or OSHA. Two- to three-month dermal application studies with cresols demonstrated evidence of tumor promotion in mice. The relevance of these findings to humans is unknown.

Remaining ingredients - Not listed by IARC, NTP, ACGIH, or OSHA.

Section 4 - First Aid Measures

Eyes: Flush eyes with plenty of water. Get medical attention.

Skin: Remove contaminated clothing and clean before reuse. Wash all exposed areas of skin with plenty of soap and water. Get medical attention if irritation develops.

Inhalation: Move individual to fresh air. Get medical attention if breathing difficulty occurs. If not breathing, provide artificial respiration assistance (mouth-to-mouth) and call a physician immediately.

Ingestion: Do not induce vomiting. Call a physician or poison control center. If available, administer activated charcoal (6-8 heaping teaspoons) with two to three glasses of water. Do not give anything by mouth to an unconscious person. Immediately transport to a medical care facility and see a physician.

Section 5 - Fire Fighting Measures

Flash Point: No applicable information found
UEL: No applicable information found
LEL: No applicable information found

Extinguishing Media: Use water, carbon dioxide, dry chemical, foam, or Halon.

Unusual Fire and Explosion Hazards: None known.

Hazardous Combustion Products: May emit toxic fumes when exposed to heat or fire.

Section 6 - Accidental Release Measures

Spills: Prevent further migration into the environment. Use absorbent/adsorbent material to solidify liquids. Sweep up or vacuum. Wear protective equipment, including eye protection, to avoid exposure (see Section 8 for specific handling precautions). m-Cresol is a CERCLA Hazardous Substance and a SARA 313 Toxic Chemical. Sodium phosphate dibasic anhydrous is a CERCLA Hazardous Substance.

Section 7 - Handling and Storage

Storage Conditions: Refrigerator: 2 to 8 C (36 to 46 F).

Section 8 - Exposure Controls / Personal Protection

See Section 2 for Exposure Guideline information.

Under normal use and handling conditions, no protective equipment is required. The following is recommended for a production setting:

Respiratory Protection: Use an approved respirator.

Eye Protection: Safety glasses.

Ventilation: Laboratory fume hood or local exhaust ventilation.

Other Protective Equipment: Chemical-resistant gloves and body covering to minimize skin contact. If handled in a ventilated enclosure, as in a laboratory setting, respirator and goggles or face shield may not be required. Safety glasses are always required.

Section 9 - Physical and Chemical Properties

Appearance: Clear solution
Odor: Odorless
Boiling Point: >100 C (212 F)
Melting Point: Not applicable
Specific Gravity: 1.004 to 1.007
pH: 7.0 to 7.8
Evaporation Rate: No applicable information found
Water Solubility: Soluble
Vapor Density: No applicable information found
Vapor Pressure: No applicable information found

Section 10 - Stability and Reactivity

Stability: Stable at normal temperatures and pressures.

Incompatibility: May react with strong oxidizing agents (e.g., peroxides, permanganates, nitric acid, etc.).

Hazardous Decomposition: May emit toxic fumes when heated to decomposition.

Hazardous Polymerization: Will not occur.

Section 11 - Toxicological Information

Acute Exposure

Data for insulin, lispro crystals, the active ingredient, are presented.

Oral: No applicable information found.

Skin: No applicable information found.

Inhalation: No applicable information found.

Intravenous:
Insulin, lispro crystals - Rat, 10 units/kg, no deaths or toxicity.
Dog, 0.1 units/kg, no deaths, decreased blood glucose values.

Subcutaneous:
Insulin, lispro crystals - Rat, 10 units/kg, no deaths or toxicity.
Dog, 2 units/kg, no deaths or toxicity.

Skin Contact: No applicable information found.

Eye Contact: No applicable information found.

Chronic Exposure

Data for Insulin, and insulin, lispro crystals are presented as indicated.

Target Organ Effects:
Insulin - Hormonal effects (decreased blood sugar).

Reproduction:
Insulin - Mixed results reported in animal studies. Effects were attributed to hypoglycemia. Insulin itself is not considered a reproduction hazard.

Sensitization:
Insulin, lispro crystals - Rhesus monkeys, extremely weak immunogenic potential.

Mutagenicity:
Insulin, lispro crystals - Negative in Ames assay.

Section 12 - Ecological Information

No applicable ecological information found.

Ecotoxicity Data:
Glycerin
Fathead minnow median lethal concentration: 44 g/L
Goldfish 24-hour median lethal concentration: >5000 mg/L
Protozoa threshold toxic concentration for cell multiplication: 3200 mg/L
Algae (M. aeruginosa) threshold toxic concentration for cell multiplication: 2900 mg/L

Environmental Fate:
Glycerin
Log Kow: -1.76
Log Koc: -0.7 to 0.5
Henry's Law constant (atm*m3/mol): 1.75 x 10(11)
5-Day biological oxygen demand: 24% to 82%
Theoretical oxygen demand (p/p): 1.22
Atmospheric half-life (hours): 33

Environmental Summary:
Glycerin - Material is practically non-toxic to aquatic organisms. Material is not expected to bioconcentrate in aquatic organisms and is expected to be highly mobile in soil. Material is not expected to readily volatilize; however, once in the atmosphere it will readily photodegrade. Material is expected to be rapidly degraded by microorganisms.

