SAFETY DATA SHEETS

This SDS packet was issued with item:

078917510

The safety data sheets (SDS) in this packet apply to the individual products listed below. Please refer to invoice for specific item number(s).

078865848 078917507 078917508 078917509

Allergan

T 800 678 1605

Allergan, plc.
100 Enterprise Dr.
Rockaway, NJ 07866
www.Allergan.com

Thank you for your recent request for information concerning Actavis Products and their Safety Data Sheets (SDS).

The intention of the enclosed information is to provide you with available data and information from published scientific and medical literature to assist you in your practice decisions. Some of this information may address off-label uses that are not currently approved by the U.S. Food and Drug Administration (FDA). If you did not request the enclosed information, please report to Allergan's Medical Information department.

An SDS does not exist for the following products and therefore we are unable to provide the documentation requested.

- Atenolol/Chlorthalidone Tablets
- Propranolol Tablets
- Doxycycline Hyclate Capsules
- Hydroxyzine Pamoate Capsules
- Metronidazole Tablets
- Primidone Tablets
- Buspirone Hydrochloride Tablets
- Minocycline Hydrochloride Capsules
- Cyclobenzaprine Hydrochloride Tablets
- Chlorzoxazone Tablets
- Diclofenac Sodium API
- Estradiol Tablets 0.5 mg 100, 1.0 mg 100, 1.0 mg 500, 2.0 mg 100, and 2.0 mg 500
- Metoclopramide Tablets, USP
- Lactulose Syrup / Lactulose Solution USP / EP Grade (No NDC provided)
- Lisinopril Tablets
- Methocarbamol Tablets 500 mg 500, Methocarbamol Tablets 500 mg 500, Methocarbamol Tablets 750 mg 100, and Methocarbamol Tablets 750 mg 100
- Simethicone and Artificial Tears Ointment (No NDC provided)
- Progesterone Capsules

The Occupational Safety and Health Administration (OSHA) exempts Safety Data Sheets (SDS) for drugs regulated by the U.S. Food and Drug Administration (FDA) that are in solid final form, including pills or tablets for direct administration to patients. In addition, drug products packaged by the chemical manufacturer intended for sale at a retail establishment to consumers (e.g., over-the-counter drugs) are exempt, as are drug products intended for personal use by employees at their work place (e.g., first aid supplies).[1]

The above information is being provided in response to your specific inquiry. Allergan, plc. makes no recommendation regarding unapproved uses. The intention is to provide a synopsis of relevant drug and medical information derived from readily available sources. The information provided may not represent all

available information on this topic. Any publication of the provided information or use beyond this intent is prohibited without written authorization from Allergan, plc. As is typical with published scientific and medical literature, some of the information presented in the enclosed or cited references may not conform to the approved labeling for the product(s) mentioned.

Please contact our Medical Communications Department at 1-800-678-1605 should you have any further questions. In addition, product prescribing information is available on the web at www.allergan.com.

Thank you for your interest in Allergan, plc. products.

Sincerely,

Global Medical Scientific Information
Allergan Medical Affairs
(800) 678-1605

Allergan

T 800 678 1605

Allergan, plc.
100 Enterprise Dr.
Rockaway, NJ 07866
www.Allergan.com

Reference:

1. Occupational Safety and Health Standards. Health Communication Statement [Subpart Z, Toxic and Hazardous Substances; 29 CFR 1910.1200(b)(6)(vii)]. Available at: http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10099. Accessed June 15, 2006.

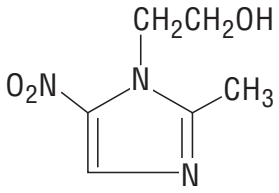
To reduce the development of drug-resistant bacteria and maintain the effectiveness of metronidazole tablets and other antibacterial drugs, metronidazole tablets should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

WARNING

Metronidazole has been shown to be carcinogenic in mice and rats. (See **PRECAUTIONS.)** Unnecessary use of the drug should be avoided. Its use should be reserved for the conditions described in the **INDICATIONS AND USAGE** section below.

DESCRIPTION

Metronidazole is an oral synthetic antiprotozoal and antibacterial agent, 1-(β-hydroxyethyl)-2-methyl-5-nitroimidazole, which has the following structural formula:



$C_6H_9N_3O_3$ M. W. 171.16

Metronidazole 250 mg and 500 mg tablets, for oral administration, contain the inactive ingredients: colloidal silicon dioxide, hydroxypropyl cellulose, lactose (anhydrous), microcrystalline cellulose, sodium starch glycolate, and stearic acid.

CLINICAL PHARMACOLOGY

METRONIDAZOLE TABLETS USP 250 mg and 500 mg
Revised: December 2010
Rx only
195584

Disposition of metronidazole in the body is similar for both oral and intravenous dosage forms, with an average elimination half-life in healthy humans of eight hours. The major route of elimination of metronidazole and its metabolites is via the urine (60 to 80% of the dose), with fecal excretion accounting for 6 to 15% of the dose. The metabolites that appear in the urine result primarily from side-chain oxidation [1-(β-hydroxyethyl)-2-hydroxymethyl-5-nitroimidazole and 2-methyl-5-nitroimidazole-1-yl-acetic acid] and glucuronide conjugation, with unchanged metronidazole accounting for approximately 20% of the total. Renal clearance of metronidazole is approximately 10 mL/min/1.73 m^2.

Metronidazole is the major component appearing in the plasma, with lesser quantities of the 2-hydroxymethyl metabolite also being present. Less than 20% of the circulating metronidazole is bound to plasma proteins. Both the parent compound and the metabolite possess *in vitro* bactericidal activity against most strains of anaerobic bacteria and *in vitro* trichomonacidal activity.

Metronidazole appears in cerebrospinal fluid, saliva, and human milk in concentrations similar to those found in plasma. Bactericidal concentrations of metronidazole have also been detected in pus from hepatic abscesses.

Following oral administration, metronidazole is well absorbed, with peak plasma concentrations occurring between one and two hours after administration. Plasma concentrations of metronidazole are proportional to the administered dose. Oral administration of 250 mg, 500 mg, or 2,000 mg produced peak plasma concentrations of 6 mcg/mL, 12 mcg/mL, and 40 mcg/mL, respectively. Studies reveal no significant bioavailability differences between males and females; however, because of weight differences, the resulting plasma levels in males are generally lower.

Decreased renal function does not alter the single-dose pharmacokinetics of metronidazole. However, plasma clearance of metronidazole is decreased in patients with decreased liver function.

Microbiology

Trichomonas vaginalis, Entamoeba histolytica. Metronidazole possesses direct trichomonacidal and amebacidal activity against *T. vaginalis* and *E. histolytica.* The *in vitro* minimal inhibitory concentration (MIC) for most strains of these organisms is 1 mcg/mL or less.

Anaerobic Bacteria. Metronidazole is active *in vitro* against most obligate anaerobes but does not appear to possess any clinically relevant activity against facultative anaerobes or obligate aerobes. Against susceptible organisms, metronidazole is generally bactericidal at concentrations equal to or slightly higher than the minimal inhibitory concentrations. Metronidazole has been shown to have *in vitro* and clinical activity against the following organisms:

Anaerobic gram-negative bacilli, including:
- *Bacteroides* species, including the *Bacteroides fragilis* group (*B. fragilis, B. distasonis, B. ovatus, B. thetaiotaomicron, B. vulgatus)*
- *Fusobacterium* species

Anaerobic gram-positive bacilli, including:
- *Clostridium* species and susceptible strains of *Eubacterium*

Anaerobic gram positive cocci, including:
- *Peptococcus niger*
- *Peptostreptococcus species*

Susceptibility Tests

Bacteriologic studies should be performed to determine the causative organisms and their susceptibility to metronidazole; however, the rapid, routine susceptibility testing of individual isolates of anaerobic bacteria is not always practical, and therapy may be started while awaiting these results.

Quantitative methods give the most precise estimates of susceptibility to antibacterial drugs. A standardized agar dilution method and a broth microdilution method are recommended.[1]

Control strains are recommended for standardized susceptibility testing. Each time the test is performed, one or more of the following strains should be included: *Clostridium perfringens* ATCC 13124, *Bacteroides fragilis* ATCC 25285, and *Bacteroides thetaiotaomicron* ATCC 29741. The mode metronidazole MICs for those three strains are reported to be 0.25, 0.25, and 0.5 mcg/mL, respectively.

A clinical laboratory is considered under acceptable control if the results of the control strains are within one doubling dilution of the mode MICs reported for metronidazole.

A bacterial isolate may be considered susceptible if the MIC value for metronidazole is not more than 16 mcg/mL. An organism is considered resistant if the MIC is greater than 16 mcg/mL. A report of "resistant" from the laboratory indicates that the infecting organism is not likely to respond to therapy.

INDICATIONS AND USAGE

Symptomatic Trichomoniasis

Metronidazole tablets are indicated for the treatment of symptomatic trichomoniasis in females and males when the presence of the trichomonad has been confirmed by appropriate laboratory procedures (wet smears and/or cultures).

Asymptomatic Trichomoniasis

Metronidazole tablets are indicated in the treatment of asymptomatic females when the organism is associated with endocervicitis, cervicitis, or cervical erosion. Since there is evidence that presence of the trichomonad can interfere with accurate assessment of abnormal cytological smears, additional smears should be performed after eradication of the parasite.

