

PART I *What is the material and what do I need to know in an emergency?***1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE****IDENTIFICATION of the SUBSTANCE or PREPARATION:**

TRADE NAME: **TOPIRAMATE CAPSULE and TABLET**
CHEMICAL NAME: Active Ingredient: 2,3:4,5-Di-O-isopropylidene-β-D-fructopyranose sulfamate
CHEMICAL CLASS: Active Ingredient: Sulfamate-Substituted Monosaccharide
THERAPEUTIC CLASS: Antiepileptic
RELEVANT USE of the SUBSTANCE: Human Pharmaceutical
HOW SUPPLIED: Capsules - NDC: 0093-7335-06: 15 mg white capsules
 - NDC: 0093-7336-06; 25 mg white capsules
 Tablets – NDC: 0093-0155-06, 0093-0155-10: 25 mg white oval tablets
 - NDC: 0093-7540-06, 0093-7540-10: 50 mg light yellow oval tablets
 - NDC: 0093-7219-06, 0093-7219-10: 100 mg yellow oval tablets
 - NDC: 0093-7220-06, 0093-7220-10: 200 mg salmon oval tablets

COMPANY/UNDERTAKING IDENTIFICATION:

U.S. SUPPLIER/MANUFACTURER'S NAME: **TEVA**
ADDRESS: 1090 Horsham Road
 North Wales, PA 19454
 215-591-3000 [08:00 AM --> 05:00 PM]
BUSINESS PHONE:
EUROPEAN SUPPLIER/MANUFACTURER'S NAME: **TEVA/TAPI**
ADDRESS: Sicor sri-Via Terrazzano
 77-20017 Cho (MI), Italy
 +39 02 93197 306 [08:00 AM --> 05:00 PM]
BUSINESS PHONE:
EMERGENCY PHONE: United States/Canada/Puerto Rico: 1-800/424-9300 (Chemtrec) [24-hrs]
 International: 01-703-527-3887 (Chemtrec) [24-hours]
EMAIL: TevaSDSRequest@tevapharm.com
DATE OF PREPARATION: December 2, 2013
DATE OF REVISION: New

ALL WHMIS required information is included in appropriate sections based on the ANSI Z400.1-2004 format. This product has been classified in accordance with the hazard criteria of the CPR and the SDS contains all the information required by the CPR. The product is also classified per the Global Harmonization Standard.

2. HAZARD IDENTIFICATION

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 exempted from classification and other criteria of 1272/2008.

EU LABELING/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: This product consists of a two-piece capsules which are white and filled with white to off-white pellets or tablets that are white (25 mg), light yellow (50 mg), yellow (100 mg), and salmon (200 mg) oval-shaped tablets. **Hazards:** In the workplace, dusts from damaged capsules or tablets may cause irritation of contaminated skin or eye. Non-therapeutic ingestion may be harmful. Therapeutic use can cause include tingling of arms and legs (paresthesia), lack of hunger, nausea, diarrhea, weight loss, nervousness, upper respiratory tract infection, fatigue, dizziness, somnolence, nervousness, psychomotor slowing, difficulty with memory, difficulty with concentration/attention, and confusion. Adverse effects on the eyes, kidneys and neurological system have been reported. Fetal harm has been reported. 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 can ignite if highly heated or if exposed to direct flame. When involved in a fire, this material may decompose and produce irritating vapors and toxic compounds (including carbon, iron, titanium, sulfur and nitrogen oxides). **Reactivity Hazards:** This product is not reactive. **Environmental Hazards:** May cause harm to aquatic organisms if accidentally released. All environmental release should be avoided. **Emergency Recommendations:** Emergency responders must wear personal protective equipment suitable for the situation to which they are responding.

3. COMPOSITION and INFORMATION ON INGREDIENTS

CHEMICAL NAME	CAS #	EINECS #	% w/v	LABEL CLASSIFICATION EU Classification (67/548/EEC) GHS & EU Classification (1272/2008 EC) Risk Phrases/Hazard Statements
ACTIVE INGREDIENTS				
Topiramate 2,3:4,5-Di-O-isopropylidene-β-D-fructopyranose sulfamate	97240-79-4	204-522-1	Proprietary	SELF CLASSIFICATION: <u>EU 67/548</u> Classification: Reproductive Toxicity Category 2, Toxic Risk Phrase Codes: R61, R48/22 Hazard Symbol: T <u>GHS & EU 1272/2008</u> Classification: Reproductive Cat. 1B, Acute Oral Toxicity Cat. 5, STOT (Eyes, Kidneys, Neurological System) RE Cat. 1 Hazard Codes: H360D, H303, H372 Hazard Symbol/Pictogram: GHS08
EXCIPIENTS - CAPSULES				
Corn Starch	9005-25-8	232-679-6	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Ethyl Cellulose	9004-57-3	232-674-9	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Gelatin	9000-70-8	232-554-6	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Iron Oxide Black	1309-33-7	215-166-1	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Polyethylene Glycol	25322-68-3	NLP # 500-038-2	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Propylene Glycol	57-55-6	200-338-0	Proprietary	<u>EU 67/548</u> Classification Not Applicable <u>EU/GHS 1272/2008</u> Classification Not Applicable
Povidone	9003-39-8	Not Listed	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Shellac	9000-59-3	232-549-9	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Sugar Spheres/Sucrose	57-50-1	200-334-9	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Talc	14807-96-6	238-877-9	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Titanium Dioxide	13463-67-7	236-675-7	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Triethyl Citrate	77-93-0	201-070-7	Proprietary	EU 67/548: Classification: Not applicable GHS & EU 1272/2008: Classification: Not applicable.
EXCIPIENTS - TABLETS				
Colloidal Silicon Dioxide	112945-52-5	Not Listed	Proprietary	SELF-CLASSIFICATION <u>EU 67/548</u> Classification: Not Applicable Risk Phrase Codes: Not Applicable Hazard Symbols: Not Applicable <u>GHS and EU 1272/2008</u> Classification: Acute Oral Toxicity Cat. 5 Hazard Codes: H303 Hazard Symbol/Pictogram: Not Applicable
Corn Starch	9005-25-8	232-679-6	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
FD&C Blue No 2 (200 mg only)	860-22-0	212-728-8	Proprietary	SELF CLASSIFICATION <u>EU (67/548/EEC)</u> : Classification: Harmful Risk Phrases: R22 Symbol: Xn <u>EU/GHS 1272/2008</u> : Classification: Acute Oral Toxicity Cat. 4 Hazard Statement Codes: H302 Hazard Symbols/Pictograms: GHS07
FD& C Red No. 40 (200 mg only)	4548-53-2	224-909-9	Proprietary	SELF CLASSIFICATION <u>EU (67/548/EEC)</u> : Classification: Not Applicable Risk Phrases: Not Applicable Symbol: Not Applicable <u>EU/GHS 1272/2008</u> : Classification: Acute Oral Toxicity Cat. 5 Hazard Statement Codes: H303 Hazard Symbols/Pictograms: Not Applicable
Hypromellose (excluding 50 mg)	9004-65-3	Not Listed	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Iron Oxide Black (100 mg only)	1309-33-7	215-166-1	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Iron Oxide Red (200 mg only)	1309-37-1	215-168-2	Proprietary	EU 67/548: Classification: Not Applicable. GHS & EU 1272/2008: Classification: Not Applicable.
Iron Oxide Yellow (50 an 100 mg only)	20344-49-4	243-746-4	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.

See Section 16 for full classification information of product and components.

3. COMPOSITION and INFORMATION ON INGREDIENTS (Continued)

CHEMICAL NAME	CAS #	EINECS #	% w/v	LABEL CLASSIFICATION EU Classification (67/548/EEC) GHS & EU Classification (1272/2008 EC) Risk Phrases/Hazard Statements
EXCIPIENTS – TABLETS (CONTINUED)				
Lactose Monohydrate	64044-51-5	Anhydrous: 200-559-2	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Magnesium Stearate	557-04-0	209-150-3	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Microcrystalline Cellulose	9004-34-6	232-674-9	Proprietary	EU 67/54: Classification: Not applicable. GHS & EU 1272/2008 Classification: Not applicable.
Partially Hydrolyzed Polyvinyl Alcohol	25213-24-5	Not Listed	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Polydextrose (25 and 100 mg only)	68424-04-4	Not Listed	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Polyethylene Glycol	25322-68-3	NLP # 500- 038-2	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Talc (50 mg only)	14807-96-6	238-877-9	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Titanium Dioxide	13463-67-7	236-675-7	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.

See Section 16 for full classification information of product and components.

PART II *What should I do if a hazardous situation occurs?*

4. FIRST-AID MEASURES

DESCRIPTION OF FIRST AID MEASURES: Contaminated individuals must be taken for medical attention if any adverse effects occur. Remove contaminated clothing and shoes. Take a copy of this SDS to health professional with victim. Wash clothing and thoroughly clean shoes before reuse.

SKIN EXPOSURE: No specific effect is expected from skin contact. If this product contaminates the skin and adverse effect occurs, begin decontamination with running water. The contaminated individual must seek medical attention if any adverse effects occur after flushing.

EYE EXPOSURE: If dusts from product enter the eyes, open contaminated individual's eyes while under gently running water. Use sufficient force to open eyelids. Have contaminated individual "roll" eyes. Minimum flushing is for 20 minutes. Contaminated individual must seek medical attention if adverse effect continues after flushing.

INHALATION: If dusts of this product are inhaled, remove victim to fresh air. The contaminated individual must seek medical attention if any adverse effects occur.

INGESTION: If this product is swallowed, CALL PHYSICIAN OR POISON CONTROL CENTER FOR MOST CURRENT INFORMATION. If professional advice is not available, seek immediate medical attention. If alert, victim should drink up to three glasses of water. Do not induce vomiting. Never induce vomiting or give diluents (milk or water) to someone who is unconscious, having convulsions, or unable to swallow. If victim is convulsing, maintain an open airway and obtain emergency medical attention.

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: In therapeutic use, pre-existing glaucoma and other eye disorders, migraine, metabolic acidosis, kidney disorders and renal impairment may be aggravated. Workplace exposure may also aggravate these conditions. Persons who may have hypersensitivity reactions to this material 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.

5. FIRE-FIGHTING MEASURES

FLASH POINT: Not available.

AUTOIGNITION TEMPERATURE: Not available.

FLAMMABLE LIMITS (in air by volume, %): Not applicable.

FIRE EXTINGUISHING MEDIA: Unless incompatibilities exist for surrounding materials, carbon dioxide, water spray, 'ABC' type chemical extinguishers, foam, dry chemical and halon extinguishers can be used to fight fires involving this product.

UNSUITABLE FIRE EXTINGUISHING MEDIA: None known.

