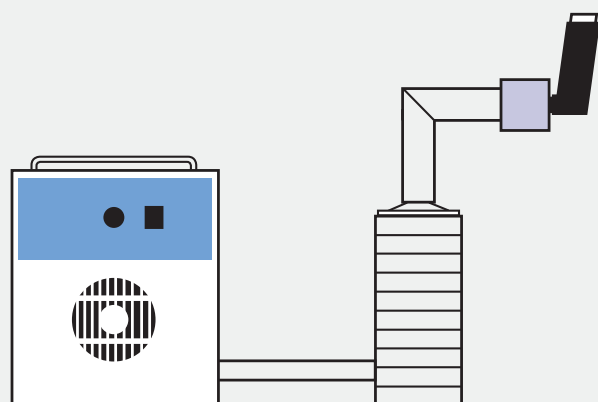
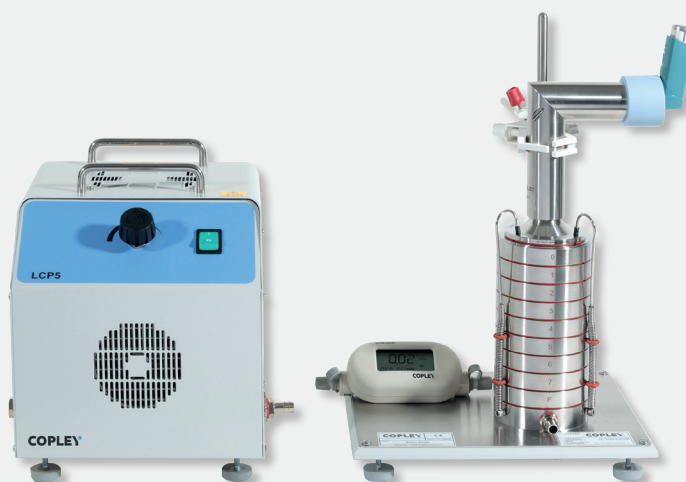


Andersen Cascade Impactor (ACI)

↓ Schematic of ACI with Pump for testing MDIs



↓ ACI with Pump for testing MDIs



INTRODUCTION

The ACI, manufactured by Copley, is an 8-stage cascade impactor that has been designed for measuring the APSD generated by MDIs and DPIs.

It complies with the specifications laid down in USP Chapter <601>, Ph.Eur. 2.9.18 and ChP 2015.

IMPACTOR USE (METERED-DOSE INHALERS)

The standard ACI is designed for use at 28.3 L/min (which is equivalent to 1 cubic foot/min).

The 8 stages have the following particle size collection bands:

- Stage 0 9.0 + microns
- Stage 1 5.8 – 9.0 microns
- Stage 2 4.7 – 5.8 microns
- Stage 3 3.3 – 4.7 microns
- Stage 4 2.1 – 3.3 microns
- Stage 5 1.1 – 2.1 microns
- Stage 6 0.7 – 1.1 microns
- Stage 7 0.4 – 0.7 microns

The ACI, like other cascade impactors, is designed such that as the aerosol stream passes through each stage, particles having sufficient inertia will impact upon that

particular stage collection plate, whilst smaller particles with insufficient inertia will remain entrained in the air stream and pass to the next impactation stage.

By analysing the amount of active drug deposited on the various stages, it is then possible to calculate the Fine Particle Dose (FPD) and Fine Particle Fraction (FPF) and following further manipulation, the Mass Median Aerodynamic Distribution (MMAD) and Geometric Standard Deviation (GSD) of the active drug particles collected.

IMPACTOR USE (DRY POWDER INHALERS)

The same impactor can be used for determining the particle size of Dry Powder Inhalers (DPIs).

In this instance, however, a **preseparator** is interposed between the induction port and stage 0 of the impactor in order to collect the large mass of non-inhalable powder boluses typically emitted from a DPI prior to their entry into the impactor.

