SAFETY DATA SHEET

Prepared to U.S. OSHA, CMA, ANSI, Canadian WHMIS Standards, European Union CLP EC 1272/2008 and the Global Harmonization Standard

1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY UNDERTAKING

PRODUCT IDENTIFIER/TRADE/MATERIAL NAME: Liletta™ (Levonorgestrel-Releasing Intrauterine Releasing System)

DESCRIPTION: Levonorgestrel-Releasing Intrauterine Releasing System (IUS)
CHEMICAL NAME: For Active Ingredient: [18,19-Dinorpregn-4-en-20-yn-3-one-13-ethyl-17-hydroxy-, (17α)- (-)-]
CHEMICAL FAMILY: For Active: Progesterone Hormone
FORMULA: For Active Ingredient: $C_{21}H_{28}O_2$
RELEVANT USE of the SUBSTANCE: Human Pharmaceutical
USES ADVISED AGAINST: Non-Pharmaceutical Use
HOW SUPPLIED: Levonorgestrel 18 mcg/24 hours Intrauterine Releasing System

SUPPLIER OF THE SAFETY DATA SHEET

RESPONSIBLE PARTY U.S.:	**Actavis, Inc.**
U.S. ADDRESS:	400 Interpace Parkway, Morris Corporate Center III Parsippany, NJ 07054, USA
U.S. BUSINESS PHONE/GENERAL SDS INFORMATION:	1-800-272-5525
RESPONSIBLE PARTY EUROPE:	
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EMERGENCY PHONE (U.S./NORTH AMERICA):	CHEMTREC: 1-800-424-9300 (24 hours) U.S., Canada, Puerto Rico
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Email:	SDS@Actavis.com

NOTE: ALL United States Occupational Safety and Health Administration Standard (29 CFR 1910.1200), U.S. State equivalent Standards, Canadian WHMIS [Controlled Products Regulations], EU Directives through EC 1907: 2006, and European Union CLP EC 1272/2008, required information is included in appropriate sections based on the U.S. ANSI Z400.1-2010 format. This product has been classified in accordance with the hazard criteria of the countries listed above.

DATE OF PREPARATION: January 24, 2015 **DATE OF REVISION:** New

2. HAZARDS IDENTIFICATION

EU CLP REGULATION (EC) 1272/2008 LABELING AND CLASSIFICATION: According to Article 1, item 5 (a) of CLP Regulation (EC) 1272/2008, medicinal products in the finished state for human use, as defined in 2001/83/EC, are excepted from classification and other criteria of 1272/2008.

EU 67/548/EEC LABELING AND CLASSIFICATION: According to Article 1 of European Union Council Directive 92/32/EEC, medical products in the finished state for human use (as defined by European Union Council Directives 67/548/EEC and 87/21/EEC) are not subject to the regulations and administrative provisions of European Union Council Directive 92/32/EEC.

EMERGENCY OVERVIEW:

Product Description: The product consists of an inserter and levonorgestrel IUS, which is loaded at the tip of the inserter. Inserter components are an insertion tube, plunger, flange, body and slider. The device consists of a white or almost white hormone elastomer core, mounted on a T-body and covered in opaque tubing, which regulates the release of levonorgestrel. The T-body has a loop at one end and two arms at the other end. Removal threads are attached to the loop.

Health Hazards: Due to the form of this product, exposure by ingestion and inhalation is not likely. Accidental ingestion of the active ingredient due to poor hygiene while handling the product may be harmful. The active ingredient can be absorbed via intact skin and may cause systemic effects by this route if exposure is chronic. Chronic exposure may cause temporary impairment of fertility in both genders; interference with egg and sperm production. In men, exposure to female hormones has been associated with testicular atrophy, increased risk of prostate cancer, gynecomastia, loss of libido and potency. The most common effects from therapeutic use of products containing Levonorgestrel administered orally are nausea, vomiting, abdominal pain, tiredness, dizziness, changes in vaginal bleeding, breast tenderness, diarrhea, or headache. For this product and intra-uterine delivery in women, the most common adverse effects reported are uterine/vaginal bleeding including spotting, abnormal menstrual cycles and benign ovarian cysts. The active ingredient can cause harm to the fetus. May cause suppression of lactation. As a progesterone-only hormone, this material is possibly carcinogenic in humans. These effects may be possible as a result of workplace exposure. Refer to Section 11 (Toxicological Information) for additional information on adverse effects.

Flammability Hazards: This product is combustible and may ignite if involved in a fire. When involved in a fire, this material may decompose and produce irritating vapors and toxic compounds (including carbon, tin, silica and nitrogen oxides).

Reactivity Hazards: This product is not reactive.

Environmental Hazards: Components of this product, including the active ingredient may cause long-term harm to aquatic organisms. Large quantities released to the aquatic and terrestrial environment may have an adverse effect.

Emergency Considerations: Emergency responders should wear appropriate protection for situation to which they respond.

