ATTACHMENT 4
UNTOWARD EFFECTS REPORTED TO MANUFACTURERS

Table 4-1

Untoward Effects Reported to Manufacturers of OTC Capsaicin Patches, Plasters, or Poultices

Active Ingredient	Description of Untoward Effect*	Number of Times Effect Reported					
		1998	1999	2000	2001	2002	2003 (thru Aug.)
Capsaicin 0.016% - 0.025%	Serious**	0	0	0	0	0	0
	Local irritation or erythema (may include hyper-pigmentation)	5	4	1	2	2	3
	Rash or contact dermatitis	0	1	1	1	1	0
	Blistering	0	4	0	0	6	0
	Stinging, burning, and/or itching	2	2	5	4	3	2
	Bruising	0	0	0	0	0	0
	Skin removal	1	0	2	1	0	0
	Other (anxiety attack)	0	0	0	1	0	0

*More than one untoward effect may be reported for each affected individual (see Table 1 in Section V for numbers of affected individuals for each year); actual effect sometimes difficult to ascertain from consumer reports

**Serious events, as defined for FDA's MedWatch classification, include death, life-threatening occurrence, hospitalization, disability, congenital anomaly, or condition that required intervention to prevent permanent impairment or damage.

Table 4-2

Untoward Effects Reported to Manufacturers of OTC Menthol Patches, Plasters, or Poultices

Active Ingredient	Description of Untoward Effect*	Number of Times Effect Reported					
		1998	1999	2000	2001	2002	2003 (thru Aug.)
Menthol 1.25% - 5%	Serious**	0	0	0	0	0	0
	Local irritation or erythema (may include hyper-pigmentation)	1	1	2	25	18	6
	Rash or contact dermatitis	2	1	8	16	23	17
	Blistering	0	0	0	3	4	8
	Stinging, burning, and/or itching	2	1	4	30	22	11
	Bruising	0	5	4	8	13	4
	Skin removal	0	1	0	1	4	0
	Other***	0	0	5	11	19	2

*More than one untoward effect may be reported for each affected individual (see Table 2 in Section V for numbers of affected individuals for each year); actual effect sometimes difficult to ascertain from consumer reports

**Serious events, as defined for FDA's MedWatch classification, include death, life-threatening occurrence, hospitalization, disability, congenital anomaly, or condition that required intervention to prevent permanent impairment or damage.

*** "Other" includes (alone or several together) headache, dizziness, bleeding, nausea/sick feeling, diarrhea, asthma attack, weakness, swollen tongue, racing heart, swelling spasm, pain, memory loss, anxiety.

Table 4-3

Untoward Effects Reported to Manufacturers of OTC Methyl Salicylate Patches, Plasters, or Poultices

Active Ingredient	Description of Untoward Effect*	Number of Times Effect Reported					
		1998	1999	2000	2001	2002	2003 (thru Aug.)
Methyl Salicylate 10%	Serious**	--	--	--	--	0	0
	Local irritation or erythema (may include hyper-pigmentation)	--	--	--	--	2	2
	Rash or contact dermatitis	--	--	--	--	0	0
	Blistering	--	--	--	--	0	0
	Stinging, burning, and/or itching	--	--	--	--	2	0
	Bruising	--	--	--	--	0	0
	Skin removal	--	--	--	--	1	0
	Other	--	--	--	--	0	0

*More than one untoward effect may be reported for each affected individual (see Table 3 in Section V for numbers of affected individuals for each year); actual effect sometimes difficult to ascertain from consumer reports

**Serious events, as defined for FDA's MedWatch classification, include death, life-threatening occurrence, hospitalization, disability, congenital anomaly, or condition that required intervention to prevent permanent impairment or damage.

-- Product(s) not reported as sold before 2002.

