Variability in Size Distribution Measurements Obtained Using Multiple Andersen Mark II Cascade Impactors

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Purpose. Andersen Mark II cascade impactors are commonly used for the testing of pharmaceutical aerosols. The reproducibility of size distribution measurements made with various Mark II impactors was assessed theoretically and experimentally.

Methods. Stage cutpoints were calculated for fourteen Mark II impactors based on jet diameter measurements for each stage. The calculated cutpoints were used to predict differences in size distributions measured with various Mark II impactors. Five impactors were exposed to an atomizer-generated oleic acid test aerosol to experimentally verify predicted differences in size distribution measurements among impactors.

Results. Stage cutpoints were calculated to vary by up to 0.45 micron for 'identical' stages of different Mark II impactors based on jet diameter measurements. The size distributions measured with various Mark II impactors were shown to be significantly different based on theoretical and experimental observations. For one particular experiment, the amount of material collected on Stage 6 ranged from 26.8 percent of the total sampled mass to 40.9 percent depending on which Mark II was used. Theoretical calculations predicted that the amount of material collected on Stage 6 would vary from 24.0 to 43.5 percent of the total sampled mass among impactors for this experiment. A Similarity Ratio, useful for interpreting the test results, was defined and discussed.

Conclusions. Significant differences in stage cutpoints exist among Andersen Mark II impactors. These differences in stage cutpoints can result in large differences in size distribution measurements made with various Mark II impactors. By measuring jet diameters and calculating stage cutpoints, it is possible to predict the performance of a particular Mark II impactor.

KEY WORDS: Andersen cascade impactor; size distribution; metered dose inhaler (MDI); lognormal distribution; variability.

INTRODUCTION

Cascade impactors are widely used for measuring the size distribution of airborne particles. The Andersen Cascade Impactor (1 AFCM Non-Viable Ambient Particle Sizing Sampler, Graseby-Andersen Inc., Smyrna, GA) is one of the most frequently used impactors for measuring the size distributions of pharmaceutical aerosols. The eight stage Andersen impactor separates the sample aerosol into nine size intervals when used with a backup filter after the last impaction stage.

Several versions of the Andersen Cascade Impactor have been used throughout the years. The most commonly used versions in the pharmaceutical industry are the Mark I and Mark II impactors. The Mark I impactor was released in 1970 and has stages with cutpoints ranging from 0.4 to 11.0 μm. The Mark II impactor was released in 1977 and has cutpoints from 0.4 to 9.0 μm. The manufacturer reports that the two impactors have identical cutpoints except for the two upper stages on the Mark II which were redesigned to minimize wall losses and particle bounce (1).

In order to collect accurate data with any cascade impactor, it is necessary to have accurate data on the cutpoints of the stages. Information provided by the manufacturer in the Mark II User's Manual (1) has calibration data from the first version of the impactor made back in 1952. There have been several independent calibrations of the Mark II impactor including those of Mitchell et al. (2) and Vaughan (3). The cutpoints reported in these papers vary, but generally are close to those reported by the manufacturer. However, Vaughan reported a Stage 2 cutpoint of 5.7 μm as opposed to the value of 4.7 μm reported by the manufacturer (3). Deviations of this magnitude from the manufacturer's reported cutpoint could certainly cause significant errors in size distributions measured by the Mark II.

Particle size distribution measurements are almost always used as part of the acceptance testing for pharmaceutical aerosols such as metered dose inhalers (MDIs). The Andersen impactor is often used to make these size distribution measurements. Since cascade impactor tests are often used to accept or reject lots of manufactured aerosols, it is critical that reliable and accurate results be obtained from cascade impactor tests.

The situation is complicated by the fact that the cascade impactors used to set the size distribution acceptance specifications for a product are often different than the cascade impactors actually used to clear product for sale. Specifications are usually set based on cascade impactor tests run in a Research and Development laboratory during the development and stability phase of the product development cycle. Product clearance tests, which must meet the R&D generated specifications, are generally performed at a separate Quality Control laboratory using different cascade impactors. Therefore, it is extremely important that consistent results be obtained among individual impactors of the same type.

The purpose of this paper is to: (1) determine if there are differences in the stage cutpoints among various Mark II impactors; and, if so, (2) determine the consequences of these differences on the size distributions measured by various Mark II impactors.

MATERIALS AND METHODS

The performance of various Mark II impactors was examined in three phases. In Phase I, the stage cutpoints were calculated for fourteen different impactors based on jet diameter measurements for each stage. In Phase II, theoretical stage deposition characteristics of each impactor were calculated based on the stage cutpoints obtained from Phase I. In these calculations, the impactors were assumed to sample an identical lognormal size distribution and the amount of material collected on each stage was predicted. By calculating the stage deposition characteristics for the various impactors, it was possible to assess the effect of the differences in stage cutpoints among impactors on size distribution measurements obtained with these impactors. In Phase III, experiments were performed to verify any differences in stage deposition characteristics among

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impactors that were expected as a result of the calculations in Phase II.