3. COMPOSITION and INFORMATION ON INGREDIENTS

CHEMICAL NAME	CAS #	EINECS #	% w/w	LABEL ELEMENTS EU Classification (67/548/EEC) GHS & EU Classification (1272/2008 EC) Risk Phrases/Hazard Statements/Symbol
ACTIVE INGREDIENT				
Levongestrel [18,19-Dinorpregn-4-en-20-yn-3-one-13-ethyl-17-hydroxy-, (17α)- (-)-]	797-63-7	206-656-6	Proprietary	SELF CLASSIFICATION EU 67/548 Classification: Reproductive Toxicity Cat. 2, Reproductive Toxicity Cat. 3, Carcinogenic Cat. 3 Risk Phrase Codes: R61, R62, R40, R64 Hazard Symbols: T, Xn GHS and EU 1272/2008 Classification: Reproductive Toxicity Cat. 1B, Carcinogenic Cat. 2, Adverse Effects on or Via Lactation Hazard Codes: H360Df, H351, H362 Hazard Symbol/Pictogram: GHS08
DRUG RESERVOIR EXCIPIENT INGREDIENTS				
Polydimethylsiloxane	63148-62-9	Not Listed	Proprietary	EU 67/548 Classification: Not Applicable EU/GHS 1272/2008 Classification: Not Applicable
Stannous Octoate	301-10-0	206-108-6	Proprietary	SELF CLASSIFICATION EU 67/548 Classification: Irritant, Dangerous for the Environment Risk Phrase Codes: R41, R36, R43, R51/53 Hazard Symbols: Xn/Xi, N GHS and EU 1272/2008 Classification: Eye Damage/Irritation Cat. 1, Skin Irritation Cat. 2, Skin Sensitization Cat. 1B, Aquatic Chronic Toxicity Cat. 2 Hazard Codes: H318, H315, H317, H411 Hazard Symbol/Pictogram: GHS05, GHS07, GHS09
Tetra-n-Propyl Silicate	682-01-9	211-659-0	Proprietary	SELF CLASSIFICATION EU 67/548 Classification: Irritant Risk Phrase Codes: R36/37/38 Hazard Symbols: Xi GHS and EU 1272/2008 Classification: Skin Irritation Cat. 2, Eye Irritation Cat. 2A, STOT (Inhalation-Respiratory Irritation) SE Cat. 3 Hazard Codes: H315, H319, H335 Hazard Symbol/Pictogram: GHS07

See Section 16 for full classification information for components.

4. FIRST-AID MEASURES

PROTECTION OF FIRST AID RESPONDERS: First-aid responders should not attempt to treat victims of exposure to this material without adequate personal protective equipment. Rescuers should be taken for medical attention, if necessary.

DESCRIPTION OF FIRST AID MEASURES: Victim(s) must be taken for medical attention. Remove victim(s) to fresh air, as quickly as possible. Only trained personnel should administer supplemental oxygen and/or cardio-pulmonary resuscitation, when necessary. Take copy of SDS to physician or other health professional with victim(s).

Inhalation: Inhalation is not a likely route of exposure. If somehow, mists or sprays are generated and are inhaled, remove victim to fresh air. If necessary, use artificial respiration to support vital functions. Seek medical attention if adverse effect occurs after removal to fresh air.

Skin Exposure: Basic hygiene should prevent any problems. If the product contaminates the skin, and adverse effect occurs, begin decontamination with running water. Minimum flushing is for 20 minutes. Do not interrupt flushing. Remove exposed or contaminated clothing, taking care not to contaminate eyes. Seek medical attention if adverse effect occurs after flushing.

Eye Exposure: If this product enters the eyes, open victim's eyes while under gently running water. Use sufficient force to open eyelids. Have victim "roll" eyes. Minimum flushing is for 20 minutes. Do not interrupt flushing. Seek immediate medical attention after flushing if adverse effect occurs.

Ingestion Exposure: If this product is accidentally swallowed, CALL PHYSICIAN OR POISON CONTROL CENTER FOR MOST CURRENT INFORMATION. If professional advice is not available, do not induce vomiting. Rinse mouth with water immediately. Victim should drink large quantities of water. If milk is available, victim should drink it after drinking water. Never induce vomiting or give diluents (milk or water) to someone who is unconscious, having convulsions, or unable to swallow.

IMPORTANT SYMPTOMS AND EFFECTS: See Sections 2 (Hazard Identification) and 11 (Toxicological Information).

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: In therapeutic use, current or recurrent pelvic inflammatory disease, current genital infection, endometritis, cervicitis, cervical dysplasia, uterine tumors, liver tumors, acute or severe liver disease, abnormal genital bleeding conditions with increased susceptibility to infections, severe arterial disease, such as stroke or myocardial infarction, hormone dependent tumor, acute malignancies affecting the blood, recent trophoblastic disease while hCG levels remain elevated, migraine with aura, severe or very frequent headache, jaundice, high blood pressure, history of ovarian cysts, risk factors for arterial disease, thrombotic arterial or embolic disease, may be aggravated. It is not known if workplace exposure may also aggravate these conditions. Persons who may have hypersensitivity reactions to components or other disorders described in Section 11 (Toxicological Information) may experience aggravation upon exposure.

INDICATION OF IMMEDIATE MEDICAL ATTENTION AND SPECIAL TREATMENT IF NEEDED: Treat symptoms and eliminate exposure. Persons developing hypersensitivity reactions should receive medical attention.

4. FIRST-AID MEASURES (Continued)

INDICATION OF IMMEDIATE MEDICAL ATTENTION AND SPECIAL TREATMENT IF NEEDED (continued): There is no antidote for this product. Treatment should be symptomatic and supportive.

5. FIRE-FIGHTING MEASURES

FLASH POINT: Not established.

AUTOIGNITION TEMPERATURE: Not established for product.

FLAMMABLE LIMITS & METHOD OF DETERMINATION (in air by volume, %): Not established.

FIRE EXTINGUISHING MEDIA: In the event of a fire, use suppression methods for surrounding materials, including water spray (for cooling), dry extinguishing media, carbon dioxide, foam.

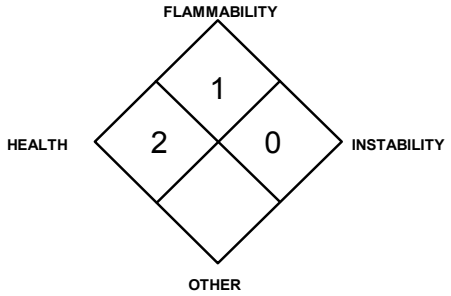
UNSUITABLE FIRE EXTINGUISHING MEDIA: None known.