Table 4-4

Untoward Effects Reported to Manufacturers of OTC Combination Counterirritant Ingredient Patches, Plasters, or Poultices

Active Ingredient	Description of Untoward Effect*	Number of Times Effect Reported					
		1998	1999	2000	2001	2002	2003 (thru Aug..)
Combination Methyl Salicylate 0.8% - 6.2% Menthol 0.4% - 5.7% Camphor 0.5% - 1.2%	Serious**	1	0	1	0	0	0
	Local irritation or erythema (may include hyper-pigmentation)	0	0	1	0	1	0
	Rash or contact dermatitis	0	1	3	1	2	0
	Blistering	0	1	1	0	2	0
	Stinging, burning, and/or itching	2	1	2	0	3	1
	Bruising	0	0	0	0	0	0
	Skin removal	1	1	1	0	0	1
	Other (reported to be related to adhesive)	0	1	2	15	4	0

*More than one untoward effect may be reported for each affected individual (see Table 4 in Section V for numbers of affected individuals for each year); actual effect sometimes difficult to ascertain from consumer reports

**Serious events, as defined for FDA's MedWatch classification, include death, life-threatening occurrence, hospitalization, disability, congenital anomaly, or condition that required intervention to prevent permanent impairment or damage. Recorded information about the two events classified as "serious" is given on the following pages.

AGE (Years)	SEX	REACTION ONSET			
		DA	MO	YR	
50 Years	F	31	Jul	1998	

CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION(exclude those used to treat reaction)

Aspirin, Prednisone 10mg bid, bronchodilators

OTHER RELEVANT HISTORY(e.g. diagnostics, allergics, pregnancy with last month of period, etc.)

Chronic obstructibe pulmonary disease, Goiter (1996), Menopausal (1996)

Salicylism (Debility, Disorientation)

First report (patient report; obtained on November 10, 1998)

The patient took aspirin for a certain period during which patches were applied at the same time (the duration and dose are unknown). The patient was hospitalized for an overdose of salicylic acid and stayed in hospital for 3 days because of disorientation.

Second report (medical report; additional information obtained on Feb. 17, 2000)

The patient took aspirin for a certain period during which patches were applied at the same time.

July 31, 1998: Chest pain occurred in the morning but it disappeared. The patient visited hospital in the afternoon due to debility and disorientation.

Her activity was restricted due to short breath, her speech was unclear and her memory was poor. As the blood salicylic acid concentration was 480 μg/ml*, the treatment of salicylism was started (excretion of salicylic acid by alkalization and diuretic).

August 2, 1998: The blood salicylic acid concentration went down and the condition of patient improved. Her respiration became stable and there was no wheeze. Accordingly, the patient was discharged.

* The manufacturer's data indicates that concurrent application of approximately 4,000 patches would be required to produce the reported concentration.

AGE (Years)	SEX	REACTION ONSET			
		DA	MO	YR	
	F	18	Jan	2000	

CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION(exclude those used to treat reaction)

hydrogen peroxide

OTHER RELEVANT HISTORY(e.g. diagnostics, allergics, pregnancy with last month of period, etc.)

NA

pain,red,swollen.

First report (patient report; obtained on January 18, 2000)

January 18,2000:She applied a patch on her right breast in order to apply "heat" occurred in top surface of breast near nipple. She felt discomfort where the patch had been applied and removed the same and her skin was very red. She applied another patch and dropped the bottle of hydrogen peroxide. She noticed her breast swollen and increased pain and redness.

January 19,2000:She went to hospital. She was pescribed antibiotics and analgetics.

January 24,2000:She admitted hospital. She was given antibiotics i.v. and morphine. After a week she was discharged.

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October 15, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 78N-0301 - External Analgesic Drug Products for Over-the-Counter Human Use; Reopening of the Administrative Record and Amendment of the Tentative Final Monograph

Dear Sir or Madam:

Enclosed are three copies (plus one original) of comments submitted by the Consumer Healthcare Products Association in response to Docket No. 78N-0301, External Analgesic Drug Products for Over-the-Counter Human Use; Reopening of the Administrative Record and Amendment of the Tentative Final Monograph. This notice was published in the *Federal Register* on July 17, 2003.

To confirm receipt, please date stamp the enclosed receipt and return it to my office in the self-addressed, stamped envelope I have included.

Thank you for your assistance.

Lorna C. Totman, Ph.D.
Senior Director of Scientific Affairs & Toxicology