Phase I—Cutpoint Calculations from Jet Diameter Measurements

Jet diameters were measured using a Measurescope MM-22 microscope (Nikon Inc., Melville, NY) equipped with a Quadra-Chek 2000 (Metronics Inc., Manchester, NH) at 50 times magnification. The Quadra-Chek has the capability to measure diameters to a resolution of 0.00005″. The position of four points on the perimeter of the jet were marked. The Quadra-Chek then calculated the best-fit circle for the four data points using a least squares technique and output the diameter of this best-fit circle. Five randomly selected jets were measured for each stage. We chose to measure five jets because the manufacturer offers a 'calibration' service where they measure five randomly selected jets on each stage. In estimating the average jet diameter for a given stage, measuring five jets proved to be adequate due to the consistent jet diameters on any given stage (the standard deviations in the jet diameter measurements were small—see Results and Discussion for further details).

The measurements of jet diameter were then used to calculate the stage cutpoints. In order to do this it is necessary to examine the equation defining the Stokes number that governs inertial impaction, where Stk is the Stokes number, ρ_0 is unit density (1.0 g/cm^3), d_a is the aerodynamic particle diameter, U is the jet velocity, C_C is the Cunningham slip correction and is a function of particle of size, η is the viscosity of the air, and D_J, is the jet diameter.

$$\mathrm{Stk} = \frac{\rho_0 d_a^2 U C_c}{9\eta D_j} \tag{1}$$

The collection efficiency for a given impactor stage is a function of the Stokes number and can be numerically or experimentally determined (4,5). The most descriptive value of an impactor stage is the Stk_{50}. This is the Stokes number at which 50% of the particles impact and are collected. The aerodynamic cutpoint of a stage, d_{a50}, is the particle diameter at which Stk = Stk_{50}. The Stk_{50} of a given impactor stage depends on the Reynolds number of the flow and the physical dimensions of the stage such as the jet diameter, the distance between the back of the impaction stage and the impaction plate, the length of the jet, and the number of jets. Previous impactor research by Marple (4), Rader and Marple (5), and others has shown that Stk_{50} is insensitive to changes in jet diameter and Reynolds' number of the magnitude that we are interested in when comparing two similar impactor stages (such as Stage 3 from two different Andersen impactors). As a result, Stk_{50} will be assumed to be a constant for identical stages of each of the impactors tested. However, the value of Stk_{50} for Stage 3 will certainly be different than the value for other stages (such as Stage 4) due to differences in the stage geometry and Reynolds number.

By rearranging the Equation 1 and substituting for jet velocity it is possible to solve for the aerodynamic cutpoint, d_{a50}, of a stage. It is necessary to iteratively solve for d_{a50},

$$d_{a_{50}} = \sqrt{\frac{9\mathrm{Stk}_{50}\eta\pi D_j^3 N}{4\rho_0 Q C_c}} \tag{2}$$

because of the dependence of slip correction, C_c, on particle diameter. In this equation Q is the total flow rate through the impactor stage and N is the total number of jets on the impactor stage. Notice that two impactors with exactly the same Stk_{50} will have different aerodynamic cutpoints if they have different jet diameters, flow rates, or number of jets.

Equation 2 was used to calculate the aerodynamic cutpoint of the stages for the fourteen Andersen impactors examined. The age and operating history of the fourteen impactors varied. Andersen serial numbers (#s) 3276 and 3278 had never been operated prior to the tests described in this paper. In general, the serial number indicates the age of the impactor-higher serial numbers indicate newer impactors. Andersen #s 3214, 3216, 3218, and 3275 had all been operated for less than twelve months. The remaining impactors had been used for testing for at least twelve months.

PHASE II—Theoretical Stage Deposition Characteristics

The stage cutpoints calculated from the jet diameter measurements were used to predict the stage deposition characteristics for each of the fourteen impactors. The impactors were assumed to sample a lognormally distributed aerosol and were assumed to have perfectly sharp stage cutoffs. The mass that would collect on each stage was calculated by determining the percent of mass for the assumed lognormal size distribution with aerodynamic diameters between the stage cutpoint and the previous stage cutpoint. It is assumed, for example, that Stage 4 will collect all of the particles smaller than the Stage 3 cutpoint but larger than the Stage 4 cutpoint for a given size distribution.

PHASE III—Laboratory Measurements of Stage Deposition Characteristics

Five Andersen Mark II impactors and a Micro-Orifice Uniform Deposit Impactor (MOUDI, MSP Corp.) (6) sampled the same atomizer-generated test aerosol in order to compare the stage deposition characteristics of different Andersen impactors. The impactors were placed in an Aerosol Test Chamber in order to ensure that they all sampled a test aerosol of uniform concentration and size distribution (7). Since the five Andersen impactors sampled an identical test aerosol, it was possible to detect differences in the stage deposition characteristics of the different impactors.

The five impactors tested were among the fourteen impactors measured in Phase I. Two previously unused impactors (Andersen #s 3276 and 3278) were examined, as well as an impactor that had been used for approximately twelve months (Andersen #3077), and two impactors that had been used for more than two years (Andersen #s 2589 and 2658).