Treatment of Asymptomatic Consorts

T. vaginalis infection is a venereal disease. Therefore, asymptomatic sexual partners of treated patients should be treated simultaneously if the organism has been found to be present, in order to prevent reinfection of the partner. The decision as to whether to treat an asymptomatic male partner who has a negative culture or one for whom no culture has been attempted is an individual one. In making this decision, it should be noted that there is evidence that a woman may become reinfected if her consort is not treated. Also, since there can be considerable difficulty in isolating the organism from the asymptomatic male carrier, negative smears and cultures cannot be relied upon in this regard. In any event, the consort should be treated with metronidazole tablets in cases of reinfection.

Amebiasis

Metronidazole tablets are indicated in the treatment of acute intestinal amebiasis (amebic dysentery) and amebic liver abscess.

In amebic liver abscess, metronidazole tablet therapy does not obviate the need for aspiration or drainage of pus.

Anaerobic Bacterial Infections

Metronidazole tablets are indicated in the treatment of serious infections caused by susceptible anaerobic bacteria. Indicated surgical procedures should be performed in conjunction with metronidazole tablet therapy. In a mixed aerobic and anaerobic infection, antimicrobials appropriate for the treatment of the aerobic infection should be used in addition to metronidazole tablets.

In the treatment of most serious anaerobic infections, the intravenous form of metronidazole is usually administered initially. This may be followed by oral therapy with metronidazole tablets at the discretion of the physician.

INTRA-ABDOMINAL INFECTIONS, including peritonitis, intra-abdominal abscess, and liver abscess, caused by *Bacteroides* species including the *B. fragilis* group (*B. fragilis, B. distasonis, B. ovatus, B. thetaiotaomicron, B. vulgatus), Clostridium* species, *Eubacterium* species, *Peptococcus niger,* and *Peptostreptococcus* species.

SKIN AND SKIN STRUCTURE INFECTIONS caused by *Bacteroides* species including the *B. fragilis* group, *Clostridium* species, *Peptococcus niger, Peptostreptococcus* species, and *Fusobacterium* species.

GYNECOLOGIC INFECTIONS, including endometritis, endomyometritis, tubo-ovarian abscess, and postsurgical vaginal cuff infection, caused by *Bacteroides* species including the *B. fragilis* group, *Clostridium* species, *Peptococcus niger,* and *Peptostreptococcus* species.

BACTERIAL SEPTICEMIA caused by *Bacteroides* species including the *B. fragilis* group, and *Clostridium* species.

BONE AND JOINT INFECTIONS, as adjunctive therapy, caused by *Bacteroides* species including the *B. fragilis* group.

CENTRAL NERVOUS SYSTEM (CNS) INFECTIONS, including meningitis and brain abscess, caused by *Bacteroides* species including the *B. fragilis* group.

LOWER RESPIRATORY TRACT INFECTIONS, including pneumonia, empyema, and lung abscess, caused by *Bacteroides* species including the *B. fragilis* group.

ENDOCARDITIS caused by *Bacteroides* species including the *B. fragilis* group. To reduce the development of drug-resistant bacteria and maintain the effectiveness of metronidazole tablets and other antibacterial drugs, metronidazole tablets should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

CONTRAINDICATIONS

Metronidazole tablets are contraindicated in patients with a prior history of hypersensitivity to metronidazole or other nitroimidazole derivatives.

In patients with trichomoniasis, metronidazole tablets are contraindicated during the first trimester of pregnancy. (See **WARNINGS.)**

WARNINGS

Convulsive Seizures and Peripheral Neuropathy

Convulsive seizures and peripheral neuropathy, the latter characterized mainly by numbness or paresthesia of an extremity, have been reported in patients treated with metronidazole. The appearance of abnormal neurologic signs demands the prompt discontinuation of metronidazole therapy. Metronidazole should be administered with caution to patients with central nervous system diseases.

PRECAUTIONS

General

Patients with severe hepatic disease metabolize metronidazole slowly, with resultant accumulation of metronidazole and its metabolites in the plasma. Accordingly, for such patients, doses below those usually recommended should be administered cautiously.

Known or previously unrecognized candidiasis may present more prominent symptoms during therapy with metronidazole and requires treatment with a candidicidal agent.

Prescribing metronidazole tablets in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of development of drug-resistant bacteria.

Information for Patients

Alcoholic beverages should be avoided while taking metronidazole tablets and for at least one day afterward. (See **Drug Interactions**).

Patients should be counseled that antibacterial drugs including metronidazole tablets should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When metronidazole tablets are prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by metronidazole tablets or other antibacterial drugs in the future.

Laboratory Tests

Metronidazole is a nitroimidazole and should be used with caution in patients with evidence of or history of blood dyscrasia. A mild leukopenia has been observed during its administration; however, no persistent hematologic abnormalities attributable to metronidazole have been observed in clinical studies. Total and differential leukocyte counts are recommended before and after therapy for trichomoniasis and amebiasis, especially if a second course of therapy is necessary, and before and after therapy for anaerobic infections.

Drug Interactions

Metronidazole has been reported to potentiate the anticoagulant effect of warfarin and other oral coumarin anticoagulants, resulting in a prolongation of prothrombin time. This possible drug interaction should be considered when metronidazole is prescribed for patients on this type of anticoagulant therapy.

The simultaneous administration of drugs that induce microsomal liver enzymes, such as phenytoin or phenobarbital, may accelerate the elimination of metronidazole, resulting in reduced plasma levels; impaired clearance of phenytoin has also been reported.

The simultaneous administration of drugs that decrease microsomal liver enzyme activity, such as cimetidine, may prolong the half-life and decrease plasma clearance of metronidazole. In patients stabilized on relatively high doses of lithium, short-term metronidazole therapy has been associated with elevation of serum lithium and, in a few cases, signs of lithium toxicity. Serum lithium and serum creatinine levels should be obtained several days after beginning metronidazole to detect any increase that may precede clinical symptoms of lithium intoxication.

Alcoholic beverages should not be consumed during metronidazole therapy and for at least one day afterward because abdominal cramps, nausea, vomiting, headaches, and flushing may occur.

Psychotic reactions have been reported in alcoholic patients who are using metronidazole and disulfiram concurrently. Metronidazole should not be given to patients who have taken disulfiram within the last two weeks.

Drug/Laboratory Test Interactions

Metronidazole may interfere with certain types of determinations of serum chemistry values, such as aspartate aminotransferase (AST, SGOT), alanine aminotransferase (ALT, SGPT), lactate dehydrogenase (LDH), triglycerides, and hexokinase glucose. Values of zero may be observed. All of the assays in which interference has been reported involve enzymatic coupling of the assay to oxidation-reduction of nicotinamide adenine dinucleotide ($NAD^+ \leftrightarrows NADH$). Interference is due to the similarity in absorbance peaks of NADH (340 nm) and metronidazole (322 nm) at pH 7.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Metronidazole has shown evidence of carcinogenic activity in a number of studies involving chronic, oral administration in mice and rats.

Prominent among the effects in the mouse was the promotion of pulmonary tumorigenesis. This has been observed in all six reported studies in that species, including one study in which the animals were dosed on an intermittent schedule (administration during every fourth

week only). At very high dose levels (approx. 500 mg/kg/day which is approximately 33 times the most frequently recommended human dose for a 50 kg adult based on mg/kg body weight) there was a statistically significant increase in the incidence of malignant liver tumors in males. Also, the published results of one of the mouse studies indicate an increase in the incidence of malignant lymphomas as well as pulmonary neoplasms associated with lifetime feeding of the drug. All these effects are statistically significant.

Several long-term, oral-dosing studies in the rat have been completed. There were statistically significant increases in the incidence of various neoplasms, particularly in mammary and hepatic tumors, among female rats administered metronidazole over those noted in the concurrent female control groups.

Two lifetime tumorigenicity studies in hamsters have been performed and reported to be negative.

Although metronidazole has shown mutagenic activity in a number of *in vitro* assay systems, studies in mammals (*in vivo)* have failed to demonstrate a potential for genetic damage.

Fertility studies have been performed in mice at doses up to six times the maximum recommended human dose based on mg per sq. m. and have revealed no evidence of impaired fertility.

Pregnancy

Teratogenic Effects

Pregnancy category B

Metronidazole crosses the placental barrier and enters the fetal circulation rapidly. Reproduction studies have been performed in rats at doses up to five times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to metronidazole. No fetotoxicity was observed when metronidazole was administered orally to pregnant mice at 20 mg/kg/day approximately one and a half times the most frequently recommended human dose (750 mg/day) based on mg/kg body weight; however in a single small study where the drug was administered intraperitoneally, some intrauterine deaths were observed. The relationship of these findings to the drug is unknown. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, and because metronidazole is a carcinogen in rodents, this drug should be used during pregnancy only if clearly needed.

Use of metronidazole for trichomoniasis during pregnancy should be restricted to those in whom alternative treatment has been inadequate. Use of metronidazole for trichomoniasis in the first trimester of pregnancy should be carefully evaluated because metronidazole crosses the placental barrier and its effects on the human fetal organogenesis are not known (see above).

Nursing Mothers

Because of the potential for tumorigenicity, shown for metronidazole in mouse and rat studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. Metronidazole is secreted in human milk in concentrations similar to those found in plasma.