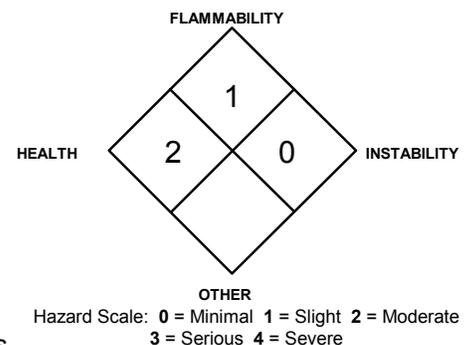
SPECIAL HAZARDS ARISING FROM THE SUBSTANCE: This product must be substantially pre-heated before ignition can occur. When involved in a fire, this material may decompose and produce irritating vapors and toxic compounds (including carbon, iron, titanium, sulfur and nitrogen oxides).

Explosion Sensitivity to Mechanical Impact: Not applicable.

Explosion Sensitivity to Static Discharge: Not sensitive.

SPECIAL PROTECTIVE ACTIONS FOR FIRE-FIGHTERS: Structural firefighters must wear Self-Contained Breathing Apparatus and full protective equipment. All personal protective gear and contaminated fire-response equipment should be decontaminated with soapy water and thoroughly rinsed before being returned to service. Move fire-exposed containers if it can be done without risk to firefighters. If possible, prevent runoff water from entering storm drains, bodies of water, or other environmentally sensitive areas.

NFPA RATING



6. ACCIDENTAL RELEASE MEASURES

PERSONAL PRECAUTIONS, PROTECTIVE EQUIPMENT AND EMERGENCY PROCEDURES: Spill kits, clearly labeled, should be kept in or near preparation and administrative areas. It is suggested that kits include a respirator, chemical splash goggles, two pairs of gloves, two sheets (12" x 12") of absorbent material, 250-mL and 1-liter spill control pillows, a small scoop to collect glass fragments (if applicable) and two large waste disposal bags. Absorbents should be able to be incinerated. Avoid generating airborne dusts of this material during spill response procedures as described below.

PROTECTIVE EQUIPMENT:

Small Spills/Spills in Hoods: Personnel wearing nitrile or other appropriate gloves, labcoat or other protective clothing and eye protection should immediately clean incidental spills of less than 5 g.

Large Spills: Use proper protective equipment, including double nitrile or appropriate gloves, and protective clothing (i.e., disposable Tyvek coveralls). When there is any danger of airborne dusts being generated, use a full-face respirator equipped with a High Efficiency Particulate (HEPA) filter. Self-Contained Breathing Apparatus (SCBA) can be used instead of an air-purifying respirator.

METHODS FOR CLEAN-UP AND CONTAINMENT:

Cleanup of Small Spills: Solids should be gently covered with wet absorbent pads. Clean spill with pad and dispose of properly. Decontaminate the spill area (three times) using a bleach and detergent solution and then rinse with clean water.

Spills in Hoods: Decontamination of all interior hood surfaces may be required after the above procedures have been followed. If the HEPA filter of a hood is contaminated, label the unit "Do not use-contaminated" and have trained personnel wearing appropriate protective equipment change and dispose of the filter properly as soon as possible.

Large Spills: Restrict access to the spill areas. For spills of greater than 5 g, be sure not to generate dusts by gently covering with damp absorbent sheets, spill-control pads, pillows, cloths, or towels. The dispersion of particles into surrounding air and the possibility of inhalation is a serious matter and should be treated as such. Do not apply chemical in-activators as they may produce hazardous by-products. Thoroughly clean all contaminated surfaces three times using a bleach and detergent solution and then rinse with clean water.

All Spills: Use procedures described above and then place all spill residues in an appropriate, labeled container and seal. Move to a secure area. Dispose of in accordance with Federal, State, and local hazardous waste disposal regulations (see Section 13, Disposal Considerations). For spills on water, contain, minimize dispersion and collect. Dispose of recovered material and report spill per regulatory requirements.

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.

REFERENCE TO OTHER SECTIONS: Review Sections 2, 8, 11, & 12 before proceeding with cleanup. See Section 13, Disposal Considerations for more information.

PART III *How can I prevent hazardous situations from occurring?*

7. HANDLING and STORAGE

PRECAUTIONS FOR SAFE HANDLING: All employees who handle this material should be thoroughly trained to handle it safely. As with all chemicals, avoid getting this material ON YOU or IN YOU. Do not eat or drink while handling this material. After handling this material, wash face and hands thoroughly prior to eating, drinking, smoking or applying cosmetics. Ensure this material is used with adequate ventilation. Appropriate personal protective equipment must be worn (see Section 8, Exposure Controls - Personal Protection). Open containers slowly on a stable surface in areas that have been designated for use of this material. Minimize all exposures to this material. Avoid generation of dusts. Areas in which this material is used should be wiped down, so that this material does not accumulate.

CONDITIONS FOR SAFE STORAGE: Containers of this material must be properly labeled. Store containers in a cool, dry location, away from direct sunlight and sources of intense heat. Recommended Storage Temperature: 20-25°C (68-77°F). Store away from incompatible materials (see Section 10, Stability and Reactivity). Material should be stored in secondary containers. Keep containers tightly closed when not in use. Inspect all incoming containers before storage, to ensure containers are properly labeled and not damaged. Have appropriate extinguishing equipment in the storage area (e.g., sprinkler system, portable fire extinguishers). Empty containers may contain residual material; therefore, empty containers should be handled with care and disposed of properly.

SPECIFIC END USE(S): This product is a human pharmaceutical.

PROTECTIVE PRACTICES DURING MAINTENANCE OF CONTAMINATED EQUIPMENT: When cleaning non-disposable equipment, wear nitrile or other appropriate gloves (double gloving is recommended), goggles, and lab coat. Prevent dispersion of particulates by wetting or dampening surfaces prior to clean up of equipment. If applicable, wash equipment using a bleach and detergent solution and then rinse with clean water

8. EXPOSURE CONTROLS - PERSONAL PROTECTION

EXPOSURE LIMITS/CONTROL PARAMETERS:

VENTILATION AND ENGINEERING CONTROLS: General: Use with adequate ventilation. Follow standard operating procedures and requirements for handling this product. Ensure eyewash stations and deluge showers are available and accessible in areas where this product is used. Wear appropriate personal protect equipment consistent with the recommendations of this SDS. Prevent accumulation of product on work surfaces by routinely cleaning areas appropriately.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION (Continued)

EXPOSURE LIMITS/CONTROL PARAMETERS (continued):

WORKPLACE EXPOSURE LIMITS/CONTROL PARAMETERS:

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	
Topiramate	97240-79-4	NE	NE	NE	NE	NE	NE	NE	Teva OEL Range µg/m ³ ≥ 10 - < 100 (established 6 March 2012)
Microcrystalline Cellulose Ethyl Cellulose Hypromellose Exposure limits are for cellulose	9004-34-6 9004-57-3 9004-65-3	10	NE	15 (total dust), 5 (resp. fraction)	NE	10 (total dust), 5 (resp. fraction)	NE	NE	NE
Colloidal Silicon Dioxide	112945-52- 5	NE	NE	20 mppcf or	80 mg/m ³ % SO ₂	6 See NIOSH Pocket Guide App. C	NE	3000	Carcinogen: IARC-3, TLV- A3
Corn Starch	9005-25-8	10	NE	15 (total dust), 5 (resp. fract.)	NE	10 (total dust), 5 (resp. fract.)	NE	NE	Carcinogen: TLV-A4
FD&C Blue No. 2	860-22-0	NE	NE	NE	NE	NE	NE	NE	NE
FD& C Red No. 40	4548-53-2	NE	NE	NE	NE	NE	NE	NE	Carcinogen: IARC-3
Gelatin	9000-70-8	NE	NE	NE	NE	NE	NE	NE	NE
Iron Oxide, Black, Iron Oxide Red, Iron Oxide Yellow, Exposure limits given are for CAS# 1309-37-1 (Fe ₂ O ₃)	1309-33-7 1309-37-1 20344-49-4	5 (resp. fraction)	NE	10 (fume)	NE	5 (dusts & fume, as Fe)	NE	2500 (dust & fume, as Fe)	Carcinogen: IARC-3, MAK- 3B, TLV-A4
Lactose Monohydrate	64044-51-5	NE	NE	NE	NE	NE	NE	NE	NE
Magnesium Stearate Exposure limits are for Stearates	557-04-0	10	NE	NE	NE	NE	NE	NE	Carcinogen: TLV-A4
Polyvinyl Alcohol Partially Hydrolyzed	25213-24-5	NE	NE	NE	NE	NE	NE	NE	NE
Polyethylene Glycol	25322-68-3	NE	NE	NE	NE	NE	NE	NE	DFG MAKs: TWA = 1000 (inhalable fraction) PEAK = 8•MAK 15 min. average value, 1-hr interval, 4 per shift DFG MAK Pregnancy Risk Classification: C AIHA WEEL: TWA = 10
Povidone	9003-39-8	NE	NE	NE	NE	NE	NE	NE	Carcinogen: IARC-3
Polydextrose	68424-04-4	NE	NE	NE	NE	NE	NE	NE	NE
Propylene Glycol	57-55-6	NE	NE	NE	NE	NE	NE	NE	AIHA WEEL: TWA = 10
Shellac	9000-59-3	NE	NE	NE	NE	NE	NE	NE	NE
Sucrose	57-50-1	10	NE	15 (total dust), 5 (resp. fraction)	NE	10 (total dust), 5 (resp. fraction)	NE	NE	Carcinogen: TLV-A4
Talc	14807-96-6	2 (resp. fraction)	NE	20 mppcf (containing < 1% quartz)	NE	2 (respirable dust) and < 1% quartz	NE	NE	Carcinogen: IARC-3, MAK- 3B (respirable fraction), TLV-A4
Titanium Dioxide	13463-67-7	10	NE	15 (total dust) 10 (vacated 1989 PEL)	NE	See NIOSH Pocket Guide Appendix A	Ca, 5000	NE	Carcinogen: IARC-2B, MAK- 3A, NIOSH-Ca, TLV-A4
Triethyl Citrate	77-93-0	NE	NE	NE	NE	NE	NE	NE	NE

NE = Not Established

See Section 16 for Definitions of Other Terms Used

INTERNATIONAL OCCUPATIONAL EXPOSURE LIMITS: Exposure limits available for some excipient components are given below.