An atomizer was used to generate the polydisperse liquid test aerosol. The atomizer solution consisted of oleic acid and beclomethasone dipropionate dissolved in methanol. The size distribution of the generated aerosols were varied in order to compare the deposition characteristics of all of the stages of the Andersen impactors tested. While a test aerosol with an MMAD of 1.0 μm and σ_g of 2.0 is appropriate for examining differences between Stages 5 through Filter, a larger aerosol is necessary for comparing the upper stages. It was possible to roughly control the size distribution of the generated aerosol by adjusting the concentration of the oleic acid and beclomethasone dipropionate in the atomizer solution.

The aerosol generated by the atomizer was diluted with filtered dry compressed air to help evaporate the methanol. The diluted test aerosol was then introduced into the Aerosol Test Chamber and sampled by the impactors. Due to the large volume of the Aerosol Test Chamber, it took about ten minutes for the aerosol to reach the Andersen impactors after it was introduced at the top of the test chamber. This allowed ample time for the methanol to completely evaporate.

Once the methanol evaporated, the particles consisted of 95% oleic acid and 5% belcomethasone dipropionate. Oleic acid was selected as the primary component of the residual particles to prevent particle bounce in the impactor. The beclomethasone dipropionate was added to the oleic acid to act as a marker for the sample measurement. The amount of beclomethasone dipropionate on each stage was measured using an HPLC (Waters™ LC I plus, Waters Corp., Milford, MA) with a UV detector measuring at 238 nm. The mobile phase was 60 percent acetonitrile in ultra-pure water and a Supelcosil™ LC-18 column (150 × 4.6 mm, 5 micron particle size; SUPELCO Inc., Bellefonte, PA) was used.

RESULTS AND DISCUSSION

PHASE I Results—Cutpoint Calculations from Jet Measurements

A summary of the jet diameter measurements can be found in Table I. This table lists the average and standard deviation of the five jet diameters measured for each stage. The largest standard deviation for a given stage was 0.0010″, but the standard deviations were typically less than 0.0003″ for a given stage. The measured differences in jet diameters among 'identical' stages (e.g. among different Stage 5s) were much larger (up to 0.0034″) than the standard deviations, indicating that there are actual differences in jet diameter. Andersen Serial #2658 was measured twice to assess the reproducibility of the measurements. There was excellent agreement in the jet diameters for the two measurements of Andersen #2658 as shown in Table I.

The measured jet diameters were compared to the manufacturer's internal specifications on jet diameters for each stage. These specifications are not published in the Mark II operating manual, but were freely provided by the manufacturer (8). These specifications apply to individual jet measurements (i.e. not on the average of several measurements). Of the 600 jets measured, 162 of the jets (27.0%) failed the manufacturer's internal specification. There did not appear to be any relationship between the age of the impactor and the diameter of the jets. As a result, it seems unlikely that the differences in jet diameter are due to the operating history of the instrument.

Equation 2 was used to calculate stage cutpoints for fourteen different Andersen impactors based on the jet diameters listed in Table I. The calculated cutpoints, in microns, are listed in Table II. In these calculation, the value of Stk_{50} for each stage number was calculated from manufacturer jet diameter and stage cutpoint data. The Stk_{50} values were not determined experimentally for each stage number in this study. Relying on Stk_{50} value calculated from manufacturer data may introduce some error into the absolute cutpoint calculations, but will have very little effect on the predicted differences in cutpoint diameters. For example, the stage cutpoint calculations for Stage 4 were predicted to vary from 1.98 to 2.31 μm (see Table II). If the Stk_{50} calculated from the manufacturer data was inaccurately high by ten percent (this would be a surprising discrepancy), the actual stage cutpoints would all be approximately five percent lower than predicted (from 1.89 to 2.20 μm). In this case, the actual cutpoints would be slightly lower than predicted, but the range in cutpoint values would be almost the same. Therefore the calculations summarized in Table II provide useful information about the cutpoint differences among similar Mark II stages.

The Quadra-Chek 2000 system used for the diameter measurements is extremely accurate for measuring diameters of jets that are round. For this exercise we assumed that the jets were round and the measured jet 'diameters' were appropriate for use in the cutpoint calculations. However, some of the jets were irregularly shaped or were partially blocked by what appeared to be metal burrs (see Figure 1). When measuring a 'slightly irregular' jet, six points along the perimeter were marked and were used in the Quadra-Chek 2000 diameter calculation. For 'extremely irregular' jets, fourteen points were used in the diameter calculation. It should be noted that fitting a least-squares circle to an irregular jet may or may not provide a jet diameter measurement that is representative of the impaction characteristics of that jet.

After the five randomly selected holes on a stage were measured, the entire stage was briefly scanned under the microscope to examine all of the jets for burrs or irregularly shaped jets. The incidence of irregular jets or burrs appeared to be very different for different stages. Most of the stages (about 60 percent of the stages measured) had virtually no burrs or irregular jets. Approximately 20 percent of the stages examined had high incidences of abnormal jets. For these stages, between 25 and 80 percent of the jets on the stage were irregular or had burrs. The remaining stages (approximately 20 percent of the stages) had less than 25 percent abnormal jets. The irregularity of some of the jets is a potential source of error in the cutpoint calculations listed in Table II.