SPECIFIC HAZARDS ARISING FROM THE SUBSTANCE: This product may be combustible and ignite if involved in a fire. When involved in a fire, the products of thermal decomposition may include irritating fumes and toxic gases (e.g., carbon, tin, silica and nitrogen oxides).

Explosion Sensitivity to Mechanical Impact: Not sensitive.

Explosion Sensitivity to Static Discharge: Not sensitive.

NFPA RATING



Hazard Scale: **0** = Minimal **1** = Slight **2** = Moderate **3** = Serious **4** = Severe

SPECIAL PROTECTIVE ACTIONS FOR FIRE-FIGHTERS: Incipient fire responders should wear eye protection. Structural firefighters must wear Self-Contained Breathing Apparatus (SCBA) and full protective equipment. If protective equipment is contaminated by this product, it should be thoroughly washed with running water prior to removal of SCBA respiratory protection. Firefighters whose protective equipment becomes contaminated should thoroughly shower with warm, soapy water and should receive medical evaluation if they experience any adverse effects. Firefighters whose protective equipment becomes contaminated should thoroughly shower with warm, soapy water and should receive medical evaluation if they experience any adverse effects.

6. ACCIDENTAL RELEASE MEASURES

PERSONAL PRECAUTIONS: In the event of a spill, clear the area and protect people.

PROTECTIVE EQUIPMENT:

Small Spills: For incidental spills (e.g., 1 package), wear double latex or nitrile disposable gloves and eye protection.

Large Spills: For large spills (e.g., carton of packages), protective apparel should be used with a respirator when there is any danger of airborne mists or sprays being generated. Minimum Personal Protective Equipment should be rubber gloves, rubber boots, face shield, and Tyvek suit. Minimum level of personal protective equipment for releases in which the level of oxygen is less than 19.5% or is unknown must be **Level B: triple-gloves (rubber gloves and nitrile gloves over latex gloves), chemical resistant suit and boots, hard hat, and Self-Contained Breathing Apparatus.**

METHODS FOR CLEANUP AND CONTAINMENT:

Small Spills: If product has been released from packaging, absorb up any spilled material with damp sponge, polypads or other suitable material. If intact packages have been spilled, pick-up, and dispose of properly.

Large Spills: Trained personnel following pre-planned procedures should handle non-incidental releases. Access to the spill areas should be restricted. Absorb any spilled product carefully, onto polypads or other non-reactive absorption material.

All Spills: Decontaminate the area of the spill thoroughly using detergent and water. Place all spill residue in an appropriate container and seal. Do not mix with wastes from other materials. If necessary, discard contaminated response equipment or rinse with soapy water before returning such equipment to service. Dispose of in accordance with applicable international, national, state, and local procedures (see Section 13, Disposal Considerations).

ENVIRONMENTAL PRECAUTIONS: Prevent material from entering sewer or confined spaces, waterways, soil or public waters. Do not flush to sewer. For spills on water, contain, minimize dispersion and collect.

7. HANDLING and USE

PRECAUTIONS FOR SAFE HANDLING: All employees who handle this material should be thoroughly trained to handle it safely. Open containers slowly on a stable surface in areas that have been designated for use of this product. As with all chemicals, avoid getting this product ON YOU or IN YOU. Ensure this product is used with adequate ventilation (refer to Section 8, Exposure Controls-Personal Protection). Remove contaminated clothing and launder. Keep container tightly closed when not in use. Keep away from heat, sparks, and other sources of ignition. Use non-sparking tools. Empty containers may contain residual material; therefore, empty containers should be handled with care. Follow SPECIFIC USE INSTRUCTIONS supplied with this product. Particular care in working with this product must be practiced in pharmacies and other preparation areas, during manufacture of this compound, and during patient administration.

PRODUCT PREPARATION INSTRUCTIONS FOR MEDICAL PERSONNEL: Handle this material following standard medical practices and following the recommendations presented on the Package Insert.

CONDITIONS FOR SAFE STORAGE: Containers of this product must be properly labeled. Recommended Storage Temperature: 20-25°C (68-77°F). Product should be stored in secondary containers or in a diked area, as appropriate. Store away from incompatible materials (see Section 10, Stability and Reactivity). Store containers in a cool, dry location, away from direct sunlight, sources of intense heat or other sources of ignition. Product should be stored in secondary containers or in a diked area, as appropriate. Store containers away from incompatible chemicals (see Section 10, Stability and Reactivity).

7. HANDLING and USE (Continued)

CONDITIONS FOR SAFE STORAGE (continued): Post warning and "NO SMOKING" signs in storage and use areas, as appropriate. Have appropriate extinguishing equipment in the storage area (i.e., sprinkler system, portable fire extinguishers). Inspect all incoming containers before storage to ensure containers are properly labeled and not damaged.

SPECIFIC END USE(S): This product is a human pharmaceutical. Follow all industry standards for use of this product.

PROTECTIVE PRACTICES DURING MAINTENANCE OF CONTAMINATED EQUIPMENT: When cleaning non-disposable equipment, wear latex or butyl rubber (double gloving is recommended), goggles, and lab coat. Wash equipment with soap and water. Wipe equipment down with damp sponge or polypad.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION

EXPOSURE LIMITS/CONTROL PARAMETERS:

Ventilation and Engineering Controls: Use with adequate ventilation. Follow standard medical product handling procedures. During decontamination of work surfaces, workers should wear the same equipment recommended in Section 6 (Accidental Release Measures) of this SDS.

