

Individual Safety Report



\*3607188-6-88-81\*

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM



Approved by FDA on 12/02/93

Mfr report # A014956

UF/Dist report #

\*+ indicates item continued

FDA Use Only

A. Patient Information

1. Patient Identifier [REDACTED] in confidence	2. Age at time of event: 32 MOS or Date of Birth: [REDACTED]	3. Sex <input type="checkbox"/> Female <input checked="" type="checkbox"/> Male	4. Weight 38.0 lbs or [REDACTED] kgs
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C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known) # 1 ZITHROMAX PEDIATRIC ORAL SUSPENSION # 2 ADVIL Cont.	2. Dose, frequency & route used # 1 UNKNOWN # 2 DAILY	3. Therapy dates (if unknown, give duration) from/to (or best estimates) # 1 04/29/99 - UNKNOWN # 2 04/29/99 - UNKNOWN	5. Event abated after use stopped or dose reduced # 1 <input type="checkbox"/> yes <input type="checkbox"/> no <input checked="" type="checkbox"/> doesn't apply # 2 <input type="checkbox"/> yes <input type="checkbox"/> no <input checked="" type="checkbox"/> doesn't apply
4. Diagnosis for use (indications) + # 1 COLD FEVER # 2 INDICATION UNKNOWN	6. Lot # (if known) # 1 UNKNOWN # 2 UNKNOWN	7. Exp. date (if known) # 1 UNKNOWN # 2 UNKNOWN	8. Event reappeared after reintroduction # 1 <input type="checkbox"/> yes <input type="checkbox"/> no <input checked="" type="checkbox"/> doesn't apply # 2 <input type="checkbox"/> yes <input type="checkbox"/> no <input checked="" type="checkbox"/> doesn't apply
9. NDC # - for product problems only (if known) N/A		10. Concomitant medical products and therapy dates (exclude treatment of event) UNKNOWN	

B. Adverse event or product problem

1.  Adverse event and/or  Product problem (e.g. defects/malfunctions)

2. Outcomes attributed to adverse event (Check all that apply)

death 04/30/99 (mo/day/yr)  
 life-threatening  
 hospitalization - initial or prolonged

disability  
 congenital anomaly  
 required intervention to prevent permanent impairment/damage  
 other:

3. Date of event 04/29/99 (mo/day/yr)

4. Date of this report 10/26/00 (mo/day/yr)

5. Describe event or problem

THIS IS A THIRD FOLLOW UP REPORT BASED ON INFORMATION REPORTED TO PFIZER ON 17OCT00. THE FIRST FOLLOW UP REPORT WAS SUBMITTED TO THE US FDA ON 02JUN00. THE SECOND FOLLOW UP WAS SUBMITTED TO THE US FDA ON 11JUL00. THE INITIAL REPORT WAS SUBMITTED TO THE US FDA ON 10MAY00.

AN ATTORNEY REPORTS THAT ZITHROMAX (AZITHROMYCIN) WAS ADMINISTERED TO A 32-MONTH-OLD MALE ON 29APR99. WITHIN MINUTES THE CHILD BEGAN TO SCREAM WITH PAIN AND WENT INTO A COMA. HE WAS RUSHED TO THE HOSPITAL WHERE HE WAS DIAGNOSED WITH A TOXIC DRUG-INDUCED HEPATIC FAILURE. THIS EVOLVED INTO SWELLING OF THE BRAIN AND THE CHILD WAS DECLARED BRAIN DEAD ON 30APR99.

FOLLOW-UP (22MAY00): THIS ATTORNEY REPORTS THAT THE VIAL OF MEDICATION WHICH WAS PRESCRIBED FOR THE CHILD HAS BEEN REFRIGERATED SINCE IT WAS INITIALLY USED. BECAUSE OF THE INSTANT AND ULTIMATELY DEADLY REACTION THE CHILD HAD WHEN THE MEDICATION WAS ADMINISTERED, HE BELIEVES THAT IT MAY BE ADULTERATED. HE REQUESTED THAT THE MEDICATION BE EVALUATED BY A RENOWNED LABORATORY IN PENNSYLVANIA. THE 2-YEAR-OLD CHILD HAD THE "SNIFFLES." ZITHROMAX WAS PRESCRIBED AND GIVEN BY THE MOTHER TO

6. Relevant tests/laboratory data, including dates

FOLLOW-UP (22MAY00):  
LIVER SAMPLES FROM THE AUTOPSY SHOWED A LIVER INFECTION.

