Safety Surveillance and Root Cause Analysis of Adverse Events Associated With the Use of Oral Cough and Cold Ingredients in Children Less Than 12 Years of Age

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Figure 1. Diagram of Relatedness with Accidental Unsupervised Ingestions/Medication Error, 2008-2016

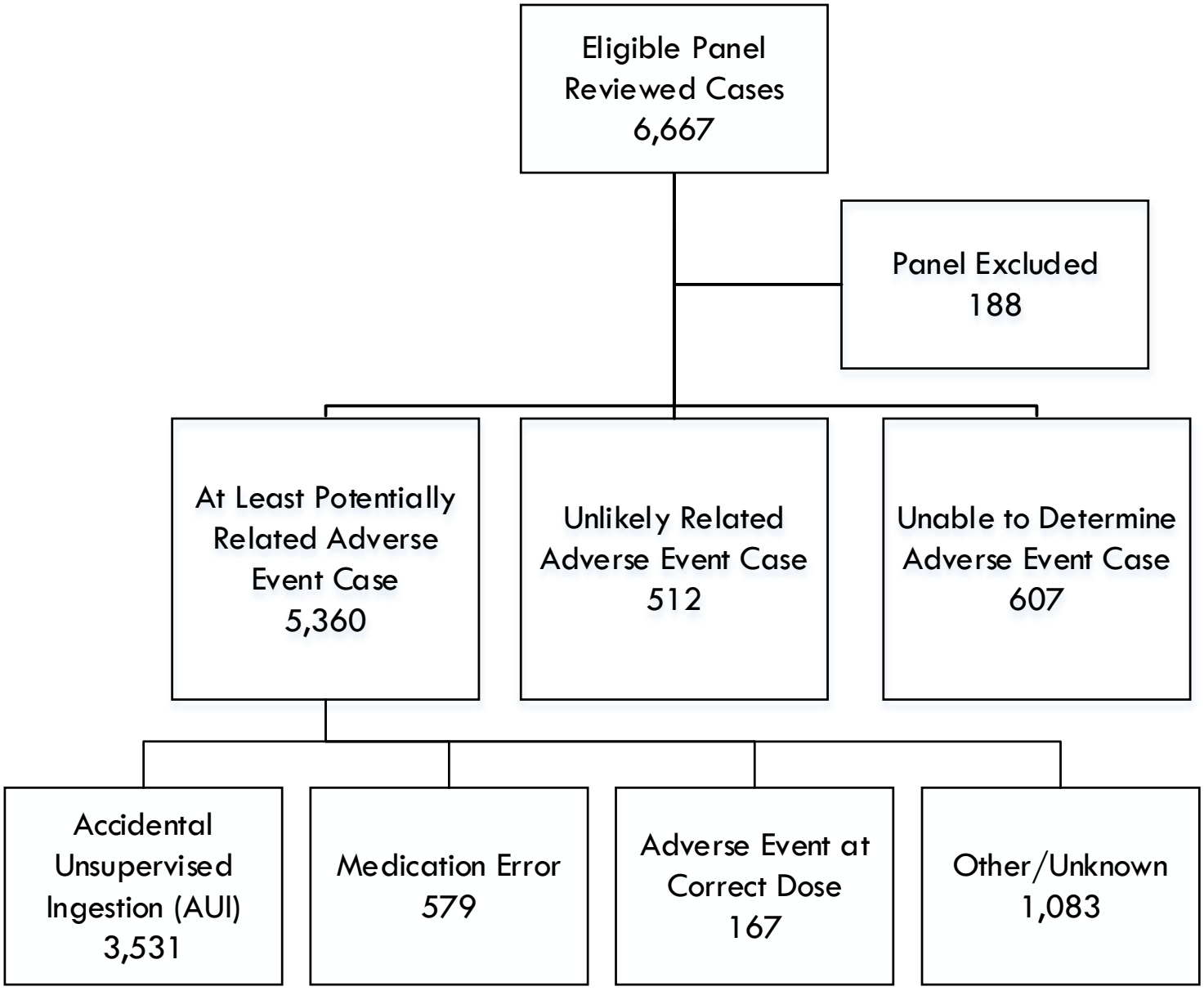

Table 1. Case Characteristics by Case Type, 2008-2016

	TOTAL Pediatric Adverse Event Cases (n=5,360)	Accidental Unsupervised Ingestion Adverse Event Cases (n=3,531)	Medication Error Adverse Event Cases (n=579)	[a]Adverse Event at Correct Dose (n=167)	Other/Unknown Reason Adverse Event Cases (n=1,083)
Age					
<6 months	29 (0.5%)	0 (0.0%)	4 (0.7%)	--	25 (2.3%)
6 months to <1 year	107 (2.0%)	83 (2.4%)	12 (2.1%)	--	12 (1.1%)
1 to <2 years	609 (11.4%)	527 (14.9%)	31 (5.4%)	--	51 (4.7%)
2 to <3 years	1,314 (24.5%)	1,175 (33.3%)	69 (11.9%)	--	70 (6.5%)
3 to <4 years	1,157 (21.6%)	1,016 (28.8%)	67 (11.6%)	--	74 (6.8%)
4 to <5 years	657 (12.3%)	519 (14.7%)	63 (10.9%)	32 (19.2%)	43 (4.0%)
5 to <6 years	344 (6.4%)	207 (5.9%)	71 (12.3%)	21 (12.6%)	45 (4.2%)
6 to <7 years	255 (4.8%)	0 (0.0%)	54 (9.3%)	35 (21.0%)	166 (15.3%)
7 to <8 years	224 (4.2%)	0 (0.0%)	48 (8.3%)	22 (13.2%)	154 (14.2%)
8 to <9 years	182 (3.4%)	0 (0.0%)	43 (7.4%)	18 (10.8%)	121 (11.2%)
9 to <10 years	127 (2.4%)	0 (0.0%)	42 (7.3%)	15 (9.0%)	70 (6.5%)
10 to <11 years	133 (2.5%)	0 (0.0%)	40 (6.9%)	13 (7.8%)	80 (7.4%)
11 to <12 years	217 (4.0%)	0 (0.0%)	35 (6.0%)	11 (6.6%)	171 (15.8%)
Exact age unknown (<12 years)	5 (0.1%)	4 (0.1%)	0 (0.0%)	--	1 (0.1%)
Gender					
Male	2,885 (53.8%)	1,948 (55.2%)	315 (54.4%)	90 (53.9%)	532 (49.1%)
Female	2,471 (46.1%)	1,582 (44.8%)	264 (45.6%)	76 (45.5%)	549 (50.7%)
Not Reported	4 (0.1%)	1 (<0.1%)	0 (0.0%)	1 (0.6%)	2 (0.2%)
Drug Administered By					
Self	4,192 (78.2%)	3,521 (99.7%)	68 (11.7%)	0 (0.0%)	603 (55.7%)

