CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20802

ENVIRONMENTAL ASSESSMENT AND/OR FONSI

MAY 21 1997

ENVIRONMENTAL ASSESSMENT
AND
FINDING OF NO SIGNIFICANT IMPACT

FOR

Excedrin® Extra Strength Tablets, Caplets and Geltabs
(Acetaminophen 250 mg, Aspirin 250 mg and Caffeine 65 mg)

NDA 20-802

FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

DIVISION HFD-550

FINDING OF NO SIGNIFICANT IMPACT

NDA 20-802

Excedrin® Extra Strength Tablets, Caplets and Geltabs (Acetaminophen 250 mg, Aspirin 250 mg and Caffeine 65 mg)

The Food and Drug Administration (FDA) recognizes the National Environmental Policy Act of 1969 (NEPA) as the national charter for protection, restoration, and enhancement of the environment. NEPA establishes policy, sets goals (section 101),and provides procedures (section 102) for carrying out the policy.

Environmental information is to be available to the public and the decision maker before decisions are made about actions that may significantly affect the quality of the human environment; FDA actions are to be supported by accurate scientific analyses; and environmental documents are to concentrate on timely and significant issues, not to amass needless detail.

***

The Food and Drug Administration Center for Drug Evaluation and Research has carefully considered the potential environmental impact of this action and has concluded that this action will not have a significant effect on the quality of the human environment and that an environmental impact statement therefore will not be prepared.

In support of their new drug application for Excedrin® Extra Strength Tablets, Caplets and Geltabs (aspirin 250 mg, acetaminophen 250 mg and caffeine 65 mg), Bristol-Myers Products (BMP) has submitted an environmental assessment (21 CFR 25.31a(a)(attached). The drug is indicated for pain associated with migraine.

Excedrin® Extra Strength Tablets have been marketed in their present formulation, since July 1977, for the relief of various aches and pains such as

headache, toothache, menstrual discomfort and muscle ache. This NDA is for an additional indication viz. to treat headaches associated with migraine. The formulation in this NDA remains unchanged.

All three active ingredients are obtained commercially. Letters from these suppliers are in Appendix B.1, stating that:

(1) they are in compliance with all environmental regulations

(2) they are in compliance with all emission requirements set forth in their permits

(3) the increase in the manufacture of the drug substance as a consequence of the approval of this NDA will not adversely affect the current emission requirements nor the current environmental laws.

Aspirin will be manufactured by Rhone-Poulenc, St. Louis, MO. Bristol-Myers Products was also purchasing aspirin from The Dow Chemical Company in Midland Michigan, ~~but now~~ has ceased to produce aspirin as of October 1996.

Acetaminophen is purchased from Mallinkrodt in Raleigh, NC; Hoechst Celanese Corp. in Bishop TX and Rhone-Poulenc Inc., Luling, TX/LA

Caffeine will be purchased from Knoll AG in Minden. Germany. Caffeine was also being purchased from Cultor Food Sciences (formerly Pfizer Food Science) in Groton, CT. Coultor has ceased the manufacture of caffeine since December of 1995.

The rejected drug substances will be returned to the respective supplier, thus minimizing the disposal of such off-specification material.

The tablets and caplets will be manufactured and packaged in the BMP facility in Morrisville, NC. The cores for the geltabs will also be manufactured at the same location. These geltab cores will be gelatin coated at Banner Pharmacaps, which is located in Chatsworth, CA. The packaging of these coated gelcaps will also take place in the BMP facility in Morrisville, NC. Banner Pharmacaps has also furnished a letter similar to that furnished by the drug substance manufacturer.

The drug product is manufactured by direct compression. During its manufacture

the air emission is controlled by filters which are 99% efficient. The waste water generated from the cleaning of manufacturing and packaging equipment, is discharged to the local waste water plant in compliance with an approved permit. No hazardous solid waste is generated during the manufacture of the drug product. The non-hazardous waste is shipped to an approved land fill facility.

Bristol-Myers Squibb (BMS) has appointed Damage Track, a commercial outfit to be the return goods processing center for expired, damaged, unwanted or unsalable product. Damage Track's processing centers are located in Atlanta, GA, Clemmons, NC, San Antonio, TX and Sparks NV. The product is packaged by Damage Track's personnel and shipped to a BMS approved incineration facility, which acknowledges receipt of the shipment and informs the center management the date(s) on which the material was actually destroyed.

The three active ingredients, aspirin, acetaminophen and caffeine, have been in use for many years without any detrimental effect on the environment.The applicant has also conducted an exhaustive literature survey, as per the suggestion of MS Nancy Sager of FDA, to show that these compounds do not have a negative impact on the environment.

The applicant has estimated the quantities of each of the actives in the fifth year of production, and calculated the Expected Introduction Concentration (EIC) of each of these actives in water (since the drug product will be taken orally for a new indication (migraine headache), and therefore the drug substances will be released in to the environment principally in the waste water system). The EIC concentrations obtained failed to place the compounds in the tier 0 catagory. But, based on the physico-chemical characteristics and literature survey, the company has demonstrated that the compounds will (1) remain in water and not be transferred to the terrestrial or the air compartments and (2) will be depleted from the water compartment by a combination of hydrolysis, biodegradation and/or photolysis.

Increased production of this drug product will increase the use of power by about 2%. There are no threatened flora or fauna species in the area where the drug product will be manufactured. The approval of this NDA will also not adversely affect any historical, architectural or archeological sites.

***

The Center for Drug Evaluation and Research has concluded that the product can be manufactured and used without any expected adverse environmental effects.

Precautions taken at the sites of manufacture of the bulk product and its final formulation are expected to minimize occupational exposures and environmental release.

4/23/97
DATE

Vispi P Bhavnagri
PREPARED BY
Vispi P. Bhavnagri Ph.D.
Review Chemist
HFD-550/830

4/29/97
DATE

Hasmukh B. Patel
DIVISION CONCURRENCE
Hasmukh B. Patel
Chemistry Team Leader

5/21/97
DATE

Nancy B Sager
Approved
Nancy B. Sager
HFD-357
Center for Drug Evaluation and Research

EXCEDRIN® EXTRA STRENGTH
ENVIRONMENTAL ASSESSMENT

Table of Contents

EXCEDRIN® EXTRA STRENGTH
ENVIRONMENTAL ASSESSMENT SUMMARY

---

1. **DATE:** December 16, 1996

2. **NAME:** Bristol-Myers Products a Div. of Bristol-Myers Squibb Co.

3. **MAILING: ADDRESS** 1350 Liberty Avenue
Hillside, N.J. 07207-6050

4. DESCRIPTION OF PROPOSED ACTION

4.A. Description of the Requested Approval

Bristol-Myers Products has filed a New Drug Application pursuant to section 505(b) of the Federal Food, Drug and Cosmetic Act for EXCEDRIN® Extra Strength Tablets (Acetaminophen 250 mg, Aspirin 250 mg, and Caffeine 65 mg). Detailed package description is attached in Appendix A.1 Detailed Package Description. An Environmental Assessment is being submitted pursuant to 21 CFR §25.31 a(a).

4.B. Need for the Proposed Action

To support the New Drug Application for EXCEDRIN® Extra Strength Tablets (Acetaminophen 250 mg, Aspirin 250 mg, and Caffeine 65 mg) for the treatment of migraine pain for Over-the-Counter (OTC) use.

4.C. Production Locations

4.C.1. Drug Substance Suppliers

The active ingredients are commercially available from the following chemical manufacturers.

Aspirin

The Dow Chemical Company
Midland, Michigan 48667
Ceased production of Aspirin in October, 1996.

Rhone-Poulenc
Specialty Chemicals Division
St. Louis, Missouri 63157

4.C. Production Locations (contd.)

4.C.1. Drug Substance Suppliers

Acetaminophen
Mallinckrodt Chemical
Raleigh, North Carolina

Hoechst Celanese
Bulk Pharmaceuticals & Intermediates
Bishop, Texas 78343

Rhone-Poulenc Inc.
Pharmaceutical Ingredients
P.O. Box 174
Luling, Louisiana 70070

Caffeine
Knoll AG, Werk Minden [Minden Works]
Karlstrasse 15, 29-35, 42-44
4950 Minden
Germany

Cultor Food Science formerly Pfizer Food Science
Groton, Ct
Ceased production of caffeine in December of 1995.

4.C.2. Drug Product Manufacturing Sites

The drug products, EXCEDRIN® Extra Strength Tablets and Caplets will be manufactured and packaged at Bristol-Myers Products Facility 9707 Chapel Hill Road (Highway 54) Morrisville, North Carolina 27560. The Morrisville facility is located on a 100 acre site within the town of Morrisville, adjacent to Research Triangle Park. The site borders on a combination of commercially and residentially zoned land uses including a railroad right-of-way. The soil is described as silty loam.

The core of the drug product, EXCEDRIN® Extra Strength Geltabs will be manufactured at the Bristol-Myers Products Facility in Morrisville, NC and will be enrobed(application of gelatin coating) at Banner Pharmacaps, Chatsworth, California. Packaging will take place at the Bristol-Myers Products Facility in Morrisville, North Carolina.

4.D. Location of Use

The subject New Drug Application, EXCEDRIN® Extra Strength Tablets, Caplets, and Geltabs will be for the treatment of migraine pain as an Over-the-Counter (OTC) use. At the present time, it is anticipated that its distribution will be to well-developed countries, particularly in the United States, Latin America, Intercontinental and Europe.

4.E. Disposal Sites

4.E.1. Drug Substance

Rejected drug substances received in Morrisville, N.C. for EXCEDRIN Extra Strength will be returned to the respective supplier. Disposal of off-specification drug substances will be minimized.

4.E.2. Drug Product

The Bristol-Myers Squibb (B.M.S.), Distribution Center has designated Damage Track, a Division of Supermarket Information Systems, Inc CHOICE facilities as the returns good processing centers for this product. The CHOICE facilities currently approved to handle pharmaceutical finished product returns include the following locations: Atlanta, GA, Clemmons, NC, San Antonio TX, and Sparks, NV. Finished product that is expired, damaged, unwanted or unsalable is returned to the centers from customers or other B.M.S. Distribution Centers, where it is checked and inventoried pending QC disposition. In accordance with the Company's approved standard operating procedure, returned goods may be placed back into available inventory subject to certain conditions, sent back to a processing site for further evaluation, or directed to disposal. All returns awaiting final disposition are held within the center in quarantine

status. Product which is slated for disposal is classified as "non-hazardous" off- specification pharmaceutical. The product is packed by facility personnel and loaded for transport to a Company approved, permitted incineration facility (See Appendix approved carrier. The shipping papers (manifests) are prepared by center personnel and accompany the waste shipment to the disposal facility. The disposal facility acknowledges receipt by signing and returning copies of the manifest back to the facility. All disposal facilities confirm in writing to center management the date(s) on which the actual destruction of the manifested materials occurred.

5. IDENTIFICATION OF SUBSTANCES THAT ARE SUBJECT TO THE PROPOSED ACTION

5.A. Drug Product

Outlined in Appendix A.2 is a description of the product active components. Material Safety Data Sheets for the active ingredients are also included. Outline in Appendix A.3 is a description of the inactive ingredients and Material Safety Data Sheets.

6. INTRODUCTION OF THE SUBSTANCES INTO THE ENVIRONMENT

All necessary actions have been or will be taken so that emissions, discharges and wastes from the production of EXCEDRIN® Extra Strength tablets will be in compliance with applicable environmental and occupational health and safety standards. EXCEDRIN® Extra Strength tablets are currently marketed under the Proposed Rule on Internal Analgesics 53 FR 45204 (November 10, 1988). This formulation has been marketed since 1978.

Introduction of EXCEDRIN® Extra Strength Tablets into the environment can occur from: (1) the formulation of the final product and packaging (2) the site of intended use (3) the disposal of drug product.

The active ingredients are commercially available and letters from the manufacturers are in Appendix B.1 stating (1) compliance with all environmental

laws; (2) in compliance with emissions requirements as set forth in all permits; and (3) that approval and the subsequent increase in production at the facilities is not expected to affect compliance with current emission requirements or compliance with environmental laws.

The following is a description of the introduction of substances into the environment from the final product manufacturing site, the site of use and the disposal of the drug product.

6.A. Substances Expected to be Emitted

The manufacturing process is that the actives (Acetaminophen, Aspirin, and Caffeine) are dry mixed together with low substituted hydroxpropyl cellulose NF, microcrystalline cellulose NF and Stearic Acid, NF. and direct compressed into a tablet/caplet form with minimal waste or emissions during the manufacturing process. The tablets/Caplets are then filmed coated with an aqueous solution. The core of the geltab dosage form is compressed as the tablet dosage form. These cores are then shipped to Banner Pharmacaps for enrobbing (application of gelatin coat).

Banner Pharmacaps has supplied a letter in Appendix B.1 stating (1) compliance with all environmental laws; (2) in compliance with emissions requirements as set forth in all permits ; and (3) that approval and the subsequent increase in production at the facilities is not expected to affect compliance with current emission requirements or compliance with environmental laws.

The manufacturing of EXCEDRIN® Extra Strength Tablets should not have any adverse impact on the environment. Its introduction into the environment as a result of manufacture is expected to be negligible. Wastes generated consist of wastewater, solid waste and air emissions. Each is described below for the final product manufacturing and packaging in Morrisville, North Carolina.

6.B. Controls Exercised

6.B.1. Air Emissions

Air emissions of particulates at the Bristol-Myers Products Morrisville site

are controlled through the use of dust control equipment. The equipment is designed with a control efficiency of 99%. The equipment is registered with the State of North Carolina, Department of Environment, Health and Natural Resources, Division of Environmental Management Air Permit No. 5309R5.

6.B.2. Liquid Waste

Wastewater will be generated from cleaning of process and packaging equipment. Waste waters from the cleaning process are discharged to the Town of Cary Sewer Authority in accordance with permit "#0004 Industrial Discharge Pretreatment Permit".

6.B.3. Solid Waste

No hazardous waste will be generated by the manufacturing and packaging processes. Solid waste generated by the manufacturing and packaging processes will be collected and sent off-site to a Subtitle D secure landfill for non-hazardous waste. The facility is Piedmont Landfill in Kernersville, N.C. (Permit # 34-06).

6.B.4. Drug Product

Disposal of rejected, returned and off-specification drug product is previously described in Section 4.E.2 of this document.

6.C. Citation of and Statement of Compliance with Applicable Emission Requirements

After due inquiry and discussion with personnel charged with responsibility for such matters, applicant certifies that all necessary actions have been or will be taken so that emissions, discharges and wastes from the production of EXCEDRIN® Extra Strength Tablets and Caplets will be in compliance with applicable environmental, occupational health and safety standards and federal, state and local emissions regulations and permits for its facility in Morrisville, North Carolina.

The Morrisville facility is under the jurisdiction of North Carolina Department of Environment, Health and Natural Resources. Federal jurisdiction is under the United States Environmental Protection Agency Region 4.

