



PROTOCOL 06-0033

**Aerosol Performance and Comparison of the SouthMedic OxyKid
Nebulizer Mask to Four other Aerosol Masks while Delivering
Albuterol during Simulated Adult Breathing**

October 24, 2006

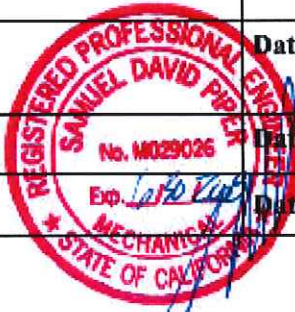
**Dave Piper, PE
Piper Medical Products
PO Box 993
Carmichael, CA. 95609
Tel 916-834-3283
Dave@PiperMedical.com
www.PiperMedical.com**

PIPER MEDICAL

Protocol 06-0033

PROTOCOL: Aerosol Performance and Comparison of the SouthMedic OxyKid Nebulizer Mask to Four other Aerosol Masks while Delivering Albuterol during Simulated Adult Breathing

Prepared By:	S. David Piper, PE	Date:	10/04/2006
Approved By:	S. David Piper, PE	Date:	10/04/2006
Tested By:	Myra Reynado, S. David Piper, PE	Date:	10/05/2006- 10/20/2006
Reported By:	S. David Piper, PE	Date:	10/24/2006
Approved By:	S. David Piper, PE	Date:	10/24/2006



1.0 Objective

- 1.1 To compare the total dose, mass median aerodynamic diameter (MMAD), geometric standard deviation (GSD), respirable mass fraction (0.5 – 5 µm), respirable mass, and treatment time of the Southmedic OxyKid Aerosol Mask to a hybrid OxyKid, Mask 45, Dragon, and Mask 90 Aerosol mask when operating under conditions of adult simulated breathing, and while aerosolizing albuterol sulfate (2.5 mg/3 ml) with a Micromist Nebulizer.

2.0 Reference

- 2.1 DRAFT VERSION "REVIEWER GUIDANCE FOR NEBULIZER, METERED DOSE INHALERS, SPACERS AND ACTUATORS" October 1993.
- 2.2 DRAFT VERSION "REVIEWER GUIDANCE FOR PREMARKET NOTIFICATION SUBMISSIONS" November 1993.
- 2.3 GOOD LABORATORY PRACTICE REGULATIONS, USFDA (21 CFR PART 58)
- 2.4 PIPER MEDICAL SOP-E-126 – SPECTOPHOTOMETER OPERATION
- 2.5 PIPER MEDICAL SOP-E-129 – CASCADE IMPACTOR OPERATION
- 2.6 PIPER MEDICAL SOP-E-130 – AEROSOL AND AIRBORNE PARTICULATE FILTER TESTING AND OPERATION

PROTOCOL: Aerosol Performance and Comparison of the SouthMedic OxyKid Nebulizer Mask to Four other Aerosol Masks while Delivering Albuterol during Simulated Adult Breathing

3.0 Acceptance Criteria

- 3.1 All equipment used will meet its pre-specified operation and calibration requirements before and after testing. All testing shall be performed per GLP.**

4.0 Equipment List

- 4.1 SouthMedic OxyKid Aerosol Mask – One sample as supplied by manufacturer.**
- 4.2 SouthMedic Hybrid OxyKid Aerosol Mask – One sample as supplied by manufacturer.**
- 4.3 Mask 45 Aerosol Mask – One sample as supplied by manufacturer (WestMed).**
- 4.4 Dragon Mask – One sample as supplied by manufacturer (KidsMed).**
- 4.5 Mask 90 Aerosol Mask – One sample as supplied by manufacturer (Hudson RCI).**
- 4.6 Hudson RCI MicroMist Nebulizer – One sample as supplied by manufacturer**
- 4.7 0-100 psig Pressure Gauge (E-008)**
- 4.8 Gilmont glass float type Rotameter (E-003)**
- 4.9 AccuLAB Standard Electronic Balance TS series (E-002)**
- 4.10 7-stage Cascade Impactor, w/ membrane filter for 8th stage (E-032)**
- 4.11 Spectrophotometer (E-113)**
- 4.12 Vacuum pump (E-009)**
- 4.13 Compressed gas source (in-house)**
- 4.14 Large Reservoir Pipette (E-033)**
- 4.15 Membrane filters – Cellulose Ester, 47 mm diameter**
- 4.16 Medication – budesonide (0.5 mg in 2.0 ml)**
- 4.17 Data Acquisition System**
- 4.18 CAHN Model C-31 Microbalance (E-031)**
- 4.19 Humidity/Temperature Meter (E-100)**
- 4.20 Frequency Generator (E-065)**
- 4.21 Oscilloscope (E-089)**
- 4.22 Aerosol Ambient Scavenging Filter Holder**
- 4.23 Valve Controller (E-090)**

