

# MATERIAL SAFETY DATA SHEET

Boehringer Ingelheim Pharmaceuticals, Inc.

**Aggrenox®**

900 Ridgebury Road  
P.O. Box 368  
Ridgefield, CT 06877

(203) 798-5521 9AM - 4PM EST

REVISED: 9/12/05

**EMERGENCY TELEPHONE NUMBER**  
**CHEMTREC - 24 hours**  
**1-800-424-9300**

## 1. SUBSTANCE IDENTIFICATION

CHEMICAL NAME: 2, 6- bis-(Diethanolamino)-4,8-dipiperidinopyrimido-(5,4-d)-pyrimidine  
& 2-Acetoxy-benzoic acid

CAS TYPE: 1

GENERIC NAME: Dipyridamole & aspirin

MOLECULAR FORMULA:  $C_{24}H_{40}N_8O_6 + C_9H_8O_4$

TRADEMARK: Aggrenox ®

MOLECULAR WEIGHT: 504.63 + 180.16

CHEMICAL FAMILY: Platelet aggregation inhibitor CAS NUMBER: 35763-39-4 Dipyridamole  
50-78-2 : 2 -Acetoxy-benzoic acid

PRODUCT USE: Antiplatelet Agent

## 2. HAZARD IDENTIFICATION

### EMERGENCY OVERVIEW

**For Product:**

**Physical State:** Hard red and ivory gelatin capsule

**WARNING!**

May be harmful if swallowed.

Aggrenox® is a combination platelet agent (dipyridamole and aspirin).

**Potential Health Effects – Product:**

**Aggrenox® is not interchangeable with the individual components of aspirin and Persantin® Tablets.**

CONTRAINDICATIONS: Hypersensitivity to **Aggrenox®** or to any other component of the therapeutic system.

ADVERSE REACTIONS TO PRODUCT: Dizziness, hypotension, headache, nausea, rash, and diarrhea may occur.

Overdosage: Hypotension, ataxia, depression, and vomiting.

ROUTES OF ENTRY: Ingestion

ACUTE EXPOSURE:

INHALATION: Not expected to be an inhalation hazard.

EYE CONTACT: Not expected to be a hazard to the eye.

SKIN CONTACT: Can cause hypersensitive reactions. Exposure may cause redness, itching and inflammation.

INGESTION: Not expected to be an ingestion hazard. May be harmful .Ingestion may cause dizziness, dyspepsia, abdominal pain, fatigue, headache, drowsiness, weakness, nausea, palpitations, hypotension, and other systemic effects.

CHRONIC EXPOSURE: Possible hypersensitization (development of abnormal sensitivity).

TARGET ORGANS: Cardiovascular system, liver, kidneys

MEDICAL CONDITIONS POTENTIALLY AGGRAVATED BY EXPOSURE: Hypersensitivity to dipyridamole, tartrazine dye or aspirin; coronary, artery disease, hypotension, hepatic or renal failure.

OSHA REGULATORY STATUS: OSHA Exempt for product.

CARCINOGENICITY: Not listed as a carcinogen or potential carcinogen by NTP, IARC Monographs or OSHA.

---

### 3. COMPONENTS PER UNIT DOSE

---

MATERIAL	EXPOSURE LIMITS
Active Ingredient:	
Dipyridamole 200 mg	1,000 ug/m <sup>3</sup> BIEL*
Aspirin 25 mg	5 mg/m <sup>3</sup> ACGIH 8-hr TLV-TWA (blood)
Excipients:	
Acacia	No TLV established
Aluminum stearate	10 mg/m <sup>3</sup> ACGIH 8-hr TLV-TWA (regulated as a member of the generics group aluminum stearates (except stearates of toxic metals) (irritation) 2 mg/m <sup>3</sup> ACGIH 8-hr TLV-TWA (aluminum, soluble salts, as Al) (except stearates of toxic metals) (irritation)
Colloidal Silicon Dioxide	10 mg/m <sup>3</sup> ACGIH 8-hr TLV-TWA (based on precipitated silica and silica gel) .8 mg/m <sup>3</sup> OSHA Z-3 8-hr TWA (silica: amorphous, including natural diatomaceous earth)
Corn starch	No TLV established
Dimethicone	No TLV established
Hydroxypropyl methylcellulose	No TLV established
Hydroxypropyl methylcellulose phthalate	No TLV established
Lactose monohydrate	No TLV established
Methacrylic acid copolymer	20 ppm ACGIH 8-hr TLV-TWA (irritation) (methacrylic acid)

