

Individual Safety Report



\*368342-2-00-01\*

TH. FDA MEDICAL PRODUCTS REPORTING PROGRAM



McNeil Consumer Healthcare  
Fort Washington, PA 19034-2299

Approved by FDA on 11/15/93

Mfr report #
UDI/Dist report #
FDA use only

Page \_\_\_\_\_ of \_\_\_\_\_

**A. Patient information**

1. Patient identifier Case 3 In confidence	2. Age at time of event: unknown or Date of birth:	3. Sex ( ) female ( ) male	4. Weight unk lbs or kgs
--	---	----------------------------------	-----------------------------------

**B. Adverse event or product problem**

1. <input checked="" type="checkbox"/> Adverse event and/or	Product problem (e.g., defects/malfunctions)
2. Outcomes attributed to adverse event (check all that apply): <input type="checkbox"/> disability <input type="checkbox"/> death (mo/day/yr) <input type="checkbox"/> life-threatening <input checked="" type="checkbox"/> hospitalization - initial or prolonged <input type="checkbox"/> congenital anomaly <input type="checkbox"/> required intervention to prevent permanent impairment/damage <input type="checkbox"/> other:	
3. Date of event (mo/day/yr) unknown	4. Date of this report (mo/day/yr) 10/18/99

5. Describe event or problem

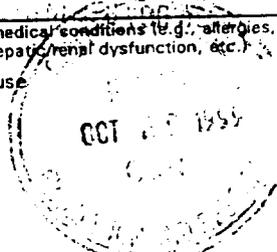
Case abstract #53 from the 1999 North American Congress of Clinical Toxicology Annual Meeting (J Toxicol Clin Toxicol 1999;37(5):604) of false positive ethylene glycol (EG) determination by enzyme assay in patients with chronic acetaminophen hepatotoxicity. According to abstract, serum EG determinations are usually performed by glycerol dehydrogenase (GDH) enzyme assay or gas chromatography. A recent report suggests that false positive results by enzymatic assay may occur in the presence of elevated LDH and/or lactate resulting in increased production of NADH, the product of GDH enzymatic reaction. Authors of abstract report on 3 pts identified as having fulminant hepatic failure (LIVER FAILURE), hx of chronic APAP abuse & high anion gap metabolic ACIDOSIS. Each pt had EG levels by GDH enzyme assay greater than or equal to 20mg/dL. Case 3 had an AST= 3612 IU/L (SGOT INCREASED) and LDH=12,713 IU/L (LDH INCREASED). In all 3 cases the elevated EG by GDH enzyme assay was later determined to be negative by (See Sect C10)

6. Relevant tests/laboratory data, including dates

unspecified time: EG=20 mg/dL, anion gap=33, pH=7.15, AST=3612 IU/L, LDH=12,713 IU/L, lactate=26.5 mmol/L

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

history of chronic acetaminophen abuse



**C. Suspect medication(s)**

1. Name (give labeled strength & mfr/labeler, if known)	
#1 unspecified acetaminophen product	
#2	
2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration) from/to (or best estimate)
#1 unknown dose, po	#1 unknown dates or duration
#2	#2
4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
#1 unknown	#1 ( ) Yes ( ) No (X) N/A
#2	#2 ( ) Yes ( ) No ( ) N/A
6. Lot # (if known)	7. Exp. date (if known)
#1 unknown	#1 unknown
#2	#2
9. NDC # - for product problems only (if known)	8. Event reappeared after reintroduction
	#1 ( ) Yes ( ) No (X) N/A
	#2 ( ) Yes ( ) No ( ) N/A
10. Concomitant medical products and therapy dates (exclude treatment of event) unknown (Sect B5 cont) gas chromatography. Authors conclude the false positive results were most likely due to increases in LDH and/or lactate associated with the liver failure and acidosis.	

**G. All manufacturers**

1. Contact office - name/address (& mfring site for devices)	2. Phone number
McNeil Consumer Healthcare Medical Affairs 7050 Camp Hill Road Ft. Washington, PA 19034	215-273-7820
4. Date received by manufacturer (mo/day/yr)	5. (A) NDA # 19-872
10/18/99	IND # PLA # pre-1938 ( ) Yes
6. If IND, protocol #	(X) health professional ( ) user facility ( ) company representative ( ) distribute. ( ) other:
7. Type of report (check all that apply)	8. Adverse event term(s)
( ) 5-day (X) 15-day ( ) 10-day ( ) periodic (X) initial ( ) follow-up #	LIVER FAILURE ACIDOSIS SGOT INCREASED LDH INC
9. Mfr. report number	
1254627A	

**E. Initial reporter**

1. Name, address & phone #	
P. Wax University of Rochester Medical Center 601 Elmwood Avenue Rochester, NY 14642	
2. Health professional?	3. Occupation
(X) Yes ( ) No	
4. Initial reporter also sent report to FDA	
( ) Yes ( ) No (X) Unk	



Facsimile Form 3500A

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.



acute griseofulvin overdose producing elevated amylase and AST. This case suggests that both amylase and hepatic transaminase be measured after large accidental pediatric ingestions of this drug.