	TOTAL Pediatric Adverse Event Cases (n=5,360)	Accidental Unsupervised Ingestion Adverse Event Cases (n=3,531)	Medication Error Adverse Event Cases (n=579)	[a]Adverse Event at Correct Dose (n=167)	Other/Unknown Reason Adverse Event Cases (n=1,083)
Parent	526 (9.8%)	0 (0.0%)	259 (44.7%)	74 (44.3%)	193 (17.8%)
Grandparent	65 (1.2%)	0 (0.0%)	36 (6.2%)	3 (1.8%)	26 (2.4%)
Other Relative	13 (0.2%)	0 (0.0%)	6 (1.0%)	0 (0.0%)	7 (0.6%)
Babysitter/Daycare	13 (0.2%)	0 (0.0%)	6 (1.0%)	0 (0.0%)	7 (0.6%)
Other Caregiver	404 (7.5%)	0 (0.0%)	167 (28.8%)	70 (41.9%)	167 (15.4%)
Multiple Caregivers	26 (0.5%)	0 (0.0%)	21 (3.6%)	1 (0.6%)	4 (0.4%)
Sibling or Other Child	28 (0.5%)	10 (0.3%)	4 (0.7%)	0 (0.0%)	14 (1.3%)
Not Reported	93 (1.7%)	0 (0.0%)	12 (2.1%)	19 (11.4%)	62 (5.7%)
Exposure Site					
Own Residence	4,872 (90.9%)	3,342 (94.6%)	532 (91.9%)	103 (61.7%)	895 (82.6%)
Other Residence	162 (3.0%)	100 (2.8%)	17 (2.9%)	0 (0.0%)	45 (4.2%)
Other Location	69 (1.3%)	28 (0.8%)	10 (1.7%)	1 (0.6%)	30 (2.8%)
Multiple Locations	9 (0.2%)	1 (<0.1%)	5 (0.9%)	2 (1.2%)	1 (0.1%)
Not Reported	248 (4.6%)	60 (1.7%)	15 (2.6%)	61 (36.5%)	112 (10.3%)
Level of Care					
Treated/evaluated and released without admission	2,374 (44.3%)	1,651 (46.8%)	278 (48.0%)	54 (32.3%)	391 (36.1%)
Received care, but admission status unknown	124 (2.3%)	50 (1.4%)	14 (2.4%)	20 (12.0%)	40 (3.7%)
Managed outside of a HCF	488 (9.1%)	240 (6.8%)	117 (20.2%)	38 (22.8%)	93 (8.6%)
Died before treatment	6 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (0.6%)

	TOTAL Pediatric Adverse Event Cases (n=5,360)	**Accidental Unsupervised Ingestion Adverse Event Cases (n=3,531)**	**Medication Error Adverse Event Cases (n=579)**	**[a]Adverse Event at Correct Dose (n=167)**	**Other/Unknown Reason Adverse Event Cases (n=1,083)**
Not Reported	217 (4.0%)	63 (1.8%)	32 (5.5%)	39 (23.4%)	83 (7.7%)
Admitted to a HCF	2,151 (40.1%)	1,527 (43.2%)	138 (23.8%)	16 (9.6%)	470 (43.4%)
Admitted to non-critical care unit	1,069 (49.7%)	750 (49.1%)	77 (55.8%)	10 (62.5%)	232 (49.4%)
Admitted to critical care unit	1,039 (48.3%)	747 (48.9%)	57 (41.3%)	4 (25.0%)	231 (49.1%)
Admitted to psychiatric care facility	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Admitted to unknown type of HCF	43 (2.0%)	30 (2.0%)	4 (2.9%)	2 (12.5%)	7 (1.5%)

[a]No adverse at correct dose for children <4 years old because CCMs are not recommended for children <4 years old.

Table 1a. Cough and Cold Medication Product Types by Case[a] Type

	TOTAL Pediatric Adverse Event Cases (n=5,360)	Accidental Unsupervised Ingestion Adverse Event Cases (n=3,531)	Medication Error Adverse Event Cases (n=579)	Adverse Event at Correct Dose (n=167)	Other/Unknown Reason Adverse Event Cases (n=1,083)
Number of Products					
Single Product	4,472 (83.4%)	3,181 (90.1%)	440 (76.0%)	118 (70.7%)	733 (67.7%)
Multiple Products (CCMs only)	143 (2.7%)	65 (1.8%)	29 (5.0%)	8 (4.8%)	41 (3.8%)
Multiple Products (CCMs + non-CCMs)	745 (13.9%)	285 (8.1%)	110 (19.0%)	41 (24.6%)	309 (28.5%)
CCM Product Type – Dosage Formulation[b]					
Liquid	3,571 (66.6%)	2,474 (70.1%)	470 (81.2%)	139 (83.2%)	488 (45.1%)
Solid	1,749 (32.6%)	1,052 (29.8%)	114 (19.7%)	27 (16.2%)	556 (51.3%)
Unknown	126 (2.4%)	34 (1.0%)	11 (1.9%)	8 (4.8%)	73 (6.7%)
CCM Product Type – Age Formulation[b]					
Pediatric	3,861 (72.0%)	2,643 (74.9%)	448 (77.4%)	128 (76.6%)	642 (59.3%)
Adult	822 (15.3%)	538 (15.2%)	56 (9.7%)	23 (13.8%)	205 (18.9%)
Unknown	778 (14.5%)	392 (11.1%)	96 (16.6%)	23 (13.8%)	267 (24.7%)
CCM Product Type – Combination Formulation[b]					
Single Ingredient CCM Product	4,001 (74.6%)	2,760 (78.2%)	409 (70.6%)	69 (41.3%)	763 (70.5%)
Fixed Combination CCM Product	1,399 (26.1%)	784 (22.2%)	189 (32.6%)	102 (61.1%)	324 (29.9%)
Unknown	69 (1.3%)	35 (1.0%)	5 (0.9%)	3 (1.8%)	26 (2.4%)

[a]Each product characteristic is only counted once for each case; some cases may involve more than one product resulting in a column total greater than the number of cases.

[b]Characteristics for cough/cold products only.

Table 1b. Cough and Cold Medications Specific Formulations by Case[a] Type

	TOTAL Pediatric Adverse Event Cases (n=5,360)	Accidental Unsupervised Ingestion Adverse Event Cases (n=3,531)	Medication Error Adverse Event Cases (n=579)	Adverse Event at Correct Dose (n=167)	Other/Unknown Reason Adverse Event Cases (n=1,083)
CCM Pediatric Formulation					
Single Ingredient Liquid	2,388 (44.6%)	1,803 (51.1%)	290 (50.1%)	43 (25.7%)	252 (23.3%)
Fixed Combination Ingredient Liquid	720 (13.4%)	416 (11.8%)	109 (18.8%)	69 (41.3%)	126 (11.6%)
Single Ingredient Solid	750 (14.0%)	426 (12.1%)	55 (9.5%)	11 (6.6%)	258 (23.8%)
Fixed Combination Ingredient Solid	30 (0.6%)	12 (0.3%)	2 (0.3%)	5 (3.0%)	11 (1.0%)
Unknown	20 (0.4%)	6 (0.2%)	7 (1.2%)	1 (0.6%)	6 (0.6%)
CCM Adult Formulation					
Single Ingredient Liquid	24 (0.4%)	16 (0.5%)	3 (0.5%)	2 (1.2%)	3 (0.3%)
Fixed Combination Ingredient Liquid	173 (3.2%)	87 (2.5%)	29 (5.0%)	16 (9.6%)	41 (3.8%)
Single Ingredient Sold	327 (6.1%)	255 (7.2%)	10 (1.7%)	0 (0.0%)	62 (5.7%)
Fixed Combination Ingredient Solid	304 (5.7%)	180 (5.1%)	15 (2.6%)	6 (3.6%)	103 (9.5%)
Unknown	2 (0.0%)	2 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CCM Unknown Formulation					
Liquid	315 (5.9%)	171 (4.8%)	58 (10.0%)	11 (6.6%)	75 (6.9%)
Solid	359 (6.7%)	191 (5.4%)	33 (5.7%)	5 (3.0%)	130 (12.0%)
Unknown	116 (2.2%)	30 (0.8%)	7 (1.2%)	8 (4.8%)	71 (6.6%)

[a]*Some cases may involve more than one cough/cold product resulting in a column total greater than the number of cases; each product characteristic is only counted once for each case.*

Table 2. Listing of Potentially Related Adverse Events in Non-Fatal Cases, 2008-2016

Medical Dictionary of Regulatory Activities (MedDRA) Preferred Term	TOTAL Non-Fatal Pediatric Adverse Event Cases (n=5,322)
Tachycardia	2,330 (43.8%)
Somnolence	1,966 (36.9%)
Hallucination	1,836 (34.5%)
Ataxia	1,320 (24.8%)
Mydriasis	1,293 (24.3%)
Hypertension	1,226 (23.0%)
Agitation	1,191 (22.4%)
Irritability	949 (17.8%)
Confusional state	888 (16.7%)
Vomiting	636 (12.0%)
Tremor	577 (10.8%)
Flushing	540 (10.1%)
Nystagmus	398 (7.5%)
Psychomotor hyperactivity	364 (6.8%)
Pyrexia	332 (6.2%)
Lethargy	309 (5.8%)
Dystonia	295 (5.5%)
Dysarthria	281 (5.3%)
Dizziness	262 (4.9%)
Electrocardiogram QT prolonged	226 (4.2%)
Abnormal behaviour	210 (3.9%)
Tachypnoea	210 (3.9%)
Mucosal dryness	197 (3.7%)
Seizure	196 (3.7%)
Hypohydrosis	154 (2.9%)
Myoclonus	136 (2.6%)
Staring	136 (2.6%)
Feeling jittery	124 (2.3%)
Nausea	122 (2.3%)
Blood creatine phosphokinase increased	108 (2.0%)
Abdominal pain	87 (1.6%)
Rash	75 (1.4%)

