

**MEMORANDUM DEPARTMENT OF HEALTH AND HUMAN
SERVICES PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION CENTER
FOR DRUG EVALUATION AND RESEARCH**

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▶ Division of Over-the-Counter Drug Products, HFD-560

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SUBJECT OPDRA SAFETY REVIEW
Review of Adult and Adolescents Exposure Data on
Acetaminophen-containing products from Two Regional Poison
Control Centers – Utah and National Capitol Area
PID #D010092

Executive summary

This document is in response to the Division of Over-the-Counter Drug Products request to review data summaries and individual case reports from two regional poison control centers – the Utah Poison Control Center (UPCC) in Salt Lake City, Utah, and the National Poison Control Center (NPCC) in Washington, DC as part of a general effort to describe the epidemiology of acetaminophen-related adverse events. These data were provided to HFD-560 by McNeil, the makers of Tylenol brand of acetaminophen-containing products. The data submitted by the sponsor included ten volumes of binders describing all exposures to any acetaminophen-containing product as the primary exposure ingredient in adults and adolescents 12 years of age and older for a one year period of time from January to December 2000.

In the year 2000, the Toxic Exposure Surveillance System (TESS) of the American Association of Poison Control Centers (AAPCC) received 2,168,248 human poisoning exposure reports from 63 participating poison control centers. The UPCC and NCPCC accounted for about 74,417 (3%) of the total exposures reported to AAPCC.

In the year 2000, the UPCC received a total of 40,856 calls for all ages and products, of which 807 (2%) calls were related to primary exposure of acetaminophen-containing products in adults and adolescents 12 years of age and older; the NCPCC received 33,561

calls for all ages and products, of which 842 (3%) were related to primary exposure of acetaminophen-containing products in adults and adolescents 12 years of age and older. The majority of these exposures in both centers was intentional – 400 (73%) at UPCC and 509 (66%) at NCPCC. Overall most adult and adolescent exposures were managed at health care facilities (66% UPCC and 78% NCPCC), but unintentional exposures were more likely to be treated "on-site" (i.e. at home) (81% UPCC and 60% NCPCC). A minority of patients, 31 (6%) UPCC and 115 (15%) NPCC experienced moderate or major outcomes as a result of the acetaminophen exposure; there were three deaths, all in the NCPCC cohort.

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In conclusion, data from two regional poison control centers confirm that acetaminophen is a source of morbidity in the U.S. Poison control centers with large numbers of patients requiring management in health care facilities including emergency departments. These referrals consume the time of health care professionals and result in health care expense.

Methods

We manually reviewed hard copies of 1,649 case reports of exposures to acetaminophen-containing product submitted to two regional poison control centers. Out of these 1,649 reports, 807 reports were received by the Utah Poison Control Center (UPCC) in Salt Lake City, and 842 by the National Poison Control Center (NPCC) in Washington, DC. These reports involved single-ingredient over-the-counter (OTC) acetaminophen products, combination OTC acetaminophen products, prescription acetaminophen products, and multiple products containing acetaminophen (multiple OTC products or OTC/prescription products or multiple prescription products). The motive for ingestion was classified as unintentional, intentional, or unknown/other. We used the following categories to classify the sites where the poisoning cases are managed a) on-site, which is usually home, b) health care facility, or c) unknown/other. For the purpose of this analysis we treated all cases that were referred to a health care facility as being assessed to require treatment at a health care facility, although a proportion of these cases were lost to follow-up or were not known to receive care. We classified the outcome of the cases into the following categories: a) none, minor or unknown (we included 'unable to follow, but judged as potentially toxic' in this category), b) moderate, c) major, and d) death. We excluded 259 and 72 calls received by UPCC and NPCC respectively since these cases represented adverse events or involved unknown or pediatric acetaminophen formulations. Additionally only exposures to acetaminophen-containing products as the primary exposure ingredient were included.

Definitions and terminology used

- *No effect* – the patient did not develop any signs or symptoms as a result of exposure.
- *Minor effect* – the patient developed signs or symptoms as a result of the exposure, but these were minimally bothersome and generally resolved rapidly with no residual disability or disfigurement.
- *Moderate effect* – the patient exhibited signs or symptoms as a result of the exposure that were more pronounced, more prolonged, or more systemic in nature than minor

symptoms. Symptoms were not life threatening and there was no residual disability or disfigurement.

- *Major effect* – the patient developed signs or symptoms as a result of the exposure that were life-threatening or resulted in significant residual disability or disfigurement.
- *Death* – a patient dies as a result of the exposure or as a direct complication of the exposure.
- *Unknown* - the patient was lost to follow-up, or was not followed but the outcome was judged as potentially toxic exposure

Management sites included 1) health care facilities such as acute care hospitals, physician offices or clinics, and freestanding emergency centers and 2) nonhealth care facilities or on-site management that generally referred to the patient's home.

Results

UPCC

Table 1 describes the data on exposure to acetaminophen-containing products from the Utah Poison Control Center (UPCC) by type of formulation, management site and outcome. Of the 146 cases of exposure to acetaminophen-containing products where the motive of ingestion was unintentional, 118 (81%) cases were treated on-site and 28 (19%) cases were treated or referred to a health care facility for further management and evaluation. In contrast, of the 400 cases of intentional or suicidal exposure to acetaminophen-containing products, 332 (83%) were treated or referred to a health care facility and 60 (15%) were treated on-site. The management site was unknown or other in the remaining 8 cases. Outcome was coded as "moderate" in 23 (4%) cases and "major" in 8 (1%) cases. There were no deaths in this group.

