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Research Paper

Mensuration and Cleaning of the Jets in Andersen Cascade Impactors

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Purpose. Fifty-three Andersen Cascade Impactors (404 stages) have been investigated using an automated visual stage mensuration technique. A cleaning method was suggested for stages with jets smaller than nominal diameters. The impact of nonapproved jet diameters on result parameters from particle size analysis was evaluated theoretically.
Methods. The jet diameters were measured using the Andersen Visual Inspection Device. A stepwise cleaning procedure was performed to recover the jets of noncompliant stages, and after each step a new stage mensuration was performed.
Results. The result of this extensive investigation, including measurements of each jet, is compared to other studies, to tolerance limits applied at AstraZeneca Lund and also to limits used by the manufacturer. Sixteen of the investigated stages were outside applied tolerance limits due to too small average diameters. Insertion of a go gauge into every jet of the stages was the only technique of those tested that increased the jet diameters toward nominal dimensions. Moreover, the relative standard deviation of the jet diameters decreased considerably after use of go gauges.
Conclusions. Stage mensuration is a valuable technique for detection of improper jet dimensions of the Andersen Cascade Impactor, and use of go gauges is an effective cleaning method especially for jets with small diameters. However, use of stop/go gauges as a periodical quality control test on a small number of randomly selected jets was a poorly discriminating test, as both compliant and noncompliant stages would most probably pass such a test.

KEY WORDS: Andersen Cascade Impactor; jet diameters; stage mensuration; visual inspection.

INTRODUCTION

The Andersen Cascade Impactor (ACI) is a frequently used multi-jet impactor for characterization of pharmaceutical aerosols. Correct jet dimensions are important to ensure proper functioning of the impactor in terms of stage cutoffs (1). It has previously been demonstrated that the jet dimensions of the impactor stages may vary significantly between different ACIs, causing variations in particle size measurements (2). Other studies, however, report satisfactory agreement between measured jet dimensions and the manufacturer's target jet dimensions (3). The difference between the observations referred to may result from use of different mensuration techniques, varying age (including variability of the manufacturing process) and frequency of impactor use, but also the number of jets measured on every stage (sample size).

The Andersen Visual Inspection Device (AVID) counts and examines every jet on an ACI stage automatically. Several parameters are evaluated for each jet, for example, average diameter, maximum diameter, minimum diameter, elongation of jet, and location of the jets on a stage in x and y coordinates. In this study, mensuration of all jets from 53 ACIs was performed.

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MATERIALS AND METHODS

Andersen Cascade Impactors

The 53 Andersen 1 ACFM ambient 8-stage (Mark II) cascade impactors (Andersen Instruments Inc., Smyrna, GA, USA) used in this study were purchased between year 1990 and 2000. The majority of these impactors had been used intensively in the laboratory for several years.

AVID Instrument

The AVID instrument (manufactured by Specac Ltd, Orpington, Kent, UK, on behalf of Andersen Instruments Inc., Smyrna, GA, USA) consists of a camera (PULNIX PE-2010) connected to a LABVIEW-based steering program (Impactor Visual Inspection Device, ver. 2.0b) and a carousel fixture for an impactor stage. The camera and the fixture are mounted and precisely aligned in a robust metal stand. One stage at a time is examined, jet-by-jet, in the carousel fixture. The steering program controls the carousel jet positions. Prior to each stage measurement, a calibration procedure was performed. The calibration routine of the instrument includes adjustment of camera intensity and focus, and calibration against traceable normals. The camera counts the number of pixels in the calibrated jet (normal), and upon entry of the diameter of this jet, the pixel size to be used in the measurement of impactor stage jets, is deduced. The normals used are dedicated ACI stages 0–6 for which one jet on each stage are regularly calibrated against a national standard.

Instrument Validation

Before use, the AVID instrument and corresponding method were validated. Various tests such as lamp intensity variation with time and stage number, jet measurements using different lamp intensities, influence of background light, repeated measurements of the reference jets and impactor stages, and validation of the software were performed. The calibration procedure is performed prior to every stage measurement using a traceable normal of equivalent jet size, resulting in a high accuracy of the measurements. The repeatability (repetitive measurement of average jet diameter for a stage) was found to be 0.00–0.17% RSD and intermediate precision (different days) 0.06–0.58% RSD.