Geriatric Use

Decreased renal function does not alter the single-dose pharmacokinetics of metronidazole. However, plasma clearance of metronidazole is decreased in patients with decreased liver function. Therefore, in elderly patients, monitoring of serum levels may be necessary to adjust the metronidazole dosage accordingly.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established, except for the treatment of amebiasis.

ADVERSE REACTIONS

Two serious adverse reactions reported in patients treated with metronidazole have been convulsive seizures and peripheral neuropathy, the latter characterized mainly by numbness or paresthesia of an extremity. Since persistent peripheral neuropathy has been reported in some patients receiving prolonged administration of metronidazole, patients should be specifically warned about these reactions and should be told to stop the drug and report immediately to their physicians if any neurologic symptoms occur.

The most common adverse reactions reported have been referable to the gastrointestinal tract, particularly nausea reported by about 12% of patients, sometimes accompanied by headache, anorexia, and occasionally vomiting; diarrhea; epigastric distress; and abdominal cramping. Constipation has also been reported.

The following reactions have also been reported during treatment with metronidazole:

Mouth:	A sharp, unpleasant metallic taste is not unusual. Furry tongue, glossitis, and stomatitis have occurred; these may be ssociated with a sudden overgrowth of Candida which may occur during therapy.
Hematopoietic:	Reversible neutropenia (leukopenia); rarely, reversible thrombocytopenia.
Cardiovascular:	Flattening of the T-wave may be seen in electrocardiographic tracings.
Central Nervous System:	Convulsive seizures, peripheral neuropathy, dizziness, vertigo, incoordination, ataxia, confusion, irritability, depression, weakness, and insomnia.
Hypersensitivity:	Urticaria, erythematous rash, flushing, nasal congestion, dryness of the mouth (or vagina or vulva), and fever.
Renal:	Dysuria, cystitis, polyuria, incontinence, and a sense of pelvic pressure. Instances of darkened urine have been reported by approximately one patient in 100,000. Although the pigment which is probably responsible for this phenomenon has not been positively identified, it is almost certainly a metabolite of metronidazole and seems to have no clinical significance.
Other:	Proliferation of Candida in the vagina, dyspareunia, decrease of libido, proctitis, and fleeting joint pains sometimes resembling "serum sickness." If patients receiving metronidazole drink alcoholic beverages, they may experience abdominal distress, nausea, vomiting, flushing, or headache. A modification of the taste of alcoholic beverages has also been reported. Rare cases of pancreatitis, which generally abated on withdrawal of the drug, have been reported.

Crohn's disease patients are known to have an increased incidence of gastrointestinal and certain extraintestinal cancers. There have been some reports in the medical literature of breast and colon cancer in Crohn's disease patients who have been treated with metronidazole at high doses for extended periods of time. A cause and effect relationship has not been established. Crohn's disease is not an approved indication for metronidazole.

OVERDOSAGE

Single oral doses of metronidazole, up to 15 g, have been reported in suicide attempts and accidental overdoses. Symptoms reported include nausea, vomiting, and ataxia.

Oral metronidazole has been studied as a radiation sensitizer in the treatment of malignant tumors. Neurotoxic effects, including seizures and peripheral neuropathy, have been reported after 5 to 7 days of doses of 6 to 10.4 g every other day.

Treatment

There is no specific antidote for metronidazole overdose; therefore, management of the patient should consist of symptomatic and supportive therapy.

DOSAGE AND ADMINISTRATION

In elderly patients, the pharmacokinetics of metronidazole may be altered, and, therefore, monitoring of serum levels may be necessary to adjust the metronidazole dosage accordingly.

Trichomoniasis

In the Female

One-day treatment — two grams of metronidazole tablets, given either as a single dose or in two divided doses of one gram each given in the same day. *Seven-day course of treatment* — 250 mg three times daily for seven consecutive days. There is some indication from controlled comparative studies that cure rates as determined by vaginal smears, signs and symptoms, may be higher after a seven-day course of treatment than after a one day treatment regimen.

The dosage regimen should be individualized. Single-dose treatment can assure compliance, especially if administered under supervision, in those patients who cannot be relied on to continue the seven day regimen. A seven-day course of treatment may minimize reinfection by protecting the patient long enough for the sexual contacts to obtain appropriate treatment. Further, some patients may tolerate one treatment regimen better than the other.

Pregnant patients should not be treated during the first trimester. (See **CONTRAINDICATIONS**.) In pregnant patients in whom alternative treatment has been inadequate, the one-day course of therapy should not be used, as it results in higher serum levels which can reach the fetal circulation (see **PRECAUTIONS, Pregnancy**).

When repeat courses of the drug are required, it is recommended that an interval of four to six weeks elapse between courses and that the presence of the trichomonad be reconfirmed by appropriate laboratory measures. Total and differential leukocyte counts should be made before and after re-treatment.

In the Male

Treatment should be individualized as for the female.

Amebiasis

Adults

For acute intestinal amebiasis (acute amebic dysentery): 750 mg orally three times daily for 5 to 10 days.

For amebic liver abscess: 500 mg or 750 mg orally three times daily for 5 to 10 days.

Pediatric Patients

35 to 50 mg/kg/24 hours, divided into three doses, orally for 10 days. **Anaerobic Bacterial Infections**

In the treatment of most serious anaerobic infections, the intravenous form of metronidazole is usually administered initially.

The usual adult *oral* dosage is 7.5 mg/kg every six hours (approx. 500 mg for a 70 kg adult). A maximum of 4 g should not be exceeded during a 24 hour period. The usual duration of therapy is 7 to 10 days; however, infections of the bone and joint, lower respiratory tract, and endocardium may require longer treatment.

Patients with severe hepatic disease metabolize metronidazole slowly, with resultant accumulation of metronidazole and its metabolites in the plasma. Accordingly, for such patients, doses below those usually recommended should be administered cautiously. Close monitoring of plasma metronidazole levels[2] and toxicity is recommended.

The dose of metronidazole tablets should not be specifically reduced in anuric patients since accumulated metabolites may be rapidly removed by dialysis.

HOW SUPPLIED

Metronidazole tablets USP, 250 mg are available as round, convex, white compressed tablets debossed with “WPI” on one side and “3969” on the other side and are packaged in bottles of 100, 250, and 500. Metronidazole tablets, 500 mg are available as oblong, scored, white compressed tablets debossed with “WPI” on one side and “39” - “70” on the other side and are packaged in bottles of 50 and 500.

Dispense in a tight, light-resistant container as defined in the USP with a child-resistant closure (as required).

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

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1. Proposed standard: PSM-11 — Proposed Reference Dilution Procedure for Antimicrobic Susceptibility Testing of Anaerobic Bacteria, National Committee for Clinical Laboratory Standards; and Sutter, et al: Collaborative Evaluation of a Proposed Reference Dilution Method of Susceptibility Testing of Anaerobic Bacteria, Antimicrob. Agents Chemother. *16:* 495-502 (Oct.) 1979; and Tally, et al.: *In Vitro* Activity of Thienamycin, Antimicrob. Agents Chemother. 14:436-438 (Sept.) 1978.
2. Ralph, E.D., and Kirby, W.M.M.: Bioassay of Metronidazole With Either Anaerobic or Aerobic Incubation, J. Infect. Dis. *132*:587-591 (Nov.) 1975; or Gulaid, et al.: Determination of Metronidazole and Its Major Metabolites in Biological Fluids by High Pressure Liquid Chromatography, Br. J. Clin. Pharmacol. 6:430-432, 1978.

Manufactured By:
Watson Pharma Private Limited
Verna, Salcette Goa 403 722 INDIA

Distributed By:
Watson Pharma, Inc.
Corona, CA 92880 USA

Revised: December 2010

SAFETY DATA SHEET

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

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 (AS LABELED):		**METRONIDAZOLE CAPSULES and TABLETS**
CHEMICAL NAME:	For Active Ingredient:	2-Methyl-5-nitroimidazole-1-ethanol
CHEMICAL CLASS:		For Active Ingredient: Nitroimidazole
THERAPEUTIC CLASS:		Antibiotic/Antimicrobial/Antiprotozoal
HOW SUPPLIED:	375 mg Opaque, Light Green Capsule: NDC:50111-884-05: 50 in 1 bottle;	
	250 mg Round, White Tablet:	NDC:50111-333-01: 100 in 1 bottle; NDC:50111-333-06: 250 in 1 bottle; NDC:50111-333-02: 500 in 1 bottle;
	500 mg Oval, White Tablet:	NDC:50111-334-01: 100 in 1 bottle; NDC:50111-334-02: 500 in 1 bottle
RELEVANT USE of the SUBSTANCE		Pharmaceutical for Human Use

COMPANY/UNDERTAKING IDENTIFICATION:

U.S. SUPPLIER/MANUFACTURER'S NAME:	**TEVA**
ADDRESS:	1090 Horsham Road North Wales, PA 19454
BUSINESS PHONE:	215-591-3000 [08:00 AM --> 05:00 PM]
EUROPEAN SUPPLIER/MANUFACTURER'S NAME:	**TEVA/TAPI**
ADDRESS:	Sicor sri-Via Terrazzano 77-20017 Cho (MI), Italy
BUSINESS PHONE:	+39 02 93197 306 [08:00 AM --> 05:00 PM]
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:	November 22, 2013
DATE OF REVISION:	New

