

PENNCENTURY™

Exclusive manufacturer of the MicroSprayer® Aerosolizer and Dry Powder Insufflator™

For intrapulmonary use

www.penncentury.com



Expanding the reach of aerosol drug delivery

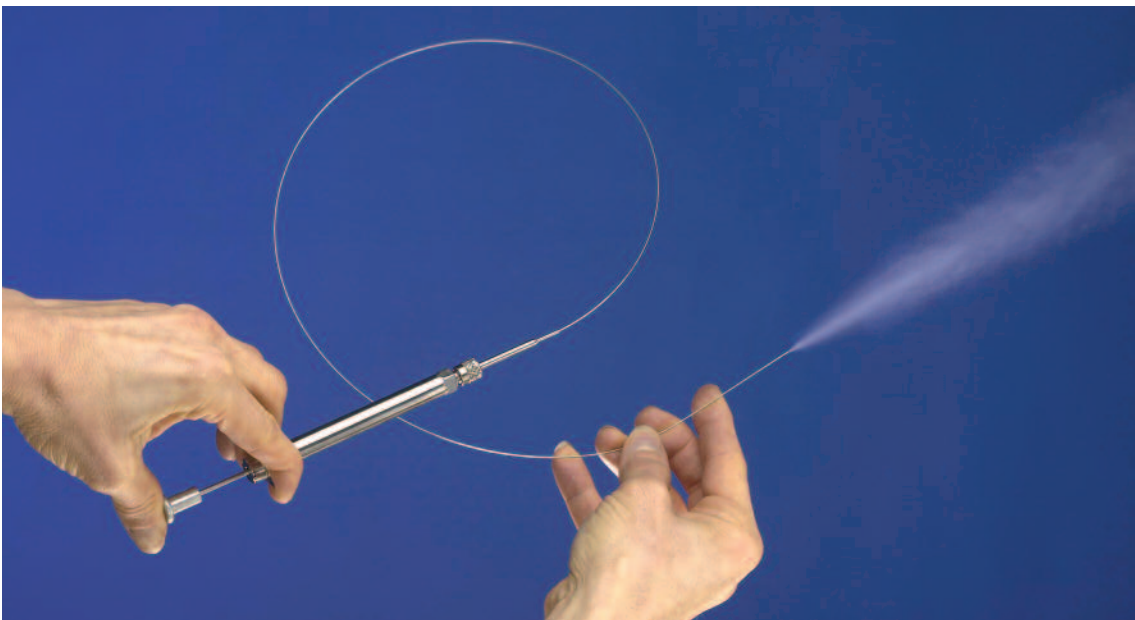
Deliver a soft mist directly to the lung with Penn-Century's unique liquid and dry powder devices

Penn-Century: Offering a new paradigm for pulmonary drug delivery

Because the lungs offer such a rapid, direct portal to the bloodstream, more and more pharmaceutical research is focusing on discovering new drugs to treat both pulmonary and systemic diseases via the lungs. However, gaining access to the lungs safely, effectively and precisely requires overcoming numerous technological and anatomical obstacles. Existing inhaler and nebulizer technologies are often highly inefficient and imprecise. Most depend on heat

or propellants that can alter the compounds delivered. The alternative method – delivering large droplets (liquid bolus) through an endotracheal tube – offers poor distribution and may create respiratory distress or unwanted immunological effects.

Penn-Century intrapulmonary devices offer a new paradigm for aerosol drug delivery that permits the user to administer aerosols safely and precisely – direct to the lungs.



Safe
Effective
Precise

Penn-Century devices have successfully delivered:

Antibiotics, anaesthetics, bronchodilators, vaccines, peptides, proteins, hormones, endotoxins, anti-inflammatories, LPS, neutrophil elastase and inhibitors of HNE, surfactant, radio-opaque tracers, epinephrine, DNA, heparin, L-dopa, stem cells, COX-2 inhibitors, monoclonal antibodies, chemotherapy, gene therapy, micro- and nanoparticles, biohazards, environmental challenges, etc.