COLLOIDAL SILICON DIOXIDE:

Australia: TWA = 2 mg/m³ (respirable dust), JUL 2008

CORN STARCH:

Belgium: TWA = 10 mg/m³, MAR 2002

Korea: TWA = 10 mg/m³, 2006

New Zealand: TWA = 10 mg/m³ (inspirable dust), JAN 2002

Russia: STEL = 10 mg/m³, JUN 2003

Switzerland: MAK-W = 3 mg/m³, DEC 2006

United Kingdom: TWA = 10 mg/m³ (inhalable dust), OCT 2007

United Kingdom: TWA = 4 mg/m³ (respirable dust), OCT 2007

CORN STARCH (continued):

In Argentina, Bulgaria, Colombia, Jordan, Singapore,

Vietnam check ACGIH TLV

GELATINS:

Russia: STEL = 10 mg/m³, JUN 2003

MAGNESIUM STEARATE:

New Zealand: TWA = 10 mg/m³ (inspirable dust), JAN 2002

Sweden: TWA = 5 mg/m³, JUN 2005

Belgium: TWA = 10 mg/m³, MAR 2002

MICROCRYSTALLINE CELLULOSE:

Belgium: TWA = 10 mg/m³, MAR 2002

France: VME = 10 mg/m³, FEB 2006

Korea: TWA = 10 mg/m³, 2006

Mexico: TWA = 10 mg/m³; STEL = 20 mg/m³, 2004

The Netherlands: MAC-TGG = 2 mg/m³, 2003

New Zealand: TWA = 10 mg/m³ (inspirable dust), JAN 2002

Russia: STEL = 10 mg/m³, JUN 2003

Switzerland: MAK-W = W 6 mg/m³, DEC 2006

United Kingdom: TWA = 10 mg/m³ (inhalable), 2005

United Kingdom: TWA = 4 mg/m³; STEL = 20 mg/m³ (respirable), 2005

In Argentina, Bulgaria, Colombia, Jordan, Singapore, Vietnam, check ACGIH TLV

8. EXPOSURE CONTROLS - PERSONAL PROTECTION (Continued)

EXPOSURE LIMITS/CONTROL PARAMETERS (continued):

INTERNATIONAL OCCUPATIONAL EXPOSURE LIMITS (continued):

IRON OXIDES:

Finland: TWA = 5 ppm (fume), JAN 1999
France: VME = 5 mg/m³ (fume), JAN 1999
Germany: MAK = 1.5 mg(Fe)/m³ (respirable), 2005
Japan: OEL = 1 mg/m³ (respirable), 4 mg/m³ (total), MAY 2006
Korea: TWA = 10 mg/m³, 2006
Korea: TWA = 5 mg/m³, 2006
Mexico: TWA = 10 mg/m³; STEL = 20 mg/m³, 2004
The Netherlands: MAC-TGG = 5 mg(Fe)/m³, 2003
The Netherlands: MAC-TGG = 10 mg/m³, 2003
New Zealand: TWA = 5 mg(Fe)/m³ (dust and fume), JAN 2002
New Zealand: TWA = 10 mg/m³ (inspirable dust), JAN 2002
Norway: TWA = 3 mg/m³, JAN 1999
The Philippines: TWA = 10 mg/m³ (fume), JAN 1993
Poland: MAC(TWA) fume = 5 mg/m³, MAC(STEL) = 10 mg/m³, JAN 1999
Russia: TWA = 6 mg/m³, JUN 2003
Sweden: NGV = 3.5 mg/m³ (fume), JAN 1999
Switzerland: MAK-W = 3 mg/m³, DEC 2006
Thailand: TWA = 10 mg/m³ (fume), JAN 1993
Turkey: TWA = 10 mg/m³ (fume), JAN 1993
United Kingdom: TWA = 4 mg/m³ (respirable), 2005
United Kingdom: TWA = 10 mg/m³ (inhalable), 2005
United Kingdom: TWA = 5 mg(Fe)/m³; STEL = 10 mg(Fe)/m³, 2005
In Argentina, Bulgaria, Colombia, Jordan, Singapore, Vietnam check ACGIH TLV

POVIDONE:

Russia: STEL = 10 mg/m³, JUN 2003

POLYETHYLENE GLYCOL:

The Netherlands: MAC-TGG = 1000 mg/m³, 2003
Russia: STEL = 10 mg/m³, JUN 2003
Denmark: TWA = 1000 mg/m³, OCT 2002
Germany: MAK = 1000 mg/m³ (inhalable), 2005

POLYETHYLENE GLYCOL:

The Netherlands: MAC-TGG = 1000 mg/m³, 2003
Russia: STEL = 10 mg/m³, JUN 2003
Denmark: TWA = 1000 mg/m³, OCT 2002
Germany: MAK = 1000 mg/m³ (inhalable), 2005

POLYVINYL ALCOHOL:

Russia: STEL = 10 mg/m³, JUN 2003

PROPYLENE GLYCOL:

Australia: TWA = 10 mg/m³ (particulates), JUL 2008
Australia: TWA = 150 ppm (474 mg/m³) (total), JUL 2008
New Zealand: TWA = 10 mg/m³ (particulates only), JAN 2002

New Zealand: TWA = 150 ppm (474 mg/m³) (vapor and particulates), JAN 2002
Russia: STEL = 7 mg/m³, JUN 2003
United Kingdom: TWA = 10 mg/m³ (particulate), 2005
United Kingdom: TWA = 150 ppm (474 mg/m³) (total vapor), 2005

TALC:

Australia: TWA = 2.5 mg/m³, JUL 2008
Belgium: TWA = 2 mg/m³, MAR 2002
Finland: TWA = 0.5 f/cc, fibrous, SEP 2009
Finland: TWA = 5 mg/m³, granulated, SEP 2009
Japan: OEL = 0.5 mg/m³ (respirable), 2 mg/m³ (total), MAY 2009
Korea: TWA = 2 mg/m³, 2006
Mexico: TWA = 2 mg/m³ (respirable), 2004
The Netherlands: MAC-TGG = 1 mg/m³, 2003
New Zealand: TWA = 2 mg/m³ (respirable dust), JAN 2002
Sweden: TWA = 2 mg/cm³ (total dust); TWA = 1 mg/cm³ (resp. dust), JUN 2005

TALC (continued):

Switzerland: MAK-W = 2 mg/m³, DEC 2006
United Kingdom: TWA = 1 mg/m³ (resp. dust), OCT 2007
In Argentina, Bulgaria, Colombia, Jordan, Singapore, Vietnam check ACGIH TLV

SUCROSE:

Belgium: TWA = 10 mg/m³, MAR 2002
France: VME = 10 mg/m³, FEB 2006
Korea: TWA = 10 mg/m³, 2006
Mexico: TWA = 10 mg/m³; STEL = 20 mg/m³, 2004
The Netherlands: MAC-TGG = 10 mg/m³, 2003
New Zealand: TWA = 10 mg/m³ (inspirable dust), JAN 2002
Peru: TWA = 10 mg/m³, JUL 2005
United Kingdom: TWA = 10 mg/m³; STEL = 20 mg/m³, OCT 2007
In Argentina, Bulgaria, Colombia, Jordan, Singapore, Singapore, Vietnam check ACGIH TLV

TITANIUM DIOXIDE:

ARAB Republic of Egypt: TWA = 15 mg/m³, JAN 1993
Belgium: TWA = 10 mg/m³, MAR 2002
Denmark: TWA = 6 mg(Ti)/m³, OCT 2002
France: VME = 10 mg/m³, FEB 2006
Germany: MAK = 1.5 mg/m³ (respirable), 2005
Japan: OEL = 1 mg/m³ (respirable), 4 mg/m³ (total), APR 2007
Korea: TWA = 10 mg/m³, 2006
Mexico: TWA = 10 mg(Ti)/m³; STEL = 20 mg(Ti)/m³, 2004
The Netherlands: MAC-TGG = 10 mg/m³, 2003
New Zealand: TWA = 10 mg/m³ (inspirable dust), JAN 2002
Norway: TWA = 5 mg/m³, JAN 1999
Poland: MAC(TWA) = 10 mg(Ti)/m³, MAC(STEL) = 30 mg(Ti)/m³, JAN 1999
Russia: TWA = 10 mg/m³, JUN 2003
Sweden: TWA = 5 mg/m³ (total dust), JUN 2005
Switzerland: MAK-W = 3 mg/m³, DEC 2006
Turkey: TWA = 15 mg/m³, JAN 1993
United Kingdom: TWA = 10 mg/m³ (inhalable), 2005
United Kingdom: TWA = TWA 4 mg/m³ (respirable), 2005
In Argentina, Bulgaria, Colombia, Jordan, Singapore, Vietnam check ACGIH TLV

PROTECTIVE EQUIPMENT: *The following information on appropriate Personal Protective Equipment is provided to assist employers in complying with OSHA regulations found in 29 CFR Subpart I (beginning at 1910.132, including U.S. Federal OSHA Respiratory Protection (29 CFR 1910.134), OSHA Eye Protection 29 CFR 1910.133, OSHA Hand Protection 29 CFR 1910.138, OSHA Foot Protection 29 CFR 1910.136 and OSHA Body Protection 29 CFR 1910.132), equivalent standards of Canada (including CSA Respiratory Standard Z94.4-02, Z94.3-M1982, Industrial Eye and Face Protectors and CSA Standard Z195-02, Protective Footwear), or standards of EU member states (including EN 529:2005 for respiratory PPE, CEN/TR 15419:2006 for hand protection, and CR 13464:1999 for face/eye protection). Please reference applicable regulations and standards for relevant details.*

RESPIRATORY PROTECTION: Maintain airborne contaminant concentrations below exposure limits listed above, if applicable. For materials without listed exposure limits, minimize respiratory exposure. If necessary, use only respiratory protection authorized under appropriate regulations. Oxygen levels below 19.5% are considered IDLH by U.S. OSHA. In such atmospheres, use of a full-facepiece pressure/demand SCBA or a full facepiece, supplied air respirator with auxiliary self-contained air supply is required under U.S. OSHA's Respiratory Protection Standard (1910.134-1998).

EYE PROTECTION: Wear splash goggles or safety glasses as appropriate for the task. If necessary, refer to appropriate regulations.

HAND PROTECTION: Wash hands and wrists before putting on and after removing gloves. During manufacture or other similar industrial operations, wear the appropriate hand protection for the process. When used in medical administration of the product, double glove with nitrile or other appropriate gloves to avoid contact and/or absorption of the product. Use double gloves for spill response, as stated in Section 6 (Accidental Release Measures) of this SDS. Because all gloves are to some extent permeable and their permeability increases with time, they should be changed regularly (hourly is preferable) or immediately if torn or punctured. If necessary refer to appropriate regulations.

SKIN PROTECTION: Use appropriate protective clothing for the task (e.g., lab coat, etc.). If necessary, refer to the U.S. OSHA Technical Manual (Section VII: Personal Protective Equipment) or other appropriate regulations.

9. PHYSICAL and CHEMICAL PROPERTIES

The following information is for the product as a whole.

PHYSICAL FORM: Two-piece capsules, filled with white spheres.

ODOR: Practically odorless.

MOLECULAR WEIGHT: Mixture.

HOW TO DETECT THIS SUBSTANCE (identification/warning properties): The appearance may be a distinguishing characteristic of this product in event of accidental release.