Occupational/Workplace Exposure Limits/Guidelines (continued):

CHEMICAL NAME	CAS #	EXPOSURE LIMITS IN AIR							
		ACGIH-TLVs		OSHA-PELs		NIOSH-RELs		NIOSH	OTHER
		TWA mg/m^3	STEL mg/m^3	TWA mg/m^3	STEL mg/m^3	TWA mg/m^3	STEL mg/m^3	IDLH mg/m^3	mg/m^3
Levonorgestrel	767-63-7	NE	NE	NE	NE	NE	NE	NE	Actavis OEL: 0.03 $\mu g/m^3$ Carcinogen: IARC-2B (progestin-only hormones)
Polydimethyl-siloxane	63148-62-9	NE	NE	NE	NE	NE	NE	NE	NE
Stannous Octoate Exposure limits given are for tin, organic compounds, as Sn	301-10-0	0.1 (skin)	NE	0.1	NE	0.1 (skin)	NE	25 (as Sn)	DFG MAKs: TWA: 0.1 (inhalable fraction), skin PEAK: 2•MAK 15 min. average value, 4 per shift, 1-hr interval, skin DFG MAK Pregnancy Classification: D Carcinogen: TLV-A4
Tetra-n-Propyl Silicate	682-01-9	NE	NE	NE	NE	NE	NE	NE	NE

NE = Not Established

International Occupational Exposure Limits: Currently the following additional international exposure limits are in place for components of this product. Limits change and are added should be checked frequently.

STANNOUS OCTOATE: United Kingdom: TWA = 0.1 mg(Sn)/m^3; STEL = 0.2 mg(Sn)/m^3, OCT 2007

PERSONAL PROTECTIVE EQUIPMENT: Use of personal protective equipment must be in compliance with U.S. OSHA 29 CFR Subpart I (beginning at 1910.132), Canadian CSA Standards Z94.4-02 and Z94.3-02, EU EN 529:2005, CEN/TR 15419:2006, and CR 13464:1999. Please reference applicable regulations and standards for relevant details.

Respiratory Protection: A respirator is not required for routine conditions of use with adequate engineering controls. A full-face Air-Purifying Respirator with high-efficiency particulate filter or a Supplied-Air Respirator must be worn during operations where engineering controls are not sufficient, large spill cleanup, or when processing generates airborne aerosols. If respiratory protection is needed, use only respiratory protection authorized under appropriate regional regulations.

Eye Protection: During operations in which mists or sprays may be generated, splash goggles or safety glasses should be considered.

Hand Protection: During manufacture or other similar industrial operations, wear the appropriate hand protection for the process. Use double gloves for spill response, as stated in Section 6 (Accidental Release Measures) of this SDS.

Body Protection: Use appropriate protective clothing for the task (e.g., lab coat, etc.)

9. PHYSICAL and CHEMICAL PROPERTIES

The following information is available for the product.

FORM: As described in Section 2.
COLOR: As described in Section 2.
ODOR: Mild odor.
ODOR THRESHOLD: Not available.
HOW TO DETECT THIS SUBSTANCE (identification/warning properties): The appearance of this product may act as a distinguishing characteristic.

The following information is available for the active ingredient, Levonorgestrel.

FORM: Crystalline solid.
COLOR: white.
MOLECULAR WEIGHT: 312.4
MOLECULAR FORMULA: $C_{21}H_{28}O_2$
ODOR: Odorless.
ODOR THRESHOLD: Not applicable.
BOILING POINT @ 760 mmHg: 459.14°C (858.5°F) [predict.]
MELTING POINT: 236-240°C (456.8-464°F)
VAPOR PRESSURE (air = 1) @ 25°C: 0 mmHg [predict.]
SPECIFIC GRAVITY (water = 1): 1.139 g/cm^3
EVAPORATION RATE (nBuAc = 1): Not applicable.
FLASH POINT: 195.45°C (383.8°F) [predict.]
SOLUBILITY IN WATER: Insoluble; 8.991 mg/L (est.)
OTHER SOLUBILITIES: Soluble in ethanol (1 in 120), chloroform (1 in 15), diethyl ether (1 in 400) and dioxane.
COEFFICIENT WATER/OIL DISTRIBUTION: Log P = 3.368 [predict.]

10. STABILITY and REACTIVITY

CHEMICAL STABILITY: This product is stable.

DECOMPOSITION PRODUCTS: ***Combustion:*** If exposed to extremely high temperatures, the products of thermal decomposition may include irritating fumes and toxic gases (e.g., carbon, tin, silica and nitrogen oxides). ***Hydrolysis:*** None known.

MATERIALS WITH WHICH SUBSTANCE IS INCOMPATIBLE: This product is generally compatible with other common materials in a medical facility.

POSSIBILITY OF HAZARDOUS REACTIONS OR POLYMERIZATION: Will not occur.

CONDITIONS TO AVOID: Avoid heat, light, and contact with incompatible chemicals.

11. TOXICOLOGICAL INFORMATION

SYMPTOMS OF EXPOSURE BY ROUTE OF EXPOSURE: The health hazard information provided below is pertinent to medical employees using this product in an occupational setting. The following paragraphs describe the symptoms of exposure by route of exposure.

Inhalation: Inhalation is an unlikely route of exposure for this product due to its form.

Contact with Skin or Eyes: Contact with the skin may cause mild irritation, which is alleviated upon rinsing. Prolonged or repeated skin contact may cause dermatitis (dry, red skin). Contact of this product with the eyes may cause irritation, redness and tearing.

Skin Absorption: Absorption of hormones through the skin may contribute to the effects of exposure as described in "Other Potential Health Effects".

Ingestion: Ingestion is not a significant route of occupational exposure and is unlikely due to form of product. Ingestion of this material (i.e., through poor hygiene practices) may lead to acute poisoning resulting in mild, self limiting effects, usually involving the gastrointestinal tract. Nausea, vomiting and occasionally vaginal breakthrough bleeding may occur. Symptoms of chronic ingestion may include those described for "Other Potential Health Effects".