ALL WHMIS required information is included in appropriate sections based on the ANSI Z400.1-2010 format. This material has been classified in accordance with the hazard criteria of the CPR and the SDS contains all the information required by the CPR. The material is also classified per all applicable EU Directives through EC 1907: 2006, the European Union CLP EC 1272/2008 and 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 excepted 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 is supplied as capsules that are opaque light green and white round and oval tablets. **Health Hazards:** In the workplace, exposure via inhalation and skin contact may cause irritation. Eye contact with drug product can cause mechanical irritation. Accidental ingestion may be harmful. In therapeutic use, the most common adverse effects reported are nausea, headache, anorexia, and occasionally vomiting, diarrhea, epigastric distress, and abdominal cramping, sharp, metallic taste, overgrowth of Candida. Constipation has also been reported. Rare cases of pancreatitis have been reported. May cause adverse effects on neurological, cardiovascular system, Prolonged therapeutic use may cause super-infections. Use of alcohol while taking Metronidazole can cause an accumulation of systemic acetaldehyde, which can lead to serious effects or be fatal. Animal studies indicate significant carcinogenic potential. Limited evidence of mutagenic effects, based on animal data. 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 requires substantial pre-heating before ignition occurs. When involved in a fire, this product may decompose and produce irritating vapors and toxic compounds (including carbon, iron, magnesium, sodium, silicon, titanium and nitrogen oxides). **Reactivity Hazards:** This product is not reactive. **Environmental Hazards:** This product contains a compound that can cause long-term harm to aquatic organisms. **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/w	LABEL ELEMENTS EU Classification (67/548/EEC) GHS & EU Classification (1272/2008 EC) Risk Phrases/Hazard Statements
ACTIVE INGREDIENT				
Metronidazole 2-Methyl-5-nitroimidazole-1-ethanol	443-48-1	207-136-1	Proprietary	SELF CLASSIFICATION EU 67/548 Classification: Carcinogenic Cat. 2, Germ Cell Mutagen Cat. 3, Harmful, Irritant, Dangerous for the Environment Risk Phrase Codes: R45, R68, R22, R38, R52 Hazard Symbols: T, Xn/Xi GHS and EU 1272/2008 Classification: Carcinogenic Cat. 1B, Germ Cell Mutagen Cat. 2, Acute Oral Toxicity Cat. 4, Skin Irritation Cat. 2, Aquatic Chronic Toxicity Cat. 3 Hazard Codes: H350, H341, H302, H315, H412 Hazard Symbol/Pictogram: GHS07, GHS08
EXCIPIENTS				
Black Iron Oxide, Synthetic (capsules only)	1317-61-9	215-277-5	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Colloidal Silicon Dioxide (tablets only)	112945-52-5	Not Listed	Proprietary	SELF-CLASSIFICATION EU 67/548 Classification: Not Applicable Risk Phrase Codes: Not Applicable Hazard Symbols: Not Applicable GHS and EU 1272/2008 Classification: Acute Oral Toxicity Cat. 5 Hazard Codes: H303 Hazard Symbol/Pictogram: Not Applicable
Corn Starch/Pregelatinized Starch (capsules only)	9005-25-8	232-679-6	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Crospovidone (tablets only)	9003-39-8	Not Listed	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
D&C Yellow No. 10 (capsules only)	25013-16-5	Not Listed	Proprietary	SELF CLASSIFICATION EU 67/548 Classification: Harmful Risk Phrase Codes: R22 Hazard Symbols: Xn GHS & EU 1272/2008 Classification: Acute Oral Toxicity Cat. 4 Hazard Codes: H302 Hazard Symbol/Pictogram: GHS07
FD& C Blue # 1 (capsules only)	3844-45-9	223-339-4	Proprietary	SELF CLASSIFICATION EU (67/548/EEC): Classification: Harmful Risk Phrases: R22 Symbol: Xn EU/GHS 1272/2008: Classification: Acute Oral Toxicity Cat. 4 Hazard Statement Codes: H302 Hazard Symbols/Pictograms: GHS07
FD&C Blue No 2 (capsules only)	860-22-0	212-728-8	Proprietary	SELF CLASSIFICATION EU (67/548/EEC): Classification: Harmful Risk Phrases: R22 Symbol: Xn EU/GHS 1272/2008: Classification: Acute Oral Toxicity Cat. 4 Hazard Statement Codes: H302 Hazard Symbols/Pictograms: GHS07
FD&C Green # 3(capsules only)	2353-45-9	219-091-5	Proprietary	SELF CLASSIFICATION EU (67/548/EEC): Classification: Harmful Risk Phrases: R22 Symbol: Xn EU/GHS 1272/2008: Classification: Acute Oral Toxicity Cat. 4 Hazard Statement Codes: H302 Hazard Symbols/Pictograms: GHS07
FD& C Red No. 40 (capsules only)	4548-53-2	224-909-9	Proprietary	SELF CLASSIFICATION EU (67/548/EEC): Classification: Harmful Risk Phrases: R22 Symbol: Xn EU/GHS 1272/2008: Classification: Acute Oral Toxicity Cat. 4 Hazard Statement Codes: H302 Hazard Symbols/Pictograms: GHS07
Hydrogenated Cottonseed Oil (tablets only)	2001-29-4	232-280-7	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Magnesium Stearate (capsules only)	557-04-0	209-150-3	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.

See Section 16 for full classification information.

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
EXCIPIENTS (continued)				
Microcrystalline Cellulose (tablets only)	9004-34-6	232-674-9	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Gelatin (capsules only)	9000-70-8	232-554-6	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Propylene Glycol (capsules only)	57-55-6	200-338-0	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Shellac (capsules only)	9000-59-3	232-549-9	Proprietary	EU 67/548: Classification: Not applicable. GHS & EU 1272/2008: Classification: Not applicable.
Titanium Dioxide (capsules only)	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.

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: If skin contact with this product occurs, flush affected area with water. Minimum flushing is for 20 minutes. 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 occurs or continues after flushing.

Inhalation: If dusts 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 renal conditions, hepatic disease, active alcoholism, gastrointestinal disease, or Crohn's disease may be aggravated. Workplace exposure may also aggravate these conditions. Persons who may have hypersensitivity reactions to this product 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. There is no specific antidote for Metronidazole; therefore, management of the patient should consist of symptomatic and supportive therapy.

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.

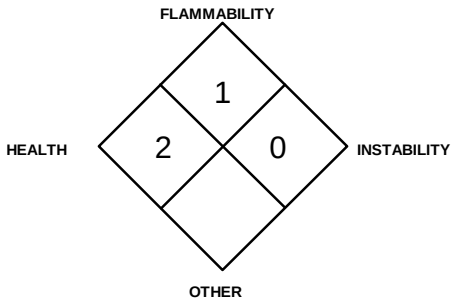
UNSUITABLE FIRE EXTINGUISHING MEDIA: None known.

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, magnesium, sodium, silicon, titanium and nitrogen oxides).

Explosion Sensitivity to Mechanical Impact: Not applicable.

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: 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.

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 product during spill response procedures as described below.

6. ACCIDENTAL RELEASE MEASURES (Continued)

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 (e.g. a single container).

Large Spills: For large spills (e.g., a pallet of containers), 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: Pick-up or wipe-up spilled capsules or tablets with damp absorbent sheets to prevent generation of dusts. Decontaminate the spill area (three times) using a bleach and detergent solution and then rinse with clean water.

Large Spills: Restrict access to the spill areas. Gently wet down area and carefully sweep up spilled product, avoiding the generation of airborne dusts. 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 product and report spill per regulatory requirements.

ENVIRONMENTAL PRECAUTIONS: Prevent product 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 and 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 product should be thoroughly trained to handle it safely. As with all chemicals, avoid getting this product ON YOU or IN YOU. Do not eat or drink while handling this product. After handling this product, wash face and hands thoroughly prior to eating, drinking, smoking or applying cosmetics. Ensure this product 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 product. Minimize all exposures to this product. Avoid generation of dusts. Areas in which this product is used should be wiped down, so that this dusts from product do not accumulate.

CONDITIONS FOR SAFE STORAGE: Containers of this product 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). Product 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 product; 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.