FOLLOW-UP 17OCT00:  
29APR99-TEMPERATURE 105 DEGREES FAHRENHEIT  
30APR99-VITAL SIGNS WERE HEART RATE 110 AND RESPIRATIONS 30.  
LONGER PUNCTURE: INCREASED INTRACRANIAL PRESSURE  
INITIAL LAB RESULTS: ELEVATED LIVER FUNCTION TESTS (LFT)/NO

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking & alcohol use, hepatic/renal dysfunction, etc.)

ALLERGIC AMOXICILLIN  
HISTORY OF TREATMENT WITH ALBUTEROL INHALER  
FEVER OF 105 DEGREES:  
- 24 HOURS PRIOR TO DEATH  
SEVERAL EPISODES OF UPPER RESPIRATORY INFECTION WITH FEVER

NOV 3 2000

G. All manufacturers

1. Contact office - name/address (& mfring site for devices) PFIZER REGULATORY SAFETY PFIZER PHARMACEUTICALS 235 EAST 42 STREET NEW YORK, N.Y. 10017 U.S.A.	2. Phone number 212-573-3129	3. Report source (check all that apply) <input type="checkbox"/> foreign <input type="checkbox"/> study <input type="checkbox"/> literature <input checked="" type="checkbox"/> consumer <input checked="" type="checkbox"/> health professional <input type="checkbox"/> user facility <input type="checkbox"/> company representative <input type="checkbox"/> distributor <input type="checkbox"/> other
4. Date received by manufacturer (mo/day/yr) 10/17/00	5. (A) NDA # NOA #50-710 IND # PLA # pre-1938 <input type="checkbox"/> yes OTC product <input type="checkbox"/> yes	8. Adverse event term(s) COMA PAIN SUDDEN DEATH PROBABLE VIRAL HEPATITIS BUN INCREASED ACIDOSIS PROTEINEMIA DECREASED BRAIN EDEMA HEPATITIS GASTROINTESTINAL HEMORRHAGE
6. If IND, protocol # N/A	7. Type of report (check all that apply) <input type="checkbox"/> 5-day <input type="checkbox"/> 10-Day <input type="checkbox"/> initial <input checked="" type="checkbox"/> 15-day <input type="checkbox"/> periodic <input checked="" type="checkbox"/> follow-up # 3	9. Mfr. report number A014956

E. Initial reporter

1. Name, address & phone #  
[REDACTED]  
Tel. - UNKNOWN

2. Health professional? <input type="checkbox"/> yes <input checked="" type="checkbox"/> no	3. Occupation ATTORNEY	4. Initial reporter also sent report to FDA <input type="checkbox"/> yes <input type="checkbox"/> no <input checked="" type="checkbox"/> link
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\*3607180-6-00-02\*

Approved by FDA on 12/02/93

Mfr report # A014956
UF/Dist report #
FDA Use Only

**C. Suspect medication(s)**

<b>1. Name (give labeled strength &amp; mfr/labeler, if known)</b> # 3 ACETAMINOPHIN # 4	
<b>2. Dose, frequency &amp; route used</b> # 3 DAILY:RECTAL # 4	<b>3. Therapy dates (if unknown, give duration) from/to (or best estimates)</b> # 3 04/29/99 - UNKNOWN # 4
<b>4. Diagnosis for use (indications)</b> # 3 INDICATION UNKNOWN # 4	<b>5. Event abated after use stoped or dose reduced</b> # 3 <input type="checkbox"/> yes <input type="checkbox"/> no <input checked="" type="checkbox"/> doesn't apply # 4 <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> doesn't apply
<b>6. Lot # (if known)</b> # 3 UNKNOWN # 4	<b>7. Exp. date (if known)</b> # 3 UNKNOWN # 4
<b>8. Event reappeared after reintroduction</b> # 3 <input type="checkbox"/> yes <input type="checkbox"/> no <input checked="" type="checkbox"/> doesn't apply # 4 <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> doesn't apply	

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## Pfizer Regulatory Safety, Pfizer Pharmaceuticals - Mfr. report # A014956

## B5. EVENT DESCRIPTION - Continued

HER CHILD WHO INSTANTLY REACTED AND WENT INTO A COMA. A MEDICAL TEAM COULD NOT REVIVE THE CHILD. THE DIAGNOSIS WAS A POSSIBLE TOXIC DRUG REACTION. LIVER SAMPLES FROM THE AUTOPSY SHOWED A LIVER INFECTION BUT ACCORDING TO THE PLAINTIFF'S COUNSEL, THE CHILD WAS NEVER JAUNDICED. THE ATTORNEY REPORTED THIS AS AN ALLEGED SUDDEN DEATH OF A 2 YR. 8 MO. OLD BOY AFTER RECEIVING ONE DOSE OF ZITHROMAX PEDIATRIC SYRUP IN APR99.