PROTOCOL: Aerosol Performance and Comparison of the SouthMedic OxyKid Nebulizer Mask to Four other Aerosol Masks while Delivering Albuterol during Simulated Adult Breathing

Testing Procedure

5.1 Patient Simulation Setup

5.1.1 A simulated adult breathing pattern will be created alternately turning

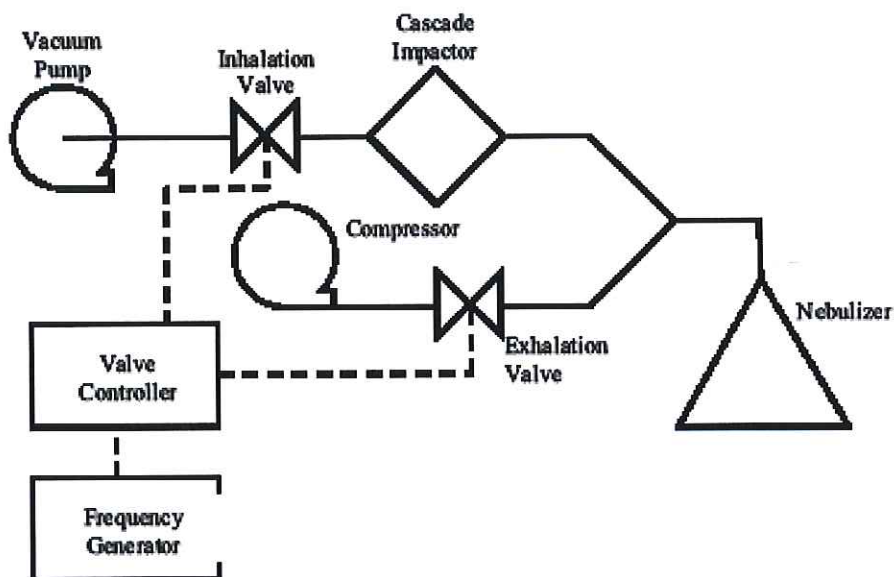


Figure 1 showing the patient simulation setup used for the aerosol testing

on an inhalation or exhalation valve and maintaining a constant flow of gas through each valve when open. As shown in Figure 1, connect the frequency generator to the valve controller. Connect the exhalation valve to a compressor. Connect the inhalation valve between a vacuum source and the cascade impactor.

5.1.2 Adjust the inhalation valve to have a flow of 28 l/min while connected to the cascade impactor and in the open condition. Similarly, adjust the exhalation valve to have a flow of 18.7 l/min when in the open condition.

5.1.3 Connect the two valves to a 22 mm wye connector. Place a 6" length of 22 mm corrugate tubing through the backside of the mouth opening in the Aerosol Mask Mannequin head. Connect each mask to the mannequin head and attach to nebulizer per instructions. Set the

PROTOCOL: Aerosol Performance and Comparison of the SouthMedic OxyKid Nebulizer Mask to Four other Aerosol Masks while Delivering Albuterol during Simulated Adult Breathing

frequency generator to an inspiratory time of 1.28 seconds and an exhalation time of 1.92 seconds. Verify with an oscilloscope.