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	mg/m^3
Metronidazole	443-48-1	NE	NE	NE	NE	NE	NE	NE	**Teva OEL TWA = 200 µg/m³** (established 20Nov2012) Carcinogen: IARC-2B, NTP-R
Corn Starch/Pregelatinized Starch	9005-25-8	10	NE	15 (total dust), 5 (respirable fraction)	NE	10 (total dust), 5 (respirable fraction)	NE	NE	Carcinogen: TLV-A4

NE = Not Established

8. EXPOSURE CONTROLS - PERSONAL PROTECTION (Continued)

EXPOSURE LIMITS/CONTROL PARAMETERS (continued):

Workplace Exposure Limits/Control Parameters (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
Black Iron Oxide, Synthetic Exposure limits given are for CAS# 1309-37-1 (Fe2O3)	1317-61-9	5 (resp. fract.)	NE	10 (fume)	NE	5 (dusts & fume, as Fe)	NE	2500 (dust & fume, as Fe)	Carcinogen: IARC-3, MAK-3B, TLV-A4
Microcrystalline Sodium Exposure limits are for celluloses	9004-34-6	10	NE	15 (total dust), 5 (resp. fract.)	NE	10 (total dust), 5 (resp. fract.)	NE	NE	NE
Crospovidone	9003-39-8	NE	NE	NE	NE	NE	NE	NE	Carcinogen: IARC-3
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
D&C Yellow No. 10	25013-16-5	NE	NE	NE	NE	NE	NE	NE	NE
FD&C Blue No. 1	3844-45-9	NE	NE	NE	NE	NE	NE	NE	Carcinogen: IARC-3
FD&C Blue No. 2	860-22-0	NE	NE	NE	NE	NE	NE	NE	NE
FD&C Green No. 3	2353-45-9	NE	NE	NE	NE	NE	NE	NE	Carcinogen: IARC-3
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
Hydrogenated Cottonseed Oil Exposure limits given are for vegetable oil mist	8001-29-4	NE	NE	15 (total dust), 5 (resp. fract.)	NE	10 (total dust), 5 (resp. fract.)	NE	NE	NE
Magnesium Stearate Exposure limits are for Stearates	557-04-0	10	NE	NE	NE	NE	NE	NE	Carcinogen: TLV-A4
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
Titanium Dioxide	13463-67-7	10	NE	15 (total dust) 10 (vacated 1989 PEL)	NE	See NIOSH Pocket Guide Appendix A		Ca, 5000	Carcinogen: IARC-2B, MAK-3A, NIOSH-Ca, TLV-A4; NIC: TLV-A3

NE = Not Established NIC = Notice of Intended Change

International Occupational Exposure Limits: Exposure limits available for some excipient components are given below.

COLLOIDAL SILICON DIOXIDE:
Australia: TWA = 2 mg/m^3 (respirable dust), JUL 2008
CORN STARCH:
Belgium: TWA = 10 mg/m^3, MAR 2002
Korea: TWA = 10 mg/m^3, 2006
New Zealand: TWA = 10 mg/m^3 (inspirable dust), JAN 2002
Russia: STEL = 10 mg/m^3, JUN 2003
Switzerland: MAK-W = 3 mg/m^3, DEC 2006
United Kingdom: TWA = 10 mg/m^3 (inhalable dust), OCT 2007
United Kingdom: TWA = 4 mg/m^3 (respirable dust), OCT 2007
In Argentina, Bulgaria, Colombia, Jordan, Singapore, Vietnam check ACGIH TLV
GELATINS:
Russia: STEL = 10 mg/m^3, JUN 2003
MAGNESIUM STEARATE:
New Zealand: TWA = 10 mg/m^3 (inspirable dust), JAN 2002
Sweden: TWA = 5 mg/m^3, JUN 2005
Belgium: TWA = 10 mg/m^3, MAR 2002
IRON OXIDES:
ARAB Republic of Egypt: TWA = 3 ppm (5 mg/m^3) (fume), JAN 1993
Australia: TWA = 0.1 mg(Fe)/m^3, JUL 2008
Australia: TWA = 5 mg(Fe)/m^3 (fume), JUL 2008
Belgium: TWA = 2 ppm (5 mg(Fe)/m^3) (fume), MAR 2002
Denmark: TWA = 3.5 mg(Fe)/m^3, OCT 2002
Finland: TWA = 5 mg(Fe)/m^3, fume, SEP 2009
France: VME = 5 mg(Fe)/m^3 (fume), FEB 2006
Germany: MAK = 1.5 mg(Fe)/m^3 (respirable), 2005
Hungary: TWA = 6 mg/m^3 (resp), SEP2000
Japan: OEL = 1 mg/m^3 (respirable), 4 mg/m^3 (total), APR 2007
Korea: TWA = 10 mg/m^3, 2006
Korea: TWA = 5 mg/m^3, 2006
Mexico: TWA = 10 mg/m^3; STEL = 20 mg/m^3, 2004
The Netherlands: MAC-TGG = 5 mg(Fe)/m^3, 2003
The Netherlands: MAC-TGG = 10 mg/m^3, 2003
New Zealand: TWA = 5 mg(Fe)/m^3 (dust and fume), JAN 2002

IRON OXIDES (continued):
New Zealand: TWA = 10 mg/m^3 (inspirable dust), JAN 2002
Norway: TWA = 3 mg/m^3, JAN 1999
The Philippines: TWA = 10 mg/m^3 (fume), JAN 1993
Poland: MAC(TWA) fume = 5 mg/m^3, MAC(STEL) = 10 mg/m^3, JAN 1999
Russia: TWA = 6 mg/m^3, JUN 2003
Sweden: TWA = 3.5 mg(Fe)/m^3 (resp. dust), JUN 2005
Switzerland: MAK-W = 3 mg/m^3, DEC 2006
Thailand: TWA = 10 mg/m^3 (fume), JAN1993
Turkey: TWA = 10 mg/m^3 (fume), JAN 1993
United Kingdom: TWA = 4 mg/m^3 (respirable), 2005
United Kingdom: TWA = 10 mg/m^3 (inhalable), 2005
United Kingdom: TWA = 5 mg(Fe)/m^3;STEL = 10 mg(Fe)/m^3, 2005
In Argentina, Bulgaria, Colombia, Jordan, Singapore, Vietnam check ACGIH TLV
MICROCRYSTALLINE CELLULOSE:
Belgium: TWA = 10 mg/m^3, MAR 2002
France: VME = 10 mg/m^3, FEB 2006
Korea: TWA = 10 mg/m^3, 2006
Mexico: TWA = 10 mg/m^3; STEL = 20 mg/m^3, 2004
The Netherlands: MAC-TGG = 2 mg/m^3, 2003
New Zealand: TWA = 10 mg/m^3 (inspirable dust), JAN 2002
Russia: STEL = 10 mg/m^3, JUN 2003
Switzerland: MAK-W = W 6 mg/m^3, DEC 2006
United Kingdom: TWA = 10 mg/m^3 (inhalable), 2005
United Kingdom: TWA = 4 mg/m^3; STEL = 20 mg/m^3 (respirable), 2005
In Argentina, Bulgaria, Colombia, Jordan, Singapore, Vietnam, check ACGIH TLV
POVIDONE:
Russia: STEL = 10 mg/m^3, JUN 2003
PROPYLENE GLYCOL:
Australia: TWA = 10 mg/m^3 (particulates), JUL 2008
Australia: TWA = 150 ppm (474 mg/m^3) (total), JUL 2008
New Zealand: TWA = 10 mg/m^3 (particulates only), JAN 2002
New Zealand: TWA = 150 ppm (474 mg/m^3) (vapor and particulates), JAN 2002
Russia: STEL = 7 mg/m^3, JUN 2003
United Kingdom: TWA = 10 mg/m^3 (particulate), 2005
United Kingdom: TWA = 150 ppm (474 mg/m^3) (total vapor), 2005

8. EXPOSURE CONTROLS - PERSONAL PROTECTION (Continued)

EXPOSURE LIMITS/CONTROL PARAMETERS (continued):

International Occupational Exposure Limits (continued):

TITANIUM DIOXIDE:
ARAB Republic of Egypt: TWA = 15 mg/m^3, JAN 1993
Belgium: TWA = 10 mg/m^3, MAR 2002
Denmark: TWA = 6 mg(Ti)/m^3, OCT 2002
France: VME = 10 mg/m^3, FEB 2006
Germany: MAK = 1.5 mg/m^3 (respirable), 2005
Japan: OEL = 1 mg/m^3 (respirable), 4 mg/m^3 (total), APR 2007
Korea: TWA = 10 mg/m^3, 2006
Mexico: TWA = 10 mg(Ti)/m^3; STEL = 20 mg(Ti)/m^3, 2004
The Netherlands: MAC-TGG = 10 mg/m^3, 2003
New Zealand: TWA = 10 mg/m^3 (inspirable dust), JAN 2002

TITANIUM DIOXIDE (continued):
Norway: TWA = 5 mg/m^3, JAN 1999
Poland: MAC(TWA) = 10 mg(Ti)/m^3, MAC(STEL) = 30 mg(Ti)/m^3, JAN 1999
Russia: TWA = 10 mg/m^3, JUN 2003
Sweden: TWA = 5 mg/m^3 (total dust), JUN 2005
Switzerland: MAK-W = 3 mg/m^3, DEC 2006
Turkey: TWA = 15 mg/m^3, JAN 1993
United Kingdom: TWA = 10 mg/m^3 (inhalable), 2005
United Kingdom: TWA = TWA 4 mg/m^3 (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 CFR1910.132*), 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: Capsules and tablets.
COLOR: As described in Section 2.
ODOR: Practically odorless.
ODOR THRESHOLD: Not applicable.
MOLECULAR WEIGHT: Mixture.
MOLECULAR FORMULA: Mixture.
HOW TO DETECT THIS SUBSTANCE (identification/warning properties): The appearance may be a distinguishing characteristic of this product in event of accidental release.

The following information is for the Metronidazole active ingredient.

