

Dosage Unit Sampling Apparatus (DUSA) for MDIs

INTRODUCTION

The Delivered Dose is the **total** amount of drug emitted from the device and hence available to the patient.

Its uniformity is a Critical Quality Attribute (CQA) in determining the safety, quality and efficacy of an orally inhaled and nasal drug product (OINDP).

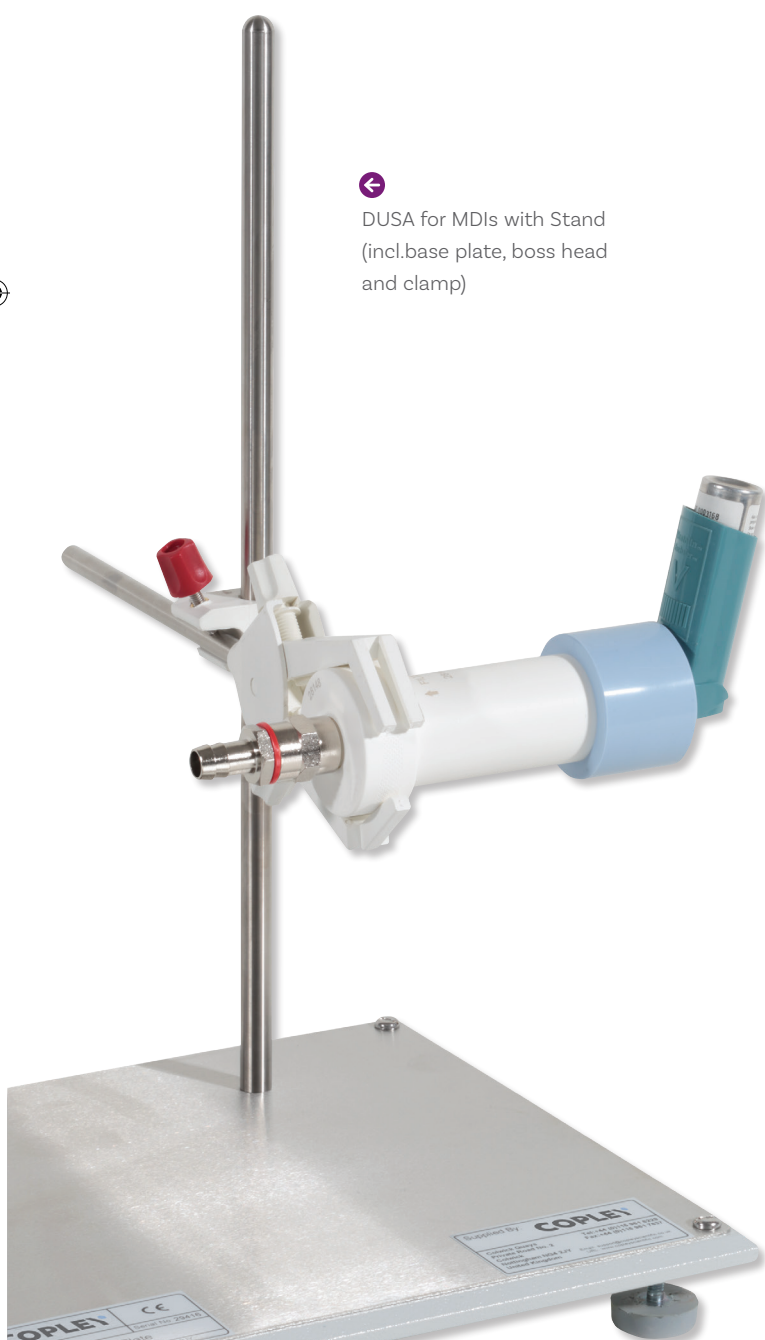
Based on an original design by Charles Thiel in 3M's laboratories in Minneapolis, USA, the **Dosage Unit Sampling Apparatus (DUSA) for MDIs** has been designed specifically for the

sampling and testing of MDIs and Nasal Aerosols.

It is used to perform those tests specified in the Pharmacopoeias relating to "delivered" or "emitted" dose, namely "Uniformity of Delivered Dose", "Dose Content Uniformity (DCU)" and "DDU or DCU through container life".

Over the years, the design of the sampling apparatus has been refined to improve user-friendliness and productivity whilst maintaining the critical internal dimensions specified by the Pharmacopoeias.