Medical Dictionary of Regulatory Activities (MedDRA) Preferred Term	**TOTAL Non-Fatal Pediatric Adverse Event Cases (n=5,322)**
Urinary retention	69 (1.3%)
Insomnia	64 (1.2%)
Pruritus	64 (1.2%)
Skin warm	59 (1.1%)
Gastrointestinal sounds abnormal	57 (1.1%)
Urticaria	54 (1.0%)
Restlessness	51 (1.0%)
Feeling abnormal	49 (0.9%)
Mental status changes	48 (0.9%)
Formication	43 (0.8%)
Respiratory depression	41 (0.8%)
Anxiety	39 (0.7%)
Urinary incontinence	38 (0.7%)
Hypotension	36 (0.7%)
Muscle twitching	36 (0.7%)
Vision blurred	36 (0.7%)
Aggression	34 (0.6%)
Coma	31 (0.6%)
Muscle rigidity	31 (0.6%)
Oedema	31 (0.6%)
Acidosis	30 (0.6%)
Headache	30 (0.6%)
Pallor	30 (0.6%)
Hypokalaemia	29 (0.5%)
Dyskinesia	27 (0.5%)
Glassy eyes	27 (0.5%)
Unresponsive to stimuli	27 (0.5%)
Disorientation	26 (0.5%)
Hyperhidrosis	26 (0.5%)
Diplopia	23 (0.4%)
Miosis	23 (0.4%)
Dyspnoea	22 (0.4%)
Delirium	20 (0.4%)

Medical Dictionary of Regulatory Activities (MedDRA) Preferred Term	**TOTAL Non-Fatal Pediatric Adverse Event Cases (n=5,322)**
Hyperglycaemia	20 (0.4%)
Pupillary reflex impaired	20 (0.4%)
Speech disorder	20 (0.4%)
Electrocardiogram QRS complex prolonged	18 (0.3%)
Decreased appetite	17 (0.3%)
Gaze palsy	16 (0.3%)
Hyperreflexia	16 (0.3%)
Drooling	15 (0.3%)
Fall	15 (0.3%)
Hypotonia	15 (0.3%)
Visual impairment	14 (0.3%)
Abdominal pain upper	13 (0.2%)
Cyanosis	13 (0.2%)
Erythema	13 (0.2%)
Hypersensitivity	13 (0.2%)
Blood glucose increased	12 (0.2%)
Clonus	12 (0.2%)
Hypoxia	12 (0.2%)
Muscular weakness	12 (0.2%)
Syncope	12 (0.2%)
Altered state of consciousness	11 (0.2%)
Bradycardia	11 (0.2%)
Chest pain	11 (0.2%)
Hypertonia	11 (0.2%)
Nervousness	11 (0.2%)
Respiratory rate decreased	10 (0.2%)
Anion gap increased	9 (0.2%)
Lip swelling	9 (0.2%)
Loss of consciousness	9 (0.2%)
Ocular hyperaemia	9 (0.2%)
Paranoia	9 (0.2%)
Apnoea	8 (0.2%)
Incoherent	8 (0.2%)

Medical Dictionary of Regulatory Activities (MedDRA) Preferred Term	TOTAL Non-Fatal Pediatric Adverse Event Cases (n=5,322)
Movement disorder	8 (0.2%)
Oliguria	8 (0.2%)
Poisoning	8 (0.2%)
Strabismus	8 (0.2%)
Swelling face	8 (0.2%)
Thirst	8 (0.2%)
Aphasia	7 (0.1%)
Dehydration	7 (0.1%)
Diarrhoea	7 (0.1%)
Euphoric mood	7 (0.1%)
Hallucination, visual	7 (0.1%)
Injury	7 (0.1%)
Abdominal distension	6 (0.1%)
Asthenia	6 (0.1%)
Bruxism	6 (0.1%)
Cough	6 (0.1%)
Crying	6 (0.1%)
Depressed level of consciousness	6 (0.1%)
Eye movement disorder	6 (0.1%)
Eye swelling	6 (0.1%)
Hypervigilance	6 (0.1%)
Nightmare	6 (0.1%)
Palpitations	6 (0.1%)
Sleep disorder	6 (0.1%)
Wheezing	6 (0.1%)
White blood cell count increased	6 (0.1%)
Arrhythmia	5 (<0.1%)
Dermatillomania	5 (<0.1%)
Fear	5 (<0.1%)
Malaise	5 (<0.1%)
Metabolic acidosis	5 (<0.1%)
Muscle contractions involuntary	5 (<0.1%)
Salivary hypersecretion	5 (<0.1%)

Medical Dictionary of Regulatory Activities (MedDRA) Preferred Term	**TOTAL Non-Fatal Pediatric Adverse Event Cases (n=5,322)**
Amnesia	4 (<0.1%)
Aspartate aminotransferase increased	4 (<0.1%)
Blood lactic acid increased	4 (<0.1%)
Blood pH decreased	4 (<0.1%)
Blood potassium decreased	4 (<0.1%)
Blood pressure increased	4 (<0.1%)
Electrolyte imbalance	4 (<0.1%)
Fatigue	4 (<0.1%)
Gait disturbance	4 (<0.1%)
Respiratory failure	4 (<0.1%)
Retching	4 (<0.1%)
Screaming	4 (<0.1%)
Sluggishness	4 (<0.1%)
Somnambulism	4 (<0.1%)
Vertigo	4 (<0.1%)
Akathisia	3 (<0.1%)
Aspiration	3 (<0.1%)
Blood creatinine increased	3 (<0.1%)
Conduction disorder	3 (<0.1%)
Constipation	3 (<0.1%)
Delusion	3 (<0.1%)
Dysuria	3 (<0.1%)
Exaggerated startle response	3 (<0.1%)
Feeling hot	3 (<0.1%)
Heart rate increased	3 (<0.1%)
Hypoglycaemia	3 (<0.1%)
Leukocytosis	3 (<0.1%)
Muscle spasms	3 (<0.1%)
Oropharyngeal oedema	3 (<0.1%)
Oxygen saturation decreased	3 (<0.1%)
Periorbital oedema	3 (<0.1%)
Photophobia	3 (<0.1%)
Pneumonitis	3 (<0.1%)

Medical Dictionary of Regulatory Activities (MedDRA) Preferred Term	TOTAL Non-Fatal Pediatric Adverse Event Cases (n=5,322)
Posturing	3 (<0.1%)
Pupil fixed	3 (<0.1%)
Respiratory acidosis	3 (<0.1%)
Serotonin syndrome	3 (<0.1%)
Slow speech	3 (<0.1%)
Swelling	3 (<0.1%)
Abdominal discomfort	2 (<0.1%)
Anal incontinence	2 (<0.1%)
Balance disorder	2 (<0.1%)
Blood urea increased	2 (<0.1%)
Conjunctival hyperaemia	2 (<0.1%)
Disturbance in attention	2 (<0.1%)
Dysphoria	2 (<0.1%)
Electrocardiogram PR prolongation	2 (<0.1%)
Excessive eye blinking	2 (<0.1%)
Eyelid ptosis	2 (<0.1%)
Face oedema	2 (<0.1%)
Hallucination, auditory	2 (<0.1%)
Head injury	2 (<0.1%)
Hyperthermia	2 (<0.1%)
Hyperventilation	2 (<0.1%)
Hypoaesthesia	2 (<0.1%)
Hypopnoea	2 (<0.1%)
Hypoventilation	2 (<0.1%)
Increased appetite	2 (<0.1%)
Lacrimation increased	2 (<0.1%)
Livedo reticularis	2 (<0.1%)
Logorrhoea	2 (<0.1%)
Oedema peripheral	2 (<0.1%)
PO2 decreased	2 (<0.1%)
Pain	2 (<0.1%)
Pressure of speech	2 (<0.1%)
Respiratory arrest	2 (<0.1%)