6.C.1. Citations of Applicable Federal, State Local Regulations

Listed below are citations of applicable Federal Sate and local emissions requirements and laws.

i. Federal - United States

Major environmental statutes with regulations promulgated by the United States Environmental Protection Agency that may impact pharmaceutical manufacturing include:

Air Quality: Clean Air Act of 1977 as amended 1990; United States Code (U.S.C.)§74011-7671q; 40 Code of Federal Regulations (C.F.R.) Parts §50-88

Waste: Resources Conservation and Recovery Act of 1976 as amended by the Hazardous and Solid Waste Act Amendments 1984; U.S.C.§6901-6992; 40 C.F.R. Parts §240-281.

Remediation: "superfund," Comprehensive Environmental Response, Compensation and Liability Act of 1980 (U.S.C.) § 9601-9675;40 C.F.R. Parts §300-311

Water: Clean Water Act of 1972; 33 (U.S.C.) §1251-1387; 33 C.F.R. Parts §320-330. 335-338; 40 C.F.R. Parts §104-140, 230-233, 401-477

Chemicals: Emergency Planning and Community Right-to-Know Act of 1986 (Superfund Amendments and Reauthorization Act Title III, SARA Title III) 42 (U.S.C.) §11001-11050; 40 C.F.R. Parts §350,355,370,372; Pollution Prevention Act of 1990 42 (U.S.C.) §13101-13209.

Occupational Safety & Health: Occupational Safety & Health Act of 1970; 29 (U.S.C.) §651-78; 29 C.F.R. Parts §1900-1910.

ii. State- North Carolina

- Title 13 Department of Labor Chapter 7 Occupational Safety & Health
- Title 15A Department of Environment, Health, and Natural Resources
  - Chapter 1 Departmental Rules
  - Chapter 2 Environmental Management
  - Chapter 13 Solid Waste Management
  - Chapter 18 Environmental Health

iii. Local- Morrisville, North Carolina

There are no applicable local ordinances at this time.

6.C.2. Emissions Permits

Listed in the following section are the emission permits/ and or registrations, according to air, liquid and solid waste streams.

i. Air Emissions
The air emissions of particulates at the Bristol-Myers Products Morrisville site are controlled through the use of dust control equipment. The equipment is designed with a control efficiency of 99%. The equipment is registered with the State of North Carolina, Department of Environment, Health and Natural Resources, Division of Environmental Management Air Permit # 5309R5.

ii. Liquid Waste
The wastewater from the Morrisville manufacturing site discharges into a Publicly Owned Treatment Works (POTW), Town of Cary Sewer Authority in accordance with permit "#0004 Industrial Discharge Pretreatment Permit".

iii. Solid Waste
The non-hazardous solid waste generated by the manufacturing and packaging processes will be collected and sent off-site to a Subtitle D secure landfill for non-hazardous waste. The facility is Piedmont Landfill

in Kernersville, N.C. (Permit # 34-06). Other ancillary solid waste generated, such as surplus packaging materials and manufacturing supplies will also be land filled.

6.D. Discussion of the Effects of Approval on Compliance with Current Emissions requirements

The operation for the manufacture of the EXCEDRIN® Extra Strength Tablets and Caplets does not involve any new construction, thus there will be not impact on land use, water quality or other natural resources from any construction activities.

The estimated fifth year production volume in the United States is listed in the Confidential Appendix B.2.

Considering the estimated fifth year production volumes, and that this formulation of EXCEDRIN® Extra Strength Tablets has been in the Over-the-Counter market place since 1978 there should be no adverse impact on the environment nor on compliance with current emissions permits or registrations at the final product manufacturing site.

6.E. Expected Introduction Concentrations

EXCEDRIN® Extra Strength tablets are administered to patients orally and will enter the environment primary through the sanitary wastewater systems, at the location where the product is administrated.

The estimated fifth year production volume of EXCEDRIN® Extra Strength Tablets, estimated from the projected total sales volumes is listed in Appendix B.2.

i. Expected Introduction Concentration From Use

The expected introduction concentration is calculated using the fifth year volume for the active ingredients, aspirin, acetaminophen and caffeine.

The Expected Introduction Concentration (EIC) entering the aquatic environment from patient use is determined as follows:

EIC -Aquatic (ppm) = A x B x C x D

Where
A = kg/year production
B = 1/liter per day entering POTWs *
C = year/365 day
D = 10^6 mg/kg

* 1.115×10^{11} liters per day entering Publicly Owned Treatment Works (POTWs) sources: 1992 Needs Survey, Report to Congress, September 1993, EPA 832-R-93-002.

EIC-Aquatic (ppm) = Refer to the Confidential Appendix for the EIC Value

The EIC value for the total production of EXCEDRIN® Extra Strength Tablets is and the EIC value for production associated with this NDA is. As discussed and referenced by letter to Nancy Seger the following sections are completed.

7. FATE OF EMITTED SUBSTANCES IN THE ENVIRONMENT

EXCEDRIN® Extra-Strength contains three active compounds:

- Aspirin (acetylsalicylic acid);
- Acetaminophen; and
- Caffeine.

A literature search was conducted to identify records describing the fate of these compounds in the environment. Files from the Hazardous Substance Database and other literature information reviewed for each compound are included in Appendix A.4. Following is a summary of the environmental fate of these compounds.

Environmental releases of aspirin, acetaminophen, and caffeine will preferentially partition to the aquatic environment. These compounds will readily dissolve in water with minimal sorption to organic solids or sediments or transfer to the atmosphere. Aspirin will be rapidly depleted from the aquatic environment by hydrolysis. Depletion of acetaminophen and caffeine will occur through biodegradation.

Physical and chemical properties that influence the distribution and fate of aspirin, acetaminophen, and caffeine in the environment are summarized below.

Compound	Water Solubility (mg/l)	Dissociation Constant (pKa)	Octanol/Water Coefficient ($LogK_{ow}$)	Vapor Pressure (mm Hg)	Henrys Law Constant ($atm\text{-}m^3/mol$)
Aspirin	4,600	3.49	1.19	2.52E-05	1.3E-09
Acetaminophen	11,660	9.0 - 10.15	0.55		
Caffeine	21,000	14	-0.07	<1E-08	1.9E-19

All three compounds will preferentially partition to the aquatic environment based on their high solubilities in water (i.e. 0.5 to 21 percent). Adsorption to soils, sediments, and other organic solids will be minimal based on the low magnitude of the octanol-water partition coefficients (all values are less than 3). Transfer from water or solids to the atmosphere will be minimal based on the low values for vapor pressure and Henrys Law constant. Preferential partitioning of these compounds to the aqueous environment (with minimal sorption to organic matter) effectively eliminates the potential accumulation of these compounds in organisms.

Depletion of these compounds from the aquatic environment will occur by natural physical, chemical, and biological processes, including hydrolysis, biodegradation, and photolysis.

Hydrolysis is the predominant depletion mechanism for aspirin released to water. Aspirin will be depleted rapidly from water by hydrolysis based on a half-life of less than 24 hours (12.5 to 1.2 hours for pHs 3.5 to 11.3). Depletion of caffeine

and acetaminophen by hydrolysis is not reported in the literature reviewed.

Biodegradation has also been reported to deplete aspirin and caffeine from aquatic systems. Depletion of acetaminophen by biodegradation is expected to occur based on the biodegradation demonstrated for other substituted phenols.

Photolysis through reaction with hydroxyl radicals has been reported to deplete aspirin in water. Depletion of acetaminophen and caffeine by photolysis is not reported in the literature reviewed.

8. ENVIRONMENTAL EFFECTS OF RELEASED SUBSTANCES

EXCEDRIN® Extra-Strength Tablets are currently marketed under the tentative final monograph for Internal Analgesics tablets. This formula containing acetaminophen, aspirin and caffeine has been marketed as an OTC drug since 1978. Aspirin and acetaminophen have been used as pain relievers for more than half century. Caffeine is a naturally occurring compound that has been used as an food additive and drug agent since at least the 1950s. A literature search was conducted to identify records describing the environmental toxicity of these compounds. Files from the Hazardous Substance Database and other literature information reviewed for each compound are included in Appendix A.3. These records do not contain any reference to adverse effects to environmental organisms from exposure to these drug entities.

9. USE OF RESOURCES AND ENERGY

9.A. Natural Resources and Energy

EXCEDRIN® Extra Strength tablets are currently marketed under the tentative final monograph for Acetaminophen, Aspirin and Caffeine tablets. This formulation has been marketed since 1978. The approximate energy consumption associated with the manufacturing as a percent of total consumption is 2% and based on plant capacity there is a minimal increased expected.

9.B. Effects on Endangered or Threatened Species

The approval of this New Drug Application is not expected to affect, directly or indirectly, endangered or threatened species.

Within a 1 to 1½ miles of the Morrisville, North Carolina facility there are two populations of significantly rare plants of North Carolina. They are Porteranthus and Stipulata of which neither are on the Federal Endangered list.

9.C. Effect on Property listed in or Eligible for Listing in the National Register of Historical Places

The approval of this New Drug Application will not adversely affect any historical, architectural, archeological or cultural sites.

10. Mitigation Measures

Means of controlling environmental releases during production are described in Section 6. Emergency plans consist of a site-specific contingency plan and are carried out by specially trained personnel.

Appropriate personnel at the production facility are provided with the appropriate personal protective equipment and Material Safety Data Sheets are available for materials handled on site. Employees are trained in the proper handling of the ingredients and equipment as required by Occupational Safety and Health Administration.

11. Alternatives for the Proposed Action

There have been no potential environmental impacts identified for the proposed action. EXCEDRIN Extra Strength Tablets have been marketed since 1978 with no known environmental impact.

12. List of Preparers

Mary Beth Koza, Associate Director-Environmental Affairs, Occupational Safety and Health Bristol-Myers Products, Hillside, New Jersey, BA Chemistry, Kean

College, MBA Fairleigh Dickinson University, Certified Hazardous Materials Manager at the Masters Level, 17 years of experience in environmental affairs, occupational safety and health.

13. Certification

The undersigned official certifies that the information presented is true, accurate and complete to the best of the knowledge of Bristol-Myers Products.

The undersigned official certifies that the environmental assessment summary document (15 pages) contains non-confidential information and acknowledges that this information will be made available to the public in accordance with 40 CFR §1506.6.

Date 1/3/97

John M. Mamone
V.P. Technical Operations
Bristol-Myers Products

Appendices

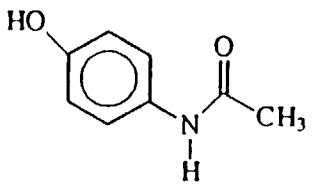
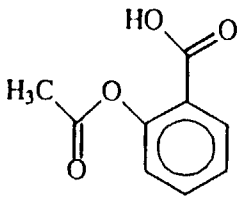
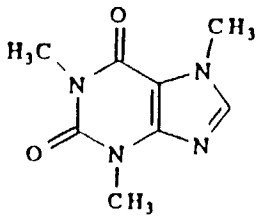
A. Non-Confidential
   - A.1. Package Description
   - A.2. Product Active Ingredients
   - A.3. Product Inactive Ingredients
   - A.4. Literature Search

B. Confidential
   - B.1. Suppliers Environmental Certification Statement (Non-confidential)
   - B.2. Manufacturing 5th Year Volume and Introduction Concentrations
   - B.3. Disposal Sites

Non-Confidential
Appendix A.2
Product Active Ingredients

BRISTOL-MYERS PRODUCTS
Hillside, New Jersey 07207

APPRENDIX A. 2
EXCEDRIN Extra Strength Tablets
Active Ingredients
Material Safety Data Sheets (attached)

Ingredient	CAS#	Molecular Weight	Formula/Description	Structure
Acetaminophen Acetanilide Acetamide, N-(4-hydroxphenyl)-	**103-90-2**	**151.17**	$C_8H_9NO_2$ White powder	
Aspirin Acetylsalicylic acid 2-(Acetyloxy)Benzoic acid Salicylic acid acetate	**50-78-2**	**180.16**	$C_9H_8O_4$ White crystalline solid	
Caffeine 1,3,7-Trimethylxanthine 1H-Purine-2,6-dione,3,7-trimethyl-	**58-08-2**	**194.19**	$C_8H_{10}N_4O_2$ White crystallien power	

EXCEDRIN® EXTRA-STRENGTH

Acetaminophen

BRISTOL-MYERS PRODUCTS
Hillside, New Jersey 07207

Mallinckrodt
Material Safety Data

Mallinckrodt provides the information contained herein in good faith but makes no representation as to its comprehensiveness or accuracy. Individuals receiving this information must exercise their independent judgment in determining its appropriateness for a particular purpose.

Mallinckrodt makes no representations, or warranties, either express or implied, of merchantability, fitness for a particular purpose with respect to the information set forth herein or to the product to which the information refers. Accordingly, Mallinckrodt will not be responsible for damages resulting from use of or reliance upon this information.

Emergency Phone Number: 314-539-1600

Performance and Laboratory Chemical Div., P.O. Box 800, Paris, KY 40362.

ACETAMINOPHEN

PRODUCT IDENTIFICATION:

Synonyms: Acetanilide, 4'-hydroxy-; acetamide, N-(4-hydroxyphenyl)-; APAP

Formula CAS No.: 103-90-2

Molecular Weight: 151.20

Chemical Formula: $C_8H_9NO_2$

Hazardous Ingredients: Acetaminophen

PRECAUTIONARY MEASURES

WARNING! HARMFUL IF SWALLOWED OR INHALED. OVERDOSAGE MAY AFFECT LIVER AND KIDNEYS. MAY CAUSE SKIN RASH OR ALLERGIC REACTION. MAY FORM COMBUSTIBLE DUST CONCENTRATIONS IN AIR.

Avoid breathing dust.
Wash thoroughly after handling.
Keep container closed.
Avoid dust cloud in presence of an ignition source.
Use with adequate ventilation.

EMERGENCY/FIRST AID

If swallowed, induce vomiting immediately as directed by medical personnel. Never give anything by mouth to an unconscious person. If inhaled, remove to fresh air. Get medical attention for any breathing difficulty. In case of contact, immediately flush eyes or skin with plenty of water for at least 15 minutes.
SEE SECTION 5.

SECTION 1 Physical Data

Appearance: White powder or granules.

Odor: Odorless.

Solubility: ca. 1.1 g/100g water @ 25°C (77°F).

Boiling Point: Not applicable.

Melting Point: ca. 170°C (338°F)

Specific Gravity: ca. 1.29

Vapor Density (Air = 1): No information found.

Vapor Pressure (mm Hg): No information found.

Evaporation Rate: No information found.

SECTION 2 Fire and Explosion Information

Fire:
As with most organic solids, fire is possible at elevated temperatures or by contact with an ignition source.

Explosion:
Fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard.

Fire Extinguishing Media:
Water spray, dry chemical, alcohol foam, or carbon dioxide.

Special Information:
In the event of a fire, wear full protective clothing and NIOSH-approved self-contained breathing apparatus with full facepiece operated in the pressure demand or other positive pressure mode.

SECTION 3 Reactivity Data

Stability:
Stable under ordinary conditions of use and storage.

Hazardous Decomposition Products:
In the presence of heat and water, substance will hydrolyze into acetic acid and p-aminophenol. Emits oxides of nitrogen when heated to decomposition.

Hazardous Polymerization:
Will not occur.

Incompatibilities:
No information found.

SECTION 4 Leak/Spill Disposal Information

Remove all sources of ignition. Ventilate area of leak or spill. Clean-up personnel may require protection from inhalation of dust.