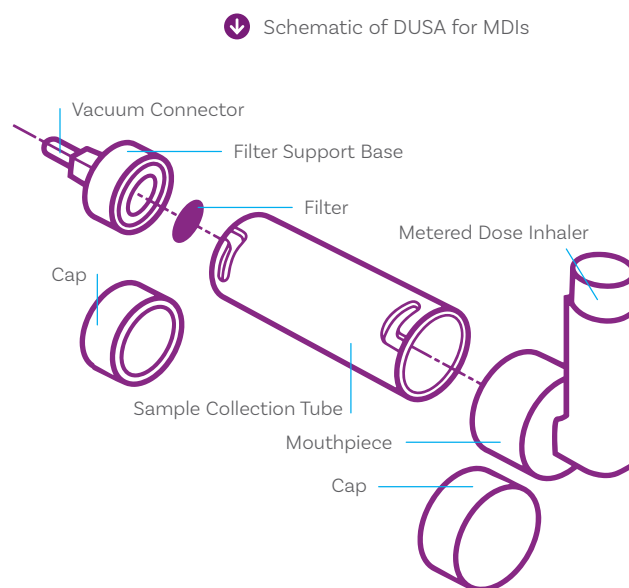
"Quick Release" bayonet caps and adapters, for example requiring a simple quarter-turn, have now replaced the more cumbersome screw thread fittings. The old fixed disc type mouthpiece adapter has been superseded by the interchangeable, and hence more versatile, sheath type mouthpiece adapter (see Page 90).



← DUSA for MDIs with Stand (incl. base plate, boss head and clamp)

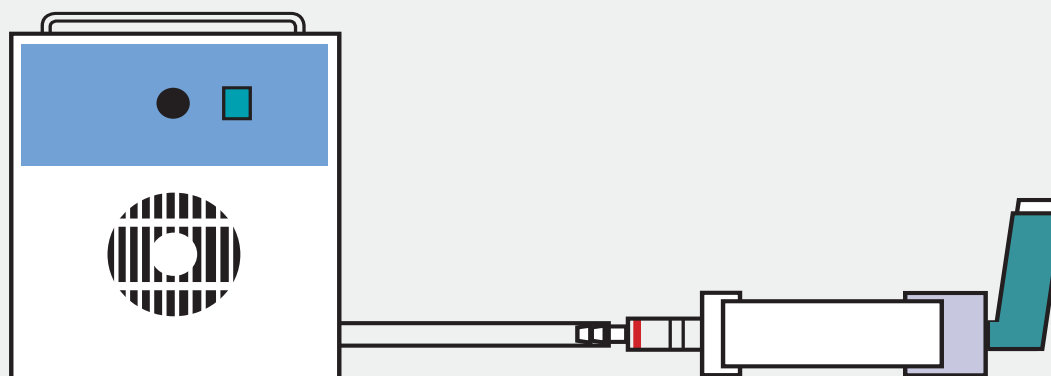


↓ Component Parts (and example MDI)



↓ Schematic of DUSA for MDIs

↓ Schematic of DUSA for MDIs with Pump (Ph.Eur.)



DESCRIPTION

The DUSA for MDIs and Nasal Aerosols consists of one collection tube, two rinsing caps, one filter support cap and one flow meter cap supplied in a handy carrying case.

The standard collection tube itself and rinsing caps are manufactured from an high-quality, inert **polypropylene**, specifically formulated for medical and pharmaceutical applications.

Alternative materials, such as aluminium and 316 stainless steel, are also available, if required. All tubes and caps are **laser numbered** to assist with traceability.

Spare collection tubes and caps are also available as individual parts.

The sample collection tube is fitted with a 25 mm glass fibre filter having a pore size of 1 micron and typical aerosol retention of 99.98% of 0.3 micron particles.

The standard unit comes with high quality silicone rubber seals. Polyethylene (LDPE) seals are available as an option, in the event of drug incompatibility or extractables being an issue with silicone rubber.

A stand comprising base plate, boss head and clamp for supporting the DUSA during use is available as an option.