- 5.2 Aerosol Testing.
- 5.2.1 Each mask will be tested with the same MicroMist nebulizer while aerosolizing a standard dose of albuterol sulfate (2.5 mg per 3.0 ml). The SouthMedic OxyKid mask will be tested three times, all other masks will be tested once (3 OxyKid Mask Tests + 1 test for other 4 masks = 7 aerosol tests).
 - 5.2.2 Connect the nebulizer to compressed air and run at 6 l/min as described in the product insert.
 - 5.2.3 Prior to starting nebulizer, turn on valve controller and verify inhalation and exhalation valve flowrates as described above. Sampling with the cascade impactor shall occur during inhalation as controlled by the valve controller. Exhalation gases will be forced out of the nebulizer as intended by the design of the nebulizer. Position aerosol ambient scavenging system 1-2 inches away from exhalation port of nebulizer. Treatment time will be measured and treatment will be determined to have ceased when visual indication of aerosol production has ceased for a period of at least 1 second. After filling nebulizer with 2 ml of medication, obtain an initial weight for the nebulizer.
 - 5.2.4 Upon completion of simulated nebulizer treatment, turn off nebulizer and valve controller, and then disassemble cascade impactor and place specimen plates and membrane filter for each stage of the cascade impactor into different specimen containers. Use a calibrated pipette to place 10 mL of water into each specimen container.
 - 5.2.5 Using standard spectrophotometer techniques (SOP-s-126), obtain concentration readings using spectrophotometer (E-113) for each cascade impactor stage. Calculate the mass of drug deposited on each cascade impactor stage.
 - 5.2.6 Upon completion of nebulization, obtain a final weight of nebulizer. Assuming normal nominal evaporation rates for nebulizers, use the gravimetric change of the nebulizer to calculate actual quantity of medication left in the nebulizer.
 - 5.2.7 Enter cascade impactor data into cascade impactor spread sheet, plot accumulated mass percents on log-log paper. Determine expulsion, MMAD, GSD, respirable mass fraction (0.5 to 5 microns), and respirable mass using standard cascade impactor data analysis techniques (SOP-s-129).
 - 5.2.8 Tabulate data and perform a comparison.

PIPER MEDICAL

Protocol 06-0033

PROTOCOL: Aerosol Performance and Comparison of the SouthMedic OxyKid Nebulizer Mask to Four other Aerosol Masks while Delivering Albuterol during Simulated Adult Breathing

RESULTS

Aerosol Performance Parameters

	OxyKid (average)	OxyKid Hybrid	Mask 45	Dragon	Mask 90
Total Dose (mg)	297	277	212	213	257
MMAD (µm)	1.7	1.8	1.8	1.7	1.7
GSD	2.4	2.4	2.8	2.4	2.4
Respirable Fraction (%0.5-5µm)	77%	79%	75%	78%	78%
Respirable Dose (mg 0.5-5µm)	228	219	159	168	201
Treatment Time (min)	11.8	11.5	9.5	11.5	10.8

Table 1 Showing the total dose of albuterol, particle size (MMAD), Geometric Standard Deviation (GSD), respirable fraction, respirable dose, and treatment time for each mask while aerosolizing albuterol sulfate with the same MicroMist nebulizer during simulated adult breathing. The results for the OxyKid mask are the average of three tests, all other mask results are for one test each.

PIPER MEDICAL

Protocol 06-0033

PROTOCOL: Aerosol Performance and Comparison of the SouthMedic OxyKid Nebulizer Mask to Four other Aerosol Masks while Delivering Albuterol during Simulated Adult Breathing