Aerosol delivery direct to the lung

Penn-Century is the exclusive manufacturer of hand-held, completely mechanical atomizers for intrapulmonary administration of liquid and dry powder aerosols. *They are currently available for laboratory use only.*

The MicroSprayer® Aerosolizer and Dry Powder Insufflator™ by Penn-Century are the only commercially available devices of their kind. They are narrow enough to be inserted down the trachea – to the carina or beyond – in anesthetized subjects. They take the guesswork out of quantifying the actual delivered dose and minimize the waste of valuable materials.

Our liquid and dry powder aerosol devices are in wide use for medical and veterinary research at pharmaceutical and biotech companies, government, academic and contract research labs and medical research centers throughout the world.

Longer custom sizes can be inserted via an endotracheal tube or bronchoscope in larger species. Shorter versions have been used intranasally. They are also small enough to access difficult-to-reach areas, such as the sinuses, colon, bladder, or uterus.

Penn-Century device feature:

- Simple and easy to use
- Portable, light-weight and hand operated
- Broader, deeper, more uniform distribution than is possible with liquid bolus/droplet instillation via an ET tube
- Precise quantification of delivered dose
- Delivery tubes can be made to any length – from mice to horses
- Rounded tip minimizes risk of injury to sensitive tissues
- Safer delivery of high concentrations
- No propellant or air burden to subjects
- Permits local and regional deposition to a lobe or lesion in larger species
- Can be sterilized with all standard heat or chemical methods
- Can deliver liquids and suspensions, as well as powders from nanoparticles to large porous particles
- Less likely to alter fragile biologics than ultrasonic and other heat-based systems
- More efficient delivery of expensive drugs



Essential tools for addressing pulmonary and systemic diseases

While not currently available for human use, these devices have been used in laboratory animals to test drugs for treating the full spectrum of pulmonary diseases, including: lung cancer,

emphysema, tuberculosis, pneumonia, asthma, cystic fibrosis, as well as systemic diseases, such as diabetes, Parkinson's disease, cardiothoracic disease, bone loss and stroke. Researchers have also found them to be very useful for creating models of disease, injury or inflammation, biohazards or environmental pollution.



Dramatic results with both liquid and dry powder administration

Penn-Century aerosolizers have been widely used in studies of pharmacological, toxicological and immunological responses in experimental subjects, across a wide range of applications. They permit more precise, efficient, targeted delivery – both of very minute and of relatively large volumes. Many studies suggest that they enable researchers to achieve a far greater impact using only a fraction of the dose that might be required by other types of drug delivery.

Extensive research results

More than 350 published papers, book chapters, posters and patents in a range of animal models have cited Penn-Century intratracheal delivery devices. They offer compelling evidence of their efficacy, not only for new drug development, but for potential clinical applications to treat a wide range of acute and chronic diseases. They have been shown to deliver far higher concentrations to the lung far more precisely than is possible via inhalation and far more safely and with far broader distribution than can be achieved by instillation of liquid droplets.

• Greater deposition and gene expression

In gene therapy studies for cystic fibrosis in monkeys, researchers found that lung deposition and gene expression were both significantly higher using the MicroSprayer® Aerosolizer. Lung deposition averaged 93% with a MicroSprayer® Aerosolizer compared to nebulizer depositions of less than 2% through a mouthpiece, laryngeal mask airway, or endotracheal tube. More significantly, delivery of the gene vector via a MicroSprayer® Aerosolizer resulted in protein expression in 62 - 80% of cells, compared to only 0.5% via a nebulized mouthpiece. (S.E. Beck, B.L. Laube, T. Flotte, 1999, 2000, 2001.)