Spills: Clean up spills in a manner that does not disperse dust into the air. Use non-sparking tools. Pick up spill for recovery or disposal and place in a closed container.

Disposal: Whatever cannot be saved for recovery may be burned in an approved incinerator or disposed in an approved waste facility.

Ensure compliance with local, state and federal regulations.

Mallinckrodt
Material Safety Data

Mallinckrodt provides the information contained herein in good faith but makes no representation as to its comprehensiveness or accuracy. Individuals receiving this information must exercise their independent judgment in determining its appropriateness for a particular purpose.

Mallinckrodt makes no representations, or warranties, either express or implied, of merchantability, fitness for a particular purpose with respect to the information set forth herein or to the product to which the information refers. Accordingly, Mallinckrodt will not be responsible for damages resulting from use of or reliance upon this information.

Emergency Phone Number: 314-539-1600

Performance and Laboratory Chemical Div., P.O. Box 800, Paris, KY 40362

SECTION 5 Health Hazard Information

A. EXPOSURE / HEALTH EFFECTS

Inhalation:
May produce an allergic response in sensitized individuals. Symptoms may include rash or wheezing.

Ingestion:
Severe overdosage may produce nausea, vomiting, perspiration, and general discomfort. Massive overdosage may produce damage to liver, kidneys, and central nervous system. Potentially toxic single dose: 10-15 grams; 25 grams is potentially fatal.

Skin Contact:
May produce allergic responses paralleling inhalation.

Eye Contact:
May cause mechanical irritation.

Chronic Exposure:
Repeated ingestion of toxic doses may produce cirrhosis of the liver.

Aggravation of Pre-existing Conditions:
Individuals exposed to alcohol or other drugs may be more susceptible to the toxic effects of this substance.

B. FIRST AID

Inhalation:
Remove to fresh air. Get medical attention for any breathing difficulty.

Ingestion:
If swallowed, induce vomiting immediately as directed by medical personnel. Never give anything by mouth to an unconscious person.

Skin Exposure:
Wash exposed area with soap and water. Get medical advice if irritation develops.

Eye Exposure:
Wash thoroughly with running water. Get medical advice if irritation develops.

C. TOXICITY DATA (RTECS, 1993)

Oral rat LD50: 2404 mg/kg; investigated as a mutagen, tumorigen, reproductive effector.

SECTION 6 Occupational Control Measures

Airborne Exposure Limits:
Mallinckrodt recommends an exposure limit of 5 mg/m^3 Time Weighted Average (TWA) for acetaminophen.

Ventilation System:
A system of local and/or general exhaust is recommended to keep employee exposures below the Airborne Exposure Limits. Local exhaust ventilation is generally preferred because it can control the emissions of the contaminant at its source, preventing dispersion of it into the general work area. Please refer to the ACGIH document, "Industrial Ventilation, A Manual of Recommended Practices", most recent edition, for details.

Personal Respirators: (NIOSH Approved)
If the exposure limit is exceeded, a half mask chemical cartridge respirator may be worn up to 50 mg/cubic meters or the maximum use concentration specified by the respirator supplier, whichever is less.

Skin Protection:
Gloves and lab coat, apron or coveralls.

Eye Protection:
Use chemical safety goggles. Contact lenses should not be worn when working with this material. Maintain eye wash fountain and quick-drench facilities in work area.

SECTION 7 Storage and Special Information

Keep in a well enclosed container stored in a cool, dry place. Acetaminophen is capable of generating a static electrical charge. If process involves dumping Acetaminophen into flammable liquid, provide inert atmosphere in vessels or maintain flammable liquid below its flashpoint.

ACEPH

ITEM 2 - 00090

Mallinckrodt
Material Safety Data

Mallinckrodt provides the information contained herein in good faith but makes no representation as to its comprehensiveness or accuracy. Individuals receiving this information must exercise their independent judgment in determining its appropriateness for a particular purpose.

Mallinckrodt makes no representations, or warranties, either express or implied, of merchantability, fitness for a particular purpose with respect to the information set forth herein or to the product to which the information refers. Accordingly, Mallinckrodt will not be responsible for damages resulting from use of or reliance upon this information.

Emergency Phone Number: 314-539-1600

Performance and Laboratory Chemical Div., P.O. Box 800, Paris, KY 40362

Addendum to Material Safety Data Sheet

REGULATORY STATUS

(Chem.Key: ACEPH)

Hazard Categories for SARA Section 311/312 Reporting

Acute	Chronic	Fire	Pressure	Reactive
X		X		

Product or Components of Product:	SARA EHS Sect. 302 RQ (lbs.)	SARA EHS Sect. 302 TPQ (lbs.)	SARA Section 313 Chemicals Name List	SARA Section 313 Chemicals Chemical Category	CERCLA Sec.103 RQ (lbs.)	RCRA Sec. 261.33
ACETAMINOPHEN (103-90-2)	No	No	No	No	No	No

SARA Section 302 EHS RQ: Reportable Quantity of Extremely Hazardous Substance, listed at 40 CFR 355.
SARA Section 302 EHS TPQ: Threshold Planning Quantity of Extremely Hazardous Substance. An asterisk (*) following a Threshold Planning Quantity signifies that if the material is a solid and has a particle size equal to or larger than 100 micrometers, the Threshold Planning Quantity = 10,000 LBS.
SARA Section 313 Chemicals: Toxic Substances subject to annual release reporting requirements listed at 40 CFR 372.65.
CERCLA Sec. 103: Comprehensive Environmental Response, Compensation and Liability Act (Superfund). Releases to air, land or water of these hazardous substances which exceed the Reportable Quantity (RQ) must be reported to the National Response Center, (800-424-8802); Listed at 40 CFR 302.4
RCRA: Resource Conservation and Recovery Act. Commercial chemical product wastes designated as acute hazards and toxic under 40 CFR 261.33

Material Safety Data Sheet

Print date -- July 18th, 1996 10:24 a.m. PS P&A PSFHV - 1.1 (1/1)

1. CHEMICAL PRODUCT and COMPANY IDENTIFICATION

Product Name: ACETAMINOPHEN, USP AND BP
Product Code: ACETAMINOPHEN
MSDS Number : 00928

SYNONYMS: APAP sieved Granular
ACETAMIDE, N-(4-HYDROXYPHENYL);
APAP;
N-ACETYL-P-AMINOPHENOL;
4-HYDROXYACETANILIDE.

HOECHST CELANESE CORPORATION BP&I
1601 LBJ FREEWAY
P.O. BOX 819005
DALLAS, TX 75381
UNITED STATES

PRODUCT USE:
Analgesic

2. COMPOSITION / INFORMATION on INGREDIENTS

COMPONENT	CAS NUMBER	
ACETAMINOPHEN, USP AND BP *	103-90-2	100%

*OSHA hazardous according to 29 CFR 1910.1200

3. HAZARDS IDENTIFICATION

POTENTIAL HEALTH EFFECTS

IMMEDIATE EFFECTS

SKIN:

Absorption: Not considered to be hazardous by dermal exposure.

Irritation: May cause allergic reaction in some individuals after repeated dermal occupational exposure.

3. HAZARDS IDENTIFICATION (Continued)

EYES:

Not an eye irritant.

INHALATION:

May cause allergic reaction in some individuals after repeated inhalation occupational exposures.

INGESTION:

May be harmful if swallowed in large quantities. Lowest reported lethal dose, in humans, is 143 mg/kg (about 10 g for a 70 kg man). Single large oral doses may result in such adverse effects as cyanosis, increased pulse rate, aplastic anemia, neutropenia, jaundice, leukopenia, skin eruptions, vomiting, fever, CNS stimulation, coma, vascular collapse, convulsions and death.

DELAYED/LONG TERM EFFECTS

Chronic ingestion may cause cyanosis, anemias, allergic skin reactions, hypoglycemia and drowsiness.

CARCINOGENIC:

This product is not listed in NTP, IARC or OSHA as a carcinogen.

MUTAGENIC:

Negative in point mutation assays. Has shown some activity in clastogenic assays.

TERATOGENIC:

Based on limited evidence, may have reproductive effects.

TARGET ORGAN EFFECTS:

Liver, skin. Excessive amounts can cause liver toxicity (HEPATOTOXIN).

4. FIRST AID MEASURES

SKIN:

Flush contaminated skin with water. If irritation (skin rash) develops, contact a physician.

EYES:

Flush with copious amounts of water. If irritation continues, contact a physician.

INHALATION:

Remove patient from contaminated area. If breathing becomes difficult, seek medical attention.

INGESTION:

Do not induce vomiting. Contact a physician immediately. Have physician call the Rocky Mountain Poison Control Center at: 1-800-525-6115.

5. FIRE FIGHTING MEASURES

Explosion limits: 1080°F dust cloud ignition temperature

EXTINGUISHING MEDIA:

Use carbon dioxide or dry chemical for small fires, alcohol-type aqueous film-forming foam (AFFF) or water spray for large fires.

FIRE FIGHTING INSTRUCTIONS:

Wear self-contained breating apparatus (SCBA).

6. ACCIDENTAL RELEASE MEASURES

Avoid eye or skin contact. Contain spill to minimize contaminated area and facilitate salvage or disposal. All clean-up and disposal should be carried out in accordance with local, state and federal regulations. If required, local and state authorities should be notified. Standard clean-up procedures such as sweeping or vacuuming should be used.

This product, when spilled or disposed of, is a non-hazardous solid waste as defined in the Resource

6. ACCIDENTAL RELEASE MEASURES (Continued)

Conservation and Recovery Act (40CFR261). Product must be disposed of properly in accordance with all local, state and federal industrial waste regulations.

7. HANDLING and STORAGE

Keep containers closed. Avoid breathing dust. Avoid contact with eyes, skin and clothing. Wash throughly with soap and water after handling. Handle in accordance with good industrial hygiene practices minimizing exposure. Avoid generation of excessive dust. Good housekeeping should be practiced to minimize dust accumulation. Equipment should be grounded to prevent build-up of electrical charge. Any operator working with the dust should wear conductive footwear. Explosion proof equipment should be used as in any chemical plant operating area. Inerting is not necessary, unless material is dumped to or used with a flammable solvent.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

HCC Workplace Exposure Limit (WEL): TWA = 5g/m³ (total)

WORK PRACTICES:

Respiratory protection: If airborne exposure is excessive, use NIOSH-approved dust respirator.

Ventilation -
Local exhaust: Recommended when appropriate to control employee exposure.
Mechanical (General): Not recommended as sole means of controlling employee exposure.

Protective gloves: Neoprene or rubber gloves.
Eye protection: Chemical safety goggles.

9. PHYSICAL and CHEMICAL PROPERTIES

Appearance: Odorless, white crystals.
Melting point: 169° to 171°C (336° to 340°F)
Specific gravity (H_2O = 1 at 20/20°C): 1.3
Solubility in water (% by weight at 20°C): 1.2
Percent volatiles by volume: 0%
Molecular weight: 151
Formula: $C_8H_9NO_2$
Chemical family: Aromatic amide

10. STABILITY and REACTIVITY

CHEMICAL STABILITY:
Chemically stable.

CONDITIONS TO AVOID:
Heat, sparks and open flame, excessive dusting due to explosion potential.

INCOMPATIBILITY:
Strong oxidizing agents.

HAZARDOUS DECOMPOSITION PRODUCTS:
Carbon monoxide and oxides of nitrogen.

HAZARDOUS POLYMERIZATION:
Will not occur.

11. TOXICOLOGICAL INFORMATION

Oral LD50 (rat): 2.4 to 6.7 g/kg
Dermal LD50 (rabbit): >7.9 g/kg

12. ECOLOGICAL INFORMATION

No information available.

13. DISPOSAL CONSIDERATIONS

This product is a non-hazardous solid waste as defined in the Resource Conservation and Recovery Act (40CFR261). Product must be disposed of in accordance with all local, state and federal regulations for industrial waste.

14. TRANSPORT INFORMATION

This product is not subject to DOT transportation regulations.

15. REGULATORY INFORMATION

This producted is regulated by the Food, Drug and Cosmetic Act.

16. OTHER INFORMATION

None.

REVISION INDICATORS:

The following sections have been revised:

SECTION 1: CHEMICAL PRODUCT & CO. IDENTIFICATION
PRODUCT USE

EXCEDRIN® EXTRA-STRENGTH

Aspirin

BRISTOL-MYERS PRODUCTS
Hillside, New Jersey 07207

Material Safety Data Sheet

The Dow Chemical Company
Midland, Michigan 48674

1. CHEMICAL PRODUCT & COMPANY IDENTIFICATION

24-Hour Emergency Phone Number: 517-636-4400

Product: ASPIRIN USP CRYSTALS NO. 80

Product Code: 00381

Effective Date: 04/27/95 Date Printed: 01/24/96 MSD: 000038

The Dow Chemical Company, Midland, MI 48674

Customer Information Center: 800-258-2436

2. COMPOSITION/INFORMATION ON INGREDIENTS

Aspirin CAS# 000050-78-2 100%

3. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

****

* White crystalline powder. Dust explosion hazard. *

* *

* *

****

POTENTIAL HEALTH EFFECTS (See Section 11 for toxicological data.)

EYE: May cause slight transient (temporary) eye irritation.

SKIN: Prolonged or repeated exposure may cause skin irritation. A single prolonged skin exposure is not likely to result in the material being absorbed through skin in harmful amounts.

INGESTION: Single dose oral toxicity is low to moderate. Small amounts swallowed incidental to normal handling are not likely to cause injury; swallowing amounts larger than that may cause injury. Ingestion may cause gastrointestinal irritation. It may also interfere with the normal blood clotting mechanism.

INHALATION: Excessive exposure may cause irritation to upper respiratory tract. May rarely cause respiratory

(Continued on page 2 , over)

sensitization in susceptible individuals.

SYSTEMIC & OTHER EFFECTS: Repeated exposures (typically by ingestion) may cause gastrointestinal irritation. Toxic or high doses may cause ringing in the ears, nausea, vomiting, and metabolic disturbances and renal failure. In animals, eye, liver and bone marrow effects have been observed at high doses.

TERATOLOGY (BIRTH DEFECTS): Has caused birth defects in laboratory animals only at doses toxic to the mother.

4. FIRST AID

EYES: Flush eyes with plenty of water.

SKIN: Wash off in flowing water or shower.

INGESTION: If swallowed, seek medical attention. Do no induce vomiting unless directed to do so by medical personnel.

INHALATION: Remove to fresh air if effects occur. Consult medical.

NOTE TO PHYSICIAN: No specific antidote. Supportive care. Treatment based on judgment of the physician in response to the reactions of the patient. In the treatment of overdoses, diuresis and hemodialysis are of benefit along with correction of water and electrolyte imbalance. Arch. Int. Med. 141:364 1981

5. FIRE FIGHTING MEASURES

FLAMMABLE PROPERTIES

FLASH POINT: Not applic.
METHOD USED:

FLAMMABILITY LIMITS
LFL: Not applic.
UFL: Not applic.

HAZARDOUS COMBUSTION PRODUCTS: Carbon dioxide, acetic acid, and salicylic acid.