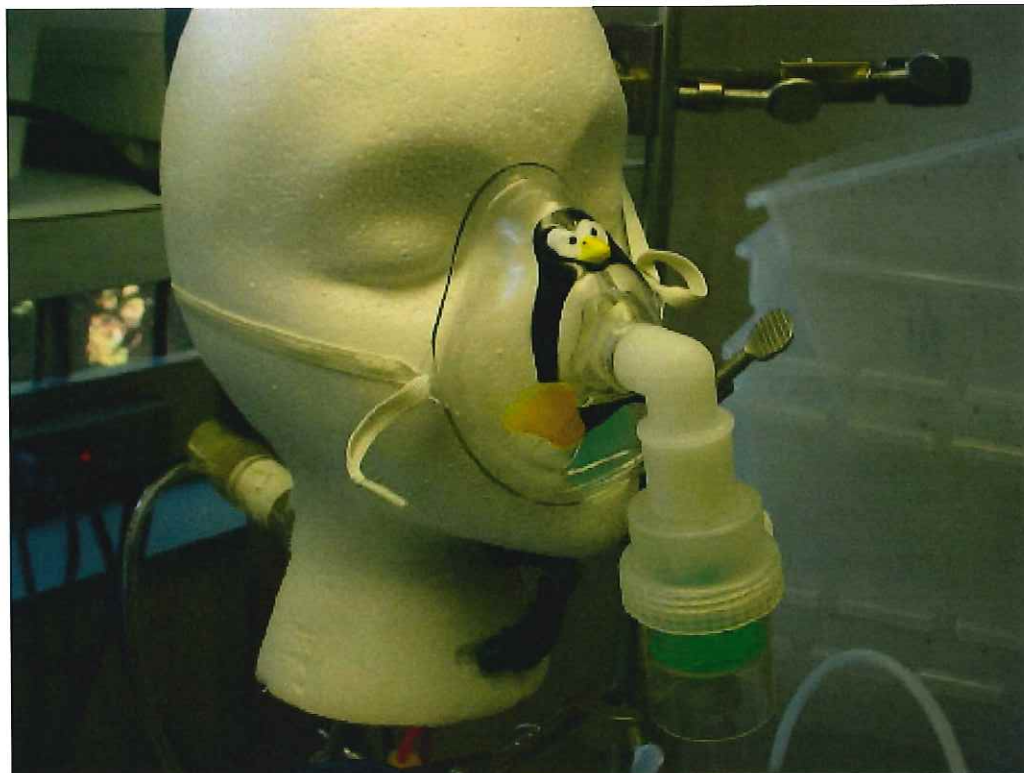


Figure 1 showing the position of the mask on the mannequin head during testing. 22 mm corrugated tubing was ported from the back of the mannequin head to the mouth position, from which aerosol was entrained to the patient simulator and cascade impactor for testing.

FIPER MEDICAL

Protocol 06-0033

PROTOCOL: Aerosol Performance and Comparison of the SouthMedic OxyKid Nebulizer Mask to Four other Aerosol Masks while Delivering Albuterol during Simulated Adult Breathing



Figure 2 showing the masks that were tested. In the upper row from left to right are the OxyKid Nebulizer Mask and the OxyKid Nebulizer Hybrid Mask. In the lower row from left to right are the Mask 45 (WestMed), Dragon Mask (KidsMed), and Mask 90 (Hudson RCI)

PIPER MEDICAL

Protocol 06-0033

PROTOCOL: Aerosol Performance and Comparison of the SouthMedic OxyKid Nebulizer Mask to Four other Aerosol Masks while Delivering Albuterol during Simulated Adult Breathing

DISCUSSION

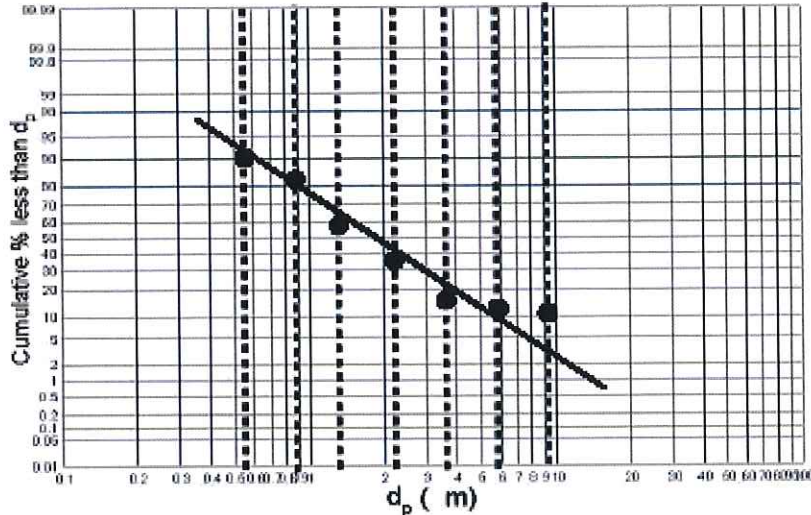
All equipment met it's specification before and after testing. There were no significant experimental variances.

The measured medication delivered during simulated adult breathing was higher when using the SouthMedic OxyKid mask than the other aerosol masks. All other aerosol performance parameters were comparable.

Piper Medical Products

Test:	1	Cascade Impactor:	E-032
Protocol:	06-0033	Impactor Flow:	28.3 l/min
Nebulizer:	Micromist @ 8 l/min	Ambient Temp:	20.4 °C
Aerosol Mask:	Oxy4d	Ambient RH%:	43.8 %
Drug:	salmeterol sulfate	PIV Volume:	3.0 ml
Simulated Breathing:	I-Flow (l/min): 28	TV(ml): 800	IE: 1:1.5

	Cutoff dia. (µm)	Diluent (mL)	Spec. Concen. (µg/mL)	Collected Mass (µg)	Percentage (%)	Cumulative (%)
Stage 1	9.30	9.79	3.42	33.52	11.0%	11.0%
Stage 2	5.81	9.79	0.86	8.41	2.7%	13.7%
Stage 3	3.63	9.79	1.17	11.48	3.8%	17.5%
Stage 4	2.25	9.79	5.53	55.13	18.1%	35.6%
Stage 5	1.41	9.79	8.82	88.77	28.8%	64.4%
Stage 6	0.88	9.79	8.05	78.84	25.8%	90.2%
Stage 7	0.55	9.79	2.33	22.85	7.5%	97.7%
Filter	0.00	9.79	3.02	29.57	9.7%	100.0%
				305	100.0%	