Microcrystalline cellulose	20 ppm OSHA Table Z-1 (skin) (methacrylic acid) 10 mg/m <sup>3</sup> ACGIH 8-hr TLV-TWA (irritation) 5 mg/m <sup>3</sup> OSHA Table Z-1 (cellulose, respirable fraction) 15 mg/m <sup>3</sup> OSHA Table Z-1 (cellulose, total dust)
Povidone	No TLV established
Stearic acid	10 mg/m <sup>3</sup> ACGIH 8-hr TLV-TWA (stearates (except stearates of toxic metals) (irritation)
Sucrose	10 mg/m <sup>3</sup> ACGIH 8-hr TLV-TWA (lung) 5 mg/m <sup>3</sup> OSHA Table Z-1 (sucrose, respirable fraction) 15 mg/m <sup>3</sup> OSHA Table Z-1 (sucrose, total dust)
Talc	2 mg/m <sup>3</sup> ACGIH 8-hr TLV-TWA (talc, containing no asbestos fibers, respirable fraction) (lung) 20 mppcf (million particles/cubic foot) OSHA Table Z-3 (silicates, less than 1% crystalline silica: talc, not containing asbestos) 0.1 mg/m <sup>3</sup> OSHA Table Z-3 (talc, not containing asbestos, 1% or more crystalline silica, respirable) 0.3 mg/m <sup>3</sup> OSHA Table Z-3 8-hr TLV-TWA (talc, not containing asbestos, 1% or more crystalline silica, total dust)
Tartaric acid	No TLV established
Titanium dioxide	10 mg/m <sup>3</sup> ACGIH 8-hr TLV-TWA (lung) 15 mg/m <sup>3</sup> OSHA Table Z-1 (titanium dioxide, total dust)
Triacetin	No TLV established *BIEL is the Boehringer Ingelheim Exposure Limit. Where governmentally imposed occupational exposure limits are lower, such limits should take precedence.

---

#### 4. EMERGENCY FIRST AID PROCEDURES

---

**Persons developing anaphylactic (life-threatening) reactions, such as difficulty in breathing or unconsciousness, must receive immediate medical attention.**

**INHALATION:** Should not pose a hazard in final form. Move to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention immediately.

**EYE CONTACT:** Should not pose a hazard in final form. Any material that contacts the eye should be washed out immediately with water. If easy to do, remove contact lenses if worn. Get medical attention if irritation persists.

**SKIN CONTACT:** Should not pose a hazard in final form. Immediately flush with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Get medical attention.

**INGESTION:** Call a physician or poison control center immediately. Only induce vomiting at the instruction of medical personnel. Never give anything by mouth to an unconscious person.

**NOTE TO PHYSICIAN:** Supportive treatment.

---

#### 5. FIRE AND EXPLOSION HAZARD DATA

---

Flash Point	Flammable Limits	
	Upper	Lower
N/A	N/A	N/A

**FIRE EXTINGUISHING MEDIA:** Water spray, dry chemical, carbon dioxide or material appropriate for surrounding fire.

SPECIAL FIRE FIGHTING PROCEDURES: Wear self-contained breathing apparatus and protective clothing. Cool fire exposed containers with water.

UNUSUAL FIRE AND EXPLOSION HAZARDS: None

HAZARDOUS COMBUSTION PRODUCTS: Carbon dioxide, carbon monoxide, nitroxides and hydrogen chloride

---

## 6. SPILL AND ACCIDENTAL RELEASE MEASURES

---

STEPS TO BE TAKEN IF SIGNIFICANT QUANTITIES OF GEL CAPSULES ARE BROKEN: Wear approved respirator, eye protection, personal protective coverings and gloves. Absorb spilled liquid and collect for disposal. Place spillage in appropriate container for waste disposal. Wash contaminated clothing before reuse.

---

## 7. PRECAUTIONS FOR SAFE HANDLING AND USE

---

HANDLING AND STORAGE PRECAUTIONS: Store in tight container. Store at temperatures 25° C (77° F). Store away from foodstuffs.

HANDLING SIGNIFICANT QUANTITIES OF BROKEN CAPSULES: Avoid contact with eyes, skin or clothing. Wash hands thoroughly after handling.

---

## 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

---

Engineering Controls: Not generally required when handling containers or capsules. (See Section 3 for exposure limits.)