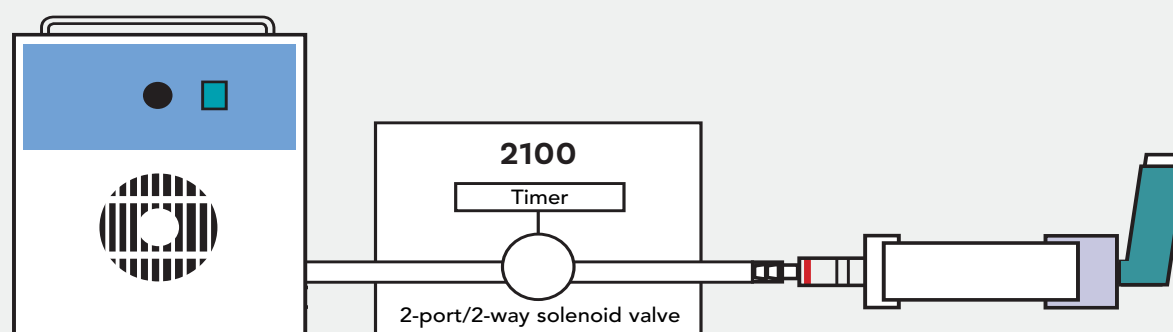
The combination of the clamp to secure the filter support cap and the boss head to alter its angle allows collection tubes to be quickly connected to the vacuum system prior to

testing and removed once the test is complete.

A further base plate option includes mounting fixtures for the Waste Shot Collector (see Page 31) and switching valve.

Using a Waste Shot Collector, a switching valve mounted on the base plate used to support the DUSA, in conjunction with a single complete DUSA, 9 spare collection tubes, 18 spare rinsing caps and 11 mouthpiece adapters (10 for the DUSA collection tubes and one for the Waste Shot Collector) can provide substantial gains in terms of throughput.

↓ Schematic of DUSA for MDIs with Pump and BAC 2100 to restrict the volume of air sampled to no more than 2 litres (USP)



Dosage Unit Sampling Apparatus (DUSA) for MDIs

System for Testing the Dose Uniformity of MDIs (incl. Waste Shot Collector and Switching Valve)



PROCEDURE (PH.EUR.)

The minimum set-up for delivered dose testing as specified by Ph.Eur. comprises a sample collection tube, fitted at one end with a suitable mouthpiece adapter to accept the inhaler under test and connected at the other end to a vacuum pump capable of continuously drawing 28.3 L/min through the assembled system (including the filter and inhaler).

A flow meter (see pages 88 - 89) should be used to adjust the flow at the inlet to the correct rate prior to testing, using the flow meter cap.

Once the device has been shaken, primed and actuated and the test is complete, the collection tube together with the filter is removed. Solvent is then added and the tube capped and agitated to assist in drug dissolution prior to recovery and analysis.

PROCEDURE (USP)

In addition to the specifications laid down in Ph.Eur., the FDA recommends, and USP specifies, that the volume of air sampled should not exceed 2 litres, this being the volume of air adjudged to be typical of the average patient.

This additional criterion can be met by positioning an electrically operated, timer controlled, two-way solenoid valve, such as that incorporated in the **Breath Actuation Controller Model BAC 2100** (see Page 86), in the line between the collection tube and the vacuum pump to control the air flow supply to the inhaler.

The BAC 2100 provides near instantaneous starting and stopping of the air flow during testing and has both delay and inhaled time functions. This allows the time that the test flow is applied to the inhaler to be adjusted

to a specific volume, for example, the 2 litres required by USP.

Operation can be triggered via the instrument front panel, foot switch, MDI Actuation Sensor or RS232 interface.

The BAC 2100 can also be used for the testing of Breath-Actuated (or Breath Operated) MDIs.

In this case, the BAC 2100 is used to initiate the flow and hence trigger the breath actuated inhaler simultaneously.

A DUSA Shaker for holding up to 21 DUSA for MDI collection tubes is available to assist in the process of drug dissolution and drug recovery (see Page 114).



DUSA for MDIs with Breath Actuation Controller Model BAC 2100 and Pump testing a Breath Actuated MDI