FORM: Crystalline solid.
COLOR: White to light yellow.
MOLECULAR WEIGHT: 171.15
MOLECULAR FORMULA: $C_6H_9N_3O_3$
ODOR: Not available.
ODOR THRESHOLD: Not available.
BOILING POINT @ 760 mmHg: 405.4°C (761.7°F) [predict.]
MELTING POINT: 159-163°C (318.2-325.4°F)
VAPOR PRESSURE (air = 1) @ 25°C: 0 mmHg [predict.]
SPECIFIC GRAVITY (water = 1): 1.452 g/cm^3 [predict.]
EVAPORATION RATE (nBuAc = 1): Not applicable.
FLASH POINT: 198.9°C (390°F) [predict.]
pH: Not available.
SOLUBILITY IN WATER @ 25°C: 11,000 mg/L
OTHER SOLUBILITIES: Soluble in dilute acids; sparingly soluble in dimethylformamide.
COEFFICIENT WATER/OIL DISTRIBUTION: Log Kow = -0.02; Log P: -0.135 [predict.]

10. STABILITY and REACTIVITY

CHEMICAL STABILITY: Stable under normal conditions.
DECOMPOSITION PRODUCTS: *Combustion:* Products of thermal decomposition may include carbon, iron, magnesium, sodium, silicon, titanium and nitrogen oxides. *Hydrolysis:* None known.
MATERIALS WITH WHICH SUBSTANCE IS INCOMPATIBLE: Incompatible with strong oxidizing agents, and 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 dusts generated by damaged capsules or tablets may slightly irritate the nose, throat, and lungs. In addition, inhalation may result in adverse effects as described under 'Other Potential Health Effects'.

SYMPTOMS OF EXPOSURE BY ROUTE OF EXPOSURE (continued):

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 information is available on possible skin absorption.

Ingestion: Accidental ingestion of this product (i.e., through poor hygiene practices) may be harmful. Other effects may occur as described under 'Other Potential Health Effects'.

Injection: Not a potential route of exposure for tablets.

OTHER POTENTIAL HEALTH EFFECTS: In therapeutic use, the most common adverse effects reported are nausea, headache, anorexia, and occasionally vomiting, diarrhea, epigastric distress, and abdominal cramping, sharp, metallic taste, overgrowth of Candida. Constipation has also been reported. Rare cases of pancreatitis have been reported. May cause adverse effects on neurological, cardiovascular system, Prolonged therapeutic use may cause super-infections. Use of alcohol while taking Metronidazole can cause an accumulation of systemic acetaldehyde, which can lead to serious effects or be fatal. Animal studies indicate significant carcinogenic potential. Limited evidence of mutagenic effects, based on animal data. Body systems adversely affected during therapeutic use are provided below. More details are also given in the Teva Active Ingredient SDS for Metronidazole.

- Body as a Whole
- Blood
- Central and Peripheral Nervous System
- Gastrointestinal System
- Hypersensitivity Reactions
- Reproductive System
- Renal System

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

HEALTH EFFECTS OR RISKS FROM EXPOSURE:

Acute: Dusts may cause irritation if inhaled and mechanical irritation to the eyes. Ingestion may be harmful or cause allergic reaction.

Chronic: Potential for carcinogenic effect. Limited evidence of mutagenic potential. Chronic exposure may cause adverse effects on the body systems described under 'Other Potential Health Effects'.

TARGET ORGANS: It is anticipated that for Occupational Exposure the target organs are: Acute: Skin, eyes, respiratory system. Chronic: Skin. In therapeutic use, product may have an impact on the body systems listed under 'Other Potential Health Effects'.

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

METRONIDAZOLE:

Standard Draize Test (Skin-Human) 0.75
Standard Draize Test (Skin-Human) 0.75%/3 weeks-continuous: Mild
Standard Draize Test (Skin-Woman) 0.75%/3 days-intermittent: Severe
Standard Draize Test (Skin-Woman) 0.75%: Moderate
Standard Draize Test (Skin-Woman) 2%: Mild
Standard Draize Test (Skin-Woman) 5
TDLo (Oral-Human) 39,600 mg/kg/4 weeks-intermittent: Peripheral Nerve and Sensation: sensory change involving peripheral nerve; Sense Organs and Special Senses (Taste): change in function; Behavioral: headache
TDLo (Oral-Woman) 40 mg/kg: Behavioral: hallucinations, distorted perceptions
TDLo (Oral-Woman) 12 mg/kg: Sense Organs and Special Senses (Eye): effect, not otherwise specified; Behavioral: tremor
TDLo (Oral-Woman) 85.8 mg/kg/14 days-intermittent: Gastrointestinal: nausea or vomiting, other changes
TDLo (Oral-Man) 3570 µg/kg/days: Liver: jaundice, other or unclassified, other changes; Nutritional and Gross Metabolic: body temperature increase
TDLo (Oral-Man) 1030 mg/kg/8 weeks: Peripheral Nerve and Sensation: paresthesis, structural change in nerve or sheath
TDLo (Intravenous-Woman) 100 mg/kg/5 days-intermittent: Behavioral: hallucinations, distorted perceptions, toxic psychosis, irritability
LD_{50} (Oral-Rat) 3 gm/kg: Behavioral: somnolence (general depressed activity); Lungs, Thorax, or Respiration: cyanosis; Nutritional and Gross Metabolic: body temperature decrease
LD_{50} (Oral-Mouse) 3800 mg/kg: Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: other oxidoreductases
LD_{50} (Oral-Mammal-Species Unspecified) 2074 mg/kg
LD_{50} (Intraperitoneal-Mouse) 870 mg/kg
LD_{50} (Intraperitoneal-Mammal-Species Unspecified) 492 mg/kg
LD_{50} (Subcutaneous-Mouse) 3640 mg/kg: Behavioral: somnolence (general depressed activity), tremor, convulsions or effect on seizure threshold
TDLo (Oral-Rat) 2500 mg/kg: Reproductive: Paternal Effects: testes, epididymis, sperm duct; Related to Chronic Data: changes in testicular weight
TDLo (Oral-Rat) 34 gm/kg/34 days-continuous: Kidney/Ureter/Bladder: hematuria; Related to Chronic Data: death, changes in testicular weight
TDLo (Oral-Rat) 219 gm/kg/2 years-continuous: Tumorigenic: carcinogenic by RTECS criteria; Liver: tumors Skin and Appendages: tumors
TDLo (Oral-Rat) 27 gm/kg/35 weeks-continuous: Tumorigenic: equivocal tumorigenic agent by RTECS criteria; Skin and Appendages: tumors; Reproductive: Tumorigenic effects: uterine tumors
TDLo (Oral-Rat) 16,800 mg/kg: male 42 day(s) pre-mating: Reproductive: Fertility: male fertility index (e.g. # males impregnating females per # males exposed to fertile non-pregnant females)
TDLo (Oral-Rat) 22,400 mg/kg: male 56 day(s) pre-mating: Reproductive: Paternal Effects: spermatogenesis (incl. genetic material, sperm morphology, motility, and count), testes, epididymis, sperm duct

METRONIDAZOLE (continued):

TDLo (Oral-Rat) 3 gm/kg/14 weeks-continuous: Tumorigenic: neoplastic by RTECS criteria; Skin and Appendages: tumors
TDLo (Oral-Rat) 22,400 mg/kg: male 56 day(s) pre-mating: Reproductive: Paternal Effects: spermatogenesis (incl. genetic material, sperm morphology, motility, and count), testes, epididymis, sperm duct
TDLo (Oral-Mouse) 7000 mg/kg/14 days-intermittent: Blood: normocytic anemia; Related to Chronic Data: changes in prostate weight, changes in testicular weight
TDLo (Oral-Mouse) 181 gm/kg/72 weeks-continuous: Tumorigenic: carcinogenic by RTECS criteria; Lungs, Thorax, or Respiration: tumors; Blood: lymphoma, including Hodgkin's disease
TDLo (Oral-Mouse) 8 gm/kg/14 weeks-continuous: Tumorigenic: neoplastic by RTECS criteria; Lungs, Thorax, or Respiration: tumors; Blood: lymphoma, including Hodgkin's disease
TDLo (Oral-Mouse) 21,800 mg/kg/2 years-intermittent: Tumorigenic: carcinogenic by RTECS criteria; Liver: tumors
TDLo (Oral-Mouse) 1680 mg/kg: Tumorigenic: carcinogenic by RTECS criteria; Reproductive: Tumorigenic effects: transplacental tumorigenesis; Lungs, Thorax, or Respiration: tumors
TDLo (Oral-Mouse) 7000 mg/kg: male 14 day(s) pre-mating: Reproductive: Specific Developmental Abnormalities: Central Nervous System; Effects on Newborn: growth statistics (e.g.%, reduced weight gain), biochemical and metabolic
TDLo (Oral-Dog) 6500 mg/kg/26 days-intermittent: Brain and Coverings: other degenerative changes; Nutritional and Gross Metabolic: weight loss or decreased weight gain; Related to Chronic Data: death
TDLo (Intraperitoneal-Rat) 1750 mg/kg: female 7 day(s) pre-mating: Reproductive: Fertility: post-implantation mortality (e.g. dead and/or resorbed implants per total number of implants)
TDLo (Intraperitoneal-Mouse) 910 mg/kg/7 days-intermittent: Reproductive: Paternal Effects: spermatogenesis (incl. genetic material, sperm morphology, motility, and count)
TDLo (Intraperitoneal-Mouse) 196 mg/kg/14 days-intermittent: Endocrine: changes in spleen weight; Blood: changes in other cell count (unspecified); Immunological Including Allergic: decreased immune response
TDLo (Intraperitoneal-Mouse) 392 mg/kg/14 days-intermittent: Blood: changes in erythrocyte (RBC) count; Immunological Including Allergic: decreased immune response; Nutritional and Gross Metabolic; weight loss or decreased weight gain
TDLo (Intraperitoneal-Mouse) 798 mg/kg/14 days-intermittent: Blood: granulocytopenia, changes in spleen; Immunological Including Allergic: decreased immune response
TDLo (Intraperitoneal-Mouse) 60 mg/kg: female 8-14 day(s) after conception: Reproductive: Effects on Embryo or Fetus: fetal death; Specific Developmental Abnormalities: other developmental abnormalities
TDLo (Unreported-Rat) 750 mg/kg: female 30 day(s) pre-mating: Reproductive: Maternal Effects: uterus, cervix, vagina
Body Fluid Assay (Human Bacteria-*Salmonella typhimurium*) 10 mg/kg
Cytogenetic Analysis (Unreported-Human) 86 mg/kg/30 days