Good general ventilation (typically 10 air changes per hour) should be used. Ventilation rates should be matched to conditions.

If operations involve crushing or other processes that may release liquid, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits.

Respiratory Protection: Not generally required when handling containers or capsules. The need for respiratory protection should be determined by an industrial hygiene survey. (See Section 3 for exposure limits.) NIOSH/MSHA approved respirators for protection should be used if respirators are found to be necessary.

PERSONAL PROTECTIVE EQUIPMENT: Not generally required when handling containers. If containers are compromised or exposure to the active ingredient or mixture is likely wear

Eye Protection: Safety goggles with side shields  
(or goggles)

Hand Protection: Neoprene or nitrile gloves

Protective Clothing: Laboratory coats

Other: Eye wash

WORK/HYGIENIC PRACTICES: Keep away from foodstuffs, beverages and feed. Immediately remove all soiled and contaminated clothing. Wash hands before breaks and at the end of work.

---

## 9. PHYSICAL/CHEMICAL CHARACTERISTICS

---

**For Product:**

APPEARANCE AND ODOR: Hard red and ivory gelatin capsule

**Dipyridamole**

APPEARANCE AND ODOR: Yellow crystalline powder with a bitter taste

Boiling Point: N/A	Specific Gravity: N/A
Vapor Pressure (mmHg): N/A	Melting Point: 163° C (325° F)
Vapor Density: N/A	Evaporation Rate: N/A
Water Solubility: practically insoluble	Autoignition Temperature: N/A
Freezing Point: N/A	Decomposition Temperature: N/A
Flammable Limits: N/A	Partition Coefficient (n-Octanol/water): N/A
Flashpoint: N/A	Volatiles, %: N/A

**Aspirin**

APPEARANCE AND ODOR: Colorless to white, crystalline powder

Boiling Point: N/A	Specific Gravity: 1.40
Vapor Pressure (mmHg): N/A	Melting Point: 135° C (rapid heating)
Vapor Density: N/A	Evaporation Rate: N/A
Water Solubility: Slightly insoluble (aspirin)	pH: N/A
Freezing Point: N/A	Autoignition Temperature: N/A
Flammable Limits: N/A	Decomposition Temperature:
Flashpoint: N/A	Partition Coefficient (n-Octanol/water):1.19
Volatiles, %: N/A	

---

## 10. REACTIVITY DATA

---

STABILITY: Stable

CONDITIONS TO AVOID: Moisture. Aspirin hydrolyzes in air into salicylic and acetic acids and acquires an odor of acetic acid.

INCOMPATIBLE MATERIALS: Strong oxidizers

HAZARDOUS DECOMPOSITION OR BY-PRODUCTS: Oxides of carbon, oxides of nitrogen

HAZARDOUS POLYMERIZATION: Will not occur.

---

## 11. TOXICOLOGICAL INFORMATION

---

ACUTE TOXICITY:

**Dipyridamole:**

Man  
TDLo - ROUTE: Oral; DOSE: 1071 ug/kg  
TOXIC EFFECTS:

*Cardiac* - Cardiomyopathy including infarction

Woman

TDLo - ROUTE: Oral; DOSE: 35 mg/kg

TOXIC EFFECTS:

*Behavioral* - General anesthetic, *Vascular* – Shock, *Lung, Thorax, or Respiration* – Dyspnea

Rat

LD50 - ROUTE: Intraperitoneal; DOSE: 1260 mg/kg

LD50 - ROUTE: Intravenous; DOSE: 195 mg/kg

TOXIC EFFECTS:

*Lung, Thorax, or Respiration* - Respiratory depression, *Gastrointestinal* - Hypermotility, diarrhea

LD50 - ROUTE: Oral; DOSE: 8400 mg/kg

TOXIC EFFECTS:

*Behavioral* - Altered sleep time (including change in righting reflex), Somnolence (general depressed activity), Irritability

LD50 - ROUTE: Subcutaneous; DOSE: 1650 mg/kg

TOXIC EFFECTS:

*Behavioral* - Somnolence (general depressed activity), ataxia, *Lung, Thorax, or Respiration* - Respiratory depression

ACUTE TOXICITY:

**Active Ingredient: Aspirin**

LD<sub>50</sub> Oral (mouse) – 250 mg/kg

LD<sub>50</sub> Oral (rabbit) – 1.010 mg/kg

LD<sub>50</sub> Oral (rat) – 200 mg/kg

LD<sub>50</sub> Intraperitoneal (rat) – 340 mg/kg

MUTAGENICITY:

**Active Ingredient: Dipyridamole**

Negative in: Ames test, In vivo chromosomal aberration tests in mice and hamsters, Micronucleus tests in mice and hamsters, and Dominant lethal test in mice

**Active Ingredient: Aspirin**

Aspirin caused induced chromosomal aberrations in cultured human fibroblasts.