PHASE II Results—Theoretical Stage Deposition Characteristics

The stage cutpoints calculated from the jet diameter measurements were used to predict the stage deposition characteristics of each impactor when sampling a given lognormal aerosol. In order to perform the calculations, the following assumptions were made: (1) each impactor was assumed to sample a perfectly lognormal aerosol; (2) the stage cutoffs were assumed to be perfectly sharp (i.e. they collect no particles smaller than the cutpoint and all particles larger than the cutpoint); and (3) the interstage losses were ignored.

The mass that would collect on a given stage was calculated by determining the percent of mass for a given lognormal size distribution with aerodynamic diameters between the stage cutpoint and the previous stage cutpoint. For example, Stage 3 would collect all of the mass corresponding to particles with aerodynamic diameters between the Stage 2 and Stage 3 cutpoints. This is a simple statistical calculation based on the properties of a lognormal distribution.

Table I. Averages and Standard Deviations from Diameter Measurements of Five Jets on Each Stage of Fourteen Andersen Mark II Impactors

Stage #	Manufacturer Specification	Andersen #2300	Andersen #2503	Andersen #2589	Andersen #2658	Andersen #2658 (retest)
0	0.0994 to 0.1014″	0.0998 ± 0.0003″	0.0995 ± 0.0003″	0.0992 ± 0.0003″	0.1009 ± 0.0003″	0.1008 ± 0.0003″
1	0.0734 to 0.0754″	0.0733 ± 0.0003″	0.0727 ± 0.0001″	0.0743 ± 0.0007″	0.0730 ± 0.0002″	0.0732 ± 0.0002″
2	0.0355 to 0.0365″	0.0357 ± 0.0002″	0.0362 ± 0.0002″	0.0361 ± 0.0000″	0.0369 ± 0.0004″	0.0369 ± 0.0005″
3	0.0275 to 0.0285″	0.0283 ± 0.0002″	0.0281 ± 0.0001″	0.0286 ± 0.0002″	0.0288 ± 0.0004″	0.0287 ± 0.0004″
4	0.0205 to 0.0215″	0.0209 ± 0.0000″	0.0210 ± 0.0001″	0.0214 ± 0.0001″	0.0203 ± 0.0002″	0.0202 ± 0.0002″
5	0.0130 to 0.0140″	0.0133 ± 0.0001″	0.0140 ± 0.0002″	0.0147 ± 0.0001″	0.0135 ± 0.0001″	0.0134 ± 0.0001″
6	0.0095 to 0.0105″	0.0103 ± 0.0001″	0.0098 ± 0.0000″	0.0091 ± 0.0001″	0.0095 ± 0.0001″	0.0095 ± 0.0001″
7	0.0095 to 0.0105″	0.0102 ± 0.0001″	0.0100 ± 0.0001″	0.0099 ± 0.0001″	0.0097 ± 0.0001″	0.0096 ± 0.0001″

Stage #	Manufacturer Specification	Andersen #2659	Andersen #2696	Andersen #3077	Andersen #3183	Andersen #3214
0	0.0994 to 0.1014″	0.0993 ± 0.0002″	0.0993 ± 0.0002″	0.1009 ± 0.0005″	0.0979 ± 0.0006″	0.0989 ± 0.0003″
1	0.0734 to 0.0754″	0.0725 ± 0.0010″	0.0735 ± 0.0002″	0.0750 ± 0.0002″	0.0733 ± 0.0002″	0.0732 ± 0.0002″
2	0.0355 to 0.0365″	0.0357 ± 0.0001″	0.0354 ± 0.0001″	0.0357 ± 0.0004″	0.0357 ± 0.0002″	0.0355 ± 0.0003″
3	0.0275 to 0.0285″	0.0284 ± 0.0001″	0.0280 ± 0.0002″	0.0276 ± 0.0002″	0.0277 ± 0.0002″	0.0281 ± 0.0000″
4	0.0205 to 0.0215″	0.0223 ± 0.0002″	0.0209 ± 0.0002″	0.0220 ± 0.0005″	0.0208 ± 0.0001″	0.0212 ± 0.0001″
5	0.0130 to 0.0140″	0.0144 ± 0.0001″	0.0136 ± 0.0002″	0.0133 ± 0.0001″	0.0134 ± 0.0001″	0.0134 ± 0.0002″
6	0.0095 to 0.0105″	0.0095 ± 0.0002″	0.0104 ± 0.0003″	0.0101 ± 0.0001″	0.0099 ± 0.0003″	0.0099 ± 0.0001″
7	0.0095 to 0.0105″	0.0091 ± 0.0001″	0.0101 ± 0.0001″	0.0099 ± 0.0001″	0.0098 ± 0.0002″	0.0100 ± 0.0003″