Medical Dictionary of Regulatory Activities (MedDRA) Preferred Term	TOTAL Non-Fatal Pediatric Adverse Event Cases (n=5,322)
Respiratory rate increased	2 (<0.1%)
Sedation	2 (<0.1%)
Skin irritation	2 (<0.1%)
Tic	2 (<0.1%)
Abdominal tenderness	1 (<0.1%)
Alkalosis	1 (<0.1%)
Anaphylactic reaction	1 (<0.1%)
Anaphylactic shock	1 (<0.1%)
Angioedema	1 (<0.1%)
Apoptosis	1 (<0.1%)
Atelectasis	1 (<0.1%)
Athetosis	1 (<0.1%)
Atrioventricular block first degree	1 (<0.1%)
Auricular swelling	1 (<0.1%)
Blood bicarbonate decreased	1 (<0.1%)
Blood calcium increased	1 (<0.1%)
Blood chloride increased	1 (<0.1%)
Bradykinesia	1 (<0.1%)
Bundle branch block right	1 (<0.1%)
Carbon dioxide decreased	1 (<0.1%)
Carbon dioxide increased	1 (<0.1%)
Cardiac arrest	1 (<0.1%)
Catatonia	1 (<0.1%)
Chills	1 (<0.1%)
Coagulopathy	1 (<0.1%)
Condition aggravated	1 (<0.1%)
Contusion	1 (<0.1%)
Coordination abnormal	1 (<0.1%)
Deafness	1 (<0.1%)
Decreased activity	1 (<0.1%)
Depressed mood	1 (<0.1%)
Drug hypersensitivity	1 (<0.1%)
Dysaesthesia	1 (<0.1%)

Medical Dictionary of Regulatory Activities (MedDRA) Preferred Term	TOTAL Non-Fatal Pediatric Adverse Event Cases (n=5,322)
Dysphagia	1 (<0.1%)
Dysphemia	1 (<0.1%)
Electrocardiogram change	1 (<0.1%)
Electroencephalogram abnormal	1 (<0.1%)
Emotional distress	1 (<0.1%)
Encephalopathy	1 (<0.1%)
Epilepsy	1 (<0.1%)
Extrapyramidal disorder	1 (<0.1%)
Eyelid oedema	1 (<0.1%)
Feeling drunk	1 (<0.1%)
Flat affect	1 (<0.1%)
Foaming at mouth	1 (<0.1%)
Focal dyscognitive seizures	1 (<0.1%)
Generalised oedema	1 (<0.1%)
Glossitis	1 (<0.1%)
Haematemesis	1 (<0.1%)
Hepatic enzyme increased	1 (<0.1%)
Hiccups	1 (<0.1%)
Hyperacusis	1 (<0.1%)
Hyperaesthesia	1 (<0.1%)
Hypoacusis	1 (<0.1%)
Hypoaesthesia oral	1 (<0.1%)
Hypocalcaemia	1 (<0.1%)
Hyponatraemia	1 (<0.1%)
Hypoperfusion	1 (<0.1%)
Hypophagia	1 (<0.1%)
Hypothermia	1 (<0.1%)
Incontinence	1 (<0.1%)
Infrequent bowel movements	1 (<0.1%)
Intentional self-injury	1 (<0.1%)
International normalised ratio increased	1 (<0.1%)
Irregular breathing	1 (<0.1%)
Limb discomfort	1 (<0.1%)

Medical Dictionary of Regulatory Activities (MedDRA) Preferred Term	TOTAL Non-Fatal Pediatric Adverse Event Cases (n=5,322)
Lip oedema	1 (<0.1%)
Lung infiltration	1 (<0.1%)
Lymphocytosis	1 (<0.1%)
Memory impairment	1 (<0.1%)
Middle insomnia	1 (<0.1%)
Musculoskeletal stiffness	1 (<0.1%)
Myalgia	1 (<0.1%)
Neck pain	1 (<0.1%)
Oromandibular dystonia	1 (<0.1%)
Pain in extremity	1 (<0.1%)
Panic reaction	1 (<0.1%)
Paraesthesia	1 (<0.1%)
Peripheral coldness	1 (<0.1%)
Peripheral swelling	1 (<0.1%)
Pharyngeal oedema	1 (<0.1%)
Piloerection	1 (<0.1%)
Platelet count increased	1 (<0.1%)
Psychomotor skills impaired	1 (<0.1%)
Psychotic disorder	1 (<0.1%)
Rales	1 (<0.1%)
Rash generalised	1 (<0.1%)
Rash maculo-papular	1 (<0.1%)
Rash pruritic	1 (<0.1%)
Restless legs syndrome	1 (<0.1%)
Rhabdomyolysis	1 (<0.1%)
Saliva altered	1 (<0.1%)
Scratch	1 (<0.1%)
Self-injurious ideation	1 (<0.1%)
Sensory loss	1 (<0.1%)
Sepsis	1 (<0.1%)
Sinus tachycardia	1 (<0.1%)
Skin abrasion	1 (<0.1%)
Skin discomfort	1 (<0.1%)

Medical Dictionary of Regulatory Activities (MedDRA) Preferred Term	**TOTAL Non-Fatal Pediatric Adverse Event Cases (n=5,322)**
Sleep talking	1 (<0.1%)
Sleep terror	1 (<0.1%)
Status epilepticus	1 (<0.1%)
Stupor	1 (<0.1%)
Swollen tongue	1 (<0.1%)
Throat irritation	1 (<0.1%)
Tongue movement disturbance	1 (<0.1%)
Torticollis	1 (<0.1%)
Transaminases increased	1 (<0.1%)
Urine output decreased	1 (<0.1%)
Ventricular tachycardia	1 (<0.1%)
Violence-related symptom	1 (<0.1%)
Visual field defect	1 (<0.1%)
Vomiting projectile	1 (<0.1%)
X-ray abnormal	1 (<0.1%)

Table 2a. Listing of All Adverse Events for Adverse Event at Correct Dose Cases, 2008-2016

Medical Dictionary of Regulatory Activities (MedDRA) Preferred Term	TOTAL Non-Fatal Pediatric Adverse Event at Correct Dose Cases (n=)
Hallucination	64 (38.3%)
Confusional state	32 (19.2%)
Mydriasis	25 (15.0%)
Tachycardia	25 (15.0%)
Agitation	16 (9.6%)
Hypertension	16 (9.6%)
Somnolence	16 (9.6%)
Tremor	16 (9.6%)
Vomiting	15 (9.0%)
Ataxia	13 (7.8%)
Irritability	12 (7.2%)
Dizziness	10 (6.0%)
Urticaria	10 (6.0%)
Dystonia	8 (4.8%)
Abnormal behaviour	7 (4.2%)
Insomnia	7 (4.2%)
Hypersensitivity	6 (3.6%)
Lethargy	6 (3.6%)
Nausea	6 (3.6%)
Mucosal dryness	5 (3.0%)
Anxiety	4 (2.4%)
Hallucination, visual	4 (2.4%)
Psychomotor hyperactivity	4 (2.4%)
Seizure	4 (2.4%)
Dysarthria	3 (1.8%)
Dyspnoea	3 (1.8%)
Flushing	3 (1.8%)
Formication	3 (1.8%)
Headache	3 (1.8%)
Hypohydrosis	3 (1.8%)
Myoclonus	3 (1.8%)
Nervousness	3 (1.8%)