OTHER FLAMMABILITY INFORMATION: Aspirin dust, when suspended in air, is flammable and if ignited poses a definite fire and

(Continued on page 3)

explosion hazard. Clouds of aspirin dust should not be exposed to possible ignition sources. Minimum explosive concentration of dry dust in air is 40 gms/cu meter. Minimum energy of ignition is 0.025 joules at 270 gms/cu meter concentration. Accumulations of aspirin dust on surfaces will burn rapidly when ignited. Good housekeeping and dust control are required.

EXTINGUISHING MEDIA: Large fire: Water fog. Small fire: CO2, halon, dry chemical.

PROTECTIVE EQUIPMENT FOR FIRE FIGHTERS: Positive-pressure, self-contained breathing apparatus required in any closed space.

6. ACCIDENTAL RELEASE MEASURES (See Section 15 for Regulatory Information)

PROTECT PEOPLE: Use appropriate clothing. Large spills may require the use of air-purifying respirators.

PROTECT THE ENVIRONMENT:

CLEANUP: Sweep up and shovel into clean, dry containers. Keep possible ignition sources away from dust.

7. HANDLING AND STORAGE

HANDLING: Aspirin dust when handled in air is flammable and poses a definite explosion hazard. Accumulations of aspirin dust on surfaces will burn rapidly when ignited. Keep aspirin dust away from ignition sources. Atmospheric levels should be maintained below the exposure guideline. When respiratory protection is required use approved air-purifying respirator.

STORAGE: Store and handle in compliance with U.S.P. Good Housekeeping Requirements (also see section 3).

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

ENGINEERING CONTROLS: Provide general and/or local exhaust ventilation to control airborne concentrations.

PERSONAL PROTECTIVE EQUIPMENT

EYE/FACE PROTECTION: Use safety glasses.

(Continued on page 4 , over)

SKIN PROTECTION: Use gloves impervious to this material when prolonged or frequently repeated contact could occur.

RESPIRATORY PROTECTION: Atmospheric levels should be maintained below the exposure guideline. When respiratory protection is required for certain operations, use an approved air-purifying respirator.

EXPOSURE GUIDELINE(S): OSHA PEL and ACGIH TLV are 5 mg/m3. Acetosalicylic acid (aspirin): ACGIH TLV and OSHA PEL are 5 mg/m3. PELS are in accord with those recommended by OSHA, as in the 1989 revision of PELS>

9. PHYSICAL AND CHEMICAL PROPERTIES

BOILING POINT: Not applicable
VAP. PRESS: Not applicable
VAP. DENSITY: Not applicable
SOL. IN WATER: 1% @ 27C, 81F
SP. GRAVITY: Not applicable
APPEARANCE: White crystalline powder.
ODOR: Not available.

10. STABILITY AND REACTIVITY

CHEMICAL STABILITY: Stable under normal storage conditions.

CONDITIONS TO AVOID: Avoid extreme heat and fire.

INCOMPATIBILITY WITH OTHER MATERIALS: Oxidizing material.

HAZARDOUS DECOMPOSITION PRODUCTS: Carbon dioxide, acetic acid, salicylic acid.

HAZARDOUS POLYMERIZATION: Will not occur.

11. TOXICOLOGICAL INFORMATION (See Section 3 for Potential Health Effects. For detailed toxicological data, write or call the address or non-emergency number shown in Section 1)

SKIN: The dermal LD50 has not been determined.

INGESTION: The oral LD50 for rats is 600-1400 mg/kg.

MUTAGENICITY: In vitro mutagenicity studies were negative.

12. ECOLOGICAL INFORMATION (For detailed Ecological data, write or call the address or non-emergency number shown in Section 1)

(Continued on page 5)

ENVIRONMENTAL FATE

DEGRADATION & PERSISTENCE:
5-Day biochemical oxygen demand (BOD5) is 1.00 p/p.
10-Day biochemical oxygen demand (BOD10) is 1.26 p/p.
20-Day biochemical oxygen demand (BOD20) is calculated to be 1.26 p/p. Theoretical oxygen demand (ThOD) is calculated to be 1.60 p/p. Biodegration under aerobic static laboratory conditions is high (BOD28/ThOD greater than 40%)

13. DISPOSAL CONSIDERATIONS (See Section 15 for Regulatory Information)

DISPOSAL METHOD: Dust is explosive. Incinerate in compliance with all local, state, and federal requirements.

14. TRANSPORT INFORMATION

U. S. DEPARTMENT OF TRANSPORTATION (D.O.T.): This product is not regulated by DOT when shipped domestically by land.

CANADIAN TDG INFORMATION:
For TDG regulatory information, if required, consult transportation regulations, product shipping papers, or your Dow representative.

15. REGULATORY INFORMATION (Not meant to be all-inclusive--selected regulations represented)

NOTICE: The information herein is presented in good faith and believed to be accurate as of the effective date shown above. However, no warranty, express or implied is given. Regulatory requirements are subject to change and may differ from one location to another; it is the buyer's responsibility to ensure that its activities comply with federal, state or provincial, and local laws. The following specific information is made for the purpose of complying with numerous federal, state or provincial, and local laws and regulations. See other sections for health and safety information.

U.S. REGULATIONS

SARA HAZARD CATEGORY: This product has been reviewed according to the EPA "Hazard Categories" promulgated under Sections 311 and 312 of the Superfund Amendment and Reauthorization Act of 1986 (SARA Title III) and is considered, under applicable definitions, to meet the following

(Continued on page 6 , over)

REGULATORY INFORMATION (CONTINUED)

categories:

Not to have met any hazard category

CANADIAN REGULATIONS

WHMIS INFORMATION: The Canadian Workplace Hazardous Materials Information System (WHMIS) Classification for this product is:

This product is not a "Controlled Product" under WHMIS.

16. OTHER INFORMATION

MSDS STATUS: Revised to 16 section format per ANSI Z400.1.

RHÔNE-POULENC

ASPIRIN 1080

Material Safety Data Sheet Date Prepared: 12/18/95 Supersedes Date: 12/11/95

1. CHEMICAL PRODUCT AND COMPANY DESCRIPTION

NORTH AMERICAN CHEMICALS ZONE
PHARMACEUTICAL INGREDIENTS
CN 7500
Cranbury NJ 08512-7500

Emergency Phone Numbers:
FOR EMERGENCIES INVOLVING A SPILL, LEAK, FIRE, EXPOSURE OR ACCIDENT CONTACT: CHEMTREC (800-424-9300) OR RHONE-POULENC (800-334-7577).

For Product Information:
(609) 860-4000

Chemical Name or Synonym:
ASPIRIN; 2-(ACETYLOXYBENZOIC) ACID; ACETOL

Molecular Formula:
$C_9H_8O_4$

2. COMPOSITION/INFORMATION ON INGREDIENTS

Component	CAS Reg Number	OSHA Hazard	Percentage
ACETYLSALICYLIC ACID	50-78-2	Y	99.5 (MIN)

3. HAZARDS IDENTIFICATION

A. EMERGENCY OVERVIEW:

Physical Appearance and Odor:
white crystalline or powder solid, odorless.

Warning Statements:
TOXIC IF SWALLOWED. EYE, SKIN AND RESPIRATORY TRACT IRRITANT. SENSITIZER. MODERATE TO SEVERE DUST EXPLOSION RISK.

B. POTENTIAL HEALTH EFFECTS:

3. HAZARDS IDENTIFICATION (Continued)

Acute Eye:
Irritant. May cause burns.

Acute Skin:
Harmful if absorbed through skin. May produce symptoms similar to those from ingestion. Irritant. Causes redness, swelling.

Acute Inhalation:
Sensitizer. Can cause respiratory tract irritation.

Acute Ingestion:
Toxic if ingested. Some people may be hypersensitive to this product. Can cause irritation, abdominal pain, nausea, bleeding, excitement, respiratory depression, heart failure, death.

Chronic Effects:
This product does not contain any ingredient designated by IARC, NTP, ACGIH or OSHA as probable or suspected human carcinogens. Prolonged contact can cause anemia, internal bleeding, decreased blood clotting ability.

4. FIRST AID MEASURES

FIRST AID MEASURES FOR ACCIDENTAL:
Eye Exposure:
Hold eyelids open and flush with a steady, gentle stream of water for at least 15 minutes. Seek medical attention.

Skin Exposure:
In case of contact, immediately wash with plenty of soap and water for at least 5 minutes. Seek medical attention if irritation develops or persists. Remove contaminated clothing and shoes. Clean contaminated clothing and shoes before re-use.

Inhalation:
Remove victim from immediate source of exposure and assure that the victim is breathing. If breathing is difficult, administer oxygen, if available. If victim is not breathing, administer CPR (cardio-pulmonary resuscitation). Seek medical attention.

4. FIRST AID MEASURES (Continued)

Ingestion:
If victim is conscious and alert, give 2-3 glasses of water to drink and induce vomiting by touching back of throat with a finger. Do not induce vomiting or give anything by mouth to an unconscious person. Seek immediate medical attention. Do not leave victim unattended. Vomiting may occur spontaneously. To prevent aspiration of swallowed product, lay victim on side with head lower than waist. If vomiting occurs and the victim is conscious, give water to further dilute the chemical.

MEDICAL CONDITIONS POSSIBLY AGGRAVATED BY EXPOSURE:
Inhalation of product may aggravate existing chronic respiratory problems such as asthma, emphysema or bronchitis. Skin contact may aggravate existing skin disease. The following potential problems relate primarily to individuals taking aspirin as a medication and are not expected to be of concern to workers, unless aspirin is accidentially ingested: (1) In persons taking anticoagulants, aspirin may accentuate anticoagulant activity; (2) Persons with influenza and some other viral illnesses may be at higher risk of developing Reye's Syndrome; and (3) Persons with rheumatoid arthritis or systemic lupus erthematosus sometimes develop hepatotoxicity.

NOTES TO PHYSICIAN:
All treatments should be based on observed signs and symptoms of distress in the patient. Consideration should be given to the possibility that overexposure to materials other than this product may have occurred.

MINIMIZE ABSORPTION: Remove salicylates by emesis with syrup of ipecac unless respiration is depressed. Do not use apomorphine. Delay absorption of the remaining poison by giving activated charcoal. If respiration is depressed, use airway-protected gastric lavage.

LABORATORY STUDIES: Determine serum salicylate levels, serum electrolytes, arterial blood gases, blood pH, coagulation studies, and renal function tests. Urine output should be done. Acid-base imbalance is common. In adults, respiratory alkalosis from hyperventilation and metabolic alkalosis from vomiting is common. In children, metabolic acidosis is often a significant problem.

TREATMENT: In mild poisoning, with adequate urine output and no vomiting, give milk and fruit juice orally every hour up to a total of 100 ml/kg in the first 24 hours.

In severe poisoning, begin hydration in the first hour with intravenous fluid, 400 ml/square meter. A 5% dextrose solution containing sodium

4. FIRST AID MEASURES (Continued)

bicarbonate, 75 meq/l, is satisfactory. However, do not use bicarbonate if the victim is alkalotic. After the first hour, the same solution can be continued at one-third the initial rate until urine flow begins, dehydration is corrected, or evidence of renal insufficiency appears. After urine flow is established, add potassium 30 meq/l of administered fluid. Discontinue potassium when serum levels reach 5 meq/l. If renal function is adequate, fluid administration should be approximately 3 liter/square meter/24 hour.

In the presence of abnormal bleeding or hypoprothrombinemia, give phytonadione, 10 mg intramuscularly. Fresh blood or platelet transfusions may be necessary.

Do not give barbiturates, paraldehyde, morphine or other central nervous system depressants.

If renal function is impaired, dialysis must be used to remove salicylates.

Reduce hyperpyrexia by tepid sponging. Do not use alcohol for sponging.

5. FIRE FIGHTING MEASURES

FIRE HAZARD DATA:

Flash Point:
Not Applicable

Extinguishing Media:
Recommended (small fires): dry chemical, carbon dioxide, Recommended (large fire): foam, water spray.

Special Fire Fighting Procedures:
Firefighters should wear NIOSH/MSHA approved self-contained breathing apparatus and full protective clothing. Dike area to prevent runoff and contamination of water sources. Dispose of fire control water later.

Unusual Fire and Explosion Hazards:
Product will burn under fire conditions. As a powder or dust, this product, (when mixed with air in critical proportions and in the presence of an ignition source) presents a moderate to high explosion hazard.

5. FIRE FIGHTING MEASURES (Continued)

Hazardous Decomposition Materials (Under Fire Conditions):
oxides of carbon

Dust Explosivity Data:

Explosibilty Index	> 10 Type of Explosion is Rated SEVERE.
Ignition Sensitivity	2.4
Explosion Severity	4.3
Cloud Ignition Temp	660 C (1220 F)
Min Cloud Ignition Energy	250 milliJoules
Layer Ignition Temp	No Data
Max. Explosion Pressure	6 Bar
Max. Rate of Pressure Rise	689 bar/second
Min. Explosion Concentration	0.05 oz/ft3

6. ACCIDENTAL RELEASE MEASURES

Evacuation Procedures and Safety:
Wear appropriate protective gear for the situation. See Personal Protection information in Section 8.

Containment of Spill:
Follow procedure described below under Cleanup and Disposal of Spill.

Cleanup and Disposal of Spill:
Shovel up into an appropriate closed container (see Section 7: Handling and Storage). Clean up residual material by washing area with water. Avoid creation of dusty conditions.

Environmental and Regulatory Reporting:
Do not flush to drain. If spilled on the ground, the affected area should be scraped clean and placed in a appropriate container for disposal. Spills may be reportable to the National Response Center (800-424-8802) and to state and/or local agencies.

7. HANDLING AND STORAGE

Minimum/Maximum Storage Temperatures:

7. HANDLING AND STORAGE (Continued)

No Data Available

Handling:
Do not ingest. Avoid direct or prolonged contact with skin and eyes. Avoid breathing dusts. This material is a pharmaceutical. Use the usual precautions associated with the handling of such products. Avoid contamination of storage containers.

THIS PRODUCT PRESENTS A MODERATE TO SEVERE DUST EXPLOSION HAZARD. It is recommended that all dust control equipment and material transport systems involved in handling of this product contain explosion relief vents or explosion suppression system or an oxygen deficient environment. In addition, all conductive elements of the system that contact this material should be electrically bonded and grounded. This powder should not be flowed through non-conductive ducts or pipes. Use only appropriately classed electrical equipment.

Storage:
Store in tightly closed containers. Store in an area that is clean, dry, away from ignition sources.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Introductory Remarks:
These recommendations provide general guidance for handling this product. Because specific work environments and material handling practices vary, safety procedures should be developed for each intended application. While developing safe handling procedures, do not overlook the need to clean equipment and piping systems for maintenance and repairs. Waste resulting from these procedures should be handled in accordance with Section 13: Disposal Considerations.

Assistance with selection, use and maintenance of worker protection equipment is generally available from equipment manufacturers.

Exposure Guidelines:
Exposure limits represent regulated or recommended worker breathing zone concentrations measured by validated sampling and analytical methods meeting OSHA requirements. The following limits (ACGIH, OSHA and other) apply to this material, where, if indicated, S=skin and

8. EXPOSURE CONTROLS/PERSONAL PROTECTION (Continued)

C=ceiling limit:

ACETYLSALICYLIC ACID

	Notes	TWA	STEL
ACGIH		5 mg/cu m	
OSHA		5 mg/cu m	

Engineering Controls:
Where engineering controls are indicated by use conditions or a potential for excessive exposure exists, the following traditional exposure control techniques may be used to effectively minimize employee exposures: local exhaust ventilation at the point of generation.

