



**VRBPAC 2007 FluMist Briefing Document
MedImmune Briefing Document Errata**

(1)

Section 6.3.2 (Protocol-Defined Wheezing in Study MI-CP111)

Manual review of data listings revealed two additional subjects 6-23 months of age with protocol-defined wheezing (MSW) within 42 days of vaccination that was associated with hospitalization: 1 FluMist recipient and 1 TIV recipient. This information was updated as indicated below.

The original text and table below (Section 6.3.2, Paragraphs 3 and 4, and Table 6-11):

A total of 18 children (11/4179 [0.3%] FluMist; 7/4173 [0.2%] TIV) were hospitalized in association with an adverse event that met the definition of protocol-defined wheezing (MSW) within 42 days of dosing (see Appendix A and Appendix B for details on these children). No deaths resulted from these 18 events, and none of the hospitalized children required mechanical ventilation or admission to an intensive care unit. Two thirds (12 of 18) of the hospitalized children were 6-23 months of age: 9/1992 [0.5%] in the FluMist group and 3/1975 [0.2%] in the TIV group. Of the 9 children in the FluMist group, 2 had a past history of wheezing or asthma, 1 had RSV infection, and 2 children had both a past history of wheezing or asthma and RSV infection. Of the 3 children in the TIV group, 1 had RSV infection, 1 had a past history of wheezing or asthma and RSV infection, and 1 had a past history of wheezing or asthma and mycoplasma infection.

Most of the hospitalized children received standard therapy including bronchodilators and steroids. The median duration of hospitalization in children 6-23 months of age was 4.5 days in the FluMist group (including one child with Down Syndrome who was hospitalized for 21 days) and 4 days in the TIV group. Thus, there was no evidence that the severity of hospitalized protocol-defined wheezing (MSW) cases differed between the FluMist and TIV treatment groups.

Table 6-11 MI-CP111: Measures of Severity of Protocol-Defined Wheezing (MSW) in Children 6-23 Months of Age

Age Subgroup (months) Outcome	FluMist			TIV		
	6-11 N=684	12-23 N=1308	6-23 N=1992	6-11 N=683	12-23 N=1292	6-23 N=1975
Number of children with protocol-defined wheezing from Day 0 through 42 days after last vaccination	47	70	117	29	46	75
Number of these children with outcome of:						
Hospitalization	4 (9%)	5 (7%)	9 (8%)	2 (7%)	1 (2%)	3 (4%)
Death	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ICU or mechanical ventilation	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
New bronchodilator prescription and not hypoxemia or respiratory distress	38 (81%)	50 (71%)	88 (75%)	20 (69%)	32 (70%)	52 (69%)
Any respiratory distress or hypoxemia	9 (19%)	20 (29%)	29 (25%)	9 (31%)	14 (30%)	23 (31%)
≥1 additional MSW episode through 180 days post final dose	18 (38%)	20 (29%)	38 (32%)	7 (24%)	14 (30%)	21 (28%)
≥2 additional MSW episodes through 180 days post final dose	2 (4%)	3 (4%)	5 (4%)	2 (31%)	2 (4%)	4 (5%)

were replaced with:

A total of 20 children (12/4179 [0.3%] FluMist; 8/4173 [0.2%] TIV) were hospitalized in association with an adverse event that met the definition of protocol-defined wheezing (MSW) within 42 days of dosing (see Appendix A and Appendix B for details on these children). No deaths resulted from these events, and none of the hospitalized children required mechanical ventilation or admission to an intensive care unit. Fourteen of the 20 hospitalized children (70%) were 6-23 months of age: 10/1992 [0.5%] in the FluMist group and 4/1975 [0.2%] in the TIV group. Of the 10 children in the FluMist group, 3 had a past history of wheeze or asthma, 1 had RSV infection, 1 had a past history of wheeze or asthma and RSV infection, and 1 had a past history of wheeze or asthma and rhinovirus infection. Of the 4 children in the TIV group, 1 had a past history of wheeze or asthma, 2 had RSV infection, and 1 had a past history of wheeze or asthma and mycoplasma infection.

Most of the hospitalized children received standard therapy including bronchodilators and steroids. The median duration of hospitalization in children 6-23 months of age was 5 days in the FluMist group (including one child with Down Syndrome who was hospitalized for 21 days) and 3.5 days in the TIV group. Thus, there was no evidence

that the severity of hospitalized protocol-defined wheezing (MSW) cases differed between the FluMist and TIV treatment groups.