### 52 A CASE OF HALOTHANE HEPATITIS FROM ORAL HALOTHANE INGESTION.

Langford J, Bosse G. *Department of Emergency Medicine, University of Louisville, Louisville, KY*

**Background:** We present an unusual case of oral halothane ingestion resulting in acute liver failure. **Case Report:** A 29-year-old male with a history of bipolar disorder and alcoholic liver disease presented to the emergency department (ED) 5 days after hosting a party where the participants were "huffing halothane". He denied using halothane personally. He also denied alcohol use for the past 5 years. The following morning he awoke to take his morning dose of gabapentin, drank approximately 2.5 ounces of a clear liquid he thought was water, realized it was halothane and immediately began to vomit. Intractable emesis continued for the next 5 days. On presentation to the ED, his temperature was 103.7, heart rate 119, respiratory rate 18, and blood pressure 155/70. Physical exam revealed an obese male in mild distress from emesis and apparent abdominal discomfort. His abdomen was non-distended with no hepatosplenomegaly. He was tender to palpation over the epigastrium. Lab results showed that the ALT was 214 IU/L, with an AST of 201 IU/L. Poison Control recommended supportive care. Since the CXR showed a right middle lobe infiltrate, he was discharged on an oral quinolone. He presented for the second time 3 days later with increased nausea, vomiting, abdominal pain. He admitted to acetaminophen use for fever and discomfort. Lab results showed an AST of 2760 IU/L, ALT of 2347 IU/L, prothrombin time of 18.8 seconds, and a partial thromboplastin time of 41.4 seconds. Toxicology screens were positive for cannabinoids. The acetaminophen level was 18 mcg/mL. The patient was admitted for acute liver failure thought to be secondary to halothane ingestion. The patient left against medical advice on hospital day 2 with AST decreased to 752 IU/L and ALT decreased to 1366 IU/L. **Conclusion:** Oral halothane ingestion resulting in acute hepatitis is extremely unusual. Treatment is supportive.

### 53 FALSE POSITIVE ETHYLENE GLYCOL DETERMINATION BY ENZYME ASSAY IN PATIENTS WITH CHRONIC ACETAMINOPHEN HEPATOTOXICITY.

Wax P, Branton T, Cobaugh D, Kwong T. *University of Rochester Medical Center, Rochester, NY*

**Background:** Serum ethylene glycol (EG) determinations are usually performed by glycerol dehydrogenase (GDH) enzyme assay or gas chromatography (GC). An advantage of the enzyme assay is that it is relatively easy to perform particularly when needed 24 hours per day. A recent report suggests that false positive results by enzymatic assay may occur in the presence of elevated LDH and/or lactate resulting in increased production of NADH, the product of the GDH enzymatic reaction. We report on 3 patients who presented with fulminant hepatic failure, a history of chronic acetaminophen abuse, and high anion gap metabolic acidosis. Ethylene glycol levels were obtained in each case. **Case Series:** Each patient had EG levels by GDH enzyme assay (Hitachi 900) that was  $\geq 20$  mg/dL. In 1 case, serial EG levels were increasing. Treatment was initiated with ethanol infusion in Case 1 and fomepizole in Case 2. The following laboratory analysis was performed:

	EG (mg/dL)	Anion gap	pH	AST (IU/L)	LDH (IU/L)	Lactate (mmol/L)
Case 1	25	31	6.8	6690	11,000	21
Case 2	50	45	7.15	12,464	39,907	14.6
Case 3	20	33	7.15	3612	12,713	26.5

In all 3 cases the elevated EG by GDH enzyme assay was later determined to be negative by GC. **Conclusion:** We conclude that the use of the EG assay by GDH enzyme technique in these 3 cases of fulminant hepatic failure from chronic acetaminophen abuse produced false positive results. These findings are most likely due to increases in LDH and/or lactate associated with the liver failure and acidosis. Elevated EG by GDH enzyme assay should trigger the ordering of serum LDH and lactate levels, and if they are elevated, GC confirmation for the presence of EG should be considered.

NOV 01 1999

OCT 29 1999