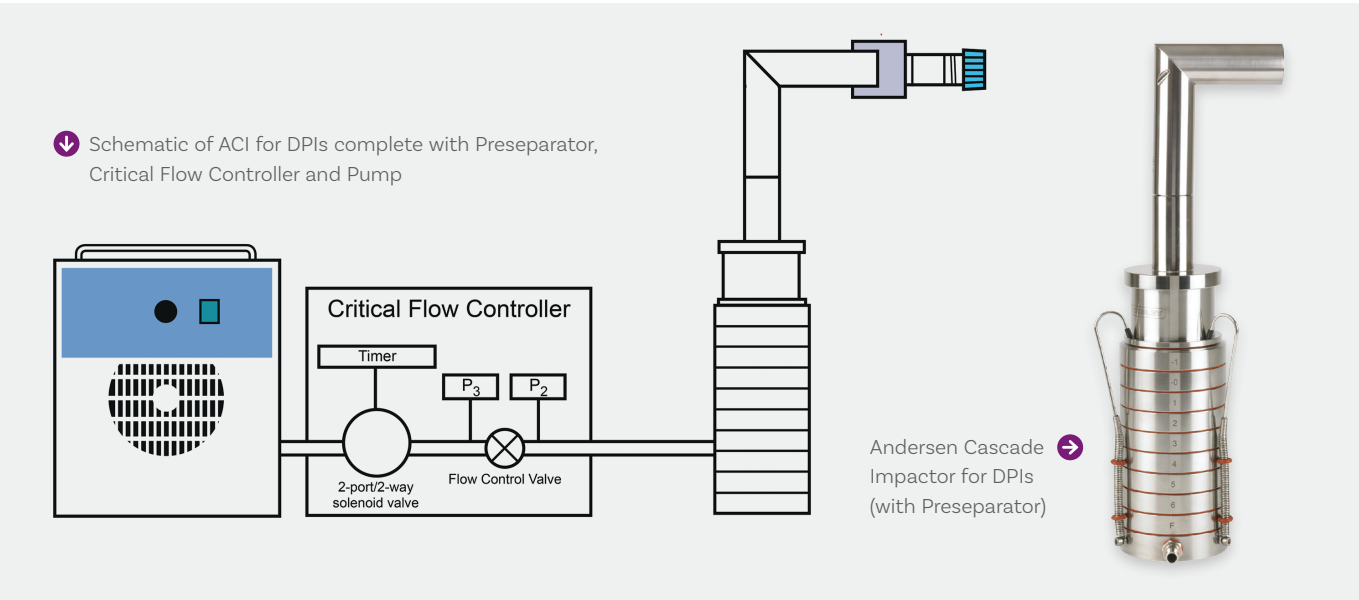
In the case of Dry Powder Inhalers (DPIs), a number of additional factors must be taken into account when testing:

- The pressure drop generated by the air drawn through the inhaler during inspiration
- The appropriate flow rate, Q, to give a pressure drop of 4 kPa
- The duration of simulated inspiration to give a volume of 4 litres
- Flow rate stability in terms of critical (sonic) flow

These factors require the use of the “General Control Equipment” for DPIs specified in USP chapter <601> and “Experimental Set Up” for testing DPIs in Ph.Eur. 2.9.18 which take all of these factors into account.

These specifications form the basis of the Critical Flow Controllers (see Page 80) which incorporate all of the equipment required into a single integrated system.

Andersen Cascade Impactor (ACI)



MODIFIED CONFIGURATIONS FOR USE AT 60 AND 90 L/MIN

In many cases (particularly with low resistance DPIs), it is necessary to operate at flow rates greater than 28.3 L/min, if a pressure drop over the inhaler of 4 kPa is to be achieved.

Whilst the ACI can be operated at flow rates greater than 28.3 L/min, it is important to consider the change in cut-points that will occur for each stage. An empirical equation can be used to calculate these cut-point changes over the range of 28.3 – 100 L/min. However, the user should be aware that reduced discrimination between the

cut-points will occur as the flow rate is increased. Furthermore, the validity of the empirical equation becomes questionable, the further the test flow rate deviates from 28.3 L/min.

In order to help address these problems, two modified configurations of the ACI are available for operating at flow rates of 60 and 90 L/min. These are described in USP Pharmacopoeial Forum Volume 28, Number 2, 2002, p. 601-603 and are now enshrined in USP chapter <601>.

In the 60 L/min version, stages 0 and 7 are removed and replaced with two additional stages, -0 and -1. Similarly, in the 90 L/min

version, stages 0, 6 and 7 are removed and replaced with three additional stages, -0, -1 and -2.