COLOR: As described in Section 2.

ODOR THRESHOLD: Not applicable.

MOLECULAR FORMULA: Mixture.

9. PHYSICAL and CHEMICAL PROPERTIES (Continued)

The following information is for the Topiramate active ingredient.

FORM: Crystalline solid.

MOLECULAR WEIGHT: 339.37

ODOR: Odorless.

BOILING POINT @ 760 mmHg: 438.7°C (821.7°F) [est.]

VAPOR PRESSURE (air = 1) @ 25°C: 6.76E-08 mmHg [predict.]

EVAPORATION RATE (nBuAc = 1): Not applicable.

FLASH POINT: 219.1°C (426.4°F) [est.]

SOLUBILITY IN WATER @ 25°C: 9.8 mg/mL

OTHER SOLUBILITIES: Soluble in acetone, chloroform, dimethylsulfoxide, and ethanol.

COEFFICIENT WATER/OIL DISTRIBUTION: Log P(oct) = -0.33 (est)

COLOR: White to off-white.

MOLECULAR FORMULA: C₁₂H₂₁NO₈S

ODOR THRESHOLD: Odorless.

MELTING POINT: 125-126°C (257-258.8°F)

SPECIFIC GRAVITY (water = 1): 1.336 g/cm³

pH: 6.3 (saturated solution)

DECOMPOSITION TEMPERATURE: Not available.

10. STABILITY and REACTIVITY

CHEMICAL STABILITY: Stable under normal conditions.

DECOMPOSITION PRODUCTS: *Combustion:* Products of thermal decomposition may include carbon, iron, titanium, sulfur and nitrogen oxides. *Hydrolysis:* None known.

MATERIALS WITH WHICH SUBSTANCE IS INCOMPATIBLE: Incompatible with oxidizing agents, strong acids.

POSSIBILITY OF HAZARDOUS REACTION/POLYMERIZATION: Will not occur.

CONDITIONS TO AVOID: Exposure to or contact with extreme temperatures, incompatible chemicals.

PART IV *Is there any other useful information about this material?*

11. TOXICOLOGICAL INFORMATION

SYMPTOMS OF EXPOSURE BY ROUTE OF EXPOSURE: The main route of occupational exposure to this product is via inhalation of dusts and skin contact. The anticipated symptoms of exposure, by route of exposure are described further in this section.

INHALATION: Inhalation of airborne dusts generated by damaged capsules of this product may slightly irritate the nose, throat, and lungs. In addition, inhalation may result in adverse effects as described under 'Other Potential Health Effects'.

CONTACT WITH SKIN or EYES: It is anticipated that this product may irritate contaminated skin or eyes. Symptoms of skin contact may include itching and redness. Symptoms of eye contact can include redness, pain, and watering (mechanical irritation).

SKIN ABSORPTION: No data is available on potential absorption of this material through intact skin.

INGESTION: Ingestion of this product (i.e., through poor hygiene practices) may be harmful or toxic by ingestion. Ingestion may cause gastrointestinal irritation, nausea, vomiting and diarrhea. Other effects may occur as described under 'Other Potential Health Effects'.

INJECTION: Not a potential route of exposure for capsules.

OTHER POTENTIAL HEALTH EFFECTS: Therapeutic use may cause tingling of the arms and legs (paresthesia), lack of hunger, nausea, diarrhea, weight loss, nervousness, upper respiratory tract infection, fatigue, dizziness, somnolence, nervousness, psychomotor slowing, difficulty with memory, difficulty with concentration/attention, and confusion. Therapeutic may also cause acute myopia and secondary angle closure glaucoma, inability to regulate body temperature, metabolic acidosis, which can lead to kidney stones, cognitive dysfunction, and excess blood ammonia. Psychological disorders, including suicidal thoughts can occur. These effects may be possible as a result of workplace exposure. The actual risk in the workplace is not known.

HEALTH EFFECTS OR RISKS FROM EXPOSURE:

Acute: Dusts from product may cause irritation if inhaled and in contact with skin or eyes.

Accidental ingestion may be harmful or cause toxic effects. Acute exposure may cause effects described in "Other Potential Health Effects".

Chronic: Chronic exposure may lead to symptoms described under 'Other Potential Health Effects'. May cause harm to fetus. No chronic effects have been reported from workplace exposure.

TARGET ORGANS: It is anticipated that for Occupational Exposure the target organs are: **Acute:** Skin, eyes, respiratory system. **Chronic:** None reported. In therapeutic use this product may have an impact on the body systems listed under 'Other Potential Health Effects'.

HAZARDOUS MATERIAL IDENTIFICATION SYSTEM

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

11. TOXICOLOGICAL INFORMATION (Continued)

TOXICITY DATA: The following toxicity data are currently available for the active ingredients. In addition, data are available for excipients, but are not provided in this SDS. Contact Teva for more information.

TOPIRAMATE:

TDLo (Oral-Human) 2.857 mg/kg: Behavioral: changes in psychophysiological tests, aggression
TDLo (Oral-Human) 4.286 mg/kg: Behavioral: tremor, headache; Gastrointestinal: nausea or vomiting
TDLo (Oral-Human) 1.43 mg/kg/2 days-intermittent: Behavioral: toxic psychosis
TDLo (Oral-Human) 5 mg/kg/2 weeks-intermittent: Skin and Appendages: dermatitis, allergic (after systemic exposure)
TDLo (Oral-Woman) 16 mg/kg: Behavioral: euphoria, hallucinations, distorted perceptions, toxic psychosis
TDLo (Oral-Woman) 1 mg/kg: Behavioral: changes in psychophysiological tests
TDLo (Oral-Woman) 16 mg/kg: Sense Organs and Special Senses (Eye): mydriasis (pupillary dilation); Behavioral: somnolence (general depressed activity), aggression
TDLo (Oral-Woman) 14.4 mg/kg: Behavioral: somnolence (general depressed activity); Blood: changes in serum composition (e.g. TP, bilirubin, cholesterol); Nutritional and Gross Metabolic: metabolic acidosis
TDLo (Oral-Woman) 3.5 mg/kg/7 days-intermittent: Blood: hemorrhage
TDLo (Oral-Woman) 280 mg/kg/10 weeks-intermittent: Peripheral Nerve and Sensation: paresthesia; Behavioral: anticonvulsant
TDLo (Oral-Man) 31.25 mg/kg: Behavioral: convulsions or effect on seizure threshold, coma; Nutritional and Gross Metabolic: metabolic acidosis
TDLo (Oral-Man) 31.3 mg/kg: Behavioral: somnolence (general depressed activity), convulsions or effect on seizure threshold; Nutritional and Gross Metabolic: metabolic acidosis
TDLo (Unreported-Human) 261 mg/kg/70 days-intermittent: Behavioral: changes in psychophysiological tests
TDLo (Unreported-Woman) 3832.5 mg/kg/3.5 years-continuous: Sense Organs and Special Senses (Eye): retinal changes (pigmentary depositions, retinitis, other)
TDLo (Unreported-Woman) 1095 mg/kg/365 days-intermittent: Sense Organs and Special Senses (Eye): visual field changes

TOPIRAMATE (continued):

TDLo (Unreported-Man) 304.59 mg/kg/213 days-intermittent: Sense Organs and Special Senses (Eye): visual field changes
TDLo (Unreported-Child) 1.875 mg/kg/3 days-intermittent: Behavioral: anticonvulsant
LD₅₀ (Intraperitoneal-Rat) > 1500 mg/kg
TDLo (Oral-Rat) 100 mg/kg: Behavioral: alteration of classical conditioning, changes in psychophysiological tests
TDLo (Oral-Rat) 140 mg/kg/7 days-intermittent: Behavioral: anti-anxiety, alteration of operant conditioning
TDLo (Oral-Rat) 105 mg/kg/1 weeks-continuous: Behavioral: alteration of classical conditioning
TDLo (Oral-Mouse) 2800 mg/kg/4 weeks-intermittent: Skin and Appendages: sweating
TDLo (Oral-Mouse) 10 mg/kg: Behavioral: anticonvulsant
TDLo (Oral-Mouse) 20 mg/kg: Brain and Coverings: recordings from specific areas of CNS; Behavioral: anticonvulsant
TDLo (Intraperitoneal-Rat) 400 mg/kg/10 days-intermittent: Brain and Coverings: other degenerative changes; Biochemical: Metabolism (Intermediary): other proteins
TDLo (Intraperitoneal-Mouse) 10 mg/kg: Behavioral: anticonvulsant
TDLo (Intraperitoneal-Mouse) 423 mg/kg: Behavioral: changes in motor activity (specific assay), ataxia
TDLo (Intraperitoneal-Mouse) 669 mg/kg: Behavioral: ataxia
TDLo (Intraperitoneal-Mouse) 1 gm/kg/5 days-intermittent: Brain and Coverings: other degenerative changes; Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: other Enzymes

CARCINOGENIC POTENTIAL OF COMPONENTS: An increase in urinary bladder tumors was observed in mice given Topiramate (20, 75, and 300 mg/kg) in the diet for 21 months. The elevated bladder tumor incidence, which was statistically significant in males and females receiving 300 mg/kg, was primarily due to the increased occurrence of a smooth muscle tumor considered histomorphologically unique to mice. Plasma exposures in mice receiving 300 mg/kg were approximately 0.5 to 1 times steady-state exposures measured in patients receiving Topiramate monotherapy at the recommended human dose (RHD) of 400 mg, and 1.5 to 2 times steady-state Topiramate exposures in patients receiving 400 mg of Topiramate plus phenytoin. The relevance of this finding to human carcinogenic risk is uncertain. No evidence of carcinogenicity was seen in rats following oral administration of Topiramate for 2 years at doses up to 120 mg/kg (approximately 3 times the RHD on an mg/m² basis).

The excipient components are listed by agencies tracking the carcinogenic potential of chemical compounds, as follows:

COLLOIDAL SILICON DIOXIDE: ACGIH TLV-A3 (Confirmed Animal Carcinogen with Unknown Relevance to Humans); IARC-3 (Unclassifiable as to Carcinogenicity in Humans)
MAGNESIUM STEARATE (as a stearate), CORN STARCH: ACGIH TLV-A4 (Not Classifiable as a Human Carcinogen)

IRON OXIDES (based on CAS# 1309-37-1): ACGIH TLV-A4 (Not Classifiable as a Human Carcinogen); IARC-3 (Unclassifiable as to Carcinogenicity in Humans); MAK-3B [respirable fraction] (Substances for Which in vitro tests or animal studies have yielded evidence of carcinogenic effects that is not sufficient for classification of the substance in one of the other categories.)