Respiratory Protection:
When respirators are required, select NIOSH/MSHA approved equipment based on actual or potential airborne concentrations and in accordance with the latest OSHA standard (29 CFR 1910.134) and/or ANSI Z88.2 recommendations.

Under normal conditions, in the absence of other airborne contaminants, the following devices should provide protection from this material up to the conditions specified by OSHA/ANSI: Air-purifying (half-mask/full-face) respirator with cartridges/canister approved for use against dusts, mists and fumes.
Under conditions immediately dangerous to life or health, or emergency conditions with unknown concentrations, use a full-face positive pressure air-supplied respirator equipped with an emergency escape air supply unit or use a self-contained breathing apparatus unit.

Eye/Face Protection:
Eye and face protection requirements will vary dependent upon work environment conditions and material handling practices. Appropriate ANSI Z87 approved equipment should be selected for the particular use intended for this material.

Eye contact should be prevented through use of chemical safety glasses with side shields or splash proof goggles. An emergency eye wash must be readily accessible to the work area.

Skin Protection:
Skin contact should be minimized through use of gloves and suitable long-sleeved clothing (i.e., shirts and pants). Consideration must be given both to durability as well as permeation resistance.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION (Continued)

Work Practice Controls:
Personal hygiene is an important work practice exposure control measure and the following general measures should be taken when working with or handling this material:

(1) Do not store, use, and/or consume foods, beverages, tobacco products, or cosmetics in areas where this material is stored.
(2) Wash hands and face carefully before eating, drinking, using tobacco, applying cosmetics, or using the toilet.
(3) Wash exposed skin promptly to remove accidental splashes of contact with this material.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical and Chemical properties here represent typical properties of this product. Contact the business area using the Product Information phone number in Section 1 for its exact specifications.

Physical Appearance:
white crystalline or powder solid.

Odor:
odorless.

pH:
Not Applicable

Specific Gravity:
1.4 at 25 C (77 F).

Water Solubility:
slightly soluble

Melting Point Range:
132 C (270 F)

Boiling Point Range:
No Data Available

Vapor Pressure:

9. PHYSICAL AND CHEMICAL PROPERTIES (Continued)

No Data Available

Vapor Density:
No Data Available

Molecular Weight:
180.17

10. STABILITY AND REACTIVITY

Chemical Stability:
This material is stable under normal handling and storage conditions described in Section 7.

Conditions To Be Avoided:
extreme humidity

Materials/Chemicals To Be Avoided:
strong bases
strong acids
strong oxidizing agents

Decomposition Temperature Range:
140 to 0 C (284 to 32 F)

The Following Hazardous Decomposition Products Might Be Expected:
Decomposition Type: hydrolysis
acetic acid
salicylic acid

Decomposition Type: thermal
oxides of carbon

Hazardous Polymerization Will Not Occur.
Avoid The Following To Inhibit Hazardous Polymerization:
not applicable

11. TOXICOLOGICAL INFORMATION

Acute Eye Irritation:
Toxicological Information and Interpretation
eye - eye irritation, rabbit.
Mild Irritant.

Acute Skin Irritation:
Toxicological Information and Interpretation
skin - skin irritation, rabbit.
Non-Irritating.

Acute Dermal Toxicity:
Toxicological Information and Interpretation
LD50 - lethal dose 50% of test species, > 7940 mg/kg, rabbit.

Acute Respiratory Irritation:
No test data found for product.

Acute Inhalation Toxicity:
No test data found for product.

Acute Oral Toxicity:
Toxicological Information and Interpretation
LD50 - lethal dose 50% of test species, 1010 mg/kg, rabbit.
LD50 - lethal dose 50% of test species, 1460 mg/kg, rat. (RP)
LD50 - lethal dose 50% of test species, 200 mg/kg, rat. (RTEC)

Chronic Toxicity:
This product does not contain any substances that are considered by OSHA, NTP, IARC or ACGIH to be "probable" or "suspected" human carcinogens.

Very large doses of aspirin have produced teratogenic effects in experimental animals.

12. ECOLOGICAL INFORMATION

Ecotoxicological Information:
No data found for product.

12. ECOLOGICAL INFORMATION (Continued)

Chemical Fate Information:
No data found for product.

13. DISPOSAL CONSIDERATIONS

Waste Disposal Method:
Chemical additions, processing or otherwise altering this material may make the waste management information presented in this MSDS incomplete, inaccurate or otherwise inappropriate. Please be advised that state and local requirements for waste disposal may be more restrictive or otherwise different from federal laws and regulations. Consult state and local regulations regarding the proper disposal of this material.

EPA Hazardous Waste - NO

14. TRANSPORTATION INFORMATION

Transportation Status:
US Department of Transportation
DOT Shipping Name:
NOT REGULATED

15. REGULATORY INFORMATION

FEDERAL REGULATIONS

TSCA Inventory Status:
All ingredients of this product are listed on the TSCA Inventory.

SARA Title III Hazard Classes:
Fire Hazard - NO
Reactive Hazard - NO

15. REGULATORY INFORMATION (Continued)

Release of Pressure - NO
Acute Health Hazard - YES
Chronic Health Hazard - YES

STATE REGULATIONS:
This product contains the following components that are regulated under California Proposition 65:

Ingredient Name	Cancer List	Reprod. List	No Sign. Risk Lvl (ug/day) California	RPI
ACETYLSALICYLIC ACID	N	Y	ND	ND

16. OTHER INFORMATION

National Fire Protection Association Hazard Ratings--NFPA(R):
1 Health Hazard Rating--Slight
1 Flammability Rating--Slight
0 Reactivity Rating--Minimal

National Paint & Coating Hazardous Materials Identification System--HMIS(R):
1 Health Hazard Rating--Slight
1 Flammability Rating--Slight
0 Reactivity Rating--Minimal

Reason for Revisions:
Conversion to ANSI MSDS format.

Key Legend Information:
NAV - Not Available
NAP - Not Applicable
ND - Not Determined
ACGIH - American Conference of Governmental Industrial Hygienists
OSHA - Occupational Safety and Health Administration
TLV - Threshold Limit Value
PEL - Permissable Exposure Limit
TWA - Time Weighted Average
STEL - Short Term Exposure Limit
NTP - National Toxicology Program
IARC - International Agency for Research on Cancer

Disclaimer:

16. OTHER INFORMATION (Continued)

The information herein is given in good faith but no warranty, expressed or implied, is made.

M A T E R I A L S A F E T Y D A T A S H E E T

RHONE-POULENC INC.
CN 7500 Cranbury, NJ 08512-7500
24-HOUR EMERGENCY TELEPHONE CHEMTREC 1-800-424-9300

Effective Date: DEC 7, 1992 Date Printed: DEC 8, 1992

PRODUCT NAME: ASPIRIN 1040

I. IDENTIFICATION

CHEMICAL NAME OF PRIMARY COMPONENT(S): Acetylsalicylic acid

FORMULA: $C_9H_8O_4$ MOLECULAR WEIGHT: 180.17

SYNONYMS: aspirin; 2-(acetyloxybenzoic)acid; acetol

CAS #: 50-78-2

II. INGREDIENTS/SUMMARY OF HAZARDS

INGREDIENT(S)	CAS Number	OSHA Hazardous (H)/ Non-Hazardous (NH)	Percent
(1) acetylsalicylic acid	50-78-2	H	99.5 (min)

NATIONAL FIRE PROTECTION ASSOCIATION RATING

HAZARDOUS MATERIALS IDENTIFICATION SYSTEM

KEY = NFPA/HMIS	NFPA	HMIS
	Health	
4=Extreme/ Severe	1	1
3=High/ Serious	Fire	
2=Moderate	1	1
1=Slight	Reactivity	
0=Minimum	0	0

SARA TITLE III HAZARD CLASSIFICATION

Immediate (acute) Health	YES
Delayed (chronic) Health	YES
Fire	NO
Sudden Release of Pressure	NO
Reactive	NO

(continued on page 2)

II. INGREDIENTS/SUMMARY OF HAZARDS (continued)

WARNING STATEMENTS:

TOXIC BY INGESTION
EYE, SKIN AND RESPIRATORY TRACT IRRITANT
SENSITIZER

CALIFORNIA PROPOSITION 65: THIS PRODUCT CONTAINS ASPIRIN, A CHEMICAL KNOWN TO THE STATE OF CALIFORNIA TO CAUSE BIRTH DEFECTS OR OTHER REPRODUCTIVE HARM.

See Section VI for complete Health Hazard Data.

DUST EXPLOSION HAZARD

III. PHYSICAL DATA

SPECIFIC GRAVITY:	1.4
BOILING POINT, 760 mm Hg, Degrees C (F):	140 (285) decomposes
MELTING POINT, Degrees C (F):	132-136 (270-276)
VAPOR PRESSURE, Degrees C:	Not known
VAPOR DENSITY (air=1):	Not known
pH:	Not known
SOLUBILITY IN WATER, @ 25 Degrees C:	1 g/300 ml water
APPEARANCE AND ODOR:	white crystalline powder; odorless

IV. FIRE AND EXPLOSION HAZARD DATA

FLASH POINT Degrees C (F): Not applicable

FLAMMABLE LIMITS IN AIR: Not applicable

AUTOIGNITION TEMPERATURE Degrees C (F): Not applicable

EXTINGUISHING MEDIA: Use carbon dioxide powder for small fires. Use water spary or foam for large fires involving this product.

SPECIAL FIRE FIGHTING PROCEDURES: Wear protective clothing and use self-contained breathing apparatus. Dike area to prevent runoff and contamination of water sources.

(continued on page 3)

RHONE-POULENC INC.
CN 7500 Cranbury, NJ 08512-7500
24-HOUR EMERGENCY TELEPHONE CHEMTREC 1-800-424-9300

Effective Date: DEC 7, 1992 Date Printed: DEC 8, 1992

PRODUCT NAME: ASPIRIN 1040

IV. FIRE AND EXPLOSION HAZARD DATA (continued)

UNUSUAL FIRE AND EXPLOSION HAZARDS:
Thermal decomposition products may be hazardous. These may include carbon monoxide and carbon dioxide.
Avoid dispersion of dust in air to reduce potential explosion hazard.
Use electrical equipment suitable for atmospheres that may contain combustible dusts.

V. REACTIVITY DATA

STABILITY:
Stable

CONDITIONS TO AVOID:
Slowly hydrolyzes in moist air to salicylic acid and acetic acids.

MATERIALS TO AVOID:
Strong oxidizing agents, strong acids, strong bases.

HAZARDOUS DECOMPOSITION PRODUCTS:
Decomposition products may be hazardous. These may include carbon monoxide and carbon dioxide.

HAZARDOUS POLYMERIZATION:
Will not occur.

VI. HEALTH HAZARD DATA/FIRST AID PROCEDURES

EXPOSURE LIMITS:
5 mg/cubic meter TWA (ACGIH TLV & OSHA PEL)

TOXICOLOGY DATA:

Oral LD50 (rats):	1010 mg/kg body weight	(1)
	1460 mg/kg body weight	(8)
Dermal LD50 (rabbits):	> 7940 mg/kg	(8)
Inhalation LC50 (rats):	No specific data available,	see below
Skin Effects (rabbits):	Non-irritating	(8)
Eye Effects (rabbits):	Mild irritant	(8)

CARCINOGENICITY, TERATOGENICITY:
This product does not contain any ingredient designated by IARC, NTP, ACGIH or OSHA as a probable human carcinogen.
Very large doses of aspirin have produced teratogenic effects in experimental animals. (2)

(continued on page 4)

VI. HEALTH HAZARD DATA/FIRST AID PROCEDURES (continued)

EFFECTS OF SINGLE OVEREXPOSURE:

Swallowing:
May cause gastrointestinal disturbances including acute irritation and bleeding. (3) Systemic effects may include central nervous system stimulation and terminal depression leading to respiratory or cardiovascular collapse.

Skin Absorption:
Percutaneous absorption of salicylates reaches toxic levels only when large areas of the skin are covered with salicylate in a suitable base or when skin has been damaged by preexisting disease. (7) Signs and symptoms same as described for swallowing.

Inhalation:
Dusts are irritating to the respiratory tract.

Skin Contact:
Causes skin irritation, seen as marked redness and swelling. (2)

Eye Contact:
Causes acute irritation and may cause a chemical burn. (2)

EFFECTS OF REPEATED OVEREXPOSURE:
Prolonged administration of large doses results in occult bleeding and may result in anemia. (2)

OTHER EFFECTS OF OVEREXPOSURE:
ALLERGEN: Aspirin is a known respiratory and systemic allergen and can produce anaphylactic phenomena even after small doses. (4)
Aspirin decreases the ability of the blood to clot. (4)

EXISTING MEDICAL CONDITIONS POSSIBLY AGGRAVATED BY EXPOSURE:
Skin irritation may be aggravated in persons with existing skin lesions.
Breathing of dust may aggravate acute or chronic asthma and chronic pulmonary disease such as emphysema and bronchitis.

The following potential problems relate primarily to individuals taking aspirin as a medication, and are not expected to be of concern to aspirin workers, unless aspirin is accidentally ingested.
- In persons taking anticoagulants, aspirin may accentuate anticoagulant activity.
- Persons with influenza and some other viral illnesses may be at higher risk of developing Reye's Syndrome.

(continued on page 5)

VI. HEALTH HAZARD DATA/FIRST AID PROCEDURES (continued)

- Persons with rheumatoid arthritis or systemic lupus erythematosus sometimes develop hepatotoxicity while taking aspirin as a medication.

EMERGENCY AND FIRST AID PROCEDURES:

Remove the patient from immediate source of exposure and assure that the individual is breathing. If not breathing, use cardio-pulmonary resuscitation or artificial respiration. GET MEDICAL ATTENTION.

Swallowing:
If patient is conscious and alert, give 2-3 glasses of water or milk to drink. If available, give one tablespoon of Syrup of Ipecac to induce vomiting. If vomiting has not occurred in 20 minutes, the same dose of Syrup of Ipecac may be repeated one additional time. Alternatively, induce vomiting by touching back of throat with finger. Do not make an unconscious person vomit. GET MEDICAL ATTENTION.

Skin:
Immediately wash skin with plenty of soap and water, while removing contaminated clothing and shoes. Wash clothing separately before reuse.

Inhalation:
Remove victim to fresh air. If not breathing, administer cardio-pulmonary resuscitation or artificial respiration. If breathing is difficult, administer oxygen. GET MEDICAL ATTENTION.

Eyes:
Hold eyelids open and flush with a steady, gentle stream of water for at least 15 minutes. GET MEDICAL ATTENTION, PREFERABLY AN OPHTHALMOLOGIST.

NOTES TO PHYSICIAN:

Treat symptomatically. Consideration should be given to the possibility that overexposure to materials other than this product may have occurred.

MINIMIZE ABSORPTION: Remove salicylates by emesis with syrup of ipecac unless respiration is depressed. Do not use apomorphine. Delay absorption of the remaining poison by giving activated charcoal. If respiration is depressed, use airway-protected gastric lavage. Enteric coated tablets can be removed by lavage with 1% sodium bicarbonate.