Medical Dictionary of Regulatory Activities (MedDRA) Preferred Term	TOTAL Non-Fatal Pediatric Adverse Event at Correct Dose Cases (n=)
Nystagmus	3 (1.8%)
Pyrexia	3 (1.8%)
Rash	3 (1.8%)
Tachypnoea	3 (1.8%)
Aggression	2 (1.2%)
Chest pain	2 (1.2%)
Drooling	2 (1.2%)
Eye swelling	2 (1.2%)
Fear	2 (1.2%)
Feeling jittery	2 (1.2%)
Hyperglycaemia	2 (1.2%)
Hyperhidrosis	2 (1.2%)
Incoherent	2 (1.2%)
Nightmare	2 (1.2%)
Oedema	2 (1.2%)
Palpitations	2 (1.2%)
Paranoia	2 (1.2%)
Pruritus	2 (1.2%)
Sleep disorder	2 (1.2%)
Staring	2 (1.2%)
Visual impairment	2 (1.2%)
Abdominal pain	1 (0.6%)
Abdominal pain upper	1 (0.6%)
Akathisia	1 (0.6%)
Amnesia	1 (0.6%)
Anaphylactic reaction	1 (0.6%)
Aphasia	1 (0.6%)
Blood glucose increased	1 (0.6%)
Bruxism	1 (0.6%)
Condition aggravated	1 (0.6%)
Crying	1 (0.6%)
Deafness	1 (0.6%)
Delirium	1 (0.6%)

Medical Dictionary of Regulatory Activities (MedDRA) Preferred Term	TOTAL Non-Fatal Pediatric Adverse Event at Correct Dose Cases (n=)
Diplopia	1 (0.6%)
Disorientation	1 (0.6%)
Dyskinesia	1 (0.6%)
Epilepsy	1 (0.6%)
Face oedema	1 (0.6%)
Gastrointestinal sounds abnormal	1 (0.6%)
Hallucination, auditory	1 (0.6%)
Hypotonia	1 (0.6%)
Intentional self-injury	1 (0.6%)
Lip swelling	1 (0.6%)
Malaise	1 (0.6%)
Memory impairment	1 (0.6%)
Mental status changes	1 (0.6%)
Movement disorder	1 (0.6%)
Muscle spasms	1 (0.6%)
Muscle twitching	1 (0.6%)
Muscular weakness	1 (0.6%)
Oedema peripheral	1 (0.6%)
Pain	1 (0.6%)
Pallor	1 (0.6%)
Panic reaction	1 (0.6%)
Photophobia	1 (0.6%)
Pupil fixed	1 (0.6%)
Respiratory depression	1 (0.6%)
Screaming	1 (0.6%)
Self-injurious ideation	1 (0.6%)
Skin warm	1 (0.6%)
Somnambulism	1 (0.6%)
Speech disorder	1 (0.6%)
Urinary incontinence	1 (0.6%)
Urinary retention	1 (0.6%)
Vertigo	1 (0.6%)
Violence-related symptom	1 (0.6%)

Medical Dictionary of Regulatory Activities (MedDRA) Preferred Term	TOTAL Non-Fatal Pediatric Adverse Event at Correct Dose Cases (n=)
Vision blurred	1 (0.6%)

Table 2b. Adverse Events and Associated Products in Adverse Event at Correct Dose Cases[a], 2008-2016

	DPH	DXM	CHL	BRO	PSE	PE	GUA	DOX	Adverse Event at Correct Dose (n=167)
Mental Status Changes	46 (27.5%)	69 (41.3%)	9 (5.4%)	6 (3.6%)	10 (6.0%)	31 (18.6%)	24 (14.4%)	5 (3.0%)	121 (72.5%)
Peripheral Anticholinergic Symptoms	16 (9.6%)	32 (19.2%)	5 (3.0%)	1 (0.6%)	8 (4.8%)	14 (8.4%)	9 (5.4%)	4 (2.4%)	50 (30.0%)
Central Motor Activity Symptoms	17 (10.2%)	24 (14.4%)	3 (1.8%)	1 (0.6%)	2 (1.2%)	9 (5.4%)	6 (3.6%)	2 (1.2%)	40 (24.0%)
Anaphylactic/ Urticarial Symptoms	1 (0.6%)	15 (9.0%)	3 (1.8%)	2 (1.2%)	1 (0.6%)	5 (3.0%)	7 (4.2%)	2 (1.2%)	18 (10.8%)
Pain Syndrome	2 (1.2%)	5 (3.0%)	1 (0.6%)	0 (0.0%)	1 (0.6%)	4 (2.4%)	0 (0.0%)	1 (0.6%)	8 (4.8%)
Other AEs[b]	13 (7.8%)	33 (19.8%)	7 (4.2%)	3 (1.8%)	7 (4.2%)	19 (11.4%)	12 (7.2%)	0 (0.0%)	50 (30.0%)
Miscellaneous AEs of Interest	6 (3.6%)	16 (9.6%)	1 (0.6%)	3 (1.8%)	4 (2.4%)	4 (2.4%)	7 (4.2%)	1 (0.6%)	25 (15.0%)
Hypertension	5 (3.0%)	10 (6.0%)	0 (0.0%)	1 (0.6%)	2 (1.2%)	1 (0.6%)	5 (3.0%)	1 (0.6%)	25 (15.0%)
Seizure	1 (0.6%)	3 (1.8%)	1 (0.6%)	0 (0.0%)	0 (0.0%)	2 (1.2%)	0 (0.0%)	0 (0.0%)	7 (4.2%)
Dyspnea	0 (0.0%)	2 (1.2%)	0 (0.0%)	1 (0.6%)	0 (0.0%)	1 (0.6%)	1 (0.6%)	0 (0.0%)	5 (3.0%)
Respiratory Depression	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	1 (0.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.2%)
Self-harm/ Ideation	0 (0.0%)	1 (0.6%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	0 (0.0%)	1 (0.6%)	0 (0.0%)	3 (1.8%)

[a]*Some cases may involve more than one adverse event resulting in a column total greater than the number of cases.*

[b]*A full listing of AE's is provided in Appendix A.*

Table 3. Rate of Adverse Event by Case Type, 2009-2016[a]

Case Type	TOTAL Pediatric Adverse Event Cases	TOTAL Rate of Pediatric Adverse Event Cases per 100 Million Dosage Units Sold (95% CI)	Dosage Units Sold per Single Adverse Event Case
All Cases	**4,756**	**6.15 (5.98, 6.33)**	**16,252,794**
Accidental Unsupervised Ingestions Cases	3,134	4.05 (3.91, 4.20)	24,664,419
Medication Error Cases	513	0.66 (0.61, 0.72)	150,678,925
Adverse Event at Correct Dose	140	0.18 (0.15, 0.21)	552,130,632
Fatal Cases	33	0.04 (0.03, 0.06)	2,342,372,378

[a]*Defined as exposures to single product, single ingredient non-RX products.*

Table 4. Case Rates of Reported Adverse Events by Product[a] Type, 2009-2016

Product Type	TOTAL Pediatric Adverse Event Cases per 100 Million Dosage Units Sold (95% CI)	Single Pediatric Adverse Event Case per Units Sold	Accidental Unsupervised Ingestion Cases per 100 Million Units Sold (95% CI)	Single Accidental Unsupervised Ingestion Cases per Units Sold	Medication Error Cases per 100 Million Dosage Units Sold (95% CI)	Dosage Units Sold per Single Medication Error Case	Adverse Event at Correct Dose Cases per 100 Million Dosage Units Sold (95% CI)	Dosage Units Sold per Single Adverse Event at Correct Dose
Liquid	16.73 (16.16, 17.31)	5,977,933	11.52 (11.05, 12.01)	8,677,644	2.28 (2.07, 2.51)	43,820,140	0.61 (0.51, 0.74)	162,760,519
Solid	2.72 (2.59, 2.86)	36,757,479	1.62 (1.52, 1.73)	61,758,834	0.17 (0.14, 0.21)	591,120,272	0.04 (0.02, 0.06)	2,758,561,271
Pediatric	9.98 (9.65, 10.31)	10,022,330	6.80 (6.53, 7.08)	14,700,541	1.19 (1.08, 1.31)	84,033,383	0.31 (0.25, 0.37)	323,684,142
Adult	1.71 (1.58, 1.83)	58,629,297	1.11 (1.01, 1.21)	90,449,471	0.11 (0.08, 0.15)	881,882,346	0.04 (0.02, 0.06)	2,490,020,742
Single Ingredient Product	9.81 (9.50, 10.13)	10,190,579	6.72 (6.46, 6.99)	14,879,694	1.01 (0.91, 1.12)	98,704,565	0.16 (0.13, 0.21)	608,147,482
Fixed Combination Product	2.95 (2.79, 3.13)	33,869,243	1.60 (1.48, 1.73)	62,351,409	0.41 (0.35, 0.48)	244,402,127	0.21 (0.17, 0.26)	477,025,838

[a]Each product characteristic is only counted once for each case; characteristics for cough/cold products only.