Injection: Not a likely route of exposure due to form of product.

HAZARDOUS MATERIAL IDENTIFICATION SYSTEM

HEALTH HAZARD	(BLUE)	2*
FLAMMABILITY HAZARD	(RED)	1
PHYSICAL HAZARD	(YELLOW)	0

PROTECTIVE EQUIPMENT

EYES	RESPIRATORY	HANDS	BODY
	SEE SECTION 8		SEE SECTION 8

For Routine Industrial Use and Handling Applications

Hazard Scale: **0** = Minimal **1** = Slight **2** = Moderate **3** = Serious **4** = Severe * = Chronic hazard

OTHER POTENTIAL HEALTH EFFECTS-Therapeutic Doses: In therapeutic use the most common adverse effects reported have included nausea, vomiting, abdominal pain, tiredness, dizziness, changes in vaginal bleeding, breast tenderness, diarrhea, or headache. May cause harm to fetus during pregnancy. Androgenic side effects such as acne, hirsutism (increased body hair growth) and weight gain occur rarely. Increased concentrations of progestins increase the normal oral flora growth rate, leading to an increase in inflammation of the gingival tissues and increased bleeding. Fluid retention may be caused by some progestins, especially high doses, and may aggravate these conditions of asthma, significant cardiac insufficiency, epilepsy, hypertension, migraine headaches or significant renal dysfunction. Individuals who have had allergic reactions to products containing progestogens may experience allergic reactions to this material. In therapeutic use, Levonorgestrel has shown carcinogenic effects. May cause harm to the fetus during pregnancy. Exposure to female hormones in men can also include testicular atrophy, increased risk of prostate cancer, loss of libido and potency, gynecomastia (the abnormal growth of breast tissue), increased risk of prostate cancer and infertility from decrease in FSH and subsequent effects on sperm maturation. Changes in FSH levels affect the ovulatory cycle in women which may lead to decreased fertility. These effects may be possible as a result of workplace exposure. The actual risk in the workplace is not known. Other adverse effects reported from therapeutic use described by body system are provided below.

- ***Body as a Whole:*** Weight gain, fluid retention and swelling.
- ***Cardiovascular System:*** High blood pressure, exacerbation of cardiovascular disorders.
- ***Central Nervous System:*** Headache. Uncommon: Migraine.
- ***Gastrointestinal System:*** Abdominal pain, nausea. Uncommon: Abdominal distention.
- ***Musculoskeletal System:*** Back pain.
- ***Psychiatric Disorders:*** Depression, nervousness, altered mood.
- ***Reproductive System:*** Harm to fetus. Menstrual bleeding changes, benign ovarian cysts, pelvic pain, painful cramps, vaginal discharge, vulvovaginitis , breast tenderness, breast pain, Uncommon: Decreased libido, pelvic inflammatory disease, endometritis, inflammation of the cervix, papanicolaou smear normal, class II. Rarely: Uterine perforation.
- ***Skin:*** Acne. Uncommon: Hair loss, increased hair growth, eczema, itching. Rarely: Hives, rash.

HEALTH EFFECTS OR RISKS FROM EXPOSURE: An Explanation in Lay Terms. Exposure to this product may cause the following health effects:

Acute: Acute ingestion of large quantities of this product caused by poor hygiene practices can cause adverse systemic effects. Skin contact may result in absorption of harmful amount of active ingredient.

Chronic: May cause harm to fetus. Carcinogenic potential. Chronic exposure to this product may cause adverse effects as described under 'Other Potential Health Effects'.

11. TOXICOLOGICAL INFORMATION (Continued)

TARGET ORGANS: Acute: *Industrial Exposure*: Skin. *Therapeutic Doses*: Reproductive system. **Chronic:** *Industrial Exposure*: Skin. *Therapeutic Doses*: In therapeutic use this material may have an impact on the body systems described under 'Other Potential Health Effects'.

SENSITIZATION OF PRODUCT: In therapeutic use rare allergic reactions including rash and hives have been reported.

IRRITANCY OF PRODUCT: This product may mildly irritate contaminated tissue if contact is prolonged.

TOXICITY DATA: The following are toxicity data for the active ingredient. Data are available for the excipient components of this product, but are not given in this SDS. Contact Actavis for more information.

LEVONORGESTREL:

TDLo (Oral-Human) 0.26 mg/kg/2 years-intermittent: Skin and Appendages: dermatitis, allergic (after systemic exposure)

TDLo (Oral-Woman) 8 µg/kg: female 1 day(s) pre-mating: Reproductive: Maternal Effects: menstrual cycle changes or disorders

TDLo (Oral-Woman) 20 µg/kg: female 1 day(s) after conception: Reproductive: Fertility:- female fertility index (e.g. # females pregnant per # sperm positive females; # females pregnant per # females mated)

TDLo (Oral-Woman) 274 µg/kg: female 52 week(s) pre-mating: Reproductive: Maternal Effects: menstrual cycle changes or disorders

TDLo (Oral-Woman) 109 µg/kg: female 26 week(s) pre-mating: Reproductive: Fertility; female fertility index (e.g. # females pregnant per # sperm positive females; # females pregnant per # females mated)

TDLo (Oral-Woman) 38,160 ng/kg: female 22 week(s) pre-mating: Reproductive: Maternal Effects: menstrual cycle changes or disorders; Fertility: female fertility index (e.g. # females pregnant per # sperm positive females; # females pregnant per # females mated)

TDLo (Oral-Woman) 5 µg/kg: female 1 day(s) after conception: Reproductive: Fertility: female fertility index (e.g. # females pregnant per # sperm positive females; # females pregnant per # females mated)