(continued on page 6)

VI. HEALTH HAZARD DATA/FIRST AID PROCEDURES (continued)

LABORATORY STUDIES to determine serum salicylate levels, serum electrolytes, arterial blood gases, blood pH, coagulation studies, and renal function tests / urine output should be done. Acid-base imbalance is common. In adults, respiratory alkalosis from hyperventilation and metabolic alkalosis from vomiting is common. In children, metabolic acidosis is often a significant problem.

TREATMENT: In mild poisoning, with adequate urine output and no vomiting, give milk and fruit juice orally every hour up to a total of 100 ml/kg in the first 24 hours.

In severe poisoning, begin hydration in the first hour with intravenous fluid, 400 ml/square meter. A 5% dextrose solution containing sodium bicarbonate, 75 meq/l, is satisfactory. However, do not use bicarbonate if the victim is alkalotic. After the first hour, the same solution can be continued at one-third the initial rate until urine flow begins, dehydration is corrected, or evidence of renal insufficiency appears. After urine flow is established, add potassium 30 meq/l of administered fluid. Discontinue potassium when serum levels reach 5 meq/l. If renal function is adequate, fluid administration should be approximately 3 l/m2/24h.

In the presence of abnormal bleeding or hypoprothrombinemia, give phytonadione, 10 mg intramuscularly. Fresh blood or platelet transfusions may be necessary.

Do not give barbiturates, paraldehyde, morphine or other central nervous system depressants.

If renal function is impaired, dialysis must be used to remove salicylates.

Reduce hyperpyrexia by tepid sponging. Do not use alcohol for sponging.

(5,6)

(continued on page 7)

VII. PRECAUTIONS FOR SAFE HANDLING AND USE

STEPS TO BE TAKEN IF MATERIAL IS RELEASED OR SPILLED:
To the extent possible, clean up spillage using shovels. Carefully scoop up loose material and place it in appropriate containers so as to avoid dust generation. Stand upwind if possible.
Residual spillage that cannot be removed by shovelling should be cleaned from hard surfaces as appropriate.
If spilled on the ground, the affected area should be scraped clean and the material placed in an appropriate container for disposal.
Do not flush material to public sewer systems or any waterways.
Wear appropriate protective clothing and equipment (see below).
Ensure adequate decontamination of tools and equipment following cleanup.

WASTE DISPOSAL METHOD:
Dispose of in accordance with local, state and federal regulations.

PRECAUTIONS TO BE TAKEN IN HANDLING AND STORING:
Store in a tightly closed container in a well ventilated area away all sources of ignition.
Dry powders can build static electricity charges when subjected to the friction of conveying, mixing, or sliding. To prevent ignition, provide adequate precautions, such as electrical grounding, or inert atmospheres when material is used in the presence of flammable materials.

VIII. SPECIAL PROTECTION INFORMATION

PROTECTIVE EQUIPMENT SHOULD BE USED DURING THE FOLLOWING PROCEDURES:
- Manufacture or formulation of this product
- Repair and maintenance of contaminated equipment
- Clean-up of leaks and spills

RESPIRATORY PROTECTION: Use NIOSH/MSHA approved respirator for dust. Use positive pressure self-contained breathing apparatus for emergency conditions where exposure limits are exceeded.

VENTILATION: Local exhaust ventilation.

PROTECTIVE CLOTHING: Work clothes, chemical-resistant gloves and boots

EYE PROTECTION: Chemical Workers Goggles.

OTHER PROTECTIVE EQUIPMENT: Maintain a sink, safety shower, eyewash fountain in work area. Have oxygen readily available.

(continued on page 8)

MATERIAL SAFETY DATA SHEET

RHONE-POULENC INC.
CN 7500 Cranbury, NJ 08512-7500
24-HOUR EMERGENCY TELEPHONE CHEMTREC 1-800-424-9300

IX. REGULATORY STATUS

TSCA Inventory :	YES
Transportation Status:	Not regulated
SARA Title III	
Section 302 Extremely Hazardous Substance List:	Not listed
Section 313 Toxic Chemicals:	Not listed
Reportable Quantity (RQ), under U.S. EPA CERCLA:	Not listed
RCRA Hazardous Waste:	Not listed
State's Right-to-Know Laws:	
California Proposition 65:	Listed - reproductive toxicity
Connecticut:	Not listed
Florida:	Toxic
Illinois:	Toxic
Louisiana:	RTK
Massachusetts:	RTK
New Jersey:	RTK, ID # 0020
New York:	Not listed
Pennsylvania:	RTK
Rhode Island:	HAZ, T note

X. REFERENCES

(1) RTECS, 76971, 3/87
(2) ACGIH Documentation of TLVs and BEIs
(3) Sittig, Handbook of Toxic and Hazardous Chemicals and Carcinogens, 2nd ed
(4) NJ Department of Health Hazardous Substance Fact Sheet
(5) Dreisbach, Handbook of Poisoning, 12th edition
(6) Arena, Poisoning, 5th edition
(7) Gosselin, Clinical Toxicology of Commercial Products, 5th ed
(8) Unpublished Rhone-Poulenc toxicology study.

(Last Page)

EXCEDRIN® EXTRA-STRENGTH

Caffeine

BRISTOL-MYERS PRODUCTS
Hillside, New Jersey 07207

MATERIAL SAFETY DATA SHEET

MANUFACTURER/ADDRESS
Food Science Group
205 East 42nd St.
New York, NY 10017

Product Identification

PFIZER PRODUCT NAME: CAFFEINE ANHYDROUS USP, FCC

PFIZER MSDS NO.: C001

EMERGENCY PHONE: (212) 573-2222

DATE: 07 08 1993

CHEMICAL NAME AND MOLECULAR FORMULA: C8 H10 N4 O2

CAS NO.(s): 58-08-2

SYNONYMS: 1-3-7 Trimethylxanthine

CHEMICAL FAMILY: Alkaloid

Hazardous Components

Materials or Components	%	Hazard Data (TLV, LD50, LC50, etc.)
Not applicable - not a mixture.		

Product Identification

BOILING POINT (DEGREE) F	352 degrees F (178 degrees C)	SPECIFIC GRAVITY (H2O = 1)	1.23
VAPOR PRESSURE (mm Hg.)	@ 178 degrees C - 760	% VOLATILE BY VOLUME (%)	0.5% max.
VAPOR DENSITY (Air = 1)	Not applicable	EVAPORATION RATE	Not applicable
SOLUBILITY IN WATER	Moderate	pH 1 % SOLN	6.5 - 7.5
APPEARANCE & ODOR	White needles of white powder; odorless with bitter taste.		

Fire & Explosion Data

FLASH POINT (Method used): Ignition Temperature: 925 degrees C

FLAMMABLE LIMITS: g/ft3

FLAMMABLE

Lel	Uel
2 min.	16 est.

EXTINGUISHING MEDIA: Water, CO2.

SPECIAL FIRE FIGHTING PROCEDURES: None

UNUSUAL FIRE AND EXPLOSION HAZARDS: Severe (Bureau of Mines Relative Explosion Hazard Rating) as dust.

Reactivity Data

STABILITY		
	UNSTABLE	
	STABLE	X

CONDITIONS TO AVOID: Not applicable

INCOMPATIBILITY (Materials to avoid): Hot alkalines, chlorine water.

HAZARDOUS DECOMPOSITION PRODUCTS: When heated to decomposition, may emit toxic fumes; composition not established.

HAZARDOUS POLYMERIZATION		CONDITIONS TO AVOID
May Occur	Will Not Occur X	Not applicable

Toxicity Classification

ORAL/PARENTERAL: 320mg/kg. oral-child LDLO; 1gm/kg oral-woman LDLO; 14,700ug/kg oral-infant TDLO; 245 mg/kg oral-rat LD50; 127mg/kg oral-mouse LD50. Other animals.

DERMAL (acute): No data available

EYE: No data available

INHALATION: No data available

CHRONIC: FDA recently proposed removal of caffeine from its "generally recognized as safe" list and is gathering additional information. Concerns with excessive use include possible reproductive effects to fetal craniofacial area, musculoskeletal system, possible bladder cancer (2 separate epidemiological studies), myocardial infarction and, to lesser degrees, constipation, palpitations, shortness of breath and depressed mental state. *Prechronic study completed.

CARCINOGENICITY:	NTP? Listed*	IARC Monographs? Not listed	OSHA Regulated? No

Health Hazard Information

Effects of Exposure

ORAL INGESTION No TLV established. May act as stimulant if excessive ingestion. Large doses (above 1g) may cause palpitation, excitement, insomnia, dizziness, headache and vomiting.

EYE CONTACT As dust or vapor, may be an irritant.

SKIN CONTACT As dust or vapor, may be an irritant.

INHALATION Avoid breathing dust. May act as stimulant on excessive inhalation. Large doses (above 1g) may cause palpitation, excitement, insomnia, dizziness, headache and vomiting.

Emergency First Aid

ORAL INGESTION If large quantities are ingested, remove to fresh air; get medical attention.

EYE CONTACT Flush eye contact with plenty of water; get medical attention.

SKIN CONTACT Flush skin contact with plenty of water; get medical attention. Launder clothing before reuse.

INHALATION If large quantities are inhaled, remove to fresh air; get medical attention.

Spill or Leak

STEPS TO BE TAKEN IN CASE MATERIAL IS RELEASED OR SPILLED Recover by vacuum, sweep or shovel into recovery containers.

WASTE DISPOSAL METHOD (Comply with applicable federal, state, and local regulations.) Wash down and flush with water. Dispose in conformance with pertinent federal, state and local regulations.

Special Protection Info.

RESPIRATORY PROTECTION (Specify Type) Approved dust mask.

VENTILATION	**LOCAL EXHAUST** Dust exhaust sys-point of use	**SPECIAL**
	MECHANICAL (general)	**OTHER**

PROTECTIVE GLOVES Standard work gloves	**EYE PROTECTION** Safety glasses

OTHER PROTECTIVE EQUIPMENT Explosion proof equipment recommended to use with dust.

Special Precautions

PRECAUTIONS TO BE TAKEN IN HANDLING AND STORING Store in tightly closed containers. Avoid breathing dust; do not ingest.

OTHER PRECAUTIONS None

This MSDS is based on a limited review of Pfizer's files and standard toxicology handbooks.

The information herein is furnished without warranty of any kind. This information should be used only as a supplement to information already in your possession concerning this product. The determination of whether and under what conditions the product should be used by your employees is yours to make.

Certificate of Analysis

Quality assurance

Knoll AG - Postfach 21 08 05 - 67008 Ludwigshafen

BASF Pharma

knc

Text	:	CAFFEINE ANHYDROUS POWDER			
Quantity	:	0,3 KG	Lot no.	:	58826
Cat no.	:	1A001BG1	Order no.	:	910541/02 // 3834897
Customer no.	:	32205101	Costcenter	:	45401 / LA1
Consignee	:	BASF CORPORATION USA CONS.PROD. & LIFE SCI.DIV. MOUNT OLIVE,NJ 07828-1234 USA			
Product	:	COFFEIN, WASSERFREI, PULVER	Specifications:		P USP0-06 / 02 / 1A001BG1
			Page	:	001 of 001

19158826
017780 / 02

Testparameters	Requirements	Results
Characters		
Appearance	Cryst. substance or granules	Test passed
Colour	White	Test passed
Odour	Odourless	Test passed
Identification	Must comply	Test passed
Melting range		
Beginning of melting	Min. 235,0 °C	236,5
End of melting	Max. 239,0 °C	237,2
Other alkaloids	Must comply	Test passed
Heavy metals, calc. as lead	Max. 10 ppm	Test passed
Readily carbonisable subst.		
Colour	Max. reference solution D	Test passed
Loss on drying	Max. 0,5 %	0,1
Residue on ignition	Max. 0,1 %	Test passed
Content	98,5 to 101,0 % in dry sub	100,3
Organic volatile impurities	Must comply	Test passed

Production site: Minden
Manufacturing date: 05 / 09 / 1996
Expiry date: 05 / 09 / 2000
(to be understood as recommended date of retesting)

Result: Caffeine, anhydrous meets the requirements of USP.

67008 Ludwigshafen, den 20.09.1996 / WOV

Klinzmann

(Dr. Klinzmann)
Quality assurance

Product # FC 5121
ABL # 58826
Kolli #
Name Caffeine Anhyd. Pwd

ITEM 3 – 01027

MATERIAL SAFETY DATA SHEET

A Unit of BASF K&F Corporation
120 East 56th Street
New York 10022
Tel: (212)752-6520

30 North Jefferson Road
Whippany, N.J. 07981
Tel: (201)887-8300

knoll

PRODUCT NUMBER:

SECTION I

*Registered Trademark

TRADE NAME: Caffeine, anhydrous

CHEMICAL NAME: 1,3,7-Trimethylxanthine

SYNONYMS: N/A

FORMULA: $C_8H_{10}N_4O_2$

CHEMICAL FAMILY: Purine derivative

MOL. WGT.: 194.19

SECTION II — INGREDIENTS

COMPONENT	CAS NO.	%	PEL/TLV — SOURCE
Caffeine, anhydrous	58-08-2	100	N/A

SECTION III — PHYSICAL DATA

MELTING POINT 760 mm Hg: 235.0 - 237.5 °C

pH: 5.5-6.5 (10g/l-H_2O)

VAPOR PRESSURE mm Hg 20 C: N/A

SPECIFIC GRAVITY OR BULK DENSITY: N/A

SOLUBILITY IN WATER: 20 °C about 20 g/l

APPEARANCE: white crystalline powder ODOR: practicaly odorless INTENSITY: N/A

SECTION IV — FIRE AND EXPLOSION HAZARD DATA

FLASH POINT (TEST METHOD): not indicated

AUTOIGNITION TEMP: N/A

FLAMMABILITY LIMITS IN AIR (%BY VOL) N/A LOWER: N/A UPPER: NA

EXTINGUISHING MEDIUM	water fog / foam / CO_2 / dry chemical / halon
SPECIAL FIREFIGHTING PROCEDURES	not required
UNUSUAL FIRE AND EXPLOSION HAZARDS	Slightly inflammable substance, no exoth. reaction up to melting point. Vapours burnable > 240°C, dust explosive St 2 under the formation of dust clouds > 50 g/m³, electrostatic charging capacity high

HPTK

received
6/8/94

PRODUCT NUMBER:

SECTION V — HEALTH DATA

TOXICOLOGICAL TEST DATA:

			RESULT:	
LD 50 oral rat:	> 261 < 383 mg/kg	source: BASF	Primary skin irritation:	non irritant — source: BASF
LD 50 dermal rat:	> 2000 mg/kg		Primary mucosal irritation:	non irritant
LC 50 inh. rat:	ca. 4,94 mg/l/4h		LD 50 i.v. rat:	105 mg/kg — source: NIOSH
LC 50 inh. rat (m):	ca. 4,94 mg/l/4h		LD 50 i.v. mouse:	68 mg/kg
LC 50 inh. rat (f):	ca. 4,1 mg/l/4h		LD 50 p.o. mouse:	620 mg/kg

EFFECTS OF OVEREXPOSURE:

a) Inhalation: Irritation of nasal, pharyngeal and tracheal mucous membranes, Cough irritation
b) Immediately: Only large amounts cause hypersensitivity reactions, muscle tremor, tachycardia, increased blood pressure, convulsions, hallucinations. Symtoms may persist for hours.
c) Skin: Slight dermal irritation
d) Eyes: Severe irritation, burning, lacrimation

FIRST AID PROCEDURES:

Should product come into contact with the eyes, immediately rinse with plenty of water.
Consult an ophthalmologist, if required. Rinse affected parts of skin with plenty of water.
Seek medical help should any symtoms occur attributable to inhalation, ingestion and contact with skin or eyes.