FOLLOW-UP (29JUN00): THE PHYSICIAN REPORTS HE IS UNABLE TO RESPOND TO THE REQUEST FOR MORE INFORMATION.

FOLLOW UP (17OCT00): AN ATTORNEY REPORTS INFORMATION FROM MEDICAL RECORDS, AN AUTOPSY REPORT, AND THE CHILD'S MOTHER. ACCORDING TO PHARMACY DATA, DURING THE PRIOR TWO YEARS, THIS CHILD HAD BEEN PRESCRIBED ERYTHROMYCIN, AUGMENTIN, CEPZIL, SULPATRIM AND ALBUTEROL INHALER. HE HAD AN ALLERGY TO AMOXICILLIN (ONSET NOT SPECIFIED.) BRIEF HISTORY FROM THE MOTHER NOTED THAT THIS CHILD WAS HEALTHY ALL HIS LIFE WITH THE EXCEPTION OF SEVERAL EPISODES OF UPPER RESPIRATORY INFECTION WITH FEVER. EARLIER ON 29APR99, HIS TEMPERATURE HAD REACHED 105° FAHRENHEIT. ACCORDING TO THE MOTHER, AFTER ONE OR TWO DOSES OF ZITHROMAX WAS GIVEN LATE ON 29APR99, THE CHILD STARTED TO SCREAM IN A VERY ODD WAY. HE WAS THEN GIVEN FOR THE FIRST TIME, ADVIL AND A TYLENOL SUPPOSITORY IN THE UPPER RANGE FOR HIS BODY WEIGHT (DOSE NOT CLEAR). HE WENT TO SLEEP, BUT WAS FOUND UNCONSCIOUS DURING THE NIGHT. AT THAT TIME HE WAS VERY COLD AND HIS EYES WERE DESCRIBED AS ROLLING TO THE BACK OF HIS HEAD. HE DID NOT WAKE UP AND WAS VERY FLOPPY. IN THE EARLY MORNING OF 30APR00, HE WAS TRANSPORTED TO THE HOSPITAL EMERGENCY ROOM BY AMBULANCE. HE WAS COMATOSE (STAGE III-IV COMA), WITH INCREASED MUSCLE TONE AND SOME RIGIDITY. HE WAS TRANSFERRED TO THE PEDIATRIC INTENSIVE CARE UNIT (PICU) AND PLACED ON A VENTILATOR. A NASOGASTRIC TUBE WAS INSERTED. LUMBAR PUNCTURE SHOWED INCREASED INTRACRANIAL PRESSURE. INITIAL LAB RESULTS SHOWED ELEVATED LIVER FUNCTION TESTS (LFT) WITH SERUM GLUTAMIC PYRUVIC TRANSAMINASE (GPT) AND ALANINE AMINOTRANSFERASE (ALT) IN THE 3000 RANGE, SERUM GLUTAMIC OXALOACETIC TRANSAMINASE (GOT) IN THE 4000 RANGE WITH NO HYPERBILIRUBINEMIA. TOTAL DIRECT BILIRUBIN WAS NORMAL AT 0.6/0.5. GLUCOSE WAS STABLE. BLOOD UREA NITROGEN (BUN) WAS SLIGHTLY ELEVATED INDICATING INABILITY TO METABOLIZE PROTEIN. COAGULOPATHY RESULTS SHOWED PT OF 19 AND PTT OF 41. AMMONIA LEVELS WERE NORMAL. NO CYANOSIS, MICROSCOPIC BLEEDING OR CARDIOVASCULAR COLLAPSE SEEN. HE WAS IN METABOLIC ACIDOSIS WITH A LOW PH IN THE BLOOD GAS, LACTIC ACIDOSIS WITH INCREASED LACTIC ACID LEVEL OF 4.4. TREATMENT WITH 10% DECAIDRON, MANNITOL FOR INTRACRANIAL PRESSURE, ZANTAC, RANITIDINE, CARAFATE, LACTULOSE 10CC TID, AND FROZEN FRESH PLASMA (FFP) EVERY FOUR HOURS TO CORRECT COAGULOPATHY WAS STARTED. CEFOTAXIME, VITAMIN K, VANCOMYCIN, ATROPINE, ATIVAN AND FENTANYL WERE GIVEN. A COMPUTERIZED TOMOGRAPH (CT) SCAN SHOWED MILD BRAIN EDEMA. CEREBRAL RIGIDITY INDICATED