TDLo (Oral-Woman) 1600 µg/kg: female 52 week(s) pre-mating: Reproductive: Fertility: female fertility index (e.g. # females pregnant per # sperm positive females; # females pregnant per # females mated)

TDLo (Oral-Rat) 1820 mg/kg/26 weeks-intermittent: Blood: changes in serum composition (e.g. TP, bilirubin, cholesterol); Biochemical: Metabolism (Intermediary): other proteins

TDLo (Oral-Rat) 10 µg/kg: female 6 day(s) after conception: Reproductive: Fertility: other measures of fertility

TDLo (Oral-Rat) 960 mg/kg: female 2 day(s) pre-mating: Reproductive: Fertility: other measures of fertility

LEVONORGESTREL (continued):

TDLo (Oral-Rat) 10 µg/kg: female 6 day(s) after conception: Reproductive: Maternal Effects: uterus, cervix, vagina

TDLo (Oral-Mouse) 29 mg/kg/69 weeks-continuous: Tumorigenic: neoplastic by RTECS criteria; Skin and Appendages: tumors

TDLo (Oral-Rabbit) 0.25 mg/kg/5 days-intermittent: Endocrine: other changes; Reproductive: Maternal Effects: uterus, cervix, vagina

TDLo (Oral-Rabbit) 0.25 mg/kg/5 days-intermittent: Endocrine: other changes

TDLo (Oral-Rabbit) 4500 µg/kg: female 3 day(s) pre-mating: Reproductive: Fertility: other measures of fertility

TDLo (Oral-Rabbit) 1875 µg/kg: female 1 day(s) pre-mating: Reproductive: Fertility: female fertility index (e.g. # females pregnant per # sperm positive females; # females pregnant per # females mated)

TDLo (Oral-Monkey) 67.4 mg/kg/2.9 years-intermittent: Reproductive: Maternal Effects: ovaries, fallopian tubes; Biochemical: Metabolism (Intermediary): other proteins

TDLo (Oral-Monkey) 1800 µg/kg: female 43 week(s) pre-mating: Reproductive: Maternal Effects: ovaries, fallopian tubes

TDLo (Oral-Dog) 1600 µg/kg: female 5 day(s) pre-mating: Reproductive: Maternal Effects: uterus, cervix, vagina

TDLo (Subcutaneous-Rat) 120 µg/kg: female 1 day(s) pre-mating: Reproductive: Fertility: other measures of fertility

TDLo (Subcutaneous-Rabbit) 0.1 mg/kg/5 days-intermittent: Endocrine: other changes; Reproductive: Maternal Effects: uterus, cervix, vagina

TDLo (Subcutaneous-Rabbit) 300 µg/kg: female 2 day(s) pre-mating 1 day(s) after conception: Reproductive: Fertility: pre-implantation mortality (e.g. reduction in number of implants per female; total number of implants per corpora lutea)

CARCINOGENIC POTENTIAL OF COMPONENTS: The following information is for the active ingredient.

Some epidemiological studies of oral contraceptive users have reported an increased relative risk of developing breast cancer, particularly at a younger age and apparently related to duration of use. These studies have predominantly involved combined oral contraceptives and there is insufficient data to determine whether the use of Progestin-only oral contraceptives similarly increases the risk. A meta-analysis of 54 studies found a small increase in the frequency of having breast cancer diagnosed for women who were currently using combined oral contraceptives or had used them within the past ten years. This increase in the frequency of breast cancer diagnosis, within ten years of stopping use, was generally accounted for by cancers localized to the breast. There was no increase in the frequency of having breast cancer diagnosed ten or more years after cessation of use. Some studies suggest that oral contraceptive use has been associated with an increase in the risk of cervical intraepithelial neoplasia in some populations of women.

However, there continues to be controversy about the extent to which such findings may be due to differences in sexual behavior and other factors. There is insufficient data to determine whether the use of Progestin-only oral contraceptives increases the risk of developing cervical intraepithelial neoplasia.

This material is listed by agencies tracking the carcinogenic potential of chemical compounds, as follows:

Levonorgestrel: IARC-2B (Possibly Carcinogenic to Humans) as Progestogen-only contraceptives

The remaining components of this product are listed as follows:

Stannous Octoate (as an organic tin compound): ACGIH TLV-A4 (Not Classifiable as a Human Carcinogen)

REPRODUCTIVE TOXICITY INFORMATION: There are no adequate and well-controlled studies of Levonorgestrel in pregnant women; however, based on its mechanism of action and findings from animal studies, this material can cause fetal harm when administered to pregnant women. In the workplace, the risk to the fetus should be communicated and the appropriate action should be taken to prevent exposure in accordance with company policy and regulatory requirements. This product is rated by the FDA for therapeutic risk as Pregnancy Risk Category X (refer to Definition of Terms for full category definitions).

Mutagenicity: No information available.

Embryotoxicity/Teratogenicity: Many studies have found no effects on fetal development associated with long-term use of contraceptive doses of oral progestins. The few studies of infant growth and development that have been conducted have not demonstrated significant adverse effects. It is nonetheless prudent to rule out suspected pregnancy before initiating any hormonal contraceptive use. However, several reports suggest an association between intrauterine exposure to progestational drugs in the first trimester of pregnancy and congenital abnormalities in male and female fetuses. Some progestational drugs induce mild virilization of the external genitalia of female fetuses. Use of synthetic progestins during pregnancy has resulted in and increase in the risk of hypospadias in a male fetus.

Reproductive Toxicity: Exposure to female hormones in men can result in infertility due to disruption of FSH levels and maturation of sperm. Irregular menstrual patterns are common among women using progestin-only oral contraceptives. If follicular development occurs, atresia of the follicle is sometimes delayed and the follicle may continue to grow beyond the size it would attain in a normal cycle. Generally these enlarged follicles disappear spontaneously. Often they are asymptomatic; in some cases they are associated with mild abdominal pain. In general, no adverse effects have been found on breastfeeding performance or on the health, growth, or development of the infant. May cause suppression of lactation.