Changes are also made to the configuration of the collection plates (with and without centre holes).

This results in a set of cut-points as per the table below.

QUALITY

A number of papers published in the late 1990s highlighted concerns relating to the manufacture and performance of the ACI manufactured by Graseby-Andersen between 1992 and 1998.

These focused on the choice of material used in their design, their construction, ease of use, accuracy, calibration and the ability to suitably qualify the impactors prior to use.

Because of these criticisms, Copley commenced manufacturing the ACI using the latest state-of-the-art production techniques.

These techniques ensure that 100% of the jets of every stage of every Copley impactor conform to the published critical dimensions for the ACI stated in USP Chapter <601> and Ph.Eur. Chapter 2.9.18.

The validity of this data is guaranteed by dimensional verification using the very latest vision inspection technology having a demonstrated optical reproducibility of 1 micron (to a 99% confidence interval).

Cut-off Diameter at	28.3	60	90	L/min
• Stage -2	-	-	8.0	microns
• Stage -1	-	8.6	6.5	microns
• Stage -0	-	6.5	5.2	microns
• Stage 0	9.0	-	-	microns
• Stage 1	5.8	4.4	3.5	microns
• Stage 2	4.7	3.2	2.6	microns
• Stage 3	3.3	1.9	1.7	microns
• Stage 4	2.1	1.2	1.0	microns
• Stage 5	1.1	0.55	0.22	microns
• Stage 6	0.7	0.26	-	microns
• Stage 7	0.4	-	-	microns

Andersen Cascade Impactor (ACI)



↓ ACI System for testing DPIs

MATERIALS OF CONSTRUCTION

The ACI was originally designed for environmental air sampling and is traditionally constructed from aluminium. However its adoption by the pharmaceutical industry has placed far harsher demands on the material because of the use of organic solvents in the drug recovery process.

Recent advances in automated, high precision machining techniques now mean that the ACI can be manufactured from **316 stainless steel** (the pharmaceutical industry's preferred material) and also **titanium**.

The main advantage of 316 stainless steel is that of superior corrosion resistance and durability, meaning that 316 stainless steel impactors manufactured by Copley are not only very competitively priced but also highly cost effective, helping to maintain accuracy and extend impactor life by reducing mechanical and chemical wear. Electrically conductive, stainless steel can also help reduce the unwanted effects of electrostatics in the impactor.

Where the weight of 316 stainless steel is a concern, Copley can also offer titanium, which has the durability of 316 stainless steel but with a 40% reduction in weight.

Copley continues to offer aluminium ACIs for those users who prefer a lower cost option or for those cases where their methods are such that corrosion resistance and durability

are not an issue. Leak-free inter-stage sealing is achieved through the use of high quality **FDA approved silicone rubber O-rings**.

Preseparators feature a one-piece seamless construction and, together with the induction ports, come with mensuration certificates as standard.

All collection plates are manufactured from 316 stainless steel. They are individually inspected for surface roughness and laser etched on the underside with batch number for traceability.

Also available as options are a one-piece 316 stainless steel induction port and specially modified 'O-ring free' 316 stainless steel inlet cone and preseparator lids for accepting the NGI style induction port.

EASE OF USE

The **"Quick Clamp"** is an optional accessory for use with the ACI which can also be retrofitted to existing impactors.

Constructed from stainless steel, the "Quick Clamp" provides a quick and easy means of assembling, clamping and dis-assembling all or part of the impactor stack (for example, less stages 6 and 7) during routine operation.

Once the assembled stack is in position, the clamping action is achieved very simply by turning a small knob through 90 degrees.

* Rounded to 0.013 in the case of USP

Andersen Cascade Impactor (ACI) - Standard 28.3 L/min Configuration		
Stage Number	Nozzles	Ph.Eur. Nozzle Diameter (mm)
0	96	2.55 +/- 0.025
1	96	1.89 +/- 0.025
2	400	0.914 +/- 0.0127*
3	400	0.711 +/- 0.0127*
4	400	0.533 +/- 0.0127*
5	400	0.343 +/- 0.0127*
6	400	0.254 +/- 0.0127*
7	201	0.254 +/- 0.0127*

Andersen Cascade Impactor (ACI)



MENSURATION, QUALIFICATION AND SYSTEM SUITABILITY

Every impactor manufactured by Copley is machined to the same precision tolerances in order to guarantee reproducibility between impactors and to ensure stage mensuration.