Table 5a. Ingredient by Case Type[a], 2008-2016

	TOTAL Pediatric Adverse Event Cases (n=5,360)	Accidental Unsupervised Ingestion Adverse Event Cases (n=3,531)	Medication Error Adverse Event Cases (n=579)	Adverse Event at Correct Dose (n=167)	Other/Unknown Reason Adverse Event Cases (n=1,083)
Diphenhydramine	3,117 (58.2%)	2,176 (61.6%)	216 (37.3%)	51 (30.5%)	674 (62.2%)
Dextromethrophan	2,062 (38.5%)	1,235 (35.0%)	337 (58.2%)	109 (65.3%)	381 (35.2%)
Phenylephrine	588 (11.0%)	333 (9.4%)	84 (14.5%)	50 (29.9%)	121 (11.2%)
Chlorpheniramine	372 (6.9%)	219 (6.2%)	46 (7.9%)	21 (12.6%)	86 (7.9%)
Pseudoephedrine	286 (5.3%)	145 (4.1%)	58 (10.0%)	19 (11.4%)	64 (5.9%)
Guaifenesin	229 (4.3%)	85 (2.4%)	35 (6.0%)	34 (20.4%)	75 (6.9%)
Brompheniramine	174 (3.2%)	84 (2.4%)	51 (8.8%)	9 (5.4%)	30 (2.8%)
Doxylamine	162 (3.0%)	85 (2.4%)	19 (3.3%)	9 (5.4%)	49 (4.5%)

[a]*Each ingredient is only counted once for each case; some cases may involve more than one cough/cold product or a combination cough/cold product with more than one ingredient resulting in a column total greater than the number of cases.*

Table 5b. Single Ingredient Cases Only by Case Type, 2008-2016

	TOTAL Pediatric Adverse Event Cases (n=3,393)	Accidental Unsupervised Ingestion Adverse Event Cases (n=2,503)	Medication Error Adverse Event Cases (n=314)	Adverse Event at Correct Dose (n=45)	Other/Unknown Reason Adverse Event Cases (n=531)
Diphenhydramine	2,251 (66.3%)	1,700 (67.9%)	128 (40.8%)	24 (53.3%)	399 (75.1%)
Dextromethorphan	1,046 (30.8%)	737 (29.4%)	176 (56.1%)	15 (33.3%)	118 (22.2%)
Pseudoephedrine	38 (1.1%)	27 (1.1%)	2 (0.6%)	3 (6.7%)	6 (1.1%)
Doxylamine	28 (0.8%)	24 (1.0%)	1 (0.3%)	0 (0.0%)	3 (0.6%)
Phenylephrine	15 (0.4%)	12 (0.5%)	2 (0.6%)	0 (0.0%)	1 (0.2%)
Chlorpheniramine	8 (0.2%)	3 (0.1%)	2 (0.6%)	0 (0.0%)	3 (0.6%)
Guaifenesin	5 (0.1%)	0 (0.0%)	1 (0.3%)	3 (6.7%)	1 (0.2%)
Brompheniramine	2 (0.1%)	0 (0.0%)	2 (0.6%)	0 (0.0%)	0 (0.0%)

Table 5c. Cases with Products Containing Diphenhydramine and/or Dextromethorphan with or without Other Ingredients

	TOTAL Pediatric Adverse Event Cases (n=5,360)	Accidental Unsupervised Ingestion Adverse Event Cases (n=3,531)	Medication Error Adverse Event Cases (n=579)	Adverse Event at Correct Dose (n=167)	Other/Unknown Reason Adverse Event Cases (n=1,083)
Dextromethorphan and diphenhydramine	86 (1.6%)	38 (1.1%)	15 (2.6%)	4 (2.4%)	29 (2.7%)
Dextromethorphan or diphenhydramine	5,093 (95.0%)	3,373 (95.5%)	538 (92.9%)	156 (93.4%)	1,026 (94.7%)

Table 6. Ingredient[a] rates per 100 Million Dosage Units Sold (95% CI), 2009-2016

	2009	2010	2011	2012	2013	2014	2015	2016
Brompheniramine	33.60 (22.14, 48.88)	19.70 (11.48, 31.54)	20.83 (12.72, 32.16)	18.96 (11.42, 29.61)	24.45 (15.50, 36.69)	28.23 (17.69, 42.74)	27.11 (16.32, 42.34)	14.42 (6.92, 26.52)
Chlorpheniramine	5.72 (4.50, 7.17)	5.23 (4.00, 6.72)	3.39 (2.34, 4.76)	3.34 (2.28, 4.71)	3.46 (2.36, 4.88)	3.14 (2.03, 4.63)	2.51 (1.49, 3.97)	3.18 (1.97, 4.86)
Dextromethorphan	7.70 (6.81, 8.68)	7.29 (6.39, 8.28)	6.49 (5.65, 7.43)	6.58 (5.74, 7.51)	7.07 (6.20, 8.03)	7.89 (6.93, 8.94)	7.39 (6.46, 8.42)	6.72 (5.83, 7.71)
Diphenhydramine	12.02 (10.81, 13.33)	11.09 (9.95, 12.33)	10.58 (9.46, 11.81)	10.85 (9.76, 12.02)	9.66 (8.69, 10.72)	11.51 (10.42, 12.68)	10.59 (9.51, 11.75)	9.69 (8.68, 10.78)
Doxylamine	2.11 (1.25, 3.33)	2.71 (1.74, 4.03)	0.82 (0.35, 1.61)	1.82 (1.10, 2.84)	1.63 (0.97, 2.58)	2.54 (1.68, 3.70)	2.12 (1.33, 3.22)	1.39 (0.78, 2.29)
Guaifenesin	0.98 (0.62, 1.47)	1.23 (0.81, 1.80)	0.62 (0.33, 1.05)	1.00 (0.63, 1.52)	1.12 (0.71, 1.66)	1.61 (1.10, 2.27)	1.24 (0.78, 1.85)	1.27 (0.81, 1.91)
Phenylephrine	3.32 (2.71, 4.02)	2.86 (2.27, 3.56)	1.94 (1.44, 2.57)	2.50 (1.93, 3.19)	2.26 (1.72, 2.90)	2.14 (1.61, 2.79)	2.11 (1.57, 2.79)	2.03 (1.50, 2.69)
Pseudoephedrine	3.86 (2.87, 5.07)	2.72 (1.92, 3.75)	1.28 (0.76, 2.03)	1.10 (0.63, 1.78)	1.79 (1.15, 2.66)	2.87 (1.99, 4.01)	2.10 (1.35, 3.13)	1.24 (0.66, 2.12)

[a]*Each ingredient is only counted once for each case; some cases may involve more than one cough/cold product or a combination cough/cold product with more than one ingredient.*