Stage #	Manufacturer Soecification	Andersen # 3216	Andersen #3218	Andersen #3275	Andersen #3276	Andersen #3278
0	0.0994 to 0.1014″	0.0988 ± 0.0003″	0.0985 ± 0.0001″	0.1012 ± 0.0001″	0.0993 ± 0.0002″	0.0982 ± 0.0007″
1	0.0734 to 0.0754″	0.0733 ± 0.0002″	0.0734 ± 0.0001″	0.0735 ± 0.0000″	0.0736 ± 0.0004″	0.0732 ± 0.0001″
2	0.0355 to 0.0365″	0.0359 ± 0.0001″	0.0357 ± 0.0001″	0.0367 ± 0.0002″	0.0359 ± 0.0001″	0.0361 ± 0.0000″
3	0.0275 to 0.0285″	0.0281 ± 0.0001″	0.0281 ± 0.0001″	0.0284 ± 0.0001″	0.0264 ± 0.0003″	0.0269 ± 0.0006″
4	0.0205 to 0.0215″	0.0209 ± 0.0002″	0.0209 ± 0.0001″	0.0216 ± 0.0001″	0.0213 ± 0.0002″	0.0212 ± 0.0001″
5	0.0130 to 0.0140″	0.0135 ± 0.0002″	0.0134 ± 0.0002″	0.0139 ± 0.0001″	0.0134 ± 0.0005″	0.0132 ± 0.0003″
6	0.0095 to 0.0105″	0.0098 ± 0.0002″	0.0096 ± 0.0003″	0.0102 ± 0.0000″	0.0103 ± 0.0001″	0.0101 ± 0.0001″
7	0.0095 to 0.0105″	0.0096 ± 0.0002″	0.0096 ± .0001″	0.0101 ± 0.0001″	0.0103 ± 0.0001″	0.0103 ± 0.0001″

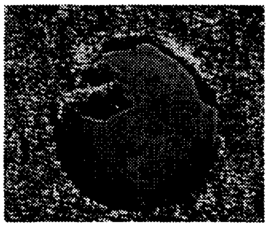
The assumption that the stages have perfectly sharp stage cutoffs introduces some error into the stage deposition calculations. In reality, a small fraction of particles larger than the Stage 3 cutpoint penetrates through Stage 3 and collects on subsequent stages. However, this is counteracted by the fact that Stage 3 collects a small fraction of particles smaller than the Stage 3 cutpoint. The net effect of this is small for impactors, such as the Andersen Mark II, that have relatively sharp stage cutoffs. The collection efficiency curves for the stages of the Mark II have been reported elsewhere (2,3).

Figure 2 shows the predicted stage deposition characteristics for fourteen different Mark II impactors sampling a lognormal aerosol with a mass median aerodynamic diameter (MMAD) of 2.40 μm and a geometric standard deviation (σ_g)

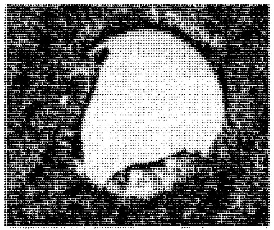
Table II. Stage Cutpoints, in Microns, Calculated for Fourteen[a] Andersen Mark II Impactors Using Equation 2 and Jet Diameter Measurements

Stage #	Reported Cutpoint (microns)	Ser. # 2300	Ser. # 2503	Ser. # 2589	Ser. # 2658	Ser. # 2658	Ser. # 2659	Ser. # 2696	Ser. # 3077	Ser. # 3183	Ser. # 3214	Ser. # 3216	Ser. # 3218	Ser. # 3275	Ser. # 3276	Ser. # 3278
0	9	8.92	8.88	8.84	9.07	9.05	8.85	8.85	9.07	8.66	8.80	8.78	8.74	9.11	8.86	8.70
1	5.8	5.67	5.60	5.79	5.63	5.66	5.58	5.69	5.87	5.67	5.66	5.67	5.68	5.69	5.70	5.66
2	4.7	4.64	4.74	4.72	4.88	4.88	4.64	4.58	4.64	4.64	4.60	4.67	4.64	4.84	4.68	4.72
3	3.3	3.35	3.32	3.41	3.45	3.43	3.37	3.30	3.23	3.25	3.32	3.32	3.32	3.37	3.02	3.10
4	2.1	2.08	2.10	2.16	1.99	1.98	2.31	2.08	2.26	2.07	2.13	2.08	2.08	2.19	2.14	2.13
5	1.1	1.07	1.17	1.26	1.10	1.09	1.22	1.11	1.07	1.09	1.09	1.10	1.09	1.15	1.09	1.06
6	0.7	0.74	0.68	0.60	0.64	0.64	0.64	0.75	0.71	0.69	0.69	0.67	0.65	0.72	0.73	0.71
7	0.4	0.41	0.40	0.39	0.38	0.37	0.34	0.41	0.39	0.39	0.40	0.37	0.37	0.41	0.42	0.42

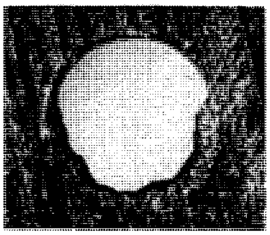
[a] Cutpoints for Andersen Serial # 2658 were calculated twice—once for each set of hole measurements listed in Table I.



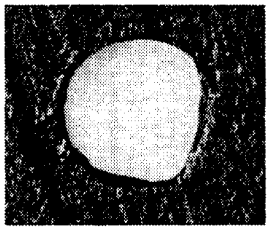
a). An unusual jet from Andersen #3183, Stage 6.



b). An unusual jet from Andersen #3218, Stage #6.



c). A typical jet from Andersen #3216, Stage 7.



d). A typical jet from Andersen #3216, Stage 6.