11. TOXICOLOGICAL INFORMATION (Continued)

TOXICITY DATA (continued):

METRONIDAZOLE (continued):
Cytogenetic Analysis (Human Lymphocyte) 500 mg/L
Cytogenetic Analysis (Oral-Human) 250 mg/kg/10 days-continuous
DNA Damage (Oral-Human) 214.3 mg/kg/10 days
DNA Damage (Human Lymphocyte) 10 mg/L/30 minutes
Sister Chromatid Exchange (Human Lymphocyte) 10 µg/kg/20 minutes
Mutation in Microorganisms (Bacteria-*Salmonella typhimurium*) 25 µg/plate
Mutation in Microorganisms (Bacteria-*Salmonella typhimurium*) 50 µg/plate
Mutation in Microorganisms (Bacteria-*Escherichia coli*) 100 µmol/L
Mutation in Microorganisms (Bacteria-*Escherichia coli*) 1 gm/L
Mutation in Microorganisms (Bacteria-*Klebsiella pneumoniae*) 20 µmol/L/20 hours
Mutation in Microorganisms (Bacteria-*Salmonella typhimurium*) 156 µg/plate/20 minutes
Mutation in Microorganisms (Bacteria-*Salmonella typhimurium*) 156 µg/plate/48 hours
Mutation in Microorganisms (Microorganism-Not Otherwise Specified) 25 µmol/L
Mutation in Microorganisms (Mold-*Neurospora crassa*) 8800 mg/L
Sister Chromatid Exchange (Monkey Lymphocyte) 10 mg/L/72 hours
Mutation Test Systems-Not Otherwise Specified (Bacteria-*Escherichia coli*) 4 mg/L
Mutation Test Systems-Not Otherwise Specified (Microorganism-Not Otherwise Specified) 5 mg/L
DNA Repair (Bacteria-*Escherichia coli*) 200 µg/disc
DNA Repair (Bacteria-*Bacillus subtilis*) 200 µg/disc
DNA Inhibition (Microorganism-Not Otherwise Specified) 1 mg/L
DNA Inhibition (Microorganism-Not Otherwise Specified) 5 mg/L
DNA Inhibition (Mouse Lymphocyte) 30 mmol/L/1 hour-continuous

METRONIDAZOLE (continued):
DNA Inhibition (Mouse Cells-Not Otherwise Specified) 100 mg/L
DNA Inhibition (Hamster Lung) 1 mmol/L/6 days-continuous
DNA Damage (Rat Liver) 3 mmol/L
DNA Damage (Mouse Lymphocyte) 30 mmol/L/4 hours-continuous
DNA Damage (Mouse Fibroblast) 300 µmol/L
DNA Adduct (Bacteria-*Escherichia coli*) 2 µmol/L
DNA Adduct (Mammal-Species Unspecified Lymphocyte) 60 µmol/L
Phage Inhibition Capacity (Bacteria-*Escherichia coli*) 500 µg/plate
Body Fluid Assay (Rat Bacteria-*Salmonella Typhimurium*) 800 mg/kg
Body Fluid Assay (Rat Bacteria-*Salmonella Typhimurium*) 100 mg/kg
Cytogenetic Analysis (Oral-Mouse) 1200 mg/kg
Cytogenetic Analysis (Oral-Mouse) 7000 mg/kg/14 days-intermittent
Cytogenetic Analysis (Hamster Lung) 10 mmol/L
Cytogenetic Analysis (Monkey Lymphocyte) 10 mg/L/72 hours
Host-Mediated Assay (Mouse Bacteria-*Salmonella Typhimurium*) 400 mg/kg/5 days
Host-Mediated Assay (Mouse Bacteria-*Escherichia coli*) 4 mg/kg/2 hours
Host-Mediated Assay (Mouse Yeast-*Saccharomyces Cerevisiae*) 25 mmol/kg
Host-Mediated Assay (Hamster Embryo) 200 mg/kg
Sister Chromatid Exchange (Oral-Hamster) 125 mg/kg
Micronucleus Test (Oral-Mouse) 7000 mg/kg/14 days-intermittent
Micronucleus Test (Intravaginal-Rat) 100 mg/kg/5 days-intermittent
Micronucleus Test (Multiple Routes-Fish-Not Otherwise Specified) 20 ppm/24 hours-continuous

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

Metronidazole has shown evidence of carcinogenic activity in a number of studies involving chronic, oral administration in mice and rats, but similar studies in the hamster gave negative results. Prominent among the effects in the mouse was the promotion of pulmonary tumorigenesis. This has been observed in all six reported studies in that species, including one study in which the animals were dosed on an intermittent schedule (administration during every fourth week only). At very high dose levels (approximately 1500 mg/m^2 which is approximately 3 times the most frequently recommended human dose for a 50 kg adult based on mg/m^2) there was a statistically significant increase in the incidence of malignant liver tumors in males. Also, the published results of one of the mouse studies indicate an increase in the incidence of malignant lymphomas as well as pulmonary neoplasms associated with lifetime feeding of the drug. All these effects are statistically significant.

Several long-term, oral-dosing studies in the rat have been completed. There were statistically significant increases in the incidence of various neoplasms, particularly in mammary and hepatic tumors, among female rats administered Metronidazole over those noted in the concurrent female control groups.

Two lifetime tumorigenicity studies in hamsters have been performed and reported to be negative.

This material is listed by agencies tracking carcinogenic potential as follows.

IARC-2B (Possibly Carcinogenic to Humans); NTP-R (Reasonably Anticipated to Be a Human Carcinogen)

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)

FD&C BLUE No. 1, FD&C Green No. 3, FD&C RED No. 40, POVIDONE: IARC-3 (Unclassifiable as to Carcinogenicity in Humans)

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.)

MAGNESIUM STEARATE (as a stearate), CORN STARCH: ACGIH TLV-A4 (Not Classifiable as a Human Carcinogen)

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); Notice of Intended Change: ACGIH TLV-A3 (Confirmed Animal Carcinogen with Unknown Relevance to Humans)

No other component of this product is 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 MATERIAL: In therapeutic use, hives, red, raised, bumpy rash, Stevens-Johnson Syndrome, toxic epidermal necrolysis (skin reaction that can cause destruction of skin and can be fatal), flushing, nasal congestion, dryness of the mouth (or vagina or vulva), inflammation of anus and lining of rectum and fever have been reported.

REPRODUCTIVE TOXICITY INFORMATION: There are no adequate and well-controlled studies of Metronidazole in pregnant women; however, when administered therapeutically, Metronidazole is not expected to cause fetal harm when administered to a pregnant woman. This product is rated by the FDA for therapeutic risk as Pregnancy Risk Category B. Refer to Definition of Terms for full Pregnancy Risk category definitions.

Mutagenicity: Metronidazole has shown mutagenic activity in a number of *in vitro* assay systems. *In vivo* studies have failed to demonstrate a potential for genetic damage.

Embryotoxicity/Teratogenicity:

Human Information: Use of Metronidazole in the first trimester should be carefully evaluated because Metronidazole crosses the placental barrier and its effects on human fetal organogenesis are not known.

Animal Information: Metronidazole crosses the placental barrier and enters the fetal circulation rapidly. Reproduction studies have been performed in rats at doses up to five times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Metronidazole. No fetotoxicity was observed when Metronidazole was administered orally to pregnant mice at 60 mg/m^2/day, which is approximately 10% of the human dose when expressed as mg/m^2. However, in a single small study where the drug was administered intraperitoneally, some intrauterine deaths were observed. The relationship of these findings to the drug is unknown.

11. TOXICOLOGICAL INFORMATION (Continued)

REPRODUCTIVE TOXICITY INFORMATION (continued):

Reproductive Toxicity: Fertility studies have been performed in mice at doses up to six times the maximum recommended human dose based on mg/m^2 and have revealed no evidence of impaired fertility. Metronidazole is secreted in human milk in concentrations similar to those found in plasma. Because there is potential for 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: Because animal reproduction studies are not always predictive of human response, and because Metronidazole is a carcinogen in rodents, this drug should be used during pregnancy only if clearly needed.

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.