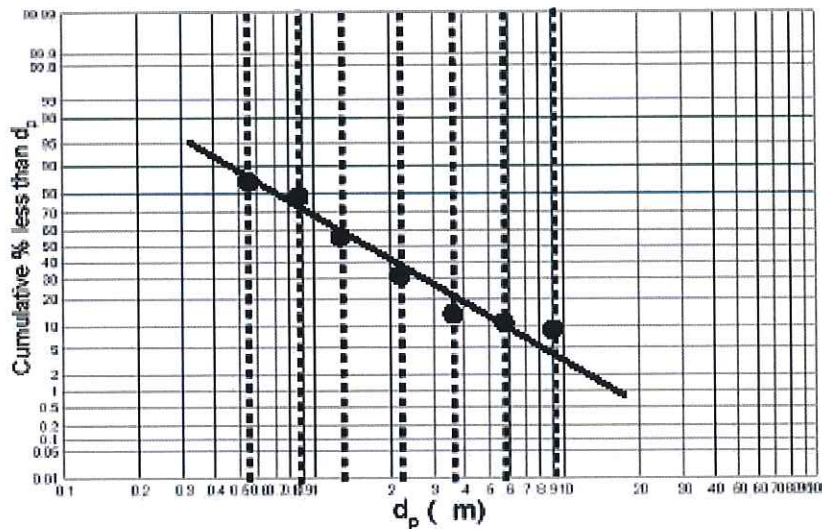


MMAD:	1.8	µm
GSD:	2.2	
Resp. Fraction:	79%	% 0.5-5 µm
Total Dose:	305	µg
Resp. Dose:	241	µg 0.5-5 µm

Piper Medical Products

Test:	2	Cascade Impactor:	E-032
Protocol:	06-0033	Impactor Flow:	28.3 l/min
Nebulizer:	Micromist @ 6 l/min	Ambient Temp:	21.7 cG
Aerosol Mask:	OxyId	Ambient RH%:	41.8 %
Drug:	albuterol sulfate	Pul Volume:	3.0 ml
Simulated Breathing:	I-Flow (l/min): 28	TV(ml): 600	IR: 1:1.5

	Cutoff dia. (µm)	Diluent (mL)	Spec. Concn. (µg/mL)	Collected Mass (µg)	Percentage (%)	Cumulative (%)
Stage 1	9.30	9.77	2.82	27.51	9.7%	9.7%
Stage 2	5.81	9.77	0.57	5.58	2.0%	11.6%
Stage 3	3.63	9.77	0.88	9.11	3.2%	14.8%
Stage 4	2.28	9.77	5.12	50.05	17.6%	32.4%
Stage 5	1.41	9.77	7.05	68.91	24.2%	56.6%
Stage 6	0.88	9.77	8.24	80.98	21.4%	78.0%
Stage 7	0.55	9.77	2.03	19.85	7.0%	84.9%
Filter	0.00	9.77	4.40	42.98	15.1%	100.0%
				285	100.0%	

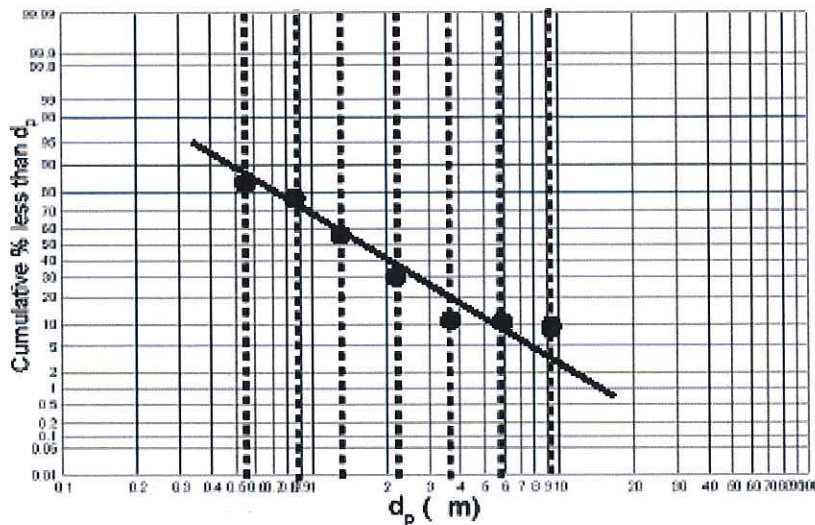


MMAD:	1.7	µm
GSD:	2.6	
Resp. Fraction:	77%	% 0.5-5 µm
Total Dose:	285	µg
Resp. Dose:	219	µg 0.5-5 µm