TERATOGENICITY:

**Active Ingredient: Dipyridamole**

Reproduction studies revealed no evidence of impaired fertility in rats at oral dosages up to 500 mg/kg/day or 3000mg/m<sup>2</sup>/day (10 times the recommended human dose on a body surface area basis).

A significant reduction in number of corpora lutea with consequent reduction in implantations and live fetus was, however observed at a dose of 1250mg/kg/day or 7500 mg/m<sup>2</sup>/day (25 times the recommended human dose on a body surface area basis). Therapeutic doses of Dipyridamole are unlikely to pose a substantial teratogenic risk, but the data are insufficient to state that there is

no risk.

Fetal loss is frequent among women with artificial heart valves who are treated during pregnancy with warfarin and may be even higher in those treated with both warfarin and dipyridamole (Ibarra-Perez et al., 1976; Sareli et al., 1989). The clinical significance of this is unclear.

No teratogenic effect is said to have occurred in unpublished studies among the offspring of pregnant mice, rats, or rabbits treated, respectively, with up to 16, 16, or 2.5 times the maximum human dose of dipyridamole (USP DI, 1998).

**REPRODUCTIVITY:**

Aspirin inhibits ovulation in rats

Cultured human fibroblasts induced chromosomal aberration test: positive

**Listed Carcinogens:** None

---

## 12. ECOLOGICAL INFORMATION

---

There are no data on the ecotoxicity of this product.

---

## 13. DISPOSAL CONSIDERATIONS

---

**WASTE DISPOSAL CONSIDERATIONS:** Dispose of in accordance with local, state and federal regulations. Incinerate.

---

## 14. TRANSPORT INFORMATION

---

**Product:**

This product is not subject to the regulations for the safe transport of hazardous materials.

DOT: Not regulated

TDG: Not regulated

IATA: Not regulated

IMDG: Not regulated

---

## 15. REGULATORY INFORMATION

---

**CANADIAN CONTROLLED PRODUCTS REGULATIONS:** This product has been classified in according to the hazard criteria of the Canadian Controlled Products Regulations, Section 33, and the MSDS contains all required information.

**WHMIS CLASSIFICATION FOR ACTIVE INGREDIENT:** Controlled. D1B, D2B

**WHMIS CLASSIFICATION FOR PRODUCT:** Not controlled.

**INVENTORY STATUS:**

This material **is not listed** on the US TSCA Inventory. (Therefore, it can only be used for TSCA exempt purposes such as R&D or drug use.)

This material **is not listed** on the DSL Inventory.

---

## 16. OTHER INFORMATION

---

### ABBREVIATIONS:

BIPI - Boehringer Ingelheim Pharmaceuticals, Inc.

N/A - Not applicable.

N/E - Not established.

### PREPARATION INFORMATION

Prepared by: BIPI. Environmental Affairs & Safety.

Date Revised: 9/12/05

Replaces: 9/6/05

REVISION INFORMATION: All sections of the MSDS updated, Exposure limits updated, Canadian Regulations added;

### SEE CURRENT PACKAGE INSERT FOR FURTHER INFORMATION

### REFERENCES

1. Ariel Research ChemExpert: Registry of Toxic Effects of Chemical Substances.
2. Ariel Research, ChemExpert: Hazardous Substance Bank.
3. Ariel Research, Global Regulatory Database.
4. National Library of Medicine, Toxline.
5. American Hospital Formulary Service, 2003.
6. BIPI MSDS, 2/03
7. BIPI MSDS 9/05
8. Physician's Desk Reference, 2003.

The opinions expressed herein are those of qualified experts within Boehringer Ingelheim Pharmaceuticals, Inc. (BIPI). We believe that the information contained within this MSDS is current as of the date issued. Since the use of this information and these opinions and the conditions of use of this material are not within the control of BIPI, it is the user's obligation to determine the conditions of safe use of this material. BIPI urges the users of this product to study this MSDS and become aware of any hazards associated with this material. In the interests of safety, the information contained in this MSDS should be made available to your employees, agents and contractors who handle this material