SECTION VI — REACTIVITY DATA

STABILITY: Preserve in well-closed containers and protected from light.
CONDITIONS TO AVOID: N/A

CHEMICAL INCOMPATIBILITY: none known

HAZARDOUS DECOMPOSITION PRODUCTS: none known

HAZARDOUS POLYMERIZATION:
CONDITIONS TO AVOID: none known

CORROSIVE TO METAL: N/A | **OXIDIZER:** N/A

SECTION VII — SPECIAL PROTECTION

RESPIRATORY PROTECTION:
Protective mask against dust nuisance

EYE PROTECTION: Protective goggles

PROTECTIVE CLOTHING: Rubber gloves, coveralls, apron

VENTILATION: local exhaust

PRODUCT NUMBER:

SECTION VIII — ENVIRONMENTAL DATA

ENVIRONMENTAL TOXICITY DATA: Possible hazard for water and sewerage plants
Biodegradability: poorly biodegradable (DIN 52 900) Analytical method: BOD
Hazardous to fish: LC 50 (96 h) ide: ca. 87 mg/l; LC 0 (48 h) ide: 50 mg/l
Hazardous to daphnia: EC 50 (48 h) : 182 mg/l Microbial toxicity: EC 10: 1530 mg/l after 17 h
source: BASF

SPILL AND LEAK PROCEDURES:
Sweep up, take up with a scoop; waste disposal cf. Waste Disposal Method

HAZARDOUS SUBSTANCE SUPERFUND: N/A RQ (lbs) N/A

WASTE DISPOSAL METHOD:
Burn in appropriate combustion plant observing environmental protection laws

HAZARDOUS WASTE 40CFR261: N/A HAZARDOUS WASTE NUMBER: N/A

CONTAINER DISPOSAL:
Dispose of in licensed facility. Recommend crushing or other means to prevent unauthorized re-use

SECTION IX — SHIPPING DATA

D.O.T. PROPER SHIPPING NAME (49CFR172.101-102)	HAZARDOUS SUBSTANCE (49CFR CERCLA LIST) REPORTABLE QUANTITY (RQ)
D.O.T. HAZARD CLASSIFICATION (CFR172.101-102) PRIMARY	SECONDARY

D.O.T. LABELS REQUIRED (49CFR172.101-102)	D.O.T. PLACARDS REQUIRED (CFR172.504)	POISON CONSTITUEN (49CFR172.203(K))
BILL OF LADING DESCRIPTION		

CC NO.	UN/NA CODE

DATE PREPARED: July 1989 UPDATED: Febr. 1992

WHILE KNOLL PHARMACEUTICALS, A UNIT OF BASF K&F CORPORATION, BELIEVES THE DATA SET FORTH HEREIN ARE ACCURATE AS OF THE DATE HEREOF, KNOLL PHARMACEUTICALS, A UNIT OF BASF K&F CORPORATION MAKES NO WARRANTY WITH RESPECT THERETO AND EXPRESSLY DISCLAIMS ALL LIABILITY FOR RELIANCE THEREON. SUCH DATA ARE OFFERED SOLELY FOR YOUR CONSIDERATION, INVESTIGATION, AND VERIFICATION.

PRODUCT NUMBER:

SECTION X — PRODUCT LABEL

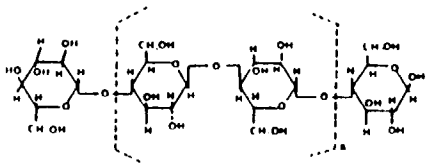
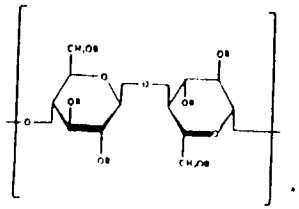
APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

Appendix A.3

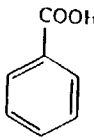
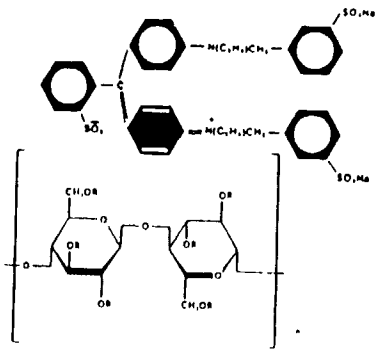
EXCEDRIN Extra Strength Tablets
Inactive Ingredients
Material Safety Data Sheets (attached)
page 1

Ingredient	CAS#	Molecular Weight	Formula/Description	Structure
Microcrystalline Cellulose,NF	9004-34-6	≈ 36000	$(C_6H_{10}O_5)x$/ white powder	
Stearic Acid,NF	57-11-4	284.48	$CH_3(CH_2)_{16}COOH$/white powder	$CH_3(CH_2)_{16}COOH$
Low substituted Hydroxypropyl Cellulose NF	9004-64-2	50,000-1,250,000	n/a / white pwder	

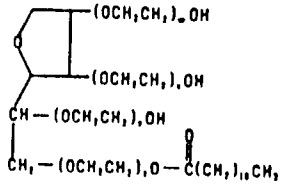
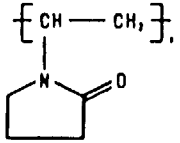
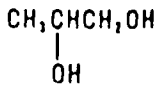
Appendix A.3

EXCEDRIN Extra Strength Tablets
Inactive Ingredients
Material Safety Data Sheets (attached)

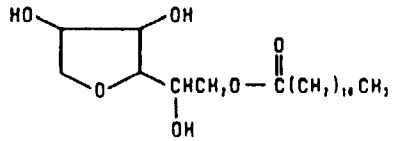
Componets-Film Coating

Ingredient	CAS#	Molecular Weight	Formula/Description	Structure
Benzoic Acid, USP Benzenecarboxylic acid	65-85-0	122.12	$C_7H_6O_2$/White powder	
FD&C Blue #1 Brilliant Blue FCF	3844-45-9	792.85	$C_{37}H_{34}N_2Na_2O_9S_3$ Dry colorant	
Hydroxypropyl Methylcellulose, USP	9004-65-3	10,000-1,500,000	not given/ white powder	
Mineral Oil, NF	8042-47-5	n/a	mixture/clear viscous liquid	Mineral oil is a mixture of refined liquid saturated hydrocarbons obtained from petroleum

Appendix A.3
EXCEDRIN Extra Strength Tablets
Inactive Ingredients
Material Safety Data Sheets (attached)

Ingredient	CAS#	Molecular Weight	Formula/Description	Structure
carnauba wax, NF	8015-86-9	n/a	n/a/pale yellow white powder	Consists of complex mixture of esters of acids and hydroxyacids.
polysorbate 20, NF	9005-64-5	1128	$C_{58}H_{114}O_{26}$/ amber liquid	
povidone, USP Plasdone K-29/32 polyvinylpyrrolidone	9003-39-8	2500- 3,000,000	$(C_6H_9NO)x$/white powder	
Propylene Glycol, USP	57-55-6	76.09	$C_3H_8O_2$/colorless liquid	

Appendix A.3
EXCEDRIN Extra Strength Tablets
Inactive Ingredients
Material Safety Data Sheets (attached)

Ingredient	CAS#	Molecular Weight	Formula/Description	Structure
Sorbitan monolaurate, NF	1338-39-2	346	$C_{18}H_{34}O_6$/amber oilyliquid	
Simethicone Emulsion, USP silicone emulsion	8050-81-5	n/a	mixture/white liquid	A mixture of dimethi cone with an average chain length of 200 to 350 dimethylsiloxane units and hydrated silica.
Water	7732-18-5	18.02	H_2O/Clear Liquid	H_2O
Titanium dioxide, USP	13463-67-7	79.88	TiO_2/white powder	TiO_2

Confidential
Appendix B.3
Disposal Sites

BRISTOL-MYERS PRODUCTS
Hillside, New Jersey 07207

EXCEDRIN® EXTRA STRENGTH
ENVIRONMENTAL ASSESSMENT

Potential Disposal Sites for EXCEDRIN ® Extra Strength Returned and Rejected Goods				
Disposal Name	**Location**	**Permit**	**Issuing Agency**	**Date**
OMS of Fairfax Inc.	9898 Furnance Road Lorton, VA	Solid Waste: #510	Commonwealth of Virginia	Issued 11/2/87 No Expiration Date
		Air: PSD-#71920	Commonwealth of Virginia	No expiration Date
		Water: A #51199	Commonwealth of Virginia	Expires 12/31/99
OMS of Babylon	125 Gleam Street West Babylon, NY 11704	Solid Waste: #1-4720-00777/00002-0	New York State Department of Environmental Conservation (NY DEC)	Expires 5/96 in process of being renewed
		Air: #1-4720-00777/00003-D	NY DEC	No expiration date indicated on permit
OMS of Huntington, LP	99 Town Line Road East Northport, NY 11731	Solid Waste: #1-4726-00790/00002-C	NY DEC	No expiration date indicated on permit
		Air: #1-4726-00790/00001-0	NY DEC	Expires 9/96

EXCEDRIN® EXTRA STRENGTH ENVIRONMENTAL ASSESSMENT

Potential Disposal Sites for EXCEDRIN ® Extra Strength Returned and Rejected Goods				
Disposal Name	**Location**	**Permit**	**Issuing Agency**	**Date**
OMS of Indianapolis, Inc.	2320 So.Harding St. Indianapolis, IN 46221	Solid Waste: FFPP #49-13	Indiana Department of Environmental Management	Expired 6/94 operating on interim permit
		Air: #0123-01	City of Indianapolis	In interim status
		Industrial Discharge: #495301	City of Indianapolis	Expires 4/97
OMS of Haverhill, Inc.	100 Recovery Way Haverhill, MA 01835	Solid Waste: NESW-CF-009	Massachusetts Department of Environmental Protection (MaDEP)	Expires 5/13/98
		Landfill: NESW-FF-011	Ma DEP	Expires 5/13/98
		Wastewater: #4391-01	Wastewater Treatment Plant of Haverhill	Expires 2/98
		Air: Mbr-86-Inc-007	MaDEP	No Expiration Date

EXCEDRIN® EXTRA STRENGTH
ENVIRONMENTAL ASSESSMENT

Potential Disposal Sites for EXCEDRIN ® Extra Strength Returned and Rejected Goods				
Disposal Name	**Location**	**Permit**	**Issuing Agency**	**Date**
OMS of Alexandria	5301 Eisenhower Ave. Alexandria, VA 22304	Air: 71895	Commonwealth of Virginia	N/A
		Water: 01-97-A-004	Commonwealth of Virginia	1/31/97
		Solid Waste: 435	Commonwealth of Virginia	N/A
OMS of Huntsville	5251 Triana Blvd. Huntsville, AL 35805	Air: 7-09-1104 X001 - X006	Alabama Dept. Environ. Mgmt.	N/A
		Water: IU0845372	Alabama Dept. Environ. Mgmt.	N/A
		Solid Waste: combined with air permit	Alabama Dept. Environ. Mgmt.	N/A

ITEM 3 – 01350

EXCEDRIN® EXTRA STRENGTH
ENVIRONMENTAL ASSESSMENT

Potential Disposal Sites for EXCEDRIN ® Extra Strength Returned and Rejected Goods				
Disposal Name	**Location**	**Permit**	**Issuing Agency**	**Date**
OMS of Lake	3830 Rogers Industrial Rd. Indianapolis, IN46221	Air: PSD-FL-113 (AC35-115379)	DEP - Tallahassee	N/A
		Water: OCD-1W-96-0440	DEP - Tallahassee	02-01-97
		Solid Waste: SO35-2793-97	DEP - Tallahassee	2-5-01
OMS of Marion	4850 Brooklake Rd., NE Brooks, OR 97305	Air & Solid Waste #364	Oregon Dept. Environ Quality	6/30/05
		Water: 89638	Oregon Dept. Environ Quality	9/30/99
OMS of Stanislaus	4040 Fink Road Crows Landing, CA 95313	Air: N-2073-1-0	San Joachin Valley A.P.C.D.	N/A
		Water No #	Stanislaus Dept. Environ Resou.	12/31/99
		Solid Waste: 50-AA-09	Calif. Integrated Waste Mgmt. Board	11/99

ITEM 3 – 01351

In a separate communication to the Agency, the applicant authorized the release of the information in Appendix B.1.

FDA 5/21/97 Non-

Confidential Appendix B.1 Suppliers Environmental Certification Statements

BRISTOL-MYERS PRODUCTS
Hillside, New Jersey 07207

EXCEDRIN® EXTRA-STRENGTH

Acetaminophen

BRISTOL-MYERS PRODUCTS
Hillside, New Jersey 07207

MALLINCKRODT CHEMICAL

Mallinckrodt Chemical, Inc.
16305 Swingley Ridge Drive
Chesterfield, Missouri 63017-1777
Telephone (314) 530-2000

September 18, 1996

Mr. Richard Eberts
Purchasing Manager - Raw Materials
Bristol-Myers Products
1350 Liberty Avenue
Hillside, NJ 07205

Re: Memo to John Steitz, September 7, 1996, Acetaminophen Environmental Assessment

Dear Mr. Eberts:

Mallinckrodt Chemical, Inc. (Mallinckrodt) has not been required to complete a "Certificate of Compliance with environmental requirements" for manufacture of acetaminophen. Therefore, Mallinckrodt is unable to provide such certificate. Mallinckrodt began manufacture of acetaminophen at Raleigh, North Carolina in 1971.

To the best of my knowledge, approval of the Bristol-Myers Products IND or NDA for products containing acetaminophen will not require Mallinckrodt to make changes to qualitative emissions.

To the best of my knowledge, Mallinckrodt's Raleigh, North Carolina facility is currently in compliance with federal, state, and local emission standards.

To the best of my knowledge, approval of the Bristol-Myers Products IND or NDA for products containing acetaminophen will not affect Mallinckrodt's ability to comply with federal, state, and local emission standards.

Sincerely,

John Steitz /sl

John Steitz
General Manager

cc: R. Boland
T. Forrester
S. Lerch

Hoechst Celanese

Bulk Pharmaceuticals & Intermediat
Hoechst Celanese Corporation
PO Box 428
Highway 77 South
Bishop, TX 78343
512 584 6000

September 26, 1996
JRA-101-96

Mr. Richard Eberts
Bristol-Myers Products
1350 Liberty Avenue
Hillside, NJ 07205

Dear Dick:

The following information is submitted in response to your letter dated September 7, 1996, regarding the FDA request for Environmental Assessment information on the Hoechst Celanese Acetaminophen process.

The manufacturing, processing, quality control testing, packaging, labeling and distribution of Hoechst Celanese Acetaminophen have been performed at the following facility for more than six years.