Fig. 1. Examples of Irregularly Shaped Jets from Andersen Mark II Stages.

of 1.70. The fourteen impactors in Figure 2 are the same impactors for which the jet diameters were measured. Based on these calculations, the mass collected on Stage 3 would vary from 15.3 to 22.8 percent of the total sampled mass depending on which impactor was used (Stage 4 would vary from 25.3 to 39.2 percent, Stage 5 from 29.0 to 38.9 percent, Stage 6 from 5.0 to 10.8, etc.). These theoretical calculations indicate that differences in jet diameter among impactors result in significant variability in size distribution measurements obtained with Andersen Mark II impactors.

Similar calculations for other size distributions predict similar differences among impactors in terms of stage deposition

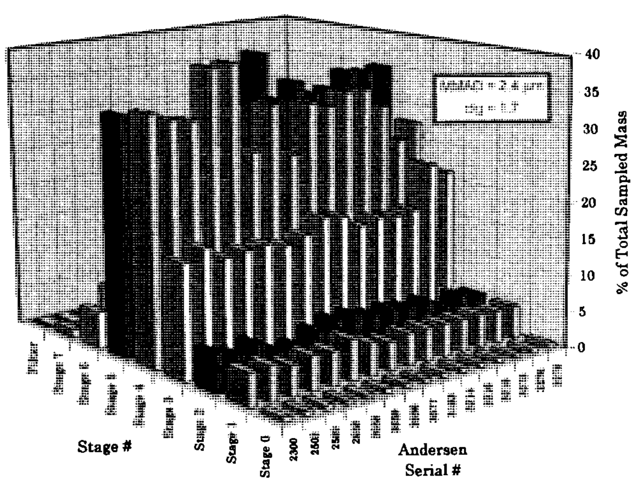


Fig. 2. Predicted Stage Deposition Characteristics for Fourteen Andersen Mark II Impactors Sampling a Lognormal Aerosol with MMAD = 2.40 μm and σ_g = 1.70.

characteristics. The magnitude of these differences are alarmingly large. For a size distribution with an MMAD of 3.50 μm and σ_g = 1.50, the mass collected on Stage 4 was predicted to vary from 24.6 to 40.2 percent of the total sampled mass. For a size distribution with an MMAD of 1.10 μm and σ_g = 1.80, the mass collected on Stage 6 was predicted to vary from 23.7 to 44.1 percent. These results indicate that the size distributions obtained with Andersen Mark II cascade impactors are strongly dependent on which impactor is used.

PHASE III Results—Laboratory Measurements of Stage Deposition Characteristics

Five Andersen Mark II impactors were tested to see if predicted differences in stage deposition characteristics could be experimentally verified. The five impactors were placed in a uniform concentration test chamber where they sampled an atomizer generated test aerosol. A recently calibrated MOUDI cascade impactor (6) was used to estimate the size distribution of the aerosol in the chamber.

Each experiment generated a comparison of stage deposition characteristics among the five Andersen impactors for the given test aerosol. Nine experiments were run in all. For each experiment, predicted stage deposition characteristics were also calculated for the impactors using the method described in Phase II. The MMAD and σ_g obtained from the MOUDI size distribution measurement were used in these calculations. The measured MMAD and σ_g for the nine test aerosols ranged from 0.94 to 4.59 μm and 1.71 to 2.12, respectively.

The measured and predicted stage deposition characteristics for Test 1 are shown in Figure 3. Based on the jet diameter measurements, Andersen #2658 was predicted to collect more mass on Stage 4 than the other four impactors (Figure 3-c). This was verified by the actual experimental data (Figure 3-a). Also notice that, as expected, Andersen #2589 collects more on Stage 6 than the other impactors (Figure 3-b and 3-d). The relative amount of aerosol collected on Stage 5 for each impactor also agrees well with the predictions.

The predictions assume that the impactors sample a perfectly lognormal aerosol. This was not the case based on the MOUDI and Andersen measurements. As a result, the amount of material measured on the filter stage was always greater than predictions based on a lognormal distribution. The amounts on Stages 0 and 1 were always less than predicted. Despite the limitation in the predictions due to the lognormal assumption, there is good agreement in the *relative* amounts collected on each stage for the different impactors.

The results from other tests showed a similar qualitative agreement between the predicted and measured stage-by-stage deposition. Quantitatively, the predictions tended to overestimate the magnitude of the difference by about 20 to 30 percent. The predictions for Test 1 estimate that the Stage 5 deposition values will range from 31.6 to 42.2 percent of the sampled mass with Andersen #3077 collecting the most and Andersen #2589 collecting the least. Thus the range in predicted values for Stage 5 was 10.6 percent of the sampled mass. The actual measurements for this test showed that Andersen #3077 did indeed collect the most (40.0 percent) and Andersen #2589 did collect the least (31.7 percent) on Stage 5. However, the measured range in values was only 8.3 percent compared to the predicted range of 10.6 percent. This difference between