Stage Cleaning

Prior to a stage measurement, the stages were cleaned in the following way:

a) The impactor was assembled (without preseparator and collection plates).

b) The outlet of the impactor was connected to a vacuum source via a bottle for solvent collection.

c) Approximately 300–500 ml ethanol was dispensed into stage 0. With the vacuum source activated, the solvent was sucked through the impactor to the bottle for 5 min.

d) The vacuum source was inactivated and the stages were washed with ethanol and allowed to dry.

As described in detail below, all jets of noncompliant stages were rinsed with go gauges with the following diameters: 2.491 mm (stage 0), 1.842 mm (stage 1), 0.510 mm (stage 4), and 0.330 mm (stage 5). The go gauges were thus slightly smaller than nominal jet diameters (Table I).

Evaluation of Jet Diameters

The evaluation of a jet diameter is performed as follows: i) the number of pixels seen through the jet and measured by the camera is converted into an area by use of the pixel size-value from the calibration procedure. ii) a diameter of a circular disk having the same area as measured in (i) is calculated (D_j). All jets on the stages were measured. For each stage, the average jet diameter of the stage (D) was calculated according to, D =Xy: please adjust size $D = \sum_j D_j/N$, where N is the number of jets of the stage and j the jet number ranging from 1 to N. Hence, D is related to the total jet area of the stage, a property which in turn is related to the linear air velocity through the jets. It is also possible to calculate the average jet diameter using the sum of the measured areas, divide with N and from the average jet area calculate the average jet diameter (assuming a circular shape). The difference between these two calculations of average diameters was very small, typically <0.1% and of no practical importance.

Calculation of Impactor Stage Cutoff

The jet diameter relates to the impactor stage cutoff (d_{50}) according to (2)

$$d_{50} = \sqrt{\frac{9\,Stk_{50}\eta\pi D^3 N}{4\rho_0 Q C_c}} \quad (1)$$

which for a specified stage can be simplified to

$$d_{50} = AD^{\frac{3}{2}}C_c^{-\frac{1}{2}} \quad (2)$$

as the viscosity of air (η), number of jets per stage (N), volumetric flow rate through the impactor (Q), and unit density (ρ_0) are constants at the same conditions. Moreover, studies have showed that Stokes number, Stk (Stk_{50} = when 50% of the particles impact and are collected) is rather insensitive to moderate changes in jet diameter for a specified stage (4). C_c is the slip correction factor, here used in its simple form, $C_c = 1 + (2.52\lambda/d_{particle})$, where the mean free path (λ) was set to 0.066 μm. Because A (see Eq. 2) is the same for both the nominal case and for the measured D-case, d_{50} of a certain stage can be determined. The determination has to be done by iteration, as C_c is dependent on particle diameter ($d_{particle}$). The determination was done according to

$$d_{50} = d_{50,nom}\left(\frac{D}{D_{nom}}\right)^{\frac{3}{2}}\left(\frac{C_{c,nom}}{C_c}\right)^{\frac{1}{2}} \quad (3)$$

Table I. Results of Stage Mensuration of All Impactor Stages from 53 Andersen Impactors[a]

	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	Stage 6	Stage 7
Nominal	2.55	1.89	0.914	0.711	0.533	0.343	0.254	0.254
Grand means of all *D*-values, before	**2.536**	**1.881**	**0.911**	**0.707**	**0.531**	**0.337**	**0.256**	**0.255**
SD, before	0.015	0.023	0.008	0.007	0.010	0.010	0.006	0.004
Grand means of all *D*-values, after	**2.537**	**1.883**	**0.911**	**0.707**	**0.531**	**0.339**	**0.256**	**0.255**
SD, after	0.013	0.019	0.008	0.007	0.010	0.008	0.006	0.004
Grand means of all *D*-values, Nichols[b]	**2.553**	**1.892**	**0.917**	**0.718**	**0.539**	**0.349**	**0.256**	**0.258**
SD, Nichols[b]	0.008	0.004	0.014	0.052	0.009	0.005	0.001	0.001
Upper limit AstraZeneca Lund	2.590	1.920	0.951	0.747	0.560	0.360	0.274	0.274
Lower limit AstraZeneca Lund	2.510	1.840	0.877	0.675	0.506	0.326	0.234	0.234
Upper limit manufacturer[c]	2.580	1.920	0.932	0.729	0.551	0.361	0.272	0.272
Lower limit manufacturer[c]	2.520	1.860	0.896	0.693	0.515	0.325	0.236	0.236