NCPCC

Table 2 describes the data on exposure to acetaminophen-containing products from the National Capital Poison Control Center (NCPCC) by type of formulation, management site and outcome. Of the 248 cases of exposure to acetaminophen-containing products where the motive of ingestion was unintentional, 149 (60%) cases were treated on-site which is usually home and 88 (35%) cases were treated or referred to a health care facility for further management and evaluation. In contrast, of the 509 cases of intentional or suicidal exposure to acetaminophen-containing products, 499 (98%) were treated or referred to a health care facility and 2 (<1%) were treated on-site. The management site was unknown or other in the remaining 8 cases. Outcome was coded as "moderate" in 85 (11%) cases and "major" in 30 (4%) cases. There were 3 deaths in this group, all intentional.

In general the two study sites were very similar in motive and outcome. There were differences in the acetaminophen product exposure type – 8% of UPCC patient exposures were from single OTC products compared to 41% of NCPCC patient exposures; 43% of UPCC patient exposures were from prescription products compared to 12% of NCPCC patient exposures.

Conclusions

This review of acetaminophen poisonings reported to TESS in two regional centers for the year 2000 shows acetaminophen poisonings account for a very small percent of all reports and result in a small percentage of serious outcomes. A large percent of patients contacting poison control centers with acetaminophen poisonings are referred to health care facilities for management. Many of the exposures in the adult age group are intentional. The generalizability of the TESS data reviewed for this analysis is unclear, particularly given that the two groups are not comparable (different product exposures).

HFD-560 Division File / Director / Team Leader / Medical Officer / Project Manager

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Table 1. Acetaminophen (APAP)(%) data from Utah Poison Control Center (UPCC), January-December 2000.*

APAP Product	Management			Outcome		
	<i>On-Site</i>	<i>Health care Facility</i>	<i>Unknown/ Other</i>	<i>None, Minor, or Unknown</i>	<i>Moderate</i>	<i>Major</i>
Single OTC (N=46)						
Unintentional (N=16)	10	6	0	16	0	0
Intentional (N=30)	1	29	0	28	1	1
Unknown/other	0	0	0	0	0	0
Combination OTC(N=241)						
Unintentional(N=49)	39	10		49	0	0
Intentional (N=192)	22	164	6	181	9	2
Unknown/other	0	0	0	0	0	0
Prescription (N=234)						
Unintentional (N=68)	59	9	0	66	2	0
Intentional (N=164)	34	128	2	149	10	5
Unknown/other (N=2)	2	0	0	2	0	0
Multiple products						
All OTC (N=22)						
Unintentional (N=10)	9	1	0	10	0	0
Intentional(N=12)	2	10	0	12	0	0
Unknown/other	0	0	0	0	0	0
OTC/Prescription (N=5)						
Unintentional(N=3)	1	2	0	2	1	0
Intentional (N=2)	1	1	0	2	0	0
Unknown/other	0	0	0	0	0	0
Total (N=548)	180 (33)	360 (66)	8 (1)	517 (95)	23 (4)	8 (1)

*This table excludes adverse events and APAP unknown formulations. No deaths were noted in this group. This table only includes data for adults and adolescents 12 years of age and older. Since this data is based on manual review of case reports, it is possible that there may be some discrepancy in the counts.

Table 2. Acetaminophen (APAP)(%) data from National Capital Poison Control Center (NCPCC), January-December 2000.*

APAP Product	Management			Outcome		
	<i>On-Site</i>	<i>Health care Facility</i>	<i>Unknown/other</i>	<i>None, Minor, or Unknown</i>	<i>Moderate</i>	<i>Major/Death</i>
Single OTC (N=314)						
Unintentional (N=90)	48	37	5	85	2	3
Intentional (N=219)	1	215	3	185	20	12/2
Unknown/other (N=5)	0	4	1	5	0	0
Combination OTC (N=283)						
Unintentional (N=85)	57	25	3	80	5	0
Intentional (N=193)	0	191	2	157	29	6/1
Unknown/other (N=5)	0	5	0	4	0	1
Prescription (N=95)						
Unintentional (N=39)	20	16	3	32	7	0
Intentional (N=54)	0	52	2	40	11	3
Unknown/other (N=2)	0	2	0	2	0	0
Multiple products						
All OTC (N=51)						
Unintentional (N=26)	20	6	0	26	0	0
Intentional (N=24)	1	23	0	12	10	2
Unknown/other (N=1)	0	1	0	1	0	0
OTC/Prescription (N=15)						
Unintentional (N=4)	2	2	0	3	1	0
Intentional (N=11)	0	11	0	11	0	0
Unknown/other (N=0)	0	0	0	0	0	0
Prescription only (N=12)						
Unintentional (N=4)	2	2	0	4	0	0
Intentional (N=8)	0	7	1	8	0	0
Unknown/other (N=0)	0	0	0	0	0	0
Total=770	151 (20)	599 (78)	20 (2)	655 (85)	85 (11)	30 (4)

*This table excludes adverse reactions (N=44), pediatric formulations (N=3), and unknown formulations (N=25). Data for exposures to APAP-containing product as the primary exposure ingredient in adults and adolescents 12 years or age and older. Since this data is based on manual review of case reports, it is possible that there may be some discrepancy in the counts.

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/s/

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