FULMINANT HEPATIC FAILURE WITH ENCEPHALOPATHY OF UNKNOWN ORIGIN. HE WAS AFEBRILE, CHEST CLEAR, WITH GOOD URINE OUTPUT, AND NO LIVER DISTENSION OR SPLENOMEGALY. HIS VITAL SIGNS WERE HEART RATE 110 AND RESPIRATIONS 30. HE WAS NOT ICTERIC. SEPSIS AND GASTROINTESTINAL BLEEDING WERE SUSPECTED. A NEUROLOGIST SUSPECTED METABOLIC DEFECTS INCLUDING (MCAT) DEFICIENCY, FREE FATTY ACID DEFICIENCIES, CHRONIC HEPATITIS, HERPES SIMPLEX VIRUS (HSV) VERSUS ALPHA-1 ANTITRYPSIN DEFICIENCY, EPSTEIN BARR (EB) VIRUS HEPATITIS. FOR THIS REASON, ACYCLOVIR WAS STARTED. ZITHROMAX LIVER TOXICITY WAS SUSPECTED. AN ADVERSE REACTION, SYNERGISM, MAY HAVE OCCURRED BETWEEN ADVIL AND ZITHROMAX. ACETAMINOPHEN IS SUSPECTED IN CONTRIBUTING TO LIVER FAILURE, THOUGH THE TOXICOLOGY SCREEN WAS WITHIN NORMAL THERAPEUTIC LEVELS, 6.0MCG/ML. REYE'S SYNDROME WITH RELATED MITOCHONDRIAL INSUFFICIENCY AND FAT METABOLISM SHUT DOWN WAS ALSO SUSPECTED. HIS ARMS WERE RIGID, WHILE THE LOWER PART OF HIS BODY WAS FLOPPY. NO FLAPPING TREMOR NOTED. AN ELECTROENCEPHALOGRAM (EEG) TO RULE OUT SEIZURE AND AN ELECTROCARDIOGRAM (EKG) CONSULT REPORTED THAT NO EPILEPTIC DISCHARGES WERE SEEN ON THE EEG. THE EEG WAS ABNORMAL DUE TO DIFFUSE DELTA SLOWING WITHOUT EVIDENCE OF NORMAL SLEEP COMPLEXES AND POOR REACTIVITY. UPON LEFT FOOT STIMULATION, SOME T-4 ACTIVITY SEEN. EVIDENCE FOR SEIZURE ACTIVITY NOT SEEN. HE WAS DIAGNOSED WITH SEVERE DIFFUSE ENCEPHALOPATHY WITH NON-SPECIFIC ETIOLOGY. THE EEG REMAINED IN NORMAL SINUS. THE AUTOPSY OF 01MAY99 WAS NORMAL WITH THE EXCEPTION OF THE LIVER. THE LIVER CONTAINED NUMEROUS KUPFFER CELLS WITH FOCAL HEPATOCELLULAR DEGENERATION. OCCASIONAL NEUTROPHILS WERE SEEN. SOME CELLS SHOW CYTOPLASMIC INCLUSIONS VERSUS CELLULAR DEBRIS. IMMUNOHISTOCHEMICAL STAINING REVEALED THAT THE MAJORITY OF THE CELLS ARE KUPFFER CELLS FILLED WITH PHAGOCYTTIC DEBRIS. THE PATHOLOGICAL DIAGNOSIS INCLUDES CLINICAL HISTORY OF FEBRILE ILLNESS 24 HOURS PRIOR TO DEATH, ACUTE HEPATITIS OF PROBABLE VIRAL ETIOLOGY, POSTMORTEM TOXICOLOGY POSITIVE ONLY FOR THERAPEUTIC LEVELS OF ACETAMINOPHEN, INFLUENZA B VIRUS ISOLATED FROM POSTMORTEM NASOPHARYNGEAL AND TRACHEAL SMEARS. NEGATIVE POSTMORTEM BLOOD CULTURES FOR HANTAVIRUS SEROLOGIES. THE CAUSE OF DEATH WAS ACUTE HEPATITIS OF PROBABLE VIRAL ETIOLOGY. THE PHYSICIANS CONCUR THAT THIS EVENT DOES NOT REPRESENT A REACTION TO A DRUG NOR REYE'S SYNDROME. THE ETIOLOGY OF THE VIRUS REMAINS UNCLEAR. TISSUE SAMPLES ARE BEING SUBMITTED TO THE CENTERS FOR DISEASE CONTROL (CDC) FOR FURTHER ANALYSIS.