FD&C RED No. 40, POVIDONE: IARC-3 (Unclassifiable as to Carcinogenicity in Humans)

SUCROSE: ACGIH TLV-A4 (Not Classifiable as a Human Carcinogen)

TALC: ACGIH TLV-A4 (Not Classifiable as a Human Carcinogen); IARC-3 (Unclassifiable as to Carcinogenicity in Humans); MAK-3B [respirable fraction]: (Substances Which Cause Concern that They Could Be Carcinogenic for Man But Cannot Be Assessed Conclusively Because of Lack of Data. Substances for which in vitro tests or animal studies have yielded evidence of carcinogenic effects that is not sufficient for classification of the substance in one of the other categories.)

TITANIUM DIOXIDE: ACGIH TLV-A4 (Not Classifiable as a Human Carcinogen); IARC-2B (Possibly Carcinogenic to Humans); MAK-3A (Substances Which Cause Concern that They Could Be Carcinogenic for Man But Cannot Be Assessed Conclusively Because of Lack of Data. Substances for which the criteria for classification in Category 4 or 5 are fulfilled, but for which the database is insufficient for the establishment of a MAK value.); NIOSH-Ca (Potential Occupational Carcinogen with No Further Categorization)

No other component of this product are not found on the following lists: U.S. EPA, U.S. NTP, U.S. OSHA, U.S. NIOSH, GERMAN MAK, IARC, or ACGIH and therefore are neither considered to be nor suspected to be cancer-causing agents by these agencies.

IRRITANCY OF PRODUCT: Inhalation of dusts from this product may be irritating to the respiratory system. Dusts will also be irritating to the eyes.

SENSITIZATION TO THE PRODUCT: Therapeutic use has been reported to cause rash and allergic dermatitis.

REPRODUCTIVE TOXICITY INFORMATION: There are no adequate and well-controlled studies of Topiramate in pregnant women; however, Topiramate can cause fetal harm when administered to a pregnant woman. 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 D (refer to Definition of Terms for full category definitions).

Mutagenicity: Topiramate did not demonstrate genotoxic potential when tested in a battery of in vitro and in vivo assays. Topiramate was not mutagenic in the Ames test or the *in vitro* mouse lymphoma assay; it did not increase unscheduled DNA synthesis in rat hepatocytes in vitro; and it did not increase chromosomal aberrations in human lymphocytes in vitro or in rat bone marrow in vivo.

Embryotoxicity/Teratogenicity:

Human Information: Topiramate during pregnancy can cause fetal harm, including an increased risk for cleft lip and/or cleft palate (oral clefts), which occur early in pregnancy before many women know they are pregnant. There may also be risks to the fetus from chronic metabolic acidosis with use of Topiramate during pregnancy.

11. TOXICOLOGICAL INFORMATION (Continued)

REPRODUCTIVE TOXICITY INFORMATION (continued):

Embryotoxicity/Teratogenicity (continued):

Animal Information: In rat studies (oral doses of 20, 100, and 500 mg/kg or 0.2, 2.5, 30, and 400 mg/kg), the frequency of limb malformations (ectrodactyly, micromelia, and amelia) was increased among the offspring of dams treated with 400 mg/kg (10 times the RHD on a mg/m² basis) or greater during the organogenesis period of pregnancy. Embryotoxicity (reduced fetal body weights, increased incidence of structural variations) was observed at doses as low as 20 mg/kg (0.5 times the RHD on a mg/m² basis). Clinical signs of maternal toxicity were seen at 400 mg/kg and above, and maternal body weight gain was reduced during treatment with 100 mg/kg or greater.

In rabbit studies (20, 60, and 180 mg/kg or 10, 35, and 120 mg/kg orally during organogenesis), embryo/fetal mortality was increased at 35 mg/kg (2 times the RHD on a mg/m² basis) or greater, and teratogenic effects (primarily rib and vertebral malformations) were observed at 120 mg/kg (6 times the RHD on a mg/m² basis). Evidence of maternal toxicity (decreased body weight gain, clinical signs, and/or mortality) was seen at 35 mg/kg and above.

When female rats were treated during the latter part of gestation and throughout lactation (0.2, 4, 20, and 100 mg/kg or 2, 20, and 200 mg/kg), offspring exhibited decreased viability and delayed physical development at 200 mg/kg (5 times the RHD on a mg/m² basis) and reductions in pre-and/or post-weaning body weight gain at 2 mg/kg (0.05 times the RHD on a mg/m² basis) and above. Maternal toxicity (decreased body weight gain, clinical signs) was evident at 100 mg/kg or greater.

In a rat embryo/fetal development study with a postnatal component (0.2, 2.5, 30 or 400 mg/kg during organogenesis; noted above), pups exhibited delayed physical development at 400 mg/kg (10 times the RHD on a mg/m² basis) and persistent reductions in body weight gain at 30 mg/kg (1 times the RHD on a mg/m² basis) and higher.

Reproductive Toxicity: No adverse effects on male or female fertility were observed in rats at doses up to 100 mg/kg (2.5 times the RHD on a mg/m² basis). Limited data on 5 breastfeeding infants exposed to Topiramate showed infant plasma Topiramate levels equal to 10 to 20% of the maternal plasma level. 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.

Non-Teratogenic Effects: Topiramate treatment can cause metabolic acidosis. The effect of Topiramate-induced metabolic acidosis has not been studied in pregnancy; however, metabolic acidosis in pregnancy (due to other causes) can cause decreased fetal growth, decreased fetal oxygenation, and fetal death, and may affect the fetus' ability to tolerate labor.

BIOLOGICAL EXPOSURE INDICES: Currently, there are no Biological Exposure Indices (BEIs) 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 soils. No predicted values are available.

PERSISTENCE AND BIODEGRADABILITY: This product has not been tested for persistence and biodegradability. No predicted values are available.

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

ECOTOXICITY: This product may be harmful or fatal to contaminated plant and animal-life (especially if large quantities are released). This product has not been tested for aquatic toxicity. No aquatic toxicity data are available for components of this product.

OTHER ADVERSE EFFECTS: The components of this product are not listed as having ozone depletion potential.

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. This product, if unaltered by use, may be disposed of by treatment at a permitted facility or as advised by your local hazardous waste regulatory authority. All protective clothing, gloves, and disposable materials used in the preparation or handling of this drug should be disposed of in accordance with established hazardous waste disposal procedures. It is the responsibility of the generator to determine at the time of disposal whether the product meets the criteria of a hazardous waste per regulations of the area in which the waste is generated and/or disposed. Incineration is recommended for the product and disposable equipment. Shipment of wastes must be done with appropriately permitted and registered transporters. Reusable equipment should be cleaned with soap and water and thoroughly rinsed.

DISPOSAL CONTAINERS: Waste materials must be placed in and shipped in appropriate 5-gallon or 55-gallon poly or metal waste pails or drums. Permeable cardboard containers are not appropriate and should not be used. Ensure that any required marking or labeling of the containers be done to all applicable regulations.

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

U.S. EPA WASTE NUMBER: Not applicable.

EWC WASTE CODE: 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: 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 material does not meet the criteria of classification of Dangerous Goods, per regulations of Transport Canada.

INTERNATIONAL AIR TRANSPORT ASSOCIATION (IATA): This product does not meet the criteria as Dangerous Goods, per rules of IATA.

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

EUROPEAN AGREEMENT CONCERNING THE INTERNATIONAL CARRIAGE OF DANGEROUS GOODS BY ROAD (ADR): This product does not meet the criteria as Dangerous Goods of the United Nations Economic Commission for Europe.

TRANSPORT IN BULK ACCORDING TO THE IBC CODE: Not applicable.

ENVIRONMENTAL HAZARDS: This product does not meet the criteria of environmentally hazardous according to the criteria of the UN Model Regulations (as reflected in the IMDG Code, ADR, RID, and ADN) and no component is not

15. REGULATORY INFORMATION

ADDITIONAL U.S. 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 THRESHOLD PLANNING QUANTITY: There are no specific Threshold Planning Quantities for components of this product. The default Federal SDS submission and inventory requirement filing threshold of 10,000 lb (4,540 kg) may apply, per 40 CFR 370.20.

U.S. SARA HAZARD CATEGORIES (SECTION 311/312, 40 CFR 370-21): ACUTE: Yes; CHRONIC: Yes; FIRE: No; REACTIVE: No; SUDDEN RELEASE: No

U.S. CERCLA REPORTABLE QUANTITY (RQ): Not applicable.

U.S. TSCA INVENTORY STATUS: This product is regulated under Food and Drug Administration standards; this product is not subject to requirements under TSCA

OTHER U.S. FEDERAL REGULATIONS: 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.

CALIFORNIA SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT (PROPOSITION 65): No component of this product is listed on the California Proposition 65 Lists.

ADDITIONAL CANADIAN REGULATIONS:

CANADIAN DSL/NDSL STATUS: This product is regulated by the Therapeutic Products Programme (TPP) of Health Canada; it is exempt from the requirements of CEPA.

OTHER CANADIAN REGULATIONS: Not applicable.

CANADIAN ENVIRONMENTAL PROTECTION ACT (CEPA) PRIORITY SUBSTANCES LISTS: The components of this product are not on the CEPA Priority Substances Lists.

CANADIAN WHMIS CLASSIFICATION and SYMBOLS: 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.

ADDITIONAL EUROPEAN REGULATIONS:

SAFETY, HEALTH, AND ENVIRONMENTAL REGULATIONS/LEGISLATION SPECIFIC FOR THE PRODUCT: Formulated, finished medicinal products for human use, are 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 (Z129.1, Provided to Summarize Occupational Hazard Information): **WARNING!** NON-THERAPEUTIC INGESTION MAY BE HARMFUL. MAY CAUSE RESPIRATORY SYSTEM, EYE, AND SKIN IRRITATION. LIMITED EVIDENCE OF POSSIBLE HARM TO FETUS DURING PREGNANCY, BASED ON ANIMAL DATA. COMBUSTIBLE IF EXPOSED TO HIGH TEMPERATURES. Do not taste or swallow. Avoid contact with skin, eyes, and clothing. Keep container closed. Use gloves, safety glasses, and appropriate respiratory and body protection. **FIRST-AID:** If exposed, seek immediate medical attention. If swallowed, do not induce vomiting. If alert, give victim up to three glasses of water. Never give anything by mouth to an unconscious person. In case of contact, immediately flush skin with copious amounts of warm water for 20 minutes. Remove contaminated clothing and shoes. If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. **IN CASE OF FIRE:** Use water fog, dry chemical or CO₂, or alcohol foam. **IN CASE OF SPILL:** Refer to Safety Data Sheet for complete spill response procedures. Spill response should be performed by persons properly trained to do so. Decontaminate area with bleach and detergent solution and triple rinse area. Place spill debris in a suitable container. Refer to SDS for additional information.

16. OTHER INFORMATION (Continued)

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 exempted from classification and other criteria of 1272/2008.