11. TOXICOLOGICAL INFORMATION (Continued)

REPRODUCTIVE TOXICITY INFORMATION (continued):

Reproductive Toxicity (continued): Small amounts of progestins pass into the breast milk of nursing mothers, resulting in detectable steroid levels in infant plasma. Very rarely, adverse effects in the infant/child have been reported, including jaundice. Because of the potential for serious adverse reactions in nursing infants, nursing mothers should be advised of these effects and the appropriate action should be taken to prevent exposure.

ACGIH BIOLOGICAL EXPOSURE INDICES (BEIs): Currently, ACGIH Biological Exposure Indices (BEIs) have not been determined for the components of this product.

12. ECOLOGICAL INFORMATION

ALL WORK PRACTICES MUST BE AIMED AT ELIMINATING ENVIRONMENTAL CONTAMINATION.

MOBILITY: This product has not been tested for mobility in soil.

PERSISTENCE AND BIODEGRADABILITY: This product has not been tested for persistence or biodegradability.

BIO-ACCUMULATION POTENTIAL: This product has not been tested for bio-accumulation potential.

ECOTOXICITY: This product may be harmful to contaminated plant and animal life, especially in large quantities. All releases to terrestrial, atmospheric and aquatic environments should be avoided. No specific data is available for this product. The following aquatic toxicity data are currently available for the active component of this product.

LEVONORGESTREL:

LC_{50} (Fish) 96 hours = > 100 mg/L

EC_{50} (*Daphnia magna*) 48 hours = > 1.3 mg/L

OTHER ADVERSE EFFECTS: This product does not contain any component with known ozone depletion potential.

RESULTS OF PBT AND vPvB ASSESSMENT: No Data Available. PBT and vPvB assessments are part of the chemical safety report required for some substances in European Union Regulation (EC) 1907/2006, Article 14.

ENVIRONMENTAL EXPOSURE CONTROLS: Controls should be engineered to prevent release to the environment, including procedures to prevent spills, atmospheric release and release to waterways.

13. DISPOSAL CONSIDERATIONS

WASTE TREATMENT/DISPOSAL METHODS: Waste disposal must be in accordance with appropriate Federal, State, and local regulations. Waste containers should be handled with uncontaminated gloves. Reusable equipment should be decontaminated using 0.05M Boric acid solution adjusted to pH 9 with 10 N sodium hydroxide followed by a detergent wash and then clean water rinse or by using a bleach solution (triple wash) and a detergent solution followed by clean water rinse.

PRECAUTIONS TO BE FOLLOWED DURING WASTE HANDLING: Wear proper protective equipment when handling waste materials.

U.S. EPA WASTE NUMBER: Wastes of the liquid should be tested to see if they meet the criteria for D001 (Characteristic/Ignitability).

EUROPEAN WASTE CODES: Wastes from Human or Animal Health Care or Related Research: 18 01 08: Medicines Other Than Those Mentioned in 18 01 07.

14. TRANSPORTATION INFORMATION

U.S. DEPARTMENT OF TRANSPORTATION REGULATIONS: This product is NOT classified as dangerous goods, per U.S. DOT regulations, under 49 CFR 172.101.

TRANSPORT CANADA TRANSPORTATION OF DANGEROUS GOODS REGULATIONS: This product is NOT classified as Dangerous Goods, per regulations of Transport Canada.

INTERNATIONAL AIR TRANSPORT ASSOCIATION (IATA): This product is NOT classified as Dangerous Goods, by rules of IATA.

INTERNATIONAL MARITIME ORGANIZATION (IMO) DESIGNATION: This product is NOT classified as Dangerous Goods by the International Maritime Organization.

UNITED NATIONS ECONOMIC COMMISSION FOR EUROPE (UNECE): This product is NOT classified by the United Nations Economic Commission for Europe to be dangerous goods. Refer to current regulations for all additional provisions other information not given here.

TRANSPORT IN BULK ACCORDING TO THE IBC CODE: See the information under the UN ADR and IMO, in this section.

ENVIRONMENTAL HAZARDS: This compound is neither environmentally hazardous according to the criteria of the UN Model Regulations (as reflected in the IMDG Code, ADR, RID, and ADN) nor a marine pollutant according to the IMDG Code and is not listed in Annex III under MARPOL 73/78.

15. REGULATORY INFORMATION

UNITED STATES REGULATIONS:

U.S. SARA Reporting Requirements: The components of this product are not subject to the reporting requirements of Sections 302, 304, and 313 of Title III of the Superfund Amendments and Reauthorization Act.

U.S. SARA Section 302 Extremely Hazardous Threshold Planning Quantity (TPQ): Not applicable.

U.S. SARA Section 304 Extremely Hazardous Reportable Quantity (RQ): Not applicable.

U.S. CERCLA Reportable Quantities (RQ): Not applicable.

U.S. TSCA Inventory Status: This product is regulated under Food and Drug Administration standards; it is not subject to requirements under TSCA.

California Safe Drinking Water and Toxic Enforcement Act (Proposition 65): When used in contraceptive implants,

Levonorgestrel is on the California Proposition 65 lists. WARNING! This material is a chemical known to the state of California to cause female reproductive harm.

Other U.S. Federal Regulations: Regulations of the FDA under the Federal Food, Drug and Cosmetic Act are applicable when this material is used in pharmaceutical preparations. Under the Hazard Communication Standard (HCS), Section (b)(5)(ii) drugs are subject to labeling requirements by the FDA under the Federal Food, Drug and Cosmetic Act and are exempt from labeling provisions of the HCS; this section of the HCS exempts only labeling requirements and not requirements for a Safety Data Sheet for drugs.