Piper Medical Products

Test:	3	Cascade Impactor:	E-032
Protocol:	06-0033	Impactor Flow:	28.3 l/min
Nebulizer:	Micromist @ 6 l/min	Ambient Temp:	23.1 °C
Aerosol Mask:	Oxyfid	Ambient RH%:	39.5 %
Drug:	sibutrol sulfate	PW Volume:	3.0 ml
Simulated Breathing:	I-Flow (l/min): 28	TV(ml): 800	IR: 1:1.5

	Cutoff dia. (µm)	Diluent (mL)	Spec. Concn. (µg/mL)	Collected Mass (µg)	Percentage (%)	Cumulative (%)
Stage 1	9.30	9.80	2.89	28.30	9.4%	9.4%
Stage 2	5.81	9.80	0.41	4.05	1.3%	10.7%
Stage 3	3.63	9.80	0.46	4.49	1.5%	12.2%
Stage 4	2.26	9.80	5.57	55.51	18.5%	30.7%
Stage 5	1.41	9.80	7.31	71.80	23.6%	54.4%
Stage 6	0.88	9.80	8.75	86.18	28.0%	78.4%
Stage 7	0.55	9.80	2.38	22.18	7.4%	83.8%
Fiber	0.00	9.80	4.99	48.90	16.2%	100.0%
				301	100.0%	

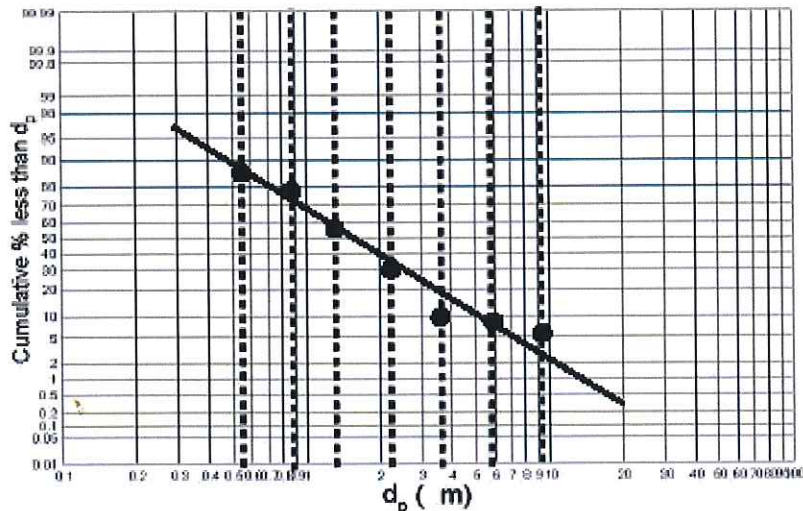


MMAD:	1.7	µm
GSD:	2.4	
Resp. Fraction:	74%	% 0.5-5 µm
Total Dose:	301	µg
Resp. Dose:	223	µg 0.5-5 µm

Piper Medical Products

Test:	4	Cascade Impactor:	E-032
Protocol:	06-0033	Impactor Flow:	28.3 l/min
Nebulizer:	Micromist @ 6 l/min	Ambient Temp:	23.9 °C
Aerosol Mask:	Oxyd Hybrid	Ambient RH%:	38.7 %
Drug:	sibutercil sulfate	PW Volume:	3.0 ml
Simulated Breathing:	I-Flow (l/min): 28	TV(ml): 800	IR: 1:1.5

	Cutoff dia. (µm)	Diluent (mL)	Spec. Concn. (µg/mL)	Collected Mass (µg)	Percentage (%)	Cumulative (%)
Stage 1	9.30	9.77	1.81	15.73	5.7%	5.7%
Stage 2	5.81	9.77	0.47	4.54	1.6%	7.3%
Stage 3	3.83	9.77	0.70	6.83	2.5%	9.8%
Stage 4	2.25	9.77	8.15	80.10	21.7%	31.5%
Stage 5	1.41	9.77	7.30	71.31	25.6%	57.3%
Stage 6	0.88	9.77	5.95	58.15	21.0%	78.3%
Stage 7	0.55	9.77	2.09	20.08	7.3%	85.6%
Fiber	0.00	9.77	4.10	40.06	14.6%	100.0%
				277	100.0%	