67/548/EEC EU LABELING/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 FOR COMPONENTS:

Full Text Global Harmonization AND EU CLP Regulation (EC) 1272/2008:

Topiramate: This is a self-classification.

Classification: Reproductive Toxicity Category 1B, Acute Oral Toxicity Category 5, Specific Target Organ Toxicity (Eyes, Kidneys, Neurological System) Repeated Exposure Category 1

Hazard Statement Codes: H360D: May damage the unborn child. H303: May be harmful if swallowed. H372: Causes damages to eyes, kidneys and neurological system through prolonged or repeated exposure.

Colloidal Silicon Dioxide, FD&C Red No. 40: This is a self-classification.

Classification: Acute Oral Toxicity Category 5

Hazard Statement Codes: H303: May be harmful if swallowed.

FD&C Blue No. 2: This is a self-classification.

Classification: Acute Oral Toxicity Category 4

Hazard Statement Codes: H302: Harmful if swallowed.

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

Full Text EU 67/548/EEC:

Topiramate: This is a self-classification.

Classification: Reproductive Toxicity Category 2, Toxic

Risk Phrases: R61: May cause harm to the unborn child. R48/22: Harmful: danger of serious damage to health by prolonged exposure if swallowed.

FD&C Blue No. 2: This is a self-classification.

Classification: Harmful

Risk Phrases: R22: Harmful if swallowed.

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

REVISION DETAILS: New.

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 product.

The Vendee (or any other third party) assumes full risk and responsibility for any injury or damage that may occur from the manufacture, use or other exposure to the material. No warranty is expressed or implied regarding the accuracy of the data set forth herein or the results that may be obtained from the use or reliance thereof. Teva, Inc. assumes no responsibility for any injury that may arise from the manufacture, use or other exposure to the material if reasonable safety procedures are not adhered to as stipulated in the data sheet attached hereto. Additionally, Teva, Inc. assumes no responsibility for injury to any person proximately caused by the inappropriate or unintended use of the material even if such reasonable safety procedures are followed.

DEFINITIONS OF TERMS

For information on medical terms used in this SDS consult an on-line database such as Medline Plus: <http://www.nlm.nih.gov/medlineplus/druginformation.html>. A large number of abbreviations and acronyms appear on a SDS. Some of these, which are commonly used, include the following:

EXPOSURE LIMITS IN AIR:

CAS #: This is the Chemical Abstract Service Number that uniquely identifies each constituent.

CEILING LEVEL: The concentration that shall not be exceeded during any part of the working exposure.

ACGIH - American Conference of Governmental Industrial Hygienists, a professional association which establishes exposure limits. **TLV** - Threshold Limit Value - an airborne concentration of a substance which represents conditions under which it is generally believed that nearly all workers may be repeatedly exposed without adverse effect. The duration must be considered, including the 8-hour Time Weighted Average (**TWA**), the 15-minute Short Term Exposure Limit, and the instantaneous Ceiling Level (**C**). Skin absorption effects must also be considered.

DFG MAK Germ Cell Mutagen Categories: **1:** Germ cell mutagens which have been shown to increase the mutant frequency in the progeny of exposed humans. **2:** Germ cell mutagens which have been shown to increase the mutant frequency in the progeny of exposed mammals. **3A:** Substances which have been shown to induce genetic damage in germ cells of human of animals, or which produce mutagenic effects in somatic cells of mammals *in vivo* and have been shown to reach the germ cells in an active form. **3B:** Substances which are suspected of being germ cell mutagens because of their genotoxic effects in mammalian somatic cell *in vivo*; in exceptional cases, substances for which there are no *in vivo* data, but which are clearly mutagenic *in vitro* and structurally related to known *in vivo* mutagens. **4:** Not applicable (Category 4 carcinogenic substances are those with non-genotoxic mechanisms of action. By definition, germ cell mutagens are genotoxic. Therefore, a Category 4 for germ cell mutagens cannot apply. At some time in the future, it is conceivable that a Category 4 could be established for genotoxic substances with primary targets other than DNA [e.g. purely aneugenic substances] if research results make this seem sensible.) **5:** Germ cell mutagens, the potency of which is considered to be so low that, provided the MAK value is observed, their contribution to genetic risk for humans is expected not to be significant.

DFG MAK Pregnancy Risk Group Classification: **Group A:** A risk of damage to the developing embryo or fetus has been unequivocally demonstrated. Exposure of pregnant women can lead to damage of the developing organism, even when MAK and BAT (Biological Tolerance Value for Working Materials) values are observed. **Group B:** Currently available information indicates a risk of damage to the developing embryo or fetus must be considered to be probable. Damage to the developing organism cannot be excluded when pregnant women are exposed, even when MAK and BAT values are observed. **Group C:** There is no reason to fear a risk of damage to the developing embryo or fetus when MAK and BAT values are observed. **Group D:** Classification in one of the groups A-C is not yet possible because, although the data available may indicate a trend, they are not sufficient for final evaluation.

IDLH-Immediately Dangerous to Life and Health: This level represents a concentration from which one can escape within 30-minutes without suffering escape-preventing or permanent injury.

LOQ: Limit of Quantitation.

MAK: Federal Republic of Germany Maximum Concentration Values in the workplace.

NE: Not Established. When no exposure guidelines are established, an entry of NE is made for reference.

NIC: Notice of Intended Change.

NIOSH CEILING: The exposure that shall not be exceeded during any part of the workday. If instantaneous monitoring is not feasible, the ceiling shall be assumed as a 15-minute TWA exposure (unless otherwise specified) that shall not be exceeded at any time during a workday.

NIOSH RELS: NIOSH's Recommended Exposure Limits.

PEL-Permissible Exposure Limit: OSHA's Permissible Exposure Limits. This exposure value means exactly the same as a TLV, except that it is enforceable by OSHA. The OSHA Permissible Exposure Limits are based in the 1989 PELs and the June, 1993 Air Contaminants Rule (**Federal Register**: 58: 35338-35351 and 58: 40191). Both the current PELs and the vacated PELs are indicated. The phrase, "Vacated 1989 PEL," is placed next to the PEL that was vacated by Court Order.

SKIN: Used when there is a danger of cutaneous absorption.

STEL-Short Term Exposure Limit: Short Term Exposure Limit, usually a 15-minute time-weighted average (TWA) exposure that should not be exceeded at any time during a workday, even if the 8-hr TWA is within the TLV-TWA, PEL-TWA or REL-TWA.

TLV-Threshold Limit Value: An airborne concentration of a substance that represents conditions under which it is generally believed that nearly all workers may be repeatedly exposed without adverse effect. The duration must be considered, including the 8-hour.

TWA-Time Weighted Average: Time Weighted Average exposure concentration for a conventional 8-hr (TLV, PEL) or up to a 10-hr (REL) workday and a 40-hr workweek.

HAZARDOUS MATERIALS IDENTIFICATION SYSTEM HAZARD RATINGS:

This rating system was developed by the National Paint and Coating Association and has been adopted by industry to identify the degree of chemical hazards.

HEALTH HAZARD: 0 (Minimal Hazard): No significant health risk, irritation of skin or eyes not anticipated. **Skin Irritation:** Essentially non-irritating. PII or Draize = "0". **Eye Irritation:** Essentially non-irritating, or minimal effects which clear in < 24 hours [e.g. mechanical irritation]. Draize = "0". **Oral Toxicity LD₅₀ Rat:** < 5000 mg/kg. **Dermal Toxicity LD₅₀Rat or Rabbit:** < 2000 mg/kg. **Inhalation Toxicity 4-hrs LC₅₀ Rat:** < 20 mg/L.; **1 (Slight Hazard):** Minor reversible injury may occur; slightly or mildly irritating. **Skin Irritation:** Slightly or mildly irritating. **Eye Irritation:** Slightly or mildly irritating. **Oral Toxicity LD₅₀ Rat:** > 500-5000 mg/kg. **Dermal Toxicity LD₅₀Rat or Rabbit:** > 1000-2000 mg/kg. **Inhalation Toxicity LC₅₀ 4-hrs Rat:** > 2-20 mg/L.; **2 (Moderate Hazard):** Temporary or transitory injury may occur. **Skin Irritation:** Moderately irritating; primary irritant; sensitizer. PII or Draize > 0, < 5. **Eye Irritation:** Moderately to severely irritating and/or corrosive; reversible corneal opacity; corneal involvement or irritation clearing in 8-21 days. Draize > 0, ≤ 25. **Oral Toxicity LD₅₀ Rat:** > 50-500 mg/kg. **Dermal Toxicity LD₅₀Rat or Rabbit:** > 200-1000 mg/kg. **Inhalation Toxicity LC₅₀ 4-hrs Rat:** > 0.5-2 mg/L.; **3 (Serious Hazard):** Major injury likely unless prompt action is taken and medical treatment is given; high level of toxicity; corrosive. **Skin Irritation:** Severely irritating and/or corrosive; may destroy dermal tissue, cause skin burns, dermal necrosis. PII or Draize > 5-8 with destruction of tissue. **Eye Irritation:** Corrosive, irreversible destruction of ocular tissue; corneal involvement or irritation persisting for more than 21 days. Draize > 80 with effects irreversible in 21 days. **Oral Toxicity LD₅₀ Rat:** > 1-50 mg/kg. **Dermal Toxicity LD₅₀Rat or Rabbit:** > 20-200 mg/kg. **Inhalation Toxicity LC₅₀ 4-hrs Rat:** > 0.05-0.5 mg/L.; **4 (Severe Hazard):** Life-threatening; major or permanent damage may result from single or repeated exposure. **Skin Irritation:** Not appropriate. Do not rate as a "4", based on skin irritation alone. **Eye Irritation:** Not appropriate. Do not rate as a "4", based on eye irritation alone. **Oral Toxicity LD₅₀ Rat:** ≤ 1 mg/kg. **Dermal Toxicity LD₅₀Rat or Rabbit:** ≤ 20 mg/kg. **Inhalation Toxicity LC₅₀ 4-hrs Rat:** ≤ 0.05 mg/L).