[a] The average jet diameters of the stages (D) were used for calculation of the statistical parameters shown. Jet diameters and standard deviation (SD) in mm. Mean of all $\bar{d}_{stage}$-values and SD are shown before and after rinsing of jets of 16 noncompliant stages (see text).
[b] From Ref. 3, in which 37 ACIs were examined and 22–33% of the jets were measured.
[c] M. Smurthwaite, Westech Instrument Services Ltd., personal correspondence, November 2003, limit applied for each jet.

RESULTS

The outcome of the stage mensuration of all stages is summarized in Table I, where nominal diameters, average diameters obtained in this study, tolerance limits applied at AstraZeneca Lund and tolerance limits of the manufacturer (M. Smurthwaite. Westech Instrument Services Ltd, personal correspondence, November 2003) are shown. The found number of jets equaled the nominal number of jets for all examined stages. Literature data from a similar study by Nichols (3) is also included in Table I. For all stages, the grand means of *D*-values were within the limits applied by AstraZeneca Lund as well as the specifications limits of the manufacturer. This does not mean, however, that all individual *D*-values were inside the two specification limits (see below). The differences between nominal jet diameter values and grand means of *D*-values in this study were small, typically in the order of 0.7%. Except for stages 6 and 7, all grand means of *D*-values were smaller than the nominal diameter values. All grand means obtained in the study by Nichols, see Table I, were larger than nominal diameters. The standard deviations of the D-values in this study and in Nichols study were of the same order, ranging from 0.001 to 0.052 mm.

After the jet mensuration of 404 stages, 16 stages were found to have smaller *D*-values than applied tolerance limits at AstraZeneca Lund (limits revised after the presented investigation, see Table I). A decrease of the jet diameters is probably a result of either accumulation of aerosol particles not successfully rinsed off or corrosion inside the jets. Different methods were tested to increase the jet diameters on one selected stage 5. The tested methods were (in working sequence):

a) Pressurized air through the jets using a handheld device of pistol type.

b) Sonication in ethanol for 10 min. The stages were completely covered with ethanol.

c) Use of a go gauge of suitable diameter on every jet followed by pressurized air, see a), through the jets.

After each of the procedures a stage mensuration was performed and the result is shown in Fig. 1. The first two steps, pressurized air and sonication, produced only small changes of the jet diameters (see below). Use of a go gauge increased the jet diameters substantially (Fig. 1) and thus step 3 was performed for all noncompliant stages. The data from stage mensuration for the sixteen stages are shown in Tables I and II. Jet diameters before and after the use of go gauges, shown in Table II, were used to calculate the corresponding stage cutoff values, see Table III.

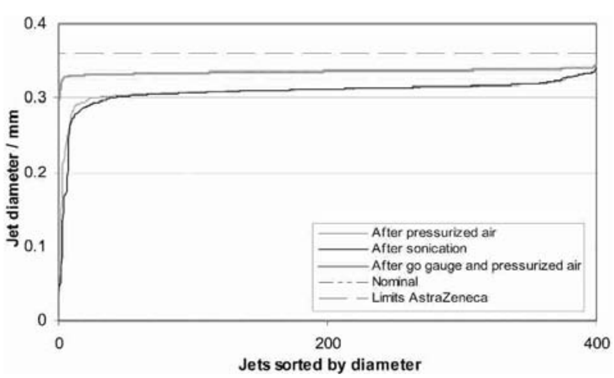

Fig. 1. Jet diameters sorted by size, from one impactor, stage 5. The limits (plain dashed lines) are AstraZeneca Lund limits, 0.326–0.361 mm.