• Greater efficacy at a fraction of the dose

In a rat model of brain injury, intratracheal aerosol delivery of only 2 mg of flurbiprofen with a MicroSprayer® Aerosolizer afforded almost complete (90%) neuroprotection, while oral administration of 50 mg of flurbiprofen was necessary to provide almost complete (66 – 86%) preservation of behavioral and histological indices. (H. Salzberg-Brenhouse et al. 2003)

• Greater concentration with fewer systemic effects

In a mouse model of lung cancer, local/regional administration of aerosolized chemotherapy with a MicroSprayer® Aerosolizer resulted in either no visible tumor development or significantly smaller tumor development than in the group receiving standard intravenous delivery. Lung concentration of radio-labeled, aerosolized chemotherapy was "50-fold higher" than i.v. administration – while using less than half the standard i.v. dosage, and with no pulmonary toxicity. (F. Gagnadoux et al. 2005)



MicroSprayer® Aerosolizer – Model IA-1C and FMJ-250 High Pressure Syringe

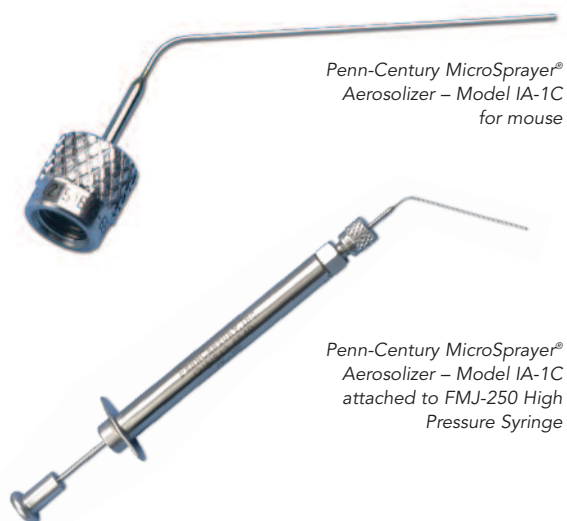
Liquid Aerosol Delivery

For mice, rats or larger species



The MicroSprayer® Aerosolizer – Model IA-1C operates with our FMJ-250 High-Pressure Syringe to generate a plume of soft mist directly into the lungs without any propellant or compressed air. Available in any length, and made entirely of sterilizable components, the Model IA-1C MicroSprayer® Aerosolizer can be inserted deep into the trachea up to the carina, or even in selected secondary airways of larger species. It produces a much deeper and more uniform distribution than is possible with liquid bolus or droplet instillation,

while permitting greater concentration, quantifiability and control than is possible with inhaler/nebulizer delivery. Aerosol is generated by a unique, patented atomizer at the very tip of the device. Standard sizes are available for mouse that measure (1 1/4") or rat (2") after a 120-degree bend. Custom sizes and configurations on request for nasal sprayers, straight tubes, or longer lengths for guinea pig, rabbit, dog, monkey, horse or other larger species.



*Penn-Century MicroSprayer®
Aerosolizer – Model IA-1C
for mouse*

*Penn-Century MicroSprayer®
Aerosolizer – Model IA-1C
attached to FMJ-250 High
Pressure Syringe*

Model IA-1C Specifications

- Based on 23-gauge stainless steel, thin-wall needle tubing with an outer diameter (o.d.) of .025" (.64 millimeters), except at the very tip which is .028" and an inner diameter (i.d.) of .017"
- Fully sterilizable, autoclavable, stainless steel and chemically-resistant internal components
- 1/4-28 tpi threaded female hub
- Available in any length or configuration (straight or with standard 120-degree bend)
- Suitable for insertion into an endotracheal tube or the working channel of a bronchoscope

FMJ-250 High Pressure Syringe Specifications

- Required for use with our Model IA-1C MicroSprayer® Aerosolizer
- Constructed of stainless steel and chemically-resistant components with a replaceable plunger with a Teflon® tip
- Fully sterilizable and autoclavable at standard temperatures
- Operates at 3000 psi
- Capacity: 250 µl. A set of clips is provided with each syringe to permit precise dosing of 25 or 50 µl, or combinations of those amounts

Particle size: When analyzed with laser defraction, the Model IA-1C produced a particle size distribution with a Mass Median Diameter (MMD) of 16-22 µm – when used with our special FMJ-250 High Pressure Syringe (sold separately). Results may vary, depending upon method of particle size analysis used, material delivered and sprayer tip length.