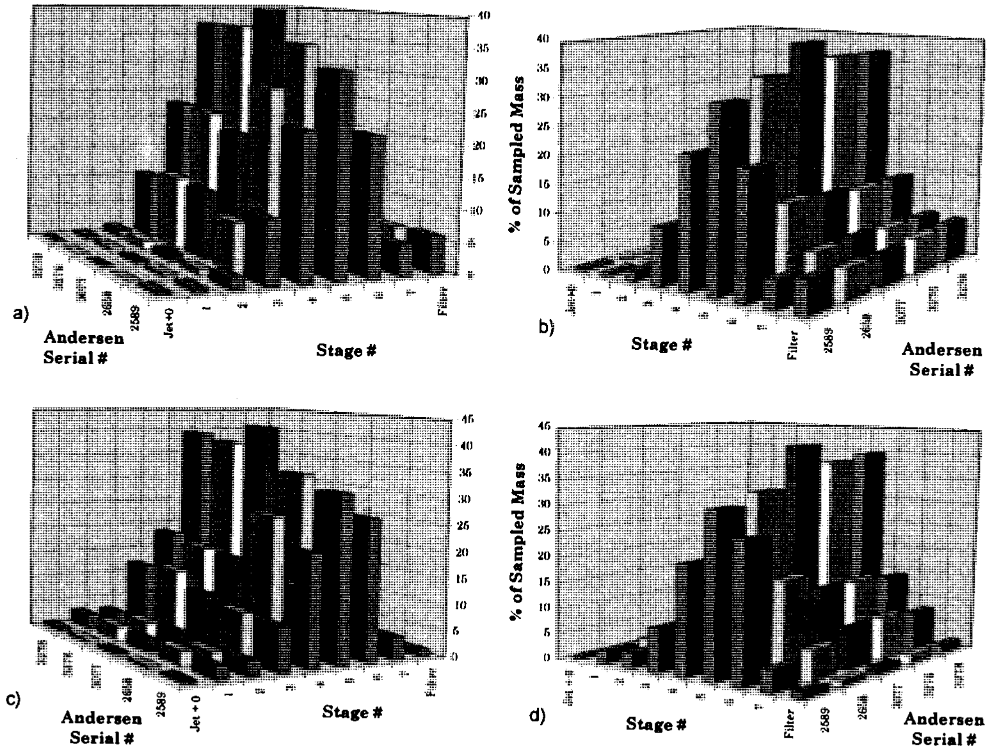


Fig. 3. Measured and Predicted Stage Deposition Characteristics for Five Andersen Mark II Impactors Sampling an Identical Aerosol (MMAD = 1.70 μm and σ_g = 1.94). a) Measured values for Test 1 (front view); b) Measured values for Test 1 (back view); c) Predicted values for Test 1 (front view); d) Predicted values for Test 1 (back view).

the measured and predicted ranges was typical of all of the experiments. The fact that the stage cutoffs are not perfectly sharp and the aerosol is not perfectly lognormal probably contribute to the difference between the predicted and measured range in measured values.

The maximum range observed in the nine tests for a given stage number was 14.1 percent of the sampled mass. For this particular experiment (Test 5), the MMAD and σ_g estimated by the MOUDI were 0.94 μm and 1.90, respectively. For this test aerosol, Andersen #2589 collected 40.9 percent of the sampled mass on Stage 6 compared to 26.8 percent collected on Stage 6 of Andersen #3278. It was predicted that Andersen #2589 would collect 43.5 percent on Stage 6 compared to 24.0 percent for Andersen #3278. It should be noted that the range in predicted values was larger than the range in measured values (19.5 percent to 14.1 percent). Nevertheless, we must not overlook the fact that a large difference was observed in Stage 6 deposition and that this large difference was predicted based on calculations using the measured jet diameters.

This theoretical and experimental comparison of various Andersen Mark II impactors has implications on the practice of using the Mark II as an instrument for Quality Control testing of MDIs. This experiment demonstrates that it is difficult to obtain consistent results with various Mark II impactors sampling the same aerosol. In these experiments, several Mark II impactors sampled a stable liquid aerosol—an ideal aerosol for obtaining consistent impactor results. Obviously, it will be much more difficult to obtain consistent results when measuring the dynamic aerosol of an MDI plume.

The results in Table III summarize the mass collected on each stage of the five Mark II impactors used during Test 8 (MMAD = 1.73 μm, σ_g = 2.00). Due to space limitations it is not possible to present results from all of the tests conducted. Each test is unique because the generated size distribution was different for each test. However, the magnitude of the differences in stage deposition characteristics observed among the five impactors for Test 8 was typical of the other eight tests. The values in Table III are in percent of the total sampled mass. Notice that the amounts for various groupings of stages are also listed. The Average value and the Range of values (maximum minus minimum value) for each stage or stage grouping are listed as well. A new parameter, called the Similarity Ratio for the stage or stage grouping, is listed in the last column of Table III. This is defined as the Average value divided by the Range of values. A high Similarity Ratio indicates the ability to obtain consistent results regardless of which impactor is used. A low Similarity Ratio indicates that the size distribution measurements obtained are very dependent on which impactor is used for the measurements.