FLAMMABILITY HAZARD: 0 (Minimal Hazard-Materials that will not burn in air when exposure to a temperature of 815.5°C [1500°F] for a period of 5 minutes.); 1 (Slight Hazard-Materials that must be pre-heated before ignition can occur. Material require considerable pre-heating, under all ambient temperature conditions before ignition and combustion can occur, including:

HAZARDOUS MATERIALS IDENTIFICATION SYSTEM HAZARD RATINGS (continued):

FLAMMABILITY HAZARD (continued): 1 (continued): Materials that will burn in air when exposed to a temperature of 815.5°C (1500°F) for a period of 5 minutes or less; Liquids, solids and semisolids having a flash point at or above 93.3°C [200°F] (e.g. OSHA Class IIIB, or; Most ordinary combustible materials [e.g. wood, paper, etc.]; **2 (Moderate Hazard-Materials that must be moderately heated or exposed to relatively high ambient temperatures before ignition can occur. Materials in this degree would not, under normal conditions, form hazardous atmospheres in air, but under high ambient temperatures or moderate heating may release vapor in sufficient quantities to produce hazardous atmospheres in air, including:** Liquids having a flash-point at or above 37.8°C [100°F]; Solid materials in the form of course dusts that may burn rapidly but that generally do not form explosive atmospheres; Solid materials in a fibrous or shredded form that may burn rapidly and create flash fire hazards (e.g. cotton, sisal, hemp; Solids and semisolids that readily give off flammable vapors.); **3 (Serious Hazard-Liquids and solids that can be ignited under almost all ambient temperature conditions. Materials in this degree produce hazardous atmospheres with air under almost all ambient temperatures, or, unaffected by ambient temperature, are readily ignited under almost all conditions, including:** Liquids having a flash point below 22.8°C [73°F] and having a boiling point at or above 38°C [100°F] and below 37.8°C [100°F] [e.g. OSHA Class IB and IC]; Materials that on account of their physical form or environmental conditions can form explosive mixtures with air and are readily dispersed in air [e.g., dusts of combustible solids, mists or droplets of flammable liquids]; Materials that burn extremely rapidly, usually by reason of self-contained oxygen [e.g. dry nitrocellulose and many organic peroxides]; **4 (Severe Hazard-Materials that will rapidly or completely vaporize at atmospheric pressure and normal ambient temperature or that are readily dispersed in air, and which will burn readily, including:** Flammable gases; Flammable cryogenic materials; Any liquid or gaseous material that is liquid while under pressure and has a flash point below 22.8°C [73°F] and a boiling point below 37.8°C [100°F] [e.g. OSHA Class IA; Material that ignite spontaneously when exposed to air at a temperature of 54.4°C [130°F] or below [e.g. pyrophoric].

PHYSICAL HAZARD: 0 (Water Reactivity): Materials that do not react with water. **Organic Peroxides:** Materials that are normally stable, even under fire conditions and will not react with water. **Explosives:** Substances that are Non-Explosive. **Unstable Compressed Gases:** No Rating. **Pyrophorics:** No Rating. **Oxidizers:** No "0" rating allowed. **Unstable Reactives:** Substances that will not polymerize, decompose, condense or self-react.; **1 (Water Reactivity):** Materials that change or decompose upon exposure to moisture. **Organic Peroxides:** Materials that are normally stable, but can become unstable at high temperatures and pressures. These materials may react with water, but will not release energy. **Explosives:** Division 1.5 & 1.6 substances that are very insensitive explosives or that do not have a mass explosion hazard. **Compressed Gases:** Pressure below OSHA definition. **Pyrophorics:** No Rating. **Oxidizers:** Packaging Group III; **Solids:** any material that in either concentration tested, exhibits a mean burning time less than or equal to the mean burning time of a 3:7 potassium bromate/cellulose mixture and the criteria for Packing Group I and II are not met. **Liquids:** any material that exhibits a mean pressure rise time less than or equal to the pressure rise time of a 1:1 nitric acid (65%) / cellulose mixture and the criteria for Packing Group I and II are not met. **Unstable Reactives:** Substances that may decompose, condense or self-react, but only under conditions of high temperature and/or pressure and have little or no potential to cause significant heat generation or explosive hazard. Substances that readily undergo hazardous polymerization in the absence of inhibitors.; **2 (Water Reactivity):** Materials that may react violently with water. **Organic Peroxides:** Materials that, in themselves, are normally unstable and will readily undergo violent chemical change, but will not detonate. These materials may also react violently with water. **Explosives:** Division 1.4 – Explosive substances where the explosive effect are largely confined to the package and no projection of fragments of appreciable size or range are expected. An external fire must not cause virtually instantaneous explosion of almost the entire contents of the package. **Compressed Gases:** Pressurized and meet OSHA definition but < 514.7 psi absolute at 21.1°C (70°F) [500 psig]. **Pyrophorics:** No Rating. **Oxidizers:** Packaging Group II **Solids:** any material that, in either concentration tested, exhibits a mean burning time of less than or equal to the mean burning time of a 2:3 potassium bromate/cellulose mixture and the criteria for Packing Group I are not met. **Liquids:** any material that exhibits a mean pressure rise time less than or equal to the pressure rise of a 1:1 aqueous sodium chlorate solution (40%) / cellulose mixture and the criteria for Packing Group I are not met. **Unstable Reactives:** Substances that may polymerize, decompose, condense, or self-react at ambient temperature and/or pressure, but have a low potential for significant heat generation or explosion. Substances that readily form peroxides upon exposure to air or oxygen at room temperature); **3 (Water Reactivity):** Materials that may form explosive reactions with water. **Organic Peroxides:** Materials that are capable of detonation or explosive reaction, but require a strong initiating source, or must be heated under confinement before initiation; or materials that react explosively with water. **Explosives:** Division 1.2 – Explosive substances that have a fire hazard and either a minor blast hazard or a minor projection hazard or both, but do not have a mass explosion hazard. **Compressed Gases:** Pressure ≥ 514.7 psi absolute at 21.1°C (70°F) [500 psig]. **Pyrophorics:** No Rating. **Oxidizers:** Packaging Group I **Solids:** any material that, in either concentration tested, exhibits a mean burning time less than the mean burning time of a 3:2 potassium bromate/cellulose mixture. **Liquids:** Any material that spontaneously ignites when mixed with cellulose in a 1:1 ratio, or which exhibits a mean pressure rise time less than the pressure rise time of a 1:1 perchloric acid (50%) / cellulose mixture. **Unstable Reactives:** Substances that may polymerize, decompose, condense or self-react at ambient temperature and/or pressure and have a moderate potential to cause significant heat generation or explosion.; **4 (Water Reactivity):** Materials that react explosively with water without requiring heat or confinement. **Organic Peroxides:** Materials that are readily capable of detonation or explosive decomposition at normal temperature and pressures. **Explosives:** Division 1.1 & 1.2-explosive substances that have a mass explosion hazard or have a projection hazard. A mass explosion is one that affects almost the entire load instantaneously. **Compressed Gases:** No Rating. **Pyrophorics:** Add to the definition of Flammability "4". **Oxidizers:** No "4" rating. **Unstable Reactives:** Substances that may polymerize, decompose, condense or self-react at ambient temperature and/or pressure and have a high potential to cause significant heat generation or explosion).

NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS:

HEALTH HAZARD: 0 Materials that, under emergency conditions, would offer no hazard beyond that of ordinary combustible materials. Gases and vapors with an LC₅₀ for acute inhalation toxicity greater than 10,000 ppm. Dusts and mists with an LC₅₀ for acute inhalation toxicity greater than 200 mg/L. Materials with an LD₅₀ for acute dermal toxicity greater than 2000 mg/kg. Materials with an LD₅₀ for acute oral toxicity greater than 2000 mg/kg. Materials essentially non-irritating to the respiratory tract, eyes, and skin. **1** Materials that, under emergency conditions, can cause significant irritation. Gases and vapors with an LC₅₀ for acute inhalation toxicity greater than 5,000 ppm but less than or equal to 10,000 ppm. Dusts and mists with an LC₅₀ for acute inhalation toxicity greater than 10 mg/L but less than or equal to 200 mg/L. Materials with an LD₅₀ for acute dermal toxicity greater than 1000 mg/kg but less than or equal to 2000 mg/kg. Materials that slightly to moderately irritate the respiratory tract, eyes and skin. Materials with an LD₅₀ for acute oral toxicity greater than 500 mg/kg but less than or equal to 2000 mg/kg.

DEFINITIONS OF TERMS (Continued)

NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS (continued):

HEALTH HAZARD (continued): 2 Materials that, under emergency conditions, can cause temporary incapacitation or residual injury. Gases with an LC₅₀ for acute inhalation toxicity greater than 3,000 ppm but less than or equal to 5,000 ppm. Any liquid whose saturated vapor concentration at 20°C (68°F) is equal to or greater than one-fifth its LC₅₀ for acute inhalation toxicity, if its LC₅₀ is less than or equal to 5000 ppm and that does not meet the criteria for either degree of hazard 3 or degree of hazard 4. Dusts and mists with an LC₅₀ for acute inhalation toxicity greater than 2 mg/L but less than or equal to 10 mg/L. Materials with an LD₅₀ for acute dermal toxicity greater than 200 mg/kg but less than or equal to 1000 mg/kg. Compressed liquefied gases with boiling points between -30°C (-22°F) and -55°C (-66.5°F) that cause severe tissue damage, depending on duration of exposure. Materials that are respiratory irritants. Materials that cause severe, but reversible irritation to the eyes or are lachrymators. Materials that are primary skin irritants or sensitizers. Materials whose LD₅₀ for acute oral toxicity is greater than 50 mg/kg but less than or equal to 500 mg/kg. Dusts and mists with an LC₅₀ for acute inhalation toxicity greater than 10 mg/L but less than or equal to 200 mg/L. Materials with an LD₅₀ for acute dermal toxicity greater than 1000 mg/kg but less than or equal to 2000 mg/kg. Materials that slightly to moderately irritate the respiratory tract, eyes and skin. Materials with an LD₅₀ for acute oral toxicity greater than 500 mg/kg but less than or equal to 2000 mg/kg. 3 (materials that, under emergency conditions, can cause serious or permanent injury): Gases and vapors whose LC₅₀ for acute inhalation toxicity is greater than 1,000 ppm but less than or equal to 3,000 ppm. Dusts and mists whose LC₅₀ for acute inhalation toxicity is greater than 0.5 mg/L but less than or equal to 2 mg/L. Materials whose LD₅₀ for acute dermal toxicity is greater than 40 mg/kg but less than or equal to 200 mg/kg. Materials whose LD₅₀ for acute oral toxicity is greater than 5 mg/kg but less than or equal to 50 mg/kg. Any liquid whose saturated vapor concentration at 20°C (68°F) is equal to or greater than one-fifth its LC₅₀ for acute inhalation toxicity, if its LC₅₀ is less than or equal to 3000 ppm and that does not meet the criteria for degree of hazard 4. Compressed liquefied gases with boiling points between -30°C (-22°F) and -55°C (-66.5°F) that cause frostbite and irreversible tissue damage. Materials that are respiratory irritants. Cryogenic gases that cause frostbite and irreversible tissue damage. Materials that are corrosive to the respiratory tract. Materials that are corrosive to the eyes or cause irreversible corneal opacity. Materials that are corrosive to the skin. 4 (materials that, under emergency conditions, can be lethal): Gases and vapors whose LC₅₀ for acute inhalation toxicity less than or equal to 1,000 ppm. Dusts and mists whose LC₅₀ for acute inhalation toxicity is less than or equal to 0.5 mg/L. Materials whose LD₅₀ for acute dermal toxicity is less than or equal to 40 mg/kg. Materials whose LD₅₀ for acute oral toxicity is less than or equal to 5 mg/kg. Any liquid whose saturated vapor concentration at 20°C (68°F) is equal to or greater than one-fifth its LC₅₀ for acute inhalation toxicity, if its LC₅₀ is less than or equal to 1000 ppm.