← Stand for 10 MDI Collection Tubes



BRITISH PHARMACOPOEIA

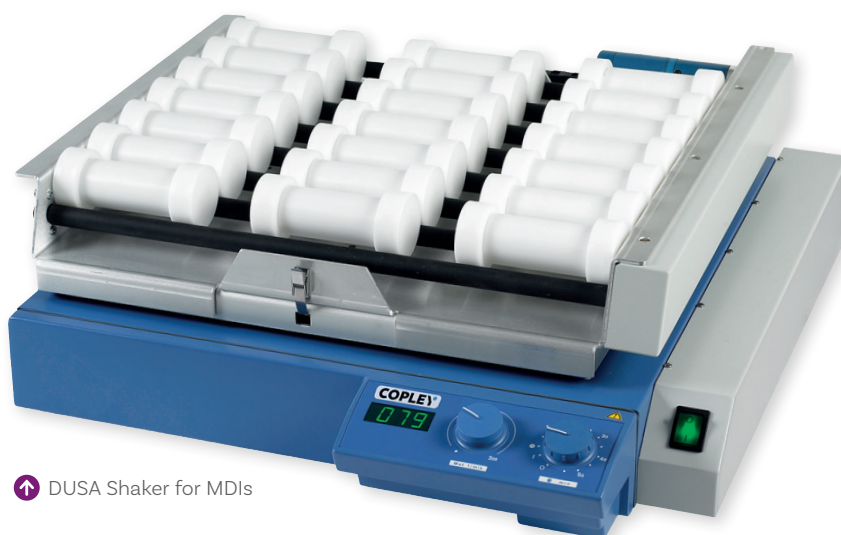
It is important to note that, in addition to the Ph. Eur. specified DUSA, the **British Pharmacopoeia** has its own unique apparatus for determining the “Content of Active Ingredient delivered by actuation of the valve”, likely retained for historical reasons.

This comprises a stainless steel base plate having three legs and a central hole to accept the actuator stem in a small vessel (to which solvent is added) suitable for shaking.

ANCILLARIES

The following ancillaries are required to complete a fully operating test system for the delivered dose testing of MDIs:

- Mouthpiece Adapter (see Page 90)
- Vacuum Pump (see Page 91)
- Breath Actuation Controller (see Page 86)
- Flow Meter (see Page 88)
- Waste Shot Collector (see Page 31)
- Option: DUSA Shaker (see Page 114)



↑ DUSA Shaker for MDIs

Cat. No. Description

- | | |
|-------|---|
| 8201 | Dosage Unit Sampling Apparatus for MDIs (Silicone Rubber Seals) |
| 8201A | Dosage Unit Sampling Apparatus for MDIs (LDPE Seals) |

Accessories

- | | |
|------|---|
| 8111 | Stand (incl. Base Plate, Boss Head and Clamp) |
| 8211 | Stand for 10 Collection Tubes |

Spare Parts

- | | |
|-------|---------------------------------------|
| 8202 | Set of 3 Silicone Rubber Seals |
| 8202A | Set of 3 LDPE Seals |
| 8203 | Collection Tube |
| 8204 | Filter Support Cap |
| 8205 | Rinsing Cap (Silicone Rubber Seal) |
| 8205A | Rinsing Cap (LDPE Seal) |
| 8206 | Flow Meter Cap (Silicone Rubber Seal) |
| 8206A | Flow Meter Cap (LDPE Seal) |
| 8207 | Stainless Steel Filter Support Disc |
| 8210 | Pack of 500 Glass Fibre Filters |

Note: Aluminium or 316 Stainless Steel DUSAs are available, if required

- | | |
|------|--|
| 8212 | BP Content Uniformity Apparatus for MDIs |
|------|--|



↑ BP Content Uniformity Apparatus for MDIs

Dosage Unit Sampling Apparatus (DUSA) for DPIs

System for testing the Dose Uniformity of DPIs (inc. Waste Shot Collector and Switching Valve.)



INTRODUCTION

A second and larger version of the Dosage Unit Sampling Apparatus (DUSA) for MDIs, capable of sampling at a variety of flow rates up to 100 L/min, is available for use with Dry Powder Inhalers (DPIs) and Nasal Powders.

The DUSA for DPIs is used to perform those tests specified by the Pharmacopoeias that relate to “delivered” or “emitted” dose, namely “Uniformity of Delivered Dose”, “Dose Content Uniformity” and “DDU or DCU through container life”. It can also be used to **characterise the flow resistance** of any DPI.

As with the system suggested for testing MDIs according to USP <601>, an electrically

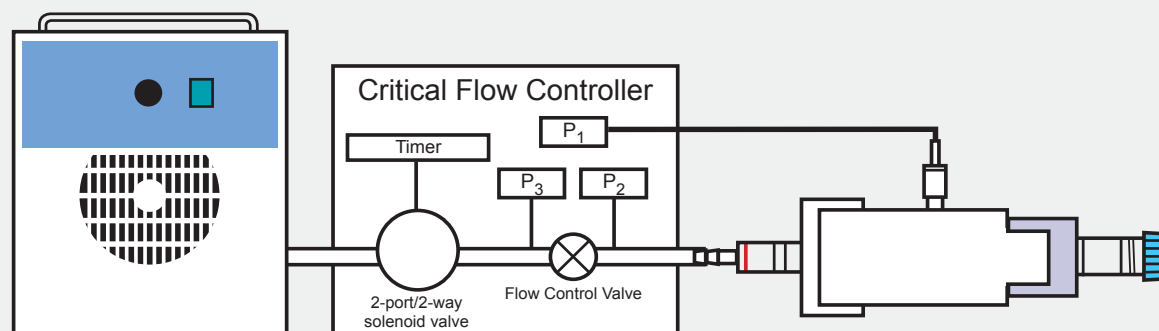
operated, timer controlled, two-way solenoid valve is positioned in the line between the collection tube and the vacuum pump to control the air flow supply to the inhaler.