MicroSprayer® Aerosolizer – Model IA-1B

Liquid Aerosol Delivery

For rat, guinea pig and larger species



The MicroSprayer® Aerosolizer – Model IA-1B generates a plume of soft mist directly into the lungs without any propellant or compressed air. (The tubing used is somewhat larger than the Model IA-1C and not suitable for mouse.) Aerosol is generated by a unique, patented atomizer at the very tip of the delivery tube, producing a far higher concentration than is possible with a nebulizer/inhalation device and more uniform distribution than is possible with instillation of a liquid bolus or droplets. Available in any length, the Model IA-1B MicroSprayer®

can be inserted directly into the trachea – near to but not touching the carina – or via an endotracheal tube. Made entirely of sterilizable components, it operates with a disposable 1 cc polycarbonate syringe, one of which is provided with every device. It is available in standard sizes suitable for use in rat (2") or guinea pig (3") after a 120-degree bend, or in custom sizes of any length for larger species or other experimental applications.

Other Specifications

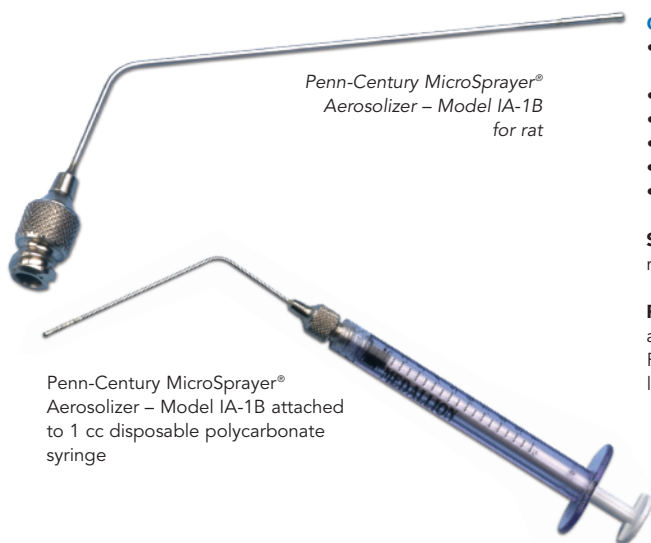
- Based on 19-gauge stainless steel, thin-wall needle tubing with an outer diameter (o.d.) of .042", except at very tip where it is .048", and an inner diameter (i.d.) of .032"
- Plasti-Mate luer hub
- Fully sterilizable, autoclavable, stainless steel and chemically-resistant internal components
- Operates at 700 psi
- Available in any length or configuration (straight or with standard 120-degree bend)
- Suitable for use with any animal except mice

Size options: Standard sizes available for rat (2") or guinea pig (3"). Custom sizes and configurations on request for nasal sprayers, straight tubes, or longer lengths for rabbit, dog, monkey or larger species.

Particle size: When analyzed with laser defraction, the Model IA-1B produced a particle size distribution with a Mass Median Diameter (MMD) of 25-30 μm – when used with a 1 cc polycarbonate syringe (provided). Results may vary, depending upon method of particle size analysis used, material delivered and sprayer tip length.

*Penn-Century MicroSprayer®
Aerosolizer – Model IA-1B
for rat*

*Penn-Century MicroSprayer®
Aerosolizer – Model IA-1B attached
to 1 cc disposable polycarbonate
syringe*



Dry Powder Insufflator™ – Model DP-4 and Model DP-4M

Dry Powder Delivery

For rat, guinea pig and larger species



Dry Powder Insufflator™ – Model DP-4

*The Dry Powder Insufflator™
– Model DP-4 for rat and
larger species (18-gauge
delivery tube)*

The Dry Powder Insufflator™ – Model DP-4 is an easy-to-use, hand-operated device designed to produce a cloud of fine powder particles from the end of a small-diameter delivery tube. The device twists open at the center to reveal a sample chamber that can be filled manually with a small amount (1 - 5 mg) of powdered material. By applying a puff of air to the device using a 3 ml plastic air syringe provided with it, it is possible to administer a range of dry powder substances to the lungs, regardless of particle size. Made of lightweight PEEK™ (polyetheretherketone) plastic and other completely sterilizable components, the Dry Powder Insufflator™ lends itself to precise quantification of the delivered dose – even of very minute quantities. It is available in standard sizes for use in a rat (2") or guinea pig (3") with a 120-degree bend, or can be ordered in custom lengths (short, long, straight) for larger species or other experimental applications.