Hoechst Celanese Corporation
Bulk Pharmaceuticals and Intermediates
1 mile South of Business Highway 77
P.O. Box 428
Bishop, Texas 78343

All facilities utilized in the production of Acetaminophen at the Bishop site are operated in full compliance with all Federal, State and local emissions requirements. Thus, approval of the subject IND or NDA will not require Hoechst Celanese Corporation to make changes to qualitative emissions. Furthermore, approval of the subject IND or NDA will not affect the ability of Hoechst Celanese Corporation to continue to comply with all Federal, State, and local emissions requirements.

Should you have any questions regarding the information submitted please feel free to contact me at (512) 584-6549.

Sincerely,

Jackie Abundo

Jackie R. Abundo
QA/QC Manager

RHÔNE-POULENC

RHÔNE-POULENC INC.

PHARMACEUTICAL INGREDIENTS
P.O. BOX 174
LULING, LOUISIANA 70070

December 15, 1996

Richard Eberts
Purchasing Manager - Raw Materials
Bristol-Myers Products
1350 Liberty Avenue
Hillside, NJ 07205

Mr. Eberts:

Following your request to complete an Environmental Assessment for the Luling site, below is Rhône Poulenc's response:

1. Rhône Poulenc's analgesics facility is located inside a Monsanto Agrochemical site. As the host company, they hold several permits including, but not limited to: State of Louisiana Department of Environmental Quality (Air and Water Permits), Parish of St. Charles Louisiana, and Federal EPA. Monsanto as well as Rhône Poulenc is presently in compliance with all Federal, State and Local permit requirements. Rhône Poulenc has been producing Acetaminophen at this facility since 1989.

2. The acetaminophen products considered by Bristol-Myers in the IND or NDA formulation are presently manufactured at the Luling analgesics facility. Therefore, qualitative emissions, directly related to the manufacturing practice, would not change.

3. As indicated in answer #1, Rhône Poulenc & Monsanto are in compliance with all Federal, State, and Local emission standards. Compliance is maintained through various reporting, sampling, and inspection criteria routinely performed at the facility.

4. Rhône Poulenc's production capabilities will be maintained well within permitted production limits. Production records are maintained at the facility, and are evaluated frequently to assure compliance with permitted levels. The desired volume of product Bristol-Myers has requested will not cause the Rhône Poulenc facility to violate any Federal, State, or Local emission criteria.

All reports and permits are maintained in the administrative offices of Monsanto.

We believe the above fulfills your request for information. If I can be of further assistance, please contact me at (504) 785-3411.

Sincerely,

Richard C. Wesley
Plant Manager
Rhône Poulenc, Luling

EXCEDRIN® EXTRA-STRENGTH

Aspirin

BRISTOL-MYERS PRODUCTS
Hillside, New Jersey 07207

The Dow Chemical Company
Midland, Michigan 48667

October 14, 1996

Mr. Richard Eberts
Bristol Myers Products
1350 Liberty Avenue
Hillside, NJ 07205

Re: Letter dated September, 7 1996 to Andrew Merlo

Dear Richard:

We received your request for a letter regarding the environmental assessment section of your new NDA or IND for your new drug substance containing Dow Chemical aspirin. As you are aware, the Dow Chemical Company will cease to produce aspirin later this year after nearly 80 years of production. In fact, we expect to be done with production in October, 1996. Since Dow will no longer be producing aspirin, our emissions related to that process will be essentially zero. Aspirin produced by Dow, for your use prior to our shutdown would have been made using the same process that was regulated by our existing environmental permits. No process changes or deviations would have been required to make the pounds of aspirin used by your company for your new product.

Sincerely,

Paul A. Adair III

Paul A. Adair, III
Production Supervisor
Salicylates Production, 1200 BLDG

CC: M. Hickey
A. Merlo
M. Thomas

RHÔNE-POULENC

SPECIALTY CHEMICALS DIVISION

140 LAFAYETTE AVENUE
PO BOX 57911
ST LOUIS MISSOURI 63157
TELEPHONE (314) 342-1300

September 23, 1996

Richard Eberts
Purchasing Manager - Raw Materials
Bristol-Myers Products
1350 Liberty Avenue
Hillside, NJ 07205

Mr. Eberts:

In your letter dated September 7, 1996, to Joseph J. Del Gandio, Bristol-Myers Products requested information to complete an Environmental Assessment. Below is Rhone-Poulenc's response:

1.) Rhone-Poulenc currently holds several permits at the St. Louis analgesics facility, including, but not limited to: City of St. Louis Air Operating Permit, Metropolitan St. Louis Sewer District (MSD) waste water discharge permit, registered EPA and Missouri Hazardous Waste Generator (MOD985771864). Rhone-Poulenc is presently in compliance with all Federal, State, and Local permit requirements. Rhone-Poulenc has produced Aspirin at the facility since 1989.

2.) The aspirin products considered by Bristol-Myers in the IND or NDA formulation are presently manufactured at the St. Louis analgesics facility. Therefore, qualitative emissions, directly related to manufacturing practice, would not change.

3.) As indicated in answer #1, above, Rhone-Poulenc is in compliance with all Federal, State, and Local emission standards. Compliance is maintained through various reporting, sampling, and inspection criteria routinely performed at the facility.

4.) Rhone-Poulenc's production capabilities will be maintained well within permitted production limits. Production records are maintained at the facility, and are evaluated frequently to assure compliance with permitted levels. The desired volume of product Bristol-Myers has requested will not cause the Rhone-Poulenc facility to violate any Federal, State, or Local emission criteria.

All reports, permits, and pertinent production records are maintained in the administrative office in fire proof cabinets. Rhone-Poulenc's record retention requirements exceed all Federal, State, and Local recommended retention periods.

We believe the above fulfills your request for information. If I have overlooked anything or can be of further assistance, please contact me at (314) 342-1364.

Sincerely,

Kenneth A. Ross
Environmental Resources Manager

EXCEDRIN® EXTRA-STRENGTH

Caffeine

BRISTOL-MYERS PRODUCTS
Hillside, New Jersey 07207

BASF Corporation

BASF

TELEFAX

Total Number of Pages: 7

Date: September 27, 1996

To: Mr. Richard Eberts
Telefax: 908-687-0186

From: Christie Ploetner - BASF Pharma
Telephone: 201-426-5358
Telefax: 201-426-5355

Re: **REQUIREMENTS FOR SUBMISSION OF IND OR NDA FOR A PRODUCT CONTAINING CAFFEINE FROM BASF**

The following pages contain the "Environmental Assessment" of Knoll AG, Minden plant which answers questions 1-3 in the letter to Edwin Kendrick dated September 7, 1996.

Concerning item 4, we can confirm that the approval of the IND or NDA submitted by Bristol Myers Products will not affect Knoll AG's ability to comply with federal, state and local emissions standards.

If there are any further questions, please do not hesitate to contact me.

Best Regards,

Christie Ploetner

Christie Ploetner

KNOLL AG
Minden Works

Minden, November 20, 1992.

ENVIRONMENTAL ASSESSMENT

Knoll AG, manufacturer of various pharmaceutical chemicals/drugs, official address:

Knoll AG, Werk Minden [Minden Works]
Karlstrasse 15, 29-35, 42-44
4950 Minden
Germany,

hereby confirms that it manufactures these pharmaceutical chemicals/drugs in accordance with all pertinent laws and regulations of the Federal Republic of Germany aimed at protecting the environment.

The establishment and operation (of plants) for the manufacture of pharmaceutical chemicals/drugs is subject to official approval under §4 of the *Bundesimmissionsschutzgesetz* (BImSchG) [Federal Immission Control Act] of Germany. This results from application of the regulations relative to industrial plants subject to official approval (4. BImSchV [4th Federal Immission Control Regulation]), which, in its Appendix, Section 4.1, specifies plants designed for the industrial production of substances by chemical conversion.

A written application for approval of this plant must be filed with the competent authorities, which do not grant approval until having thoroughly reviewed the application. Approval must not be granted unless certain prerequisites specified in §6 of the BImSchG [Federal Immission Control Act] (cf. Appendix 1) are fulfilled.

Thus, it must, for example, be ensured that the company operating a plant subject to official approval fulfills its duties and responsibilities resulting from §5 of the BImSchG [Federal

Commission Control Act]. Also, the establishment and operation of such plants must be compatible with other regulations of public interest as well as with industrial safety concerns.

§5 of the BImSchG [Federal Immission Control Act]:
Duties & Responsibilities of Companies Operating Plants Subject to Official Approval

1. Immission Control Principle

The plant shall not have any detrimental effects on the environment and/or cause any other risks, significant interference with or significant inconvenience for the general public and/or those in the vicinity of said plant.

2. Emission Control Principle

Detrimental effects on the environment shall be prevented, especially by state-of-the-art emission control measures.

3. Residue Prevention Principle

Residues shall be avoided unless they are reused according to the regulations and without any detrimental impact on the environment or, if residue prevention and/or reuse are/is technically not feasible or not reasonably acceptable, shall be eliminated as waste material in a way that does not interfere with public welfare.

4. Waste Heat Utilization Principle

Waste heat produced by said plant(s) shall be used for ((an)other) plant(s) of the company operating the aforementioned plant or made available to third parties willing to use said waste heat provided that this procedure is technically feasible and reasonably acceptable by virtue of the nature and site of said plants and compatible with principles 1 through 3.

Compliance with the above principles is typically ensured in the course of the approval procedure by linking approval to specific secondary provisions (requirements, conditions). For instance, said secondary provisions ensure that emissions from the production plant, including waste gases, solid and liquid wastes,

residues, noise, etc. are handled in an environmentally benign fashion.

Emission standards for air pollutants are set by the *TA-Luft* specifications (Official SOP of the *1. BImSchVwV* [First Clean Air Enforcement Regulation of Germany]). Compliance with said air pollutant emission standards is monitored by the initial and periodic follow-up measurements made by an agency designated by the *oberste Landesbehörde* [Supreme State Authority] (§ 26, §28 of the BImSchG [Federal Immission Control Act]). In addition, the emission levels must be reported at regular intervals in the format of a so-called Emission Declaration (§ 27 of the BImSchG).

Observance of and compliance with these regulations ensure that the industrial plants used for the manufacture of pharmaceutical chemicals/drugs are in accordance with German environmental protection legislation.

Process waste water from the pharmaceutical chemicals production plant is discharged to the fully biological central waste-water treatment plant of the Minden Works. In every approval procedure under the BImSchG [Federal Immission Control Act], the competent authorities shall, pursuant to § 6 of the BImSchG, assess whether the central waste-water treatment system ensures treatment in accordance with pertinent German statutory requirements. If this cannot be reliably assured, special pretreatment systems must be established to complement the existing central waste-water treatment plant. Only the effluent of this pretreatment system may then be discharged to the central waste-water treatment plant.

The operation of the central waste-water treatment plant is monitored by regular measurements made by the operator of the plant. Reports about these measurements are forwarded to the competent authorities. Compliance of the effluent discharged from the central waste-water treatment plant into the Weser (receiving body of water) with the standards specified in the discharge-permit issued by the water authorities is monitored by the competent authorities (*Staatliches Amt für Wasser- und*

Abfallwirtschaft [Government Agency for Water and Waste Management of Germany]) by means of independent sampling and testing, either carried out by the authority itself or contracted out.

This policy ensures that the treated process waste waters discharged from the production facilities of the Minden Works are in line with German clean water legislation.

Process residues/solid and liquid wastes resulting from the production of pharmaceutical chemicals/drugs shall be handled in accordance with the strict assessment pursuant to § 5, Section 1, No. 3 of the BImSchG [Federal Immission Control Act] and/or the requirements resulting from the provisions of the *Abfallgesetz* [German Waste Management Act].

Under these statutory provisions, residues shall be prevented or reused or, if residue prevention and/or reuse are/is technically not feasible or not reasonably acceptable, eliminated as waste in a manner that has no detrimental impact on the environment.

The above issues are reviewed and the disposal pathway is defined in each individual case in accordance with the standards of the *Abfallgesetz* [German Waste Management Act], the *Reststoffbestimmungsverordnung* [Residue Measurement Regulation], *Abfallbestimmungsverordnung* [Waste Measurement Regulation], *Abfallüberwachungsverordnung* [Waste Control Regulation], *Reststoffüberwachungsverordnung* [Residue Control Regulation], and Waste SOP. Disposal is regulated by a comprehensive auditing and approval system (disposal documentation, shipping license) along with an accurately specified accompanying document policy to ensure that each individual disposal activity can be accurately monitored and controlled. This approach ensures that waste materials can be disposed of by the statutorily defined pathway only.

Compliance with the regulations concerning residue and waste handling ensures that the process residues and wastes resulting from the production of pharmaceutical chemicals/drugs are handled in accordance with the provisions of German environmental

protection legislation.

Compliance with the statutory requirements described above is strictly enforced by us in close cooperation with the competent authorities and the designated statutory commissioners. Intentional violations of these rules and regulations constitute administrative offenses under German Law and are fineable.

Also, we should point out here that we are subject to continuous supervision by the *Staatliche Gewerbeaufsichtsamt Minden* [Minden Trade Supervisory Authority].

The accuracy of the above data, facts and statements is confirmed by the undersigned by virtue of his signature:

[signed]

Dr. Rolf Steinkamp
Werksleiter [Works Manager]
Knoll AG, *Werk Minden* [Minden Works]

Der Regierungspräsident Detmold
Die Richtigkeit der vorstehenden Angaben
wird hiermit bestätigt

Im Auftrag Detmold, den 11.04.1993

CULTOR

Food Science

JERRY O. ROLAND
Sales Manager

October 16, 1996

Mr. Richard Eberts, Jr.
Bristol-Myers Products
1350 Liberty Avenue
Hillside, NJ 07207

Dear Dick:

To confirm our recent conversation, Cultor Food Science (formerly Pfizer Food Science) ceased production of Caffeine at the Groton, CT facility in December of 1995 and no longer manufactures this product in any of its producing facilities around the world. As Cultor Food Science no longer manufactures Caffeine, Cultor's emissions cannot be in anyway materially affected by a Bristol-Myers NDA.

Dick, should you have any questions or if I can be of further service, please feel free to contact me.

Sincerely,

Jerry Roland
Sales Manager

EXCEDRIN® EXTRA-STRENGTH

Banner Pharmacaps

BRISTOL-MYERS PRODUCTS
Hillside, New Jersey 07207

BANNER
PHARMACAPS

December 10, 1996

Ms. Mary Beth Koza
Bristol-Myers Products
1350 Liberty Ave.
Hillside, NJ 07027

Dear Ms. Koza:

Please be advised that Banner Pharmacaps' Chatsworth Facility is in compliance with Local, State and Federal emissions requirements.

Excedrin Geltabs code number BM-2 are being manufactured in this facility since June of 1995. FDA's approval of your NDA and continued production of Excedrin Geltabs in Chatsworth will not change our current qualitative emissions and will not impact Banner Pharmacaps' ability to comply with current Local, State or Federal requirements.

Sincerely,

Hany Farag
Corporate Director of Compliance
and Regulatory Affairs

CC: J. Kelly, S. Marwah, J. Mitchell, E. Olsen