In the case of DPIs this is mandatory because, unlike MDIs, the majority of these devices are passive breath-actuated devices which rely on the patient’s inspiration rather than a propellant for dose emission.

The testing of DPIs is further complicated by the fact that different inhalers provide varying degrees of resistance to flow, i.e. some require more effort to inhale through than others.

Instruments such as the **Critical Flow Controller Model TPK 2100** (see Page 84) interposed between DUSA and vacuum pump simplify set-up in accordance with these pharmacopoeial recommendations, measuring and recording all the parameters required for testing and controlling flow conditions and ensuring critical (sonic) flow conditions during testing.

They also allow the time that the test flow is applied to the inhaler to be adjusted to a specific volume, for example 2 or 4 litres, to represent the inhalation volume of a typical patient.



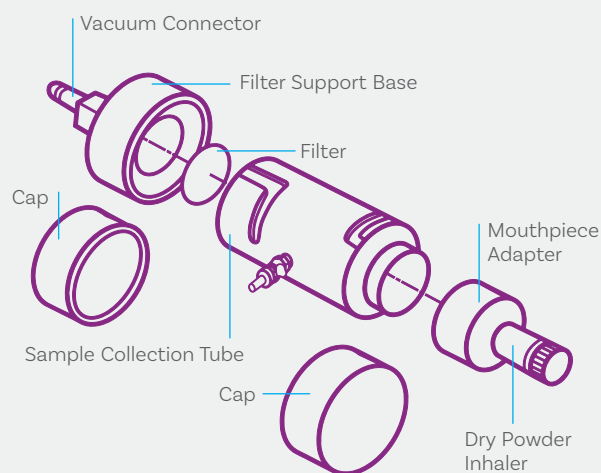
Schematic of Sampling Apparatus for DPIs with Pump and Critical Flow Controller

Dosage Unit Sampling Apparatus (DUSA) for DPIs

Component Parts (and example DPI)



Schematic of DUSA for DPIs



DESCRIPTION

The Dose Unit Sampling Apparatus (DUSA) for DPIs utilises the same materials of construction as the unit for MDIs. Alternative materials, such as aluminium and 316 stainless steel, are also available, if required.

The apparatus comprises one collection tube, two rinsing caps, one filter support cap and one flow meter cap, and comes complete in a handy carrying case.

In this case, the sample collection tube is fitted with a 47 mm glass fibre filter enabling

dosage collection at the higher flow rates – up to 100 L/min – when necessary.

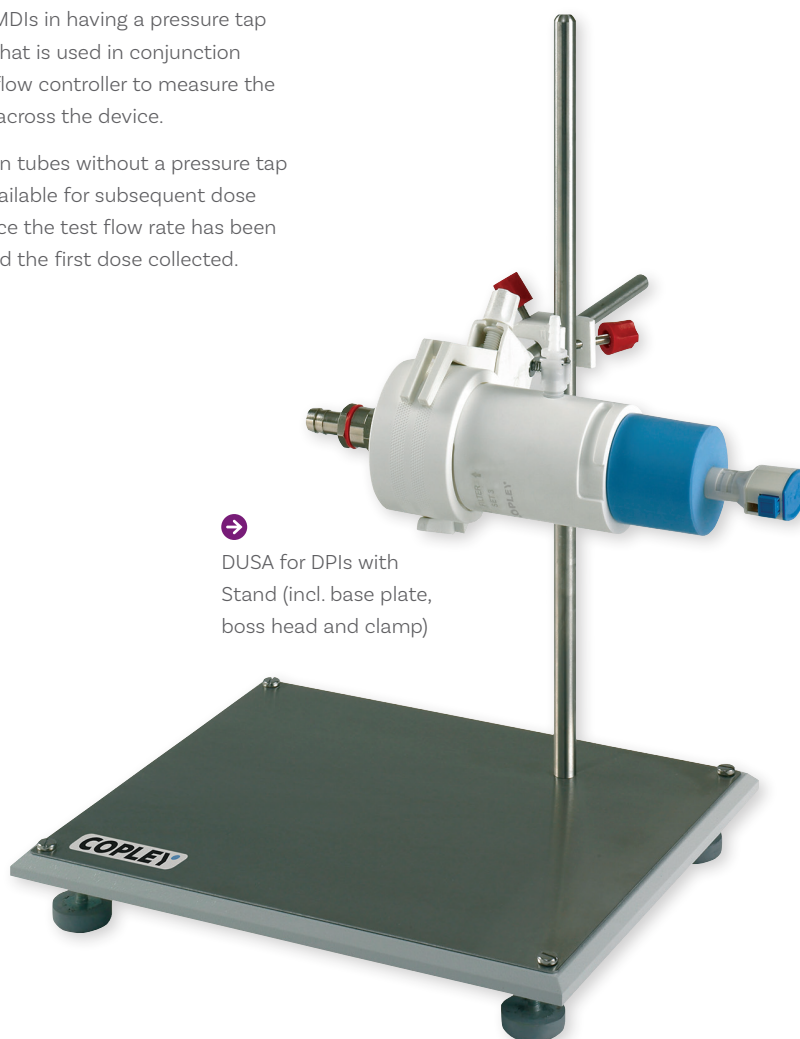
The collection tube also differs from that employed for MDIs in having a pressure tap (P1) in its wall that is used in conjunction with a critical flow controller to measure the pressure drop across the device.