Age Subgroup (months) Outcome	FluMist			TIV		
	6-11 N=684	12-23 N=1308	6-23 N=1992	6-11 N=683	12-23 N=1292	6-23 N=1975
Number of children with protocol-defined wheezing from Day 0 through 42 days after last vaccination	47	70	117	29	46	75
Number of these children with outcome of:						
Hospitalization	4 (9%)	<u>6</u> (9%)	<u>10</u> (9%)	2 (7%)	<u>2</u> (4%)	<u>4</u> (5%)
Death	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ICU or mechanical ventilation	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
New bronchodilator prescription and not hypoxemia or respiratory distress	38 (81%)	50 (71%)	88 (75%)	20 (69%)	32 (70%)	52 (69%)
Any respiratory distress or hypoxemia	9 (19%)	20 (29%)	29 (25%)	9 (31%)	14 (30%)	23 (31%)
≥1 additional MSW episode through 180 days post final dose	18 (38%)	20 (29%)	38 (32%)	7 (24%)	14 (30%)	21 (28%)
≥2 additional MSW episodes through 180 days post final dose	2 (4%)	3 (4%)	5 (4%)	<u>2</u> (7%)	2 (4%)	4 (5%)

The following information was added to Appendix A:

Appendix A SAEs of Hospitalization Associated with Medically Significant Wheezing – Subjects 6-23 Months of Age

Country	Age (mos) Gender	Past Medical History	MSW Preferred Term	# Days from Previous Dose to		Duration (dy) of		Chest X-ray Findings	Lab Results	Treatment Received	AE Severity/ Outcome	Relation of AE to Study Product ^a
				AE Onset	Hosp Onset	Hosp	AE					
FluMist TWO DOSE GROUP												
42980016 US	17 F	Diagnosed with asthma at 3 mos of age	Asthma	14 PD1	14 PD1	6	6	Right perihilar pneumonia	Negative	IV fluids, parenteral steroids, inhaled bronchodilator	Severe Recovered	Possibly
TIV TWO DOSE GROUP												
80500013 US	20 M	Diagnosed with asthma at 9 mos of age	Broncho-spasm	26 PD1	26 PD1	3	8	Expansion of 10-11 ribs, flattened diaphragm, no consolidation or effusion	Increased WBC count	O ₂ , inhaled bronchodilators, steroids, racemic epinephrine	Severe Recovered	Probably not

(2)

Section 7.3 (Efficacy by Age and History)

Two transcription errors occurred for the 36-47 month of age subgroup without a history and are corrected as below.

The original table below (Table 7-7):

Table 7-7 MI-CP111: Culture Confirmed Modified CDC-ILI Rates by Age and Past History of Wheeze or Asthma, through 180 Days After Last Vaccination

Age Group (mos)	With a History			Without a History		
	FluMist n/N (%)	TIV n/N (%)	Rate Diff	FluMist n/N (%)	TIV n/N (%)	Rate Diff
6-11	4/77 (5.2%)	9/63 (14.3%)	-9.1%	13/607 (2.1%)	31/620 (5.0%)	-2.9%
12-23	12/255 (4.7%)	27/232 (11.6%)	-6.9%	32/1053 (3.0%)	69/1060 (6.5%)	-3.5%
24-35	18/323 (5.6%)	40/337 (11.9%)	-6.3%	35/1049 (3.3%)	77/1042 (7.4%)	-4.1%
36-47	10/137 (7.3%)	15/129 (11.6%)	-4.3%	10/296 (5.1%)	33/331 (3.0%)	-4.9%
48-59	10/112 (8.9%)	17/107 (15.9%)	-7.0%	12/270 (4.4%)	32/252 (12.7%)	-8.3%

Rate difference is FluMist minus TIV. **Bold type** indicates statistically significant difference between treatment groups.

was replaced with:

Age Group (mos)	With a History			Without a History		
	FluMist n/N (%)	TIV n/N (%)	Rate Diff	FluMist n/N (%)	TIV n/N (%)	Rate Diff
6-11	4/77 (5.2%)	9/63 (14.3%)	-9.1%	13/607 (2.1%)	31/620 (5.0%)	-2.9%
12-23	12/255 (4.7%)	27/232 (11.6%)	-6.9%	32/1053 (3.0%)	69/1060 (6.5%)	-3.5%
24-35	18/323 (5.6%)	40/337 (11.9%)	-6.3%	35/1049 (3.3%)	77/1042 (7.4%)	-4.1%
36-47	10/137 (7.3%)	15/129 (11.6%)	-4.3%	15/296 (5.1%)	33/331 (10.0%)	-4.9%
48-59	10/112 (8.9%)	17/107 (15.9%)	-7.0%	12/270 (4.4%)	32/252 (12.7%)	-8.3%

Rate difference is FluMist minus TIV. **Bold type** indicates statistically significant difference between treatment groups.