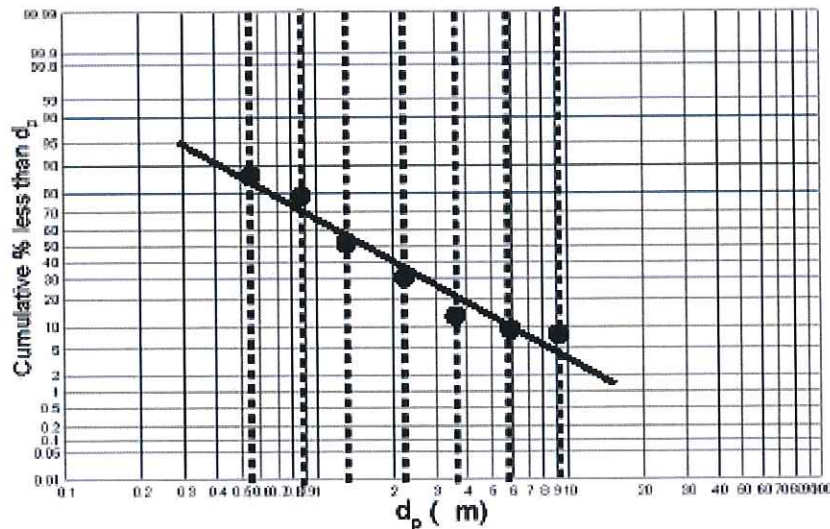


MMAD:	1.8	µm
GSD:	2.4	
Resp. Fraction:	78%	% 0.5-5 µm
Total Dose:	277	µg
Resp. Dose:	219	µg 0.5-5 µm

Piper Medical Products

Test: 5 **Cascade Impactor:** E-032
Protocol: 06-0033 **Impactor Flow:** 28.3 l/min
Nebulizer: Micromist @ 6 l/min **Ambient Temp:** 19.4 °C
Aerosol Mask: Mask 45 **Ambient RH%:** 39.0 %
Drug: albuterol sulfate **Fill Volume:** 3.01 ml
Simulated Breathing: I-Flow (l/min): 28 **TV(ml):** 800 **IR:** 1:1.5

	Cutoff dia. (µm)	Diluent (mL)	Spec. Concn. (µg/mL)	Collected Mass (µg)	Percentage (%)	Cumulative (%)
Stage 1	9.30	9.74	1.69	16.40	7.7%	7.7%
Stage 2	5.81	9.74	0.46	4.38	2.1%	9.8%
Stage 3	3.63	9.74	0.69	6.68	3.2%	13.0%
Stage 4	2.26	9.74	4.34	42.21	19.9%	32.9%
Stage 5	1.41	9.74	4.28	41.48	19.6%	52.5%
Stage 6	0.88	9.74	5.62	56.69	26.6%	79.3%
Stage 7	0.55	9.74	1.65	16.03	8.6%	87.9%
Filter	0.00	9.74	2.65	25.82	12.2%	100.0%
				212	100.0%	

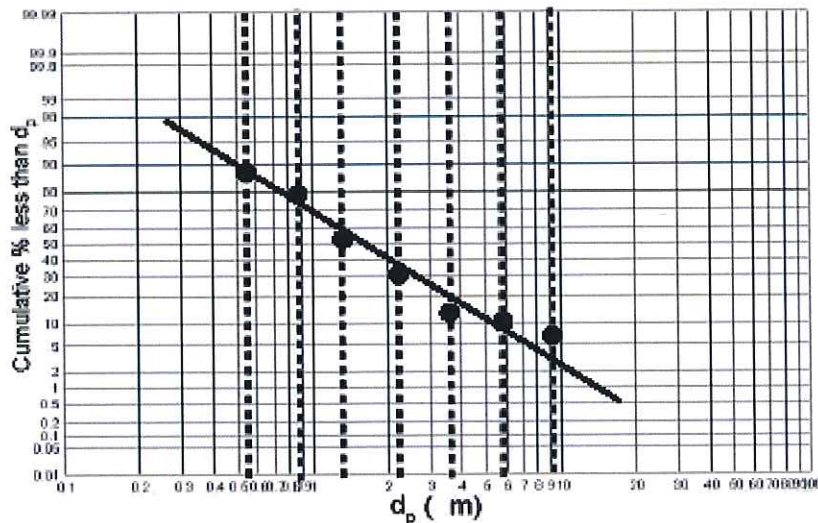


MMAD: 1.6 µm
GSD: 2.6
Resp. Fraction: 75% % 0.5-5 µm
Total Dose: 212 µg
Resp. Dose: 159 µg 0.5-5 µm