*Dry Powder Insufflator™
– Model DP-4M for mouse
(23-gauge delivery tube)*

Dry Powder Insufflator™ – Model DP-4M for Mouse

The DP-4M Dry Powder Insufflator™ is especially designed for experimental use in a mouse. The special valve system for mouse is designed to be energized by a 200 µl puff of air. Best results are obtained when operated with the Penn-Century Air Pump – Model AP-1 (shown on next page) set for 200 µl.

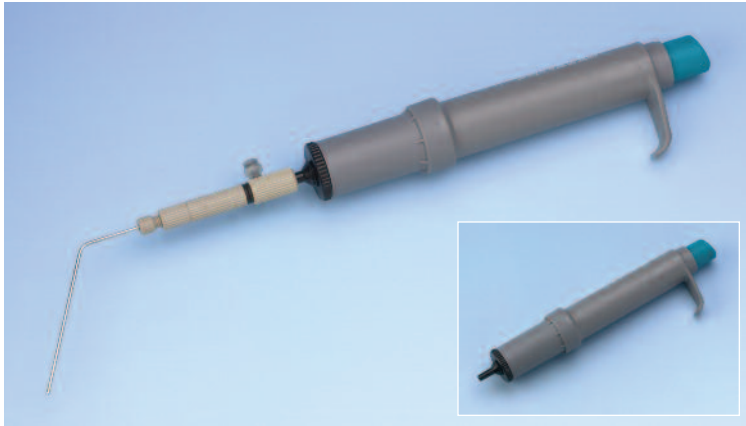
Particle size information: Based on user feedback, there are no limitations to the powder dimensions that can be delivered with the Dry Powder Insufflator™. The powdered sample can be of virtually any size formulation and is neither filtered by nor altered in any way by passage through the device.

Both the DP-4 and DP-4M have been used successfully to deliver everything from nanoparticles to macro- and large porous particles to bioactive materials.

Accessories for Penn-Century Devices

Penn-Century offers several helpful accessories for using our devices in animal models

Special air pump



Model AP-1 Air Pump

Designed to be used with our Model DP-4 and DP-4M Dry Powder Insufflator™, when a rapid succession of small air “puffs” is required, or when dosing many animals in sequence. Plastic construction with male luer slip tip. Hand-held, thumb operated.

Capacity: Because of its larger piston size and shorter thumb travel distance, this device is particularly useful in applications where dry powders are administered to mice. It is normally supplied with a displacement of 200 μ l per stroke. Air volume setting can be modified as needed, and calibrated to 0 – 5 ml of air, depending upon animal designated.

Air Pump – Model AP-1 is designed for precise, easily repeatable delivery of air to the Dry Powder Insufflator™

Visualizing the epiglottis



Model LS-2 Small Animal Laryngoscope

New and improved. Designed to clearly illuminate the trachea and epiglottis for intubation and insertion of a Penn-Century MicroSprayer® or Dry Powder Insufflator™. Now with a fiberoptic LED light source for clear, bright illumination. Each device comes with a custom-made small, tapered stainless steel blade for moving aside the animal's tongue. (Specify which animal when ordering). New easy-grip handle with curved ergonomic shape fits securely in the palm of the hand. Coated with non-slip Santoprene™ rubber. Operates with one 3-volt lithium battery (included). Autoclavable.

Small Animal Laryngoscope – Model LS-2

Accessories for Penn-Century Devices

Intracheal delivery to mouse



Mouse Intubation Platform

Simplifying intubation and pulmonary aerosol administration in mice
Endotracheal intubation of anesthetized mice can pose challenges due to the animal's small size and peculiar anatomy and the difficulty in visualizing the epiglottis. Researchers administering pulmonary aerosols to mice with Penn-Century's unique MicroSprayer® Aerosolizer and Dry Powder Insufflator™ face similar challenges. Having a platform especially designed for mouse intubation can make the process far faster, safer and easier.