DISCUSSION

The tolerance limits for *D*-values applied by AstraZeneca Lund are of the same order as the limits given by the manufacturer. Tolerance limits can, however, be applied in different ways. For instance, it is possible to apply the limits on the average diameter obtained for a whole stage, but the limits could also be applied on individual jets (M. Smurthwaite. Westech Instrument Services Ltd, personal correspondence, November 2003). We apply our limits on the *D*-value (i.e., not on individual jets). The rational when the AstraZeneca Lund limits were established was based on the data deduced in this study (data driven limits) and case studies. The latter means, for instance, determination of the impact on the result parameters from particle size determination with ACI, when jet diameters deviate from nominal. Individual jet diameters of an evaluated and approved stage may thus be outside tolerance limits, which also was considered when the AstraZeneca Lund limits were established. The manufacturer applies its tolerance limits on every jet (M. Smurthwaite. Westech Instrument Services Ltd, personal correspondence, November 2003). This approach is possible for new ACIs, but may be difficult to adopt for ACIs that have been frequently used for several years.

As seen in Table I, small differences between nominal jet diameter and the grand means of *D*-values were obtained in this study. The differences were of the same order as the data presented by Nichols (3). However, the grand means of *D*-values presented by Nichols were larger than the nominal jet diameters, whereas the *D*-values presented here are below nominal diameters. One might infer that the jet holes would become more obstructed by deposition when the ACIs are frequently used in particle size analyses.

For stages that failed according to AstraZeneca Lund tolerance limits, only a small effect on jet diameters was obtained after cleaning with pressurized air or sonication (Fig. 1). However, the average jet diameters increased considerably after use of the go gauges and came closer to nominal jet diameters than before the treatment (Table II) especially for stages with small jet diameters. The previously more or less blocked jets were enlarged which narrowed the distribution of jet diameters and is reflected in the large decrease in RSD values after the go gauge treatment (Table II). Mechanical treatment of the jets with go gauges is a gentle rinsing technique with no risk of affecting other parts of the stages. Treatment with pressurized air was necessary after the go gauge rinse in order to remove loose deposition drawn into the jets at go gauge withdrawal. The chemical composition of the obstructing material in the jets was not analyzed but is most probably corroded aluminum. If the stages are left to air-dry after the washing procedure, as part of routine analysis, liquid will stay in the jets for longer times than on the flat, surrounding surfaces. This probably causes a slow build-up of corroded aluminum. The stages that failed to comply with the tolerance limits for the average jet diameters all passed the specification after go gauge treatment. The diameters for the majority of the recovered jet diameters are, however, still lower than

Table II. Jet Diameters Measured (Noncompliant Stages According to AstraZeneca Lund Former Limits) Before and After Use of Go Gauges

		Before go gauge			After go gauge			Change	
Serial no./ stage no.	Nominal D_{nom} (mm)	D (mm)	Within stage variation %RSD	Deviation from nominal[a] (%)	D (mm)	Within stage variation %RSD	Deviation from nominal[a] (%)	ΔD^b (%)	Within stage variation decrease[c] Δ%RSD
1559/0	2.55	2.493	0.6	–2.2	2.516	0.4	–1.3	0.9	–0.2
2641/0	2.55	2.512	1.0	–1.5	2.541	0.5	–0.4	1.2	–0.5
417/0	2.55	2.510	0.4	–1.6	2.516	0.3	–1.3	0.2	–0.1
327/0	2.55	2.513	0.2	–1.5	2.518	0.2	–1.3	0.2	–0.0
2369/1	1.89	1.840	0.9	–2.6	1.847	0.2	–2.3	0.4	–0.7
2499/1	1.89	1.844	0.7	–2.4	1.848	0.3	–2.2	0.2	–0.4
2641/1	1.89	1.842	1.0	–2.5	1.856	0.4	–1.8	0.8	–0.6
2640/1	1.89	1.833	1.3	–3.0	1.847	0.5	–2.3	0.8	–0.8
2646/1	1.89	1.832	1.1	–3.1	1.859	0.3	–1.6	1.5	–0.8
2648/1	1.89	1.824	0.7	–3.5	1.845	0.5	–2.4	1.2	–0.2
2647/1	1.89	1.833	0.6	–3.0	1.851	0.3	–2.1	1.0	–0.3
2641/4	0.533	0.507	4.3	–4.9	0.512	3.6	–3.9	1.0	–0.7
2641/5	0.343	0.311	9.9	–9.3	0.331	3.8	–3.5	6.4	–6.1
159/5	0.343	0.326	1.3	–5.0	0.337	0.9	–1.7	3.4	–0.4
163/5	0.343	0.310	7.1	–9.6	0.336	1.0	–2.0	8.4	–6.1
412/5	0.343	0.329	2.5	–4.1	0.347	0.9	1.2	5.5	–1.6
Mean		NA	2.1	–3.7	NA	0.9	–1.8	2.1	–1.2