Stage mensuration replaces the need for repetitive calibration using standardised aerosols and ensures that only impactors conforming to specification are used in testing.

In practice, this means that every jet on every stage of every impactor must be individually inspected to ensure compliance.

For this reason, all cascade impactors (including induction ports and preseparators), manufactured by Copley, are checked at

every stage of manufacture using the very latest in **metrology equipment** and are provided with a **mensuration certificate** and **leak test certificate** prior to release.

SUMMARY

ACIs manufactured by Copley are:

- Available in aluminium, 316 stainless steel or titanium
- Capable of operation at 28.3, 60 or 90 L/min
- Manufactured to USP and Ph.Eur. critical dimensions
- Supplied with full stage mensuration certificate, certificate of conformity to USP/Ph.Eur. and leak test certificate

ANCILLARIES

The following ancillaries are required in addition to the ACI to complete a fully operating test system for determining the APSD of MDIs:

- Mouthpiece Adapter (see Page 90)
- Induction Port (see Page 49)
- Vacuum Pump (see Page 91)
- Flow Meter (see Page 88)
- Data Analysis Software (see Page 94)

Additionally to test DPIs:

- Preseparator (see Page 49)
- Critical Flow Controller (see Page 80)

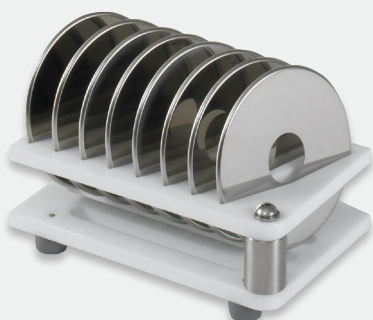
Options:

- Automation (see Page 113)





↑ Quick Clamp



↑ ACI Collection Plate Rack



↑ ACI Collection Plates
(featuring batch numbering)



↑ Preseparator, 60 L/min Conversion Kit
and Collection Plates

Cat. No. Description

Impactors

8301	28.3 L/Min Andersen Cascade Impactor*
8301-60	60 L/Min Andersen Cascade Impactor*
8301-90	90 L/Min Andersen Cascade Impactor*

Induction Ports

8501	USP Induction Port*
8510	USP Induction Port (One-piece 316 Stainless Steel)
8060	Flow Meter to Induction Port/WSC2 Adapter

Preseparators for testing DPIs

8401	28.3 L/min Preseparator*
8420	60 L/min Preseparator*
8420-90	90 L/min Preseparator*

Conversion Kits for the standard 28.3 L/min ACI

8318	Conversion Kit for 60 L/min operation*
8319	Conversion Kit for 90 L/min operation*

Options

8111	Stand (incl. Base Plate, Boss Head and Clamp)
5212	'Quick Clamp' for Andersen Cascade Impactor
5401	ACI Carrying/Wash Rack
5441	ACI Collection Plate Rack

Spare Parts

8307	Complete Set of 13 ACI Silicone Rubber O-Rings
8314	Set of 8 Stainless Steel Collection Plates (28.3 L/min)
8314-60	Set of 8 Stainless Steel Collection Plates (60 L/min)
8314-90	Set of 8 Stainless Steel Collection Plates (90 L/min)
8316	Box of 100 Glass Fibre Filters
8306	Set of 6 O-Rings for Spring Clamp
8308	Set of 3 Spring Clamps
8309	Set of 3 PVC End Caps for Spring Clamps
8403	Set of 4 O-Rings for Preseparator
8395	ACI Carrying Case
8351	Inlet Cone*
8352	Stage -2A*
8353	Stage -1A (for 90 L/min operation)*
8354	Stage -1 (for 60 L/min operation)*
8355	Stage -0*
8356	Stage 0*
8357	Stage 1*
8358	Stage 2*
8359	Stage 3*
8360	Stage 4*
8361	Stage 5*
8362	Stage 6*
8363	Stage 7*
8364	Stage F (Filter)*
8365	Base (including Hose Fitting)*

*Please specify **Aluminium (A)**, **316 Stainless Steel (S)** or **Titanium (T)** when placing your order.