To assist researchers working with our aerosol devices and other intubation procedures in mice, Penn-Century now offers a Mouse Intubation Platform. Designed by Sapio for Penn-Century, Inc., according to Bivas-Benita et al., *Eur J Pharm Biopharm*, 2005, this Plexiglass®/Perspex® platform has been extensively tested. It provides a simple, durable, lightweight, easy-to-use system for supporting the anesthetized mouse during intubation and/or insertion of our aerosol delivery devices.

The Mouse Intubation Platform includes:

- Solid Plexiglass®/Perspex® base and stainless steel support rod, easily attached to any standard lab holder/clamp setup (not included).
- Special adjustable neck support with Delrin® fittings to facilitate visualization of the trachea.
- Stainless steel posts with plastic "wire" maintain the anesthetized animal in the correct position for intubation, suspended from the front incisors.
- Two side posts to secure the mouse in position with a rubber band.
- Additional, adjustable stainless steel side posts prevent lateral movement of the mouse during intubation.

Other Specifications

The Mouse Intubation Platform is made of sterilizable Plexiglass®/Perspex® with stainless steel and Delrin® fittings. The base and fittings, including the nylon wire for suspending the animal may be cleaned with ethanol or Clorox®/Clidox® and re-used. Additional supplies provided include: hex wrench, rubber bands, additional nylon wire and screws.

Platform dimensions: 4.5" x 6 1/8 x 3/8" (15 x 23 x 6 cm)

Stainless steel support rod: 8" (20 cm)

Weight: 15.6 oz with support rod - (450 gr)

NOTE: For a detailed description of the intubation procedure with this type of platform, please refer to Bivas-Benita et al, Non-invasive pulmonary aerosol delivery in mice by the endotracheal route. *Eur J Pharm Biopharm*. 2005 Oct;61(3):214-8.

How to Order

All Penn-Century liquid and dry powder devices can be manufactured to standard or custom lengths in accordance with the needs of the customer. If you require a device that must be adapted to a particular research subject, sample material or application, or will be used in a bronchoscope or endotracheal tube, please contact us so that we may help you determine the specifications that will be most suitable for your needs.

Please note that Penn-Century devices are custom-made to order. Contact us prior to ordering to determine an estimate of delivery times.

Orders must include:

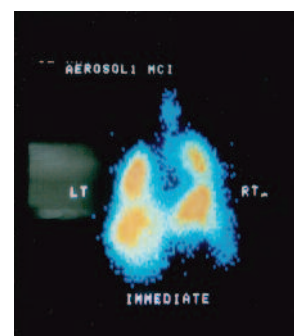
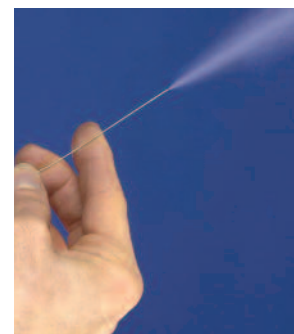
- Name of organization
- Name, address, telephone, fax and email address of researcher/investigator
- Name, address, telephone, fax and email address of purchasing agent
- Purchase Order number
- Billing address
- Shipping address with phone number of local contact
- Quantity and type of device(s). Please specify animal to be used or exact custom length, if desired.

Orders may be submitted via email to info@penncentury.com or fax (215) 220-3040

Orders can also be sent by post to:

Penn-Century, Inc.
7670 Queen St., Suite 200
Wyndmoor, PA 19038-8031 USA

Penn-Century devices are for laboratory use only.



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Ask for a copy of our bibliographic reference list

Penn-Century's line of pulmonary delivery devices is helping researchers explore new possibilities beyond the limitations of inhalation/nebulization and liquid bolus delivery systems. Ask us for a copy of our bibliographic reference chart of the more than 350 published papers, book chapters, posters and drug patents citing our devices. Learn more about what diseases are being studied and what materials delivered with them.

If you have additional questions, please contact us at info@penncentury.com.

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