FLAMMABILITY HAZARD: 0 Materials that will not burn under typical fire conditions, including intrinsically noncombustible materials such as concrete, stone, and sand: Materials that will not burn in air when exposed to a temperature of 816°C (1500°F) for a period of 5 minutes in accordance with Annex D. 1 Materials that must be preheated before ignition can occur. Materials in this degree require considerable preheating, under all ambient temperature conditions, before ignition and combustion can occur: Materials that will burn in air when exposed to a temperature of 816°C (1500°F) for a period of 5 minutes in accordance with Annex D. Liquids, solids and semisolids having a flash point at or above 93.4°C (200°F) (i.e. Class IIIB liquids). Liquids with a flash point greater than 35°C (95°F) that do not sustain combustion when tested using the *Method of Testing for Sustained Combustibility*, per 49 CFR 173, Appendix H or the UN *Recommendation on the Transport of Dangerous Goods, Model Regulations* (current edition) and the related *Manual of Tests and Criteria* (current edition). Liquids with a flash point greater than 35°C (95°F) in a water-miscible solution or dispersion with a water non-combustible liquid/solid content of more than 85 percent by weight. Liquids that have no fire point when tested by ASTM D 92 Standard Test Method for Flash and Fire Points by Cleveland Open Cup, up to a boiling point of the liquid or up to a temperature at which the sample being tested shows an obvious physical change. Combustible pellets with a representative diameter of greater than 2 mm (10 mesh). Solids containing greater than 0.5 percent by weight of a flammable or combustible solvent are rated by the closed cup flash point of the solvent. Most ordinary combustible materials. 2 Materials that must be moderately heated or exposed to relatively high ambient temperatures before ignition can occur. Materials in this degree would not under normal conditions form hazardous atmospheres with air, but under high ambient temperatures or under moderate heating could release vapor in sufficient quantities to produce hazardous atmospheres with air: Liquids having a flash point at or above 37.8°C (100°F) and below 93.4°C (200°F) (i.e. Class II and Class IIIA liquids.) Solid materials in the form of powders or coarse dusts of representative diameter between 420 microns (40 mesh) and 2 mm (10 mesh) that burn rapidly but that generally do not form explosive mixtures in air. Solid materials in fibrous or shredded form that burn rapidly and create flash fire hazards, such as cotton, sisal and hemp. Solids and semisolids that readily give off flammable vapors. Solids containing greater than 0.5 percent by weight of a flammable or combustible solvent are rated by the closed cup flash point of the solvent. 3 Liquids and solids that can be ignited under almost all ambient temperature conditions. Materials in this degree produce hazardous atmospheres with air under almost all ambient temperatures or, though unaffected by ambient temperatures, are readily ignited under almost all conditions: Liquids having a flash point below 22.8°C (73°F) and having a boiling point at or above 37.8°C (100°F) and those liquids having a flash point at or above 22.8°C (73°F) and below 37.8°C (73°F) and below 37.8°C (100°F) (i.e. Class IB and IC liquids). Materials that, on account of their physical form or environmental conditions, can form explosive mixtures with air and are readily dispersed in air. Flammable or combustible dusts with a representative diameter less than 420 microns (40 mesh). Materials that burn with extreme rapidity, usually by reason of self-contained oxygen (e.g. dry nitrocellulose and many organic peroxides). Solids containing greater than 0.5 percent by weight of a flammable or combustible solvent are rated by the closed cup flash point of the solvent. 4 Materials that will rapidly or completely vaporize at atmospheric pressure and normal ambient temperature or that are readily dispersed in air and will burn readily: Flammable gases. Flammable cryogenic materials. Any liquid or gaseous materials that is liquid while under pressure and has a flash point below 22.8°C (73°F) and a boiling point below 37.8°C (100°F) (i.e. Class IA liquids). Materials that ignite when exposed to air. Solids containing greater than 0.5 percent by weight of a flammable or combustible solvent are rated by the closed cup flash point of the solvent.

INSTABILITY HAZARD: 0 Materials that in themselves are normally stable, even under fire conditions: Materials that have an estimated instantaneous power density (product of heat of reaction and reaction rate) at 250°C (482°F) below 0.01 W/mL. Materials that do not exhibit an exotherm at temperatures less than or equal to 500°C (932°F) when tested by differential scanning calorimetry. 1 Materials that in themselves are normally stable, but that can become unstable at elevated temperatures and pressures: Materials that have an estimated instantaneous power density (product of heat of reaction and reaction rate) at 250°C (482°F) at or above 0.01 W/mL and below 10 W/mL.

NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS (continued):

INSTABILITY HAZARD (continued): 2 Materials that readily undergo violent chemical change at elevated temperatures and pressures: Materials that have an estimated instantaneous power density (product of heat of reaction and reaction rate) at 250°C (482°F) at or above 10 W/mL and below 100 W/mL. 3 Materials that in themselves are capable of detonation or explosive decomposition or explosive reaction, but that require a strong initiating source or that must be heated under confinement before initiation: Materials that have an estimated instantaneous power density (product of heat of reaction and reaction rate) at 250°C (482°F) at or above 100 W/mL and below 1000 W/mL. Materials that are sensitive to thermal or mechanical shock at elevated temperatures and pressures. 4 Materials that in themselves are readily capable of detonation or explosive decomposition or explosive reaction at normal temperatures and pressures: Materials that have an estimated instantaneous power density (product of heat of reaction and reaction rate) at 250°C (482°F) of 1000 W/mL or greater. Materials that are sensitive to localized thermal or mechanical shock at normal temperatures and pressures.

FLAMMABILITY LIMITS IN AIR:

Much of the information related to fire and explosion is derived from the National Fire Protection Association (NFPA). **Flash Point** - Minimum temperature at which a liquid gives off sufficient vapors to form an ignitable mixture with air. **Autoignition Temperature**: The minimum temperature required to initiate combustion in air with no other source of ignition. **LEL** - the lowest percent of vapor in air, by volume, that will explode or ignite in the presence of an ignition source. **UEL** - the highest percent of vapor in air, by volume, that will explode or ignite in the presence of an ignition source.

TOXICOLOGICAL INFORMATION:

Human and Animal Toxicology: Possible health hazards as derived from human data, animal studies, or from the results of studies with similar compounds are presented. Definitions of some terms used in this section are: **LD₅₀** - Lethal Dose (solids & liquids) which kills 50% of the exposed animals; **LC₅₀** - Lethal Concentration (gases) which kills 50% of the exposed animals; **ppm** concentration expressed in parts of material per million parts of air or water; **mg/m³** concentration expressed in weight of substance per volume of air; **mg/kg** quantity of material, by weight, administered to a test subject, based on their body weight in kg. Other measures of toxicity include **TDLo**, the lowest dose to cause a symptom and **TCLo** the lowest concentration to cause a symptom; **TD₀₁**, **LDLo**, and **LDO**, or **TC**, **TC₀₁**, **LCLo**, and **LCo**, the lowest dose (or concentration) to cause lethal or toxic effects. **Cancer Information:** The sources are: **IARC** - the International Agency for Research on Cancer; **NTP** - the National Toxicology Program, **RTECS** - the Registry of Toxic Effects of Chemical Substances, **OSHA** and **CAL/OSHA**. IARC and NTP rate chemicals on a scale of decreasing potential to cause human cancer with rankings from 1 to 4. Subrankings (2A, 2B, etc.) are also used. **Other Information:** **BEI** - ACGIH Biological Exposure Indices, represent the levels of determinants which are most likely to be observed in specimens collected from a healthy worker who has been exposed to chemicals to the same extent as a worker with inhalation exposure to the TLV.

REPRODUCTIVE TOXICITY INFORMATION:

A **mutagen** is a chemical which causes permanent changes to genetic material (DNA) such that the changes will propagate through generational lines. An **embryotoxin** is a chemical which causes damage to a developing embryo (i.e. within the first eight weeks of pregnancy in humans), but the damage does not propagate across generational lines. A **teratogen** is a chemical which causes damage to a developing fetus, but the damage does not propagate across generational lines. A **reproductive toxin** is any substance which interferes in any way with the reproductive process.

United States FDA Pharmaceutical Pregnancy Categories: **Pregnancy Category A:** Adequate and well-controlled human studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters). **Pregnancy Category B:** Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women OR Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester. **Pregnancy Category C:** Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. **Pregnancy Category D:** There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. **Pregnancy Category X:** Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits. **Pregnancy Category N:** FDA has not classified this drug.

ECOLOGICAL INFORMATION:

EC is the effect concentration in water. **BCF** = Bioconcentration Factor, which is used to determine if a substance will concentrate in lifeforms which consume contaminated plant or animal matter. **TL_m** = median threshold limit; Coefficient of Oil/Water Distribution is represented by **log K_{ow}** or **log K_{oc}** and is used to assess a substance's behavior in the environment.

REGULATORY INFORMATION:

U.S. and CANADA:

ACGIH: American Conference of Governmental Industrial Hygienists, a professional association which establishes exposure limits.

This section explains the impact of various laws and regulations on the material. **EPA** is the U.S. Environmental Protection Agency. **NIOSH** is the National Institute of Occupational Safety and Health, which is the research arm of the U.S. Occupational Safety and Health Administration (**OSHA**). **WHMIS** is the Canadian Workplace Hazardous Materials Information System. **DOT** and **TC** are the U.S. Department of Transportation and the Transport Canada, respectively. Superfund Amendments and Reauthorization Act (**SARA**); the Canadian Domestic/Non-Domestic Substances List (**DSL/NDSL**); the U.S. Toxic Substance Control Act (**TSCA**); Marine Pollutant status according to the **DOT**; the Comprehensive Environmental Response, Compensation, and Liability Act (**CERCLA** or **Superfund**); and various state regulations. This section also includes information on the precautionary warnings which appear on the material's package label. **OSHA** - U.S. Occupational Safety and Health Administration.

EUROPEAN AND INTERNATIONAL:

The DFG: This is the Federal Republic of Germany's Occupation Health Agency, similar to the U.S. OSHA. **EU** is the European Community (formerly known as the **EEC**, European Economic Community). **EINECS:** This is the European Inventory of Now-Existing Chemical Substances. The **ARD** is the European Agreement Concerning the International Carriage of Dangerous Goods by Road and the **RID** are the International Regulations Concerning the Carriage of Dangerous Goods by Rail. **AICS** is the Australian Inventory of Chemical Substances.