Spare collection tubes without a pressure tap (P1) are also available for subsequent dose collections, once the test flow rate has been determined and the first dose collected.

Stand for 10 DPI Collection Tubes



DUSA for DPIs with Stand (incl. base plate, boss head and clamp)



Dosage Unit Sampling Apparatus (DUSA) for DPIs



PROCEDURE

The minimum start-up requirement for DPI delivered dose testing is the same as that for MDI testing described in the preceding section, namely DUSA, mouthpiece adapter, pump and flow meter, plus the addition of a critical flow controller (e.g. TPK 2100) to measure the pressure drop across the device and control the flow conditions during testing accordingly.

Proceed as follows:

1. Assemble the system as per the schematic of the DUSA for DPIs
2. Connect the inhaler to the collection tube using a suitable mouthpiece adapter
3. Connect the tube marked P1 on the critical flow controller to the pressure tap on the collection tube
4. Switch on the pump, open the 2-way solenoid valve and adjust the flow control valve until the differential pressure on the display reads 4 kPa
5. Check that critical (sonic) flow is being achieved through the flow control valve by checking the P2 and P3 values on the display
6. Replace the inhaler with a flow meter and measure the flow rate, Q. Then, using the pre-determined flow rate, Q, and the critical flow controller timer controls, adjust the test flow duration to give an inspiration volume of 4 (or 2) L

7. Replace the inhaler and discharge the dose into the collection tube by activating the timer on the critical flow controller controlling the solenoid valve. Repeat as necessary to achieve the desired number of doses
8. Add solvent to the collection tube, apply rinsing caps and then shake the tube vigorously before assaying the contents

Note: The TPK 2100 automates much of this process (see page 84).

ANCILLARIES

The following ancillaries are required to complete a fully operating test system for the delivered dose testing of DPIs:

- Mouthpiece Adapter (see Page 90)
- Vacuum Pump (see Page 91)
- Critical Flow Controller (see Page 80)
- Flow Meter (see Page 88)
- Waste Shot Collector (see Page 31)
- Option: DUSA Shaker (see Page 114)

Cat. No.	Description
8601	Dosage Unit Sampling Apparatus for DPIs (Silicone Rubber Seals)
8601A	Dosage Unit Sampling Apparatus for DPIs (LDPE Seals)
Accessories	
8111	Stand (incl. Base Plate, Boss Head and Clamp)
8604	Stand for 10 Collection Tubes
Spare Parts	
8602	Set of 3 Silicone Rubber Seals
8602A	Set of 3 LDPE Seals
8603	Pack of 100 Glass Fibre Filters
8606	Filter Support Cap
8607	Rinsing Cap (Silicone Rubber Seal)
8607A	Rinsing Cap (LDPE Seal)
8608	Collection Tube with P1 Port
8608A	Collection Tube without P1 Port
8609	Flow Meter Cap (Silicone Rubber Seal)
8609A	Flow Meter Cap (LDPE Seal)
8610	Stainless Steel Filter Support Disc
Note: Aluminium or 316 Stainless Steel DUSAs are available, if required	