PennCentury

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Instructions for use of a Penn-Century MicroSprayer® Aerosolizer - Model IA-1C and FMJ-250 High Pressure Syringe

► For precise aerosol doses of 25-µl to 250-µl in Mouse, Rat or Custom Length



MicroSprayer®/Syringe Assembly - MSA-250

Precise, hand-operated and air-free

The Penn-Century MicroSprayer[®] Aerosolizer – Model IA-1C is a unique, patented atomizer that can be used for precise, pre-clinical aerosol administration. Together with the FMJ-250 High-Pressure Syringe that is required to operate it, the devices produce a highly concentrated, <u>air-free</u> aerosol from the end of a small-diameter delivery tube. These devices have been used to aerosolize a wide range of pharmaceutical, biologic, toxicologic and other liquids, solutions and suspensions. They permit precise administration to the lungs, nasal cavities or other *in vivo* and *in vitro* experimental applications. They are frequently used for research, analysis and testing of pulmonary drug delivery methods and inhalation and respiratory drugs and devices. These devices have unique requirements for their operation and care. They require skill and practice for best, correct use – particularly for intratracheal applications. They also require special attention to maintain in good working condition. **We urge you to review the following information completely before using these devices for the first time.**

Planning for use - What you need to know before you start

The Penn-Century MicroSprayer[®] Aerosolizer - Model IA-1C and FMJ-250 High Pressure Syringe are unlike any other hand-held atomizer. These devices have been designed to permit rapid, precise, efficient pulmonary administration of aerosols. The ability to achieve reproducible data depends entirely on the skill of the user. It takes practice, patience, skill and manual dexterity to use these devices correctly as intended, particularly for intratracheal *in vivo* applications. Because of their unique design, careful attention is also required to maintain them in good working condition.

1. Understand how this technology works

The MicroSprayer® Aerosolizer – Model IA-1C is a unique, patented <u>air-free</u> atomizer that works by manual pressure only. There are tiny components in the tip of the device that help generate an aerosol when liquids, solutions or suspensions are pushed through them with sufficient speed and force, using our patented FMJ-250 High Pressure Syringe. This syringe has been designed to provide the correct pressure for operation of the MicroSprayer® Aerosolizer – Model IA-1C. The FMJ-250 cannot be substituted for another type of syringe. The syringe contains a glass liner inside covered by a metal "jacket" on the outside.

2. All air must be eliminated from inside the syringe and MicroSprayer® before use

This atomizer generates an aerosol by manual pressure only - rather than use of compressed air or gas. If there is any air that is trapped inside of the syringe or the tubing of the MicroSprayer[®], it will produce a stream of liquid rather than a uniform cloud of aerosol. If the plunger is pushed too slowly, only a stream is produced. Because the FMJ-250 High Pressure Syringe is opaque, the user cannot see air bubbles trapped inside. Therefore, the user must learn to correctly fill the syringe and eliminate air before use by methods described below.

3. The user must practice first with water in the open air

During *in vivo* intratracheal use, the user will not be able to observe the aerosol coming from the MicroSprayer[®]. Therefore, it is essential to practice use of the device with water in the open air to experience how rapidly and with how much force the plunger of the syringe must be pushed to produce a uniform puff or plume of aerosol. If there is any air trapped inside the syringe, this will degrade the uniformity of the aerosol. Before *in vivo* use with the test formulation, the user must practice 1) loading the device correctly with water 2) eliminating any air 3) learning how fast to push the plunger to produce a uniform aerosol without streaming.

4. The user must practice attaching and using special dose measurement spacers to the syringe

Because the FMJ-250 High Pressure Syringe is opaque, the user cannot measure the dose as they would when using an ordinary glass or plastic syringe. A unique system is provided with this kit for measurement of dose volumes of 25 or 50 microliters or multiples of those volumes, up to a maximum capacity of 250 microliters. It is described in detail below. The user must practice using this special system of dose measurement prior to *in vivo* use to achieve consistent results.

5. The MicroSprayer[®] Aerosolizer must be cleaned fully to avoid blockage

As noted above, the MicroSprayer[®] Aerosolizer is a unique atomizer. <u>Contrary to appearances, it is not a hollow</u> <u>catheter, cannula or needle.</u> Aerosol is generated when formulations are pushed with sufficient speed and manual pressure through tiny patented components in the tip of the MicroSprayer[®]. <u>The inner diameter</u> <u>through these components for the Model IA-1C is about 60 microns in diameter</u>. When it is used to administer particle suspensions, additional care must be taken to clean the MicroSprayer[®] Aerosolizer according to our instructions below to prevent a build-up or agglomeration of suspended particle material in the tip that can block or clog it and interfere with performance.

6. Both the MicroSprayer® Aerosolizer and FMJ-250 High Pressure Syringe must be handled with care. The MicroSprayer® Aerosolizer is made of narrow, stainless steel tubing that is somewhat flexible. However, care must be taken not to manipulate it or force it into a sharp bend or crease, as this will damage it beyond repair. The FMJ-