Section 13 - Disposal Considerations

Waste Disposal: Dispose of any cleanup materials and waste residue according to all applicable laws and regulations. This material contains m-cresol and may be regulated under 40 CFR 261.24 when disposed in bulk quantities or in a production setting. The finished product, e.g., vials, would not be regulated under 40 CFR 261 for disposal under normal use and handling conditions.

Section 14 - Transport Information

Regulatory Organizations:

DOT: Not Regulated

ICAO/IATA: Not Regulated

IMO: Not Regulated

Section 15 - Regulatory Information

Below is selected regulatory information chosen primarily for possible Eli Lilly and Company usage. This section is not a complete analysis or reference to all applicable regulatory information. Please consider all applicable laws and regulations for your country/state.

U.S. Regulations

Insulin, lispro
TSCA - No
CERCLA - Not on this list
SARA 302 - Not on this list
SARA 313 - Not on this list
OSHA Substance Specific - No

Sodium phosphate dibasic anhydrous
TSCA - Yes
CERCLA - Name on list is sodium phosphate dibasic. RQ=5000 pounds (2270 kg)
SARA 302 - Not on this list
SARA 313 - Not on this list
OSHA Substance Specific - No

m-Cresol
TSCA - Yes
CERCLA - Name on list is m-cresol or m-cresylic acid or phenol, methyl-, or cresol, isomers and mixture. RQ = 100 pounds (45.4 kg)
SARA 302 - Not on this list
SARA 313 - Name on list is m-cresol. De minimis = 1%
OSHA Substance Specific - No

Remaining Ingredients
TSCA - Yes
CERCLA - Not on this list
SARA 302 - Not on this list
SARA 313 - Not on this list
OSHA Substance Specific - No

EU Regulations

EC Classification
Not assigned an overall EC classification.

Section 16 - Other Information

MSDS Sections Revised: Section 1.

As of the date of issuance, we are providing available information relevant to the handling of this material in the workplace. All information contained herein is offered with the good faith belief that it is accurate. THIS MATERIAL SAFETY DATA SHEET SHALL NOT BE DEEMED TO CREATE ANY WARRANTY OF ANY KIND (INCLUDING WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE). In the event of an adverse incident associated with this material, this safety data sheet is not intended to be a substitute for consultation with appropriately trained personnel. Nor is this safety data sheet intended to be a substitute for product literature which may accompany the finished product.

For additional information contact:
Eli Lilly and Company
Hazard Communication
317-651-9533

For additional copies contact:
Eli Lilly and Company
1-800-LILLY-Rx (1-800-545-5979)

GLOSSARY:

ACGIH = American Conference of Governmental Industrial Hygienists
AIHA = American Industrial Hygiene Association
BEI = Biological Exposure Index
CAS Number = Chemical Abstract Service Registry Number
CERCLA = Comprehensive Environmental Response Compensation and Liability Act (of 1980)
CHAN = Chemical Hazard Alert Notice
CHEMTREC = Chemical Transportation Emergency Center
DOT = Department of Transportation
EC = European Community
EINECS = European Inventory of Existing Chemical Substances
ELINCS = European List of New Chemical Substances
EPA = Environmental Protection Agency
HEPA = High Efficiency Particulate Air (Filter)
IARC = International Agency for Research on Cancer
ICAO/IATA = International Civil Aviation Organization/International Air Transport Association
IEG = Lilly Interim Exposure Guideline
IMO = International Maritime Organization
Kow = Octanol/Water Partition Coefficient
LEG = Lilly Exposure Guideline
LEL = Lower Explosive Limit
MSDS = Material Safety Data Sheet
MSHA = Mine Safety and Health Administration
NA = Not Applicable, except in Section 14 where NA = North America
NADA = New Animal Drug Application
NAIF = No Applicable Information Found
NCI = National Cancer Institute
NIOSH = National Institute for Occupational Safety and Health
NOS = Not Otherwise Specified
NTP = National Toxicology Program
OSHA = Occupational Safety and Health Administration
PEL = Permissible Exposure Limit (OSHA)
RCRA = Resource Conservation and Recovery Act
RQ = Reportable Quantity
RTECS = Registry of Toxic Effects of Chemical Substances
SARA = Superfund Amendments and Reauthorization Act
STEG = Lilly Short Term Exposure Guideline
STEL = Short Term Exposure Limit
TLV = Threshold Limit Value (ACGIH)
TPQ = Threshold Planning Quantity
TSCA = Toxic Substances Control Act

TWA = Time Weighted Average/8 Hours Unless Otherwise Noted
UEL = Upper Explosive Limit
UN = United Nations
WEEL = Workplace Environmental Exposure Level (AIHA)