CANADIAN REGULATIONS:

Canadian DSL Inventory Status: This product regulated by the Therapeutic Products Programme (TPP) of Health Canada and so it excepted from requirements of the DSL/NDSL Inventory.

Canadian Environmental Protection Act (CEPA) Priorities Substances Lists: The components of this product are not on the CEPA Priorities Substances Lists.

Canadian WHMIS Classification and Symbol: The WHMIS Requirements of the Hazardous Products Act does not apply in respect of the advertising, sale or importation of any cosmetic, device, drug or food within the meaning of the Food and Drugs Act.

Other Canadian Regulations: Requirements under the Canadian Heath Canada, Laboratory Biosafety Guidelines may be applicable.

EUROPEAN UNION REGULATIONS:

Safety, Health, and Environmental Regulations/Legislation Specific for the Product: When formulated in a finished medicinal compound for human use, this material is subject to Directive 2001/83/EC and subsequent amendments to the directive.

Chemical Safety Assessment: No Data Available. The chemical safety assessment is required for some substances according to European Union Regulation (EC) 1907/2006, Article 14.

16. OTHER INFORMATION

ANSI LABELING (Based on 129.1, Provided to Summarize Occupational Exposure Hazards): DANGER! CAN CAUSE HARM TO THE FETUS DURING PREGNANCY. MAY SUPPRESS LACTATION. CONTAINS SUSPECT CARCINOGEN. MAY BE ABSORBED THROUGH THE SKIN. CHRONIC EXPOSURE MAY CAUSE TEMPORARY IMPAIRMENT OF FERTILITY IN BOTH GENDERS. MAY CAUSE ALLERGIC REACTIONS FROM THERAPEUTIC USE. COMBUSTIBLE IF EXPOSED TO HIGH TEMPERATURES. Keep away from heat, sparks, and flame. Avoid contact with skin, eyes, and clothing. Avoid breathing vapors. Keep container tightly closed. Use only with adequate ventilation. Wash thoroughly after handling. Wear gloves, goggles, and appropriate body protection during handling or administration. FIRST-AID: In case of contact, flush skin or eyes with plenty of water. If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. If swallowed, do NOT induce vomiting. If vomiting occurs, have person lean forward. Call physician or poison control center immediately. Never give anything by mouth to an unconscious person. IN CASE OF FIRE: Use water fog, dry chemical, CO_2, or "alcohol" foam. IN CASE OF SPILL: Wipe up spilled product. Place residue in appropriate container and seal. Dispose of according to applicable regulations. Consult Safety Data Sheet for additional information.

GLOBAL HARMONIZATION AND EU CLP REGULATION (EC) 1272/2008 LABELING AND CLASSIFICATION: According to Article 1, item 5 (a) of CLP Regulation (EC) 1272/2008, medicinal products in the finished state for human use, as defined in 2001/83/EC, are excepted from classification and other criteria of 1272/2008.

EU 67/548/EEC LABELING AND CLASSIFICATION: According to Article 1 of European Union Council Directive 92/32/EEC, medical products in the finished state for human use (as defined by European Union Council Directives 67/548/EEC and 87/21/EEC) are not subject to the regulations and administrative provisions of European Union Council Directive 92/32/EEC.

CLASSIFICATION OF COMPONENTS:

CLP Regulation (EC) 1272/2008

Levonorgestrel: This is a self classification.

Classification: Reproductive Toxicity Category 1B, Carcinogenic Category 2, Adverse Effects on or Via Lactation

Hazard Statements: H361Df: May damage the unborn child. Suspected of damaging fertility. H351: Suspected of causing cancer. H362: May cause harm to breast-fed children.

Stannous Octoate: This is a self classification.

Classification: Eye Damage/Irritation Category 1, Skin Irritation Category 2, Skin Sensitization Category 1B, Aquatic Chronic Toxicity Category 2

Hazard Statements: H318: Causes serious eye damage. H315: Causes skin irritation. H317: May cause an allergic skin reaction. H411: Toxic to aquatic life with long-lasting effects.

Tetra-n-Propyl Silicate: This is a self classification.

Classification: Skin Irritation Category 2, Eye Irritation Category 2A, Specific Target Organ Toxicity (Inhalation-Respiratory Irritation) Single Exposure Category 3

Hazard Statements: H315: Causes skin irritation. H319: Causes serious eye irritation. H335: May cause respiratory irritation.

All Other Components: No classification has been published or is applicable.

16. OTHER INFORMATION (Continued)

CLASSIFICATION OF COMPONENTS (continued):

67/548/EEC:

Levonorgestrel: This is a self classification.

Classification: Reproductive Toxicity Category 2, Reproductive Toxicity Category 3, Carcinogenic Category 3

Risk Phrases: R61: May cause harm to the unborn child. R62: Possible risk of impaired fertility. R40: Limited evidence of a carcinogenic effect. R64: May cause harm to breast-fed babies.

Stannous Octoate: This is a self classification.

Classification: Harmful, Irritant, Dangerous for the Environment

Risk Phrases: R41: Risk of serious damage to eyes. R36: Irritating to eyes. R43: May cause sensitisation by skin contact. R51/53: Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Tetra-n-Propyl Silicate: This is a self classification.

Classification: Irritant

Risk Phrases: R36/37/38: Irritating to eyes, respiratory system and skin.

All Other Components: No classification has been published or is applicable.

REFERENCES AND DATA SOURCES: Contact the supplier for information.

METHODS OF EVALUATING INFORMATION FOR THE PURPOSE OF CLASSIFICATION: Bridging principles were used to classify this compound.

REVISION DETAILS: New

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