## B6. RELEVANT TESTS/LAB. DATA - Continued

HYPERBILIRUBINEMIA  
GPT-3000 RANGE  
ALT-3000 RANGE  
GOT-4000 RANGE  
TOTAL DIRECT BILIRUBIN-NORMAL AT 0.6/0.5  
GLUCOSE STABLE

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Pfizer Regulatory Safety, Pfizer Pharmaceuticals - Mfr. report # A014956

BLOOD UREA NITROGEN (BUN)-SLIGHTLY ELEVATED  
 COAGULOPATHY-PT OF 19 AND PTT OF 41  
 AMMONIA LEVELS-NORMAL  
 METABOLIC ACIDOSIS WITH A LOW PH IN THE BLOOD GAS  
 LACTIC ACIDOSIS WITH INCREASED LACTIC ACID LEVEL OF 4.4  
 COMPUTERIZED TOMOGRAPH (CT) SCAN-MILD BRAIN EDEMA  
 AFEBRIL-CHEST CLEAR  
 TOXICOLOGY SCREEN WAS WITHIN NORMAL THERAPEUTIC LEVELS, 6.0MCG/ML  
 EEG NO EPILEPTIC DISCHARGES, ABNORMAL DUE TO DIFFUSE DELTA SLOWING WITHOUT EVIDENCE OF NORMAL SLEEP COMPLEXES  
 AND POOR REACTIVITY-EVIDENCE FOR SEIZURE ACTIVITY NOT SEEN. SEVERE DIFFUSE ENCEPHALOPATHY WITH NON-SPECIFIC  
 ETIOLOGY.  
 EKG-UPON LEFT FOOT STIMULATION, SOME T-4 ACTIVITY SEEN. NORMAL SINUS.  
 OLIMAYS9 AUTOPSY: NORMAL WITH THE EXCEPTION OF THE LIVER  
 LIVER CONTAINED NUMEROUS KUPFFER CELLS WITH FOCAL HEPATOCELLULAR DEGENERATION. OCCASIONAL NEUTROPHILS,  
 CYTOPLASMIC INCLUSIONS VERSUS CELLULAR DEBRIS.  
 IMMUNOHISTOCHEMICAL STAINING-MAJORITY OF THE CELLS ARE KUPFFER CELLS FILLED WITH PHAGOCYTTIC DEBRIS  
 POSTMORTEM TOXICOLOGY POSITIVE FOR ONLY FOR THERAPEUTIC LEVELS OF ACETAMINOPHEN  
 INFLUENZA B VIRUS ISOLATED FROM POSTMORTEM NASOPHARYNGEAL AND TRACHEAL SMEARS. NEGATIVE POSTMORTEM BLOOD  
 CULTURES FOR HANTAVIRUS SEROLOGIES.

C4. DIAGNOSIS FOR USE (INDICATIONS) - Continued

#1  
 BRONCHITIS  
 SINUSITIS

E1. NAME AND ADDRESS OF REPORTER - Continued

[REDACTED]  
 [REDACTED] STREET  
 [REDACTED]

Tel. - [REDACTED]

[REDACTED] MD.  
 [REDACTED] PEDIATRICS  
 [REDACTED] DRIVE  
 [REDACTED]

Tel. - UNKNOWN

[REDACTED]  
 [REDACTED] STREET  
 [REDACTED]

Tel. - [REDACTED]

G8. ADVERSE EVENT TERMS - Continued

DRUG INTERACTION - AZITHROMYCIN  
 ADVIL  
 COAGULATION TIME INCREASED  
 UNSPECIFIED DRUG REACTION  
 FLU SYNDROME  
 HEPATIC FAILURE  
 SUSPECTED REYE'S SYNDROME

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