[a] Deviation from nominal jet diameter, $[(D - D_{nom})/D_{nom}] \times 100$.
[b] Jet diameter increase, $[(D_{after} - D_{before})/D_{before}] \times 100$.
[c] Relative standard deviation decrease, $\%RSD_{after} - \%RSD_{before}$.

nominal values. The reason for this is probably that the go gauges have smaller diameters than the nominal diameter values. Use of go gauges with nominal diameters would, however, disable rinsing of jets smaller than nominal diameter but still within tolerance limits.

After the cleaning with go gauges, the calculated cutoff values of the stages came closer to nominal cutoff values (Table III). Mean deviation from nominal cutoff value decreased from –2.9 to –1.4 (% of nominal). The cleaning effect seemed larger for stages with small diameters (e.g., impactor with serial no. 163, stage 5). The impact of the deviations before cleaning with go gauges (Table III) on important particle size parameters was evaluated. A typical particle size distribution from a standard inhaler analysis was used and the relative difference between use of nominal and deviating cutoffs was calculated. For impactor with serial no. 2641 in Table III, which showed most jet diameter failures (four stages), the mass median aerodynamic diameter (MMAD) differed with 1.55%, the fine particle dose (mass of particles less than 5 μm) with 0.45%, and the geometric standard deviation (GSD) with 1.22%. Substantially smaller deviations were observed for the other stages generating failures.

Table III. Calculated Cutoff Values (Noncompliant Stages) Before and After Use of Go Gauges (Cutoff Values in μm)

Serial no./ stage no.	Cutoff nominal	Cutoff before	Cutoff after	Cutoff deviation, before, % of nominal[a]	Cutoff deviation, after, % of nominal[b]
1559/0	9.0	8.85	8.91	–1.7	–1.0
2641/0	9.0	8.90	8.98	–1.1	–0.3
417/0	9.0	8.89	8.91	–1.2	–1.0
327/0	9.0	8.90	8.91	–1.1	–0.9
2369/1	5.8	5.68	5.70	–2.0	–1.7
2499/1	5.8	5.69	5.70	–1.8	–1.7
2641/1	5.8	5.69	5.72	–1.9	–1.4
2640/1	5.8	5.67	5.70	–2.3	–1.7
2646/1	5.8	5.67	5.73	–2.3	–1.2
2648/1	5.8	5.65	5.70	–2.6	–1.8
2647/1	5.8	5.67	5.71	–2.3	–1.6
2641/4	2.1	2.02	2.04	–3.8	–3.0
2641/5	1.1	1.02	1.07	–7.3	–2.7
159/5	1.1	1.06	1.09	–3.9	–1.4
163/5	1.1	1.02	1.08	–7.6	–1.6
412/5	1.1	1.07	1.11	–3.2	0.9
			Mean	–2.9	–1.4

[a] Calculated as $[(\text{cutoff}_{Before} - \text{cutoff}_{Nominal})/\text{cutoff}_{Nominal})] \times 100$.
[b] Calculated as $[(\text{cutoff}_{After} - \text{cutoff}_{Nominal})/\text{cutoff}_{Nominal})] \times 100$.

CONCLUSIONS

The result from jet diameter mensuration of more than 400 Andersen Cascade Impactor stages using the AVID instrument was of the same order as literature data and the manufacturer's nominal diameters. Some of the stages failed applied tolerance limits due to too small jet diameters and different methods were applied to increase the jet diameters. Mechanical rinsing with go gauges was found to be a suitable method. After rinsing, the stages passed the test (average jet diameter of the stage inside the tolerance limits) and the theoretically calculated cutoff values came closer to nominal.

Finally, we infer that periodic control of the jet diameters of Andersen stages should include a stage mensuration with all jets included in order to reveal incorrect jet dimensions (e.g., through use of an automatic instrument such as the AVID). Use of stop/go gauges on a small fraction of randomly selected jets of the stages should be avoided, as all stages would most probably pass such a poorly discriminating test, especially as the go gauges themselves are likely to remove deposits from the examined jets, but not from the uncontrolled jets. The consequence is that a stage may comply with the tolerance limits although the majority of the jets are outside the limits.

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