Information is available for the active ingredient, but is not presented in this SDS. More details are also given in the Teva Active Ingredient SDS for Metronidazole.

MOBILITY: Currently, there is no specific information available on the potential mobility of this product.

PERSISTENCE AND BIODEGRADABILITY: Currently, there is no specific information on persistence and biodegradability of this product. Some biodegradation is expected.

BIO-ACCUMULATION POTENTIAL: Currently, no specific information is available on the bioconcentration potential of this product.

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. The following animal and aquatic toxicity data are available for the active ingredient.

METRONIDAZOLE:

LD_{50} (*Anas platyrhynchos* Mallard duck) 19 weeks old) > 5000 mg/kg
LC_{50} (*Anas platyrhynchos* Mallard duck 17 days old) 8 days = > 5000 ppm/8 days
LC_{50} (Colinus virginianus Bobwhite quail) 12 days old) 8 days = > 5000 ppm/8 days
LC_{50} (Americamysis bahia Opossum shrimp) age 2 days) 96 hours = 182 ppm (95% confidence limit: 140-230 ppm); static /98% AI formulated product
LC_{50} (*Lepomis macrochirus* Bluegill sunfish, weight 0.1g) 96 hours = >100 ppm; static /99.4% AI formulated product
LC_{50} (*Oncorhynchus mykiss* Rainbow trout, weight 0.3 g) 96 hours = >100 ppm; static /99.4% AI formulated product
LC_{50} (*Cyprinodon variegatus* Sheepshead minnow, weight 0.46 g) 96 hours = 1060 ppm; static /98% AI formulated product
EC_{50} (*Daphnia magna* Water flea, age < 24 hr; intoxication, immobilization) 48 hours = >1000 ppm; static /99% AI formulated product
EC_{50} (*Crassostrea virginica* Eastern oyster, embryo) intoxication, immobilization) 48 hours = 1012 ppm; static /98% AI formulated product
EC_{50} (*Pseudokirchneriella subcapitata* Green algae; decreased population growth) 72 hours = 40.4 mg/L (95% confidence limit: 2.17-750 mg/L); static

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.

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 product 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.

14. TRANSPORTATION INFORMATION (Continued)

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 is not specifically listed in Annex III under MARPOL 73/78.

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 the 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 (FDA) 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): The Metronidazole component is on the California Proposition 65 Lists. WARNING! This product contains a compound known to the State of California to cause cancer.

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.
- Canadian Environmental Protection Act (CEPA) Priority Substances Lists: Components are not on the CEPA substances lists.
- Other Canadian Regulations: Requirements under the Canadian Heath Canada, Laboratory Biosafety Guidelines may be applicable.
- 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!** MAY CAUSE RESPIRATORY SYSTEM, EYE, AND SKIN IRRITATION. NON-THERAPEUTIC INGESTION MAY BE HARMFUL. ANIMAL TESTING INDICATES SIGNIFICANT CARCINOGENIC POTENTIAL. LIMITED EVIDENCE OF MUTAGENIC POTENTIAL, BASED ON ANIMAL DATA. MAY CAUSE CHRONIC EFFECTS TO AQUATIC ORGANISMS. 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 CO_2, 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.

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.

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.

16. OTHER INFORMATION (Continued)

CLASSIFICATION FOR COMPONENTS:

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

Metronidazole: This is a self-classification.

Classification: Carcinogenic Category 1B, Germ Cell Mutagen Category 2, Acute Oral Toxicity Category 4, Skin Irritation Category 2, Aquatic Chronic Toxicity Category 3

Hazard Statement Codes: H350: May cause cancer. H341: Suspected of causing genetic effects. H302: Harmful if swallowed. H315: Causes skin irritation. H412: Harmful to aquatic life with long lasting effects.

Colloidal Silicon Dioxide: This is a self-classification.

Classification: Acute Oral Toxicity Category 5

Hazard Statements: H303: May be harmful if swallowed.

D&C Yellow No. 10, FD&C Blue No. 1, FD&C Blue No. 2, FD&C Green No. 3, FD&C Red No. 40: This is a self-classification.

Classification: Acute Oral Toxicity Category 4

Hazard Statements: H302: Harmful if swallowed.

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

Full Text EU 67/548/EEC:

Metronidazole: This is a self-classification.

Classification: Carcinogenic Category 2, Germ Cell Mutagen Category 3, Harmful, Dangerous for the Environment

Risk Phrases: R45: May cause cancer. R68: Possible risk of irreversible effects. R22: Harmful if swallowed. R38: Irritating to skin. R52: Harmful to aquatic organisms.

D&C Yellow No. 10, FD&C Blue No. 1, FD&C Blue No. 2, FD&C Green No. 3, FD&C Red No. 40: 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.

PREPARED BY: CHEMICAL SAFETY ASSOCIATES, Inc. • PO Box 1961, Hilo, HI 96721-1961 • (800) 441-3365

DATE OF PRINTING: November 22, 2013

REVISION HISTORY: New.

DEFINITIONS OF TERMS

A 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:

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

EXPOSURE LIMITS IN AIR:

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.

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 a 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 LD_{50} Rat*: < 5000 mg/kg. *Dermal Toxicity LD_{50}Rat or Rabbit*: < 2000 mg/kg. *Inhalation Toxicity 4-hrs LC_{50} 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 LD_{50} Rat*: > 500-5000 mg/kg. *Dermal Toxicity LD_{50}Rat or Rabbit*: > 1000-2000 mg/kg. *Inhalation Toxicity LC_{50}* 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 LD_{50} Rat*: > 50-500 mg/kg. *Dermal Toxicity LD_{50}Rat or Rabbit*: > 200-1000 mg/kg. *Inhalation Toxicity LC_{50} 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 LD_{50} Rat*: > 1-50 mg/kg. *Dermal Toxicity LD_{50}Rat or Rabbit*: > 20-200 mg/kg. *Inhalation Toxicity LC_{50} 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 LD_{50} Rat*: ≤ 1 mg/kg. *Dermal Toxicity LD_{50}Rat or Rabbit*: ≤ 20 mg/kg. *Inhalation Toxicity LC_{50} 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: 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.];

HAZARDOUS MATERIALS IDENTIFICATION SYSTEM HAZARD RATINGS (continued):

FLAMMABILITY HAZARD (continued): 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 and 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*: Packing Group II Solids: any material that, either in 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*: Packing 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 and 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 LC_{50} for acute inhalation toxicity greater than 10,000 ppm. Dusts and mists with an LC_{50} for acute inhalation toxicity greater than 200 mg/L. Materials with an LD_{50} for acute dermal toxicity greater than 2000 mg/kg. Materials with an LD_{50} 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 LC_{50} for acute inhalation toxicity greater than 5,000 ppm but less than or equal to 10,000 ppm. Dusts and mists with an LC_{50} for acute inhalation toxicity greater than 10 mg/L but less than or equal to 200 mg/L. Materials with an LD_{50} 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 LD_{50} for acute oral toxicity greater than 500 mg/kg but less than or equal to 2000 mg/kg. **2** Materials that, under emergency conditions, can cause temporary incapacitation or residual injury. Gases with an LC_{50} for acute inhalation toxicity greater than 3,000 ppm but less than or equal to 5,000 ppm.

DEFINITIONS OF TERMS (Continued)

NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS (continued):

HEALTH HAZARD (continued): **2 (continued):** Any liquid whose saturated vapor concentration at 20°C (68°F) is equal to or greater than one-fifth its LC_{50} for acute inhalation toxicity, if its LC_{50} 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 LC_{50} for acute inhalation toxicity greater than 2 mg/L but less than or equal to 10 mg/L. Materials with an LD_{50} 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 LD_{50} for acute oral toxicity is greater than 50 mg/kg but less than or equal to 500 mg/kg. Dusts and mists with an LC_{50} for acute inhalation toxicity greater than 10 mg/L but less than or equal to 200 mg/L. Materials with an LD_{50} 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 LD_{50} 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 LC_{50} for acute inhalation toxicity is greater than 1,000 ppm but less than or equal to 3,000 ppm. Dusts and mists whose LC_{50} for acute inhalation toxicity is greater than 0.5 mg/L but less than or equal to 2 mg/L. Materials whose LD_{50} for acute dermal toxicity is greater than 40 mg/kg but less than or equal to 200 mg/kg. Materials whose LD_{50} 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 LC_{50} for acute inhalation toxicity, if its LC_{50} 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 LC_{50} for acute inhalation toxicity less than or equal to 1,000 ppm. Dusts and mists whose LC_{50} for acute inhalation toxicity is less than or equal to 0.5 mg/L. Materials whose LD_{50} for acute dermal toxicity is less than or equal to 40 mg/kg. Materials whose LD_{50} 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 LC_{50} for acute inhalation toxicity, if its LC_{50} 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 according 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 up 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. **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 100W/mL.

NATIONAL FIRE PROTECTION ASSOCIATION HAZARD RATINGS (continued):

INSTABILITY HAZARD: **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 **N**ational **F**ire **P**rotection **A**ssociation (**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: **LD_{50}** - Lethal Dose (solids and liquids) which kills 50% of the exposed animals; **LC_{50}** - 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/m^3** 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; **TDo**, **LDLo**, and **LDo**, or **TC**, **TCo**, **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. **O**ccupational **S**afety and **H**ealth **A**dministration (**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.