Table 7. Case Counts of Product Exposures by Age, 2008-2016

	<6 months (n=29)	6 months to <1 year (n=107)	1 to <2 years (n=609)	2 to <3 years (n=1,314)	3 to <4 years (n=1,157)	4 to <5 years (n=657)	5 to <6 years (n=344)	6 to <12 years (n=1,138)	Exact Age Unknown (<12 years) (n=5)
Multiple Products (CCMs only)	**1 (3.4%)**	**2 (1.9%)**	**7 (1.1%)**	**28 (2.1%)**	**26 (2.2%)**	**17 (2.6%)**	**15 (4.4%)**	**47 (4.1%)**	**0 (0.0%)**
Multiple Products (CCMs + non-CCMs)	**6 (20.7%)**	**12 (11.2%)**	**57 (9.4%)**	**114 (8.7%)**	**115 (9.9%)**	**78 (11.9%)**	**60 (17.4%)**	**303 (26.6%)**	**0 (0.0%)**
Only CCM Pediatric Formulation	**15 (51.7%)**	**32 (29.9%)**	**330 (54.2%)**	**942 (71.7%)**	**835 (72.2%)**	**462 (70.3%)**	**210 (61.0%)**	**474 (41.7%)**	**2 (40.0%)**
Single Ingredient Liquid	8 (53.3%)	12 (37.5%)	198 (60.0%)	689 (73.1%)	590 (70.7%)	310 (67.1%)	127 (60.5%)	194 (40.9%)	1 (50.0%)
Fixed Ingredient Liquid	5 (33.3%)	6 (18.8%)	66 (20.0%)	168 (17.8%)	155 (18.6%)	71 (15.4%)	37 (17.6%)	68 (14.3%)	1 (50.0%)
Single Ingredient Solid	1 (6.7%)	14 (43.8%)	66 (20.0%)	81 (8.6%)	85 (10.2%)	78 (16.9%)	43 (20.5%)	199 (42.0%)	0 (0.0%)
Fixed Combination Solid	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	4 (0.5%)	2 (0.4%)	3 (1.4%)	6 (1.3%)	0 (0.0%)
Unknown	1 (6.7%)	0 (0.0%)	0 (0.0%)	3 (0.3%)	1 (0.1%)	1 (0.2%)	0 (0.0%)	7 (1.5%)	0 (0.0%)
Only CCM Adult Formulation	**2 (6.9%)**	**47 (43.9%)**	**145 (23.8%)**	**132 (10.0%)**	**93 (8.0%)**	**46 (7.0%)**	**23 (6.7%)**	**157 (13.8%)**	**1 (20.0%)**
Single Ingredient Liquid	0 (0.0%)	0 (0.0%)	2 (1.4%)	4 (3.0%)	3 (3.2%)	4 (8.7%)	3 (13.0%)	4 (2.5%)	0 (0.0%)
Fixed Ingredient Liquid	1 (50.0%)	2 (4.3%)	19 (13.1%)	35 (26.5%)	19 (20.4%)	3 (6.5%)	6 (26.1%)	35 (22.3%)	0 (0.0%)
Single Ingredient Solid	0 (0.0%)	34 (72.3%)	86 (59.3%)	50 (37.9%)	35 (37.6%)	25 (54.3%)	7 (30.4%)	46 (29.3%)	1 (100.0%)
Fixed Combination Solid	1 (50.0%)	10 (21.3%)	38 (26.2%)	43 (32.6%)	36 (38.7%)	14 (30.4%)	7 (30.4%)	72 (45.9%)	0 (0.0%)

	<6 months (n=29)	**6 months to <1 year (n=107)**	**1 to <2 years (n=609)**	**2 to <3 years (n=1,314)**	**3 to <4 years (n=1,157)**	**4 to <5 years (n=657)**	**5 to <6 years (n=344)**	**6 to <12 years (n=1,138)**	**Exact Age Unknown (<12 years) (n=5)**
Unknown	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Only Unknown Formulation	**5 (17.2%)**	**14 (13.1%)**	**70 (11.5%)**	**98 (7.5%)**	**88 (7.6%)**	**54 (8.2%)**	**36 (10.5%)**	**157 (13.8%)**	**2 (40.0%)**
Liquid	3 (60.0%)	5 (35.7%)	31 (44.3%)	59 (60.2%)	50 (56.8%)	26 (48.1%)	14 (38.9%)	39 (24.8%)	2 (100.0%)
Solid	0 (0.0%)	9 (64.3%)	36 (51.4%)	33 (33.7%)	35 (39.8%)	28 (51.9%)	21 (58.3%)	107 (68.2%)	0 (0.0%)
Unknown	2 (40.0%)	0 (0.0%)	3 (4.3%)	6 (6.1%)	3 (3.4%)	0 (0.0%)	1 (2.8%)	11 (7.0%)	0 (0.0%)

Table 8. Fatality Case Characteristics by Case Type, 2008-2016

	TOTAL Pediatric Adverse Event Cases (n=40)	Accidental Unsupervised Ingestion Adverse Event Cases (n=3)	Medication Error Adverse Event Cases (n=2)	Other/Unknown Reason Adverse Event Cases (n=35)
Age				
<6 months	8 (20.0%)	0 (0.0%)	0 (0.0%)	8 (22.9%)
6 months to <1 year	8 (20.0%)	0 (0.0%)	0 (0.0%)	8 (22.9%)
1 to <2 years	8 (20.0%)	3 (100.0%)	0 (0.0%)	5 (14.3%)
2 to <3 years	4 (10.0%)	0 (0.0%)	1 (50.0%)	3 (8.6%)
3 to <4 years	1 (2.5%)	0 (0.0%)	1 (50.0%)	0 (0.0%)
4 to <5 years	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
5 to <6 years	4 (10.0%)	0 (0.0%)	0 (0.0%)	4 (11.4%)
6 to <7 years	4 (10.0%)	0 (0.0%)	0 (0.0%)	4 (11.4%)
7 to <8 years	1 (2.5%)	0 (0.0%)	0 (0.0%)	1 (2.9%)
8 to <9 years	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
9 to <10 years	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
10 to <11 years	1 (2.5%)	0 (0.0%)	0 (0.0%)	1 (2.9%)
11 to <12 years	1 (2.5%)	0 (0.0%)	0 (0.0%)	1 (2.9%)
Exact age unknown (<12 years)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gender				
Male	26 (65.0%)	2 (66.7%)	2 (100.0%)	22 (62.9%)
Female	14 (35.0%)	1 (33.3%)	0 (0.0%)	13 (37.1%)
Not Reported	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Drug Administered By				
Self	3 (7.5%)	3 (100.0%)	0 (0.0%)	0 (0.0%)
Parent	16 (40.0%)	0 (0.0%)	0 (0.0%)	16 (45.7%)

	TOTAL Pediatric Adverse Event Cases (n=40)	Accidental Unsupervised Ingestion Adverse Event Cases (n=3)	Medication Error Adverse Event Cases (n=2)	Other/Unknown Reason Adverse Event Cases (n=35)
Grandparent	2 (5.0%)	0 (0.0%)	0 (0.0%)	2 (5.7%)
Other Relative	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Babysitter/Daycare	3 (7.5%)	0 (0.0%)	0 (0.0%)	3 (8.6%)
Other Caregiver	4 (10.0%)	0 (0.0%)	0 (0.0%)	4 (11.4%)
Multiple Caregivers	3 (7.5%)	0 (0.0%)	1 (50.0%)	2 (5.7%)
Sibling or Other Child	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Not Reported	9 (22.5%)	0 (0.0%)	1 (50.0%)	8 (22.9%)
Exposure Site				
Own Residence	12 (30.0%)	2 (66.7%)	1 (50.0%)	9 (25.7%)
Other Residence	1 (2.5%)	0 (0.0%)	0 (0.0%)	1 (2.9%)
Other Location	6 (15.0%)	0 (0.0%)	0 (0.0%)	6 (17.1%)
Multiple Locations	2 (5.0%)	0 (0.0%)	1 (50.0%)	1 (2.9%)
Not Reported	19 (47.5%)	1 (33.3%)	0 (0.0%)	18 (51.4%)

Table 8a. Fatality[a] Cough and Cold Medication Product Types by Case[b] Type, 2008-2016