Piper Medical Products

Test:	0	Cascade Impactor:	E-032
Protocol:	00-0033	Impactor Flow:	28.3 l/min
Nebulizer:	Micromist @ 6 l/min	Ambient Temp:	21.7 °C
Aerosol Mask:	Dragon	Ambient RH%:	37.9 %
Drug:	albuterol sulfate	PW Volume:	3.0 ml
Simulated Breathing:	I-Flow (l/min): 28	TV(ml): 800	IE: 1:1.5

	Cutoff dia. (µm)	Diluent (mL)	Spec. Concn. (µg/mL)	Collected Mass (µg)	Percentage (%)	Cumulative (%)
Stage 1	9.30	9.81	1.89	18.52	7.7%	7.7%
Stage 2	5.81	9.81	0.45	4.41	2.1%	9.8%
Stage 3	3.63	9.81	0.69	6.73	3.2%	13.0%
Stage 4	2.25	9.81	4.34	42.51	19.9%	32.9%
Stage 5	1.41	9.81	4.26	41.76	19.6%	52.5%
Stage 6	0.88	9.81	5.62	57.09	26.8%	79.3%
Stage 7	0.55	9.81	1.85	18.16	8.6%	87.9%
Fiber	0.00	9.81	2.85	28.00	12.2%	100.0%
				213	100.0%	

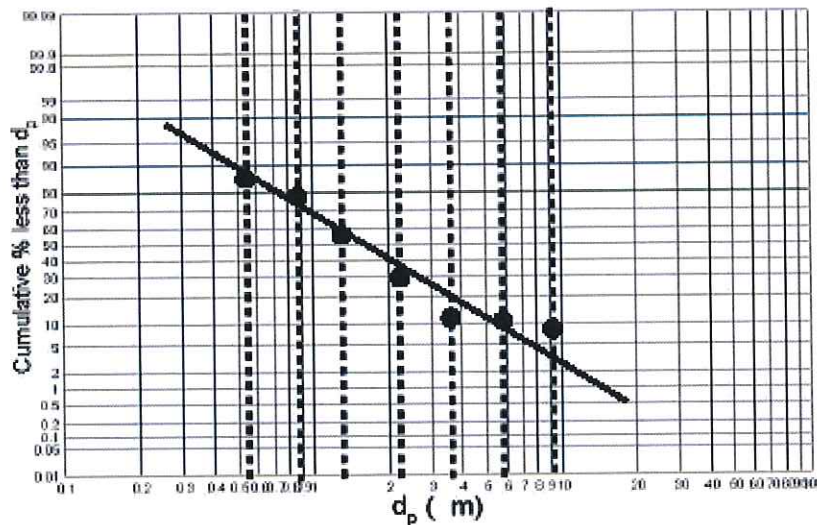


MMAD:	1.7	µm
GSD:	2.4	
Resp. Fraction:	78%	% 0.5-5 µm
Total Dose:	213	µg
Resp. Dose:	166	µg 0.5-5 µm

Piper Medical Products

Test: 7 **Cascade Impactor:** E-032
Protocol: 06-0033 **Impactor Flow:** 28.3 l/min
Nebulizer: Micromist @ 6 l/min **Ambient Temp:** 20.4 °C
Aerosol Mask: Mask 90 **Ambient RH%:** 39.0 %
Drug: albuterol sulfate **Fill Volume:** 3.0 ml
Simulated Breathing: I-Flow (l/min): 28 **TV(ml):** 800 **IR:** 1:1.5

	Cutoff dia. (µm)	Diluent (mL)	Spec. Concn. (µg/mL)	Collected Mass (µg)	Percentage (%)	Cumulative (%)
Stage 1	9.30	9.80	2.14	21.01	8.2%	8.2%
Stage 2	5.81	9.80	0.52	5.08	2.0%	10.1%
Stage 3	3.63	9.80	0.50	4.92	1.9%	12.1%
Stage 4	2.26	9.80	4.54	44.49	17.3%	29.3%
Stage 5	1.41	9.80	8.90	87.82	28.3%	55.6%
Stage 6	0.88	9.80	5.73	56.19	21.6%	77.5%
Stage 7	0.55	9.80	1.66	16.20	7.1%	84.6%
Filter	0.00	9.80	4.08	39.78	15.5%	100.0%
				257	100.0%	



MMAD: 1.7 µm
GSD: 2.4
Resp. Fraction: 78% % 0.5-5 µm
Total Dose: 257 µg
Resp. Dose: 201 µg 0.5-5 µm