The Similarity Ratios for individual stages are between 1.5 and 4.0 for Test 8. Stages 3 to 6, which collected the most mass, have Similarity Ratios between 2.7 and 3.4. When stages are grouped together, the Similarity Ratio tends to increase. In general, as more stages are grouped together the Similarity Ratio increases. This is not always the case. Notice that the Similarity Ratio when Stage 5 to Filter are grouped together is actually much smaller than when Stages 6 to Filter are grouped together.

Table III. The Percent of the Total Sampled Mass Collected on Individual Stages and Stage Groupings for Each Impactor Used During Test 8 (MMAD = 1.73 μm, σ_g = 2.00)

Stage Number	Serial #2589	Serial #2658	Serial #3077	Serial #3276	Serial #3278	Average Value	Range of Values	Similarity Ratio[a]
Jet–Stage 0	0.7	0.6	0.6	0.6	0.6	0.6	0.2	4.0
Stage 1	1.8	1.3	1.2	1.4	1.3	1.4	0.7	2.1
Stage 2	3.1	1.6	2.3	2.2	2.2	2.3	1.5	1.5
Stage 3	13.3	9.4	10.8	12.4	11.5	11.5	3.9	3.0
Stage 4	23.6	25.8	17.6	20.7	21.4	21.8	8.1	2.7
Stage 5	30.8	36.4	41.4	36.8	37.3	36.5	10.6	3.4
Stage 6	18.6	13.4	13.7	13.1	13.4	14.4	5.4	2.7
Stage 7	3.8	6.7	7.5	7.0	6.7	6.3	3.6	1.7
Filter	4.3	4.8	5.1	5.8	5.6	5.1	1.5	3.5
Stages	**Serial #2589**	**Serial #2658**	**Serial #3077**	**Serial #3276**	**Serial #3278**	**Average Value**	**Range of Values**	**Similarity Ratio**
Jet–Stage 0	0.7	0.6	0.6	0.6	0.6	0.6	0.2	4.0
Stages 1–2	5.0	2.9	3.4	3.6	3.5	3.7	2.0	1.8
Stages 3–4	36.8	35.1	28.4	33.2	32.9	33.3	8.4	4.0
Stages 5–6	49.3	49.8	55.0	49.9	50.7	51.0	5.7	9.0
Stages 7–F	8.1	11.5	12.5	12.7	12.3	11.4	4.6	2.5
Stages	**Serial #2589**	**Serial #2658**	**Serial #3077**	**Serial #3276**	**Serial #3278**	**Average Value**	**Range of Values**	**Similarity Ratio**
Jet–Stage 2	5.7	3.5	4.0	4.2	4.1	4.3	2.2	2.0
Stages 3–5	67.6	71.6	69.8	69.9	70.2	69.8	4.0	17.6
Stages 6–F	26.7	24.9	26.2	25.9	25.7	25.9	1.8	14.6
Stages	**Serial #2589**	**Serial #2658**	**Serial #3077**	**Serial #3276**	**Serial #3278**	**Average Value**	**Range of Values**	**Similarity Ratio**
Jet–Stage 4	42.5	38.6	32.4	37.4	37.0	37.6	10.1	3.7
Stages 5–F	57.5	61.4	67.6	62.6	63.0	62.4	10.1	6.2

[a] The Similarity Ratio is defined as the Average Value for a given stage or stage grouping divided by the Range of Values for that stage or stage grouping.

Unfortunately, it is not possible to determine a set of stage groupings that will maximize the Similarity Ratio in all cases as this depends on the size distribution of the test aerosol and the stage cutpoints of the group of impactors used for testing. While grouping stages together can help reduce the impact of differences in stage cutpoints, it does not eliminate the variability that these cutpoint differences cause.

CONCLUSION

Stage cutpoints for fourteen Andersen Mark II impactors were evaluated theoretically. Based on measurements of jet diameters it was determined that the actual cutpoints for a given stage number vary substantially from one Mark II impactor to another. A large portion of the jets measured (27%) had diameters outside of the manufacturer's internal jet diameter specifications. In addition, many of the jets were determined to be irregular or to have metal burrs partially obstructing the hole.

Stage-by-stage deposition characteristics were calculated for these Mark II impactors based on the calculated stage cutpoints and the properties of a lognormal aerosol size distribution. These calculations indicate that different Mark II impactors collect very different amounts of material on a given stage (e.g. Stage 4) even if they sample an identical aerosol. Experiments were performed to confirm this. The experiments confirmed that the mass collected on any given stage number does indeed differ from impactor to impactor. There is excellent qualitative agreement between the measured and predicted stage collection characteristics. Quantitatively, the experimentally measured differences among impactors are smaller than the predicted differences by about 20 to 30 percent. However, the differences in the mass collected on a given stage number are large (up to 14.1 percent of the sampled mass). Grouping stages together tends to help reduce the variability in results due to impactor differences, but it does not eliminate this variability. It is important to consider the precision of the Mark II impactor when interpreting results obtained with it.

The theoretical calculations and experimental measurements reported in this paper indicate that there are large differences in the results obtained with different Andersen Mark II impactors sampling an ideal aerosol. These differences among impactors and the dynamic nature of MDI generated aerosols result in inherent variability in size distribution measurements of MDIs made with Andersen Mark II impactors.

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