	TOTAL Pediatric Adverse Event Cases (n=40)	Accidental Unsupervised Ingestion Adverse Event Cases (n=3)	Medication Error Adverse Event Cases (n=2)	Other/Unknown Reason Adverse Event Cases (n=35)
Number of Products				
Single Product	13 (32.5%)	2 (66.7%)	0 (0.0%)	11 (31.4%)
Multiple Products (CCMs only)	2 (5.0%)	0 (0.0%)	0 (0.0%)	2 (5.7%)
Multiple Products (CCMs + non-CCMs)	25 (62.5%)	1 (33.3%)	2 (100.0%)	22 (62.9%)
CCM Product Type – Dosage Formulation[c]				
Liquid	8 (20.0%)	0 (0.0%)	1 (50.0%)	7 (20.0%)
Solid	8 (20.0%)	3 (100%)	0 (0.0%)	5 (14.3%)
Unknown	26 (65.0%)	0 (0.0%)	2 (100%)	24 (68.6%)
CCM Product Type – Age Formulation[c]				
Pediatric	7 (17.5%)	0 (0.0%)	1 (50.0%)	6 (17.1%)
Adult	5 (12.5%)	2 (66.7%)	0 (0.0%)	3 (8.6%)
Unknown	30 (75.0%)	1 (33.3%)	2 (100%)	27 (77.1%)
CCM Product Type – Combination Formulation[b]				
Single Ingredient CCM Product	28 (70.0%)	3 (100%)	1 (50.0%)	24 (68.6%)
Fixed Combination CCM Product	7 (17.5%)	0 (0.0%)	1 (50.0%)	6 (17.1%)
Unknown	6 (15.0%)	0 (0.0%)	1 (50.0%)	5 (14.3%)

[a]Fatalities only included if exposures were not related to a prescription product.

[b]Each product characteristic is only counted once for each case; some cases may involve more than one product resulting in a column total greater than the number of case.

[c]Characteristics for cough/cold products only.

Table 8b. Fatality Cough and Cold Medications Specific Formulations by Case[a] Type, 2008-2016

	TOTAL Pediatric Adverse Event Cases (n=40)	Accidental Unsupervised Ingestion Adverse Event Cases (n=3)	Medication Error Adverse Event Cases (n=2)	Other/Unknown Reason Adverse Event Cases (n=35)
CCM Pediatric Formulation				
Single Ingredient Liquid	3 (7.5%)	0 (0.0%)	0 (0.0%)	3 (8.6%)
OTC Fixed Combination Ingredient Liquid	2 (5.0%)	0 (0.0%)	1 (50.0%)	1 (2.9%)
Single Ingredient Solid	2 (5.0%)	0 (0.0%)	0 (0.0%)	2 (5.7%)
OTC Fixed Combination Ingredient Solid	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unknown	1 (2.5%)	0 (0.0%)	0 (0.0%)	1 (2.9%)
CCM Adult Formulation				
Single Ingredient Liquid	1 (2.5%)	0 (0.0%)	0 (0.0%)	1 (2.9%)
OTC Fixed Combination Ingredient Liquid	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Single Ingredient Solid	3 (7.5%)	2 (66.7%)	0 (0.0%)	1 (2.9%)
OTC Fixed Combination Ingredient Solid	1 (2.5%)	0 (0.0%)	0 (0.0%)	1 (2.9%)
Unknown	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CCM Unknown Formulation				
Liquid	2 (5.0%)	0 (0.0%)	0 (0.0%)	2 (5.7%)
Solid	3 (7.5%)	1 (33.3%)	0 (0.0%)	2 (5.7%)
Unknown	25 (62.5%)	0 (0.0%)	2 (100%)	23 (65.7%)

[a]Each product characteristic is only counted once for each case; Some cases may involve more than one cough/cold product resulting in a column total greater than the number of cases.

APPENDIX A: LISTING OF POTENTIALLY RELATED ADVERSE EVENTS IN ADVERSE EVENT AT CORRECT DOSE CASES, 2008-2016

Adverse Event Category	Adverse Event at Correct Dose	N (%) (n=167)
Mental Status Change	Hallucination	64 (38.3%)
	Confusional state	32 (19.2%)
	Agitation	16 (9.6%)
	Somnolence	16 (9.6%)
	Irritability	12 (7.2%)
	Dizziness	10 (6.0%)
	Abnormal behaviour	7 (4.2%)
	Insomnia	7 (4.2%)
	Lethargy	6 (3.6%)
	Anxiety	4 (2.4%)
	Hallucination, visual	4 (2.4%)
	Psychomotor hyperactivity	4 (2.4%)
	Nervousness	3 (1.8%)
	Aggression	2 (1.2%)
	Fear	2 (1.2%)
	Incoherent	2 (1.2%)
	Nightmare	2 (1.2%)
	Paranoia	2 (1.2%)
	Sleep disorder	2 (1.2%)
	Staring	2 (1.2%)
	Amnesia	1 (0.6%)
	Crying	1 (0.6%)
	Delirium	1 (0.6%)
	Disorientation	1 (0.6%)
	Hallucination, auditory	1 (0.6%)
	Malaise	1 (0.6%)

Adverse Event Category	Adverse Event at Correct Dose	N (%) (n=167)
	Memory impairment	1 (0.6%)
	Mental status changes	1 (0.6%)
	Panic reaction	1 (0.6%)
	Screaming	1 (0.6%)
	Somnambulism	1 (0.6%)
	Violence-related symptom	1 (0.6%)
Peripheral Anticholinergic Symptoms	Mydriasis	25 (15.0%)
	Tachycardia	25 (15.0%)
	Mucosal dryness	5 (3.0%)
	Flushing	3 (1.8%)
	Hypohydrosis	3 (1.8%)
	Pyrexia	3 (1.8%)
	Visual impairment	2 (1.2%)
	Diplopia	1 (0.6%)
	Gastrointestinal sounds abnormal	1 (0.6%)
	Photophobia	1 (0.6%)
	Pupil fixed	1 (0.6%)
	Skin warm	1 (0.6%)
	Urinary retention	1 (0.6%)
	Vision blurred	1 (0.6%)
Central Motor Activity Symptoms	Ataxia	13 (7.8%)
	Dystonia	8 (4.8%)
	Dysarthria	3 (1.8%)
	Formication	3 (1.8%)
	Myoclonus	3 (1.8%)
	Nystagmus	3 (1.8%)

Adverse Event Category	Adverse Event at Correct Dose	N (%) (n=167)
	Feeling jittery	2 (1.2%)
	Akathisia	1 (0.6%)
	Aphasia	1 (0.6%)
	Bruxism	1 (0.6%)
	Dyskinesia	1 (0.6%)
	Movement disorder	1 (0.6%)
	Speech disorder	1 (0.6%)
	Vertigo	1 (0.6%)
Anaphylactic/Urticarial Symptoms	Urticaria	10 (6.0%)
	Hypersensitivity	6 (3.6%)
	Rash	3 (1.8%)
	Eye swelling	2 (1.2%)
	Oedema	2 (1.2%)
	Pruritus	2 (1.2%)
	Anaphylactic reaction	1 (0.6%)
	Face oedema	1 (0.6%)
	Lip swelling	1 (0.6%)
	Oedema peripheral	1 (0.6%)
Pain Syndrome	Headache	3 (1.8%)
	Chest pain	2 (1.2%)
	Abdominal pain	1 (0.6%)
	Abdominal pain upper	1 (0.6%)
	Pain	1 (0.6%)
Other AE	Tremor	16 (9.6%)
	Vomiting	15 (9.0%)
	Nausea	6 (3.6%)
	Tachypnoea	3 (1.8%)

Adverse Event Category	Adverse Event at Correct Dose	N (%) (n=167)
	Drooling	2 (1.2%)
	Hyperglycaemia	2 (1.2%)
	Hyperhidrosis	2 (1.2%)
	Palpitations	2 (1.2%)
	Blood glucose increased	1 (0.6%)
	Condition aggravated	1 (0.6%)
	Deafness	1 (0.6%)
	Epilepsy	1 (0.6%)
	Hypotonia	1 (0.6%)
	Intentional self-injury	1 (0.6%)
	Muscle spasms	1 (0.6%)
	Muscle twitching	1 (0.6%)
	Muscular weakness	1 (0.6%)
	Pallor	1 (0.6%)
	Urinary incontinence	1 (0.6%)
Misc. AE of Interest	Hypertension	16 (9.6%)
	Seizure	4 (2.4%)
	Dyspnoea	3 (1.8%)
	Respiratory depression	1 (0.6%)
	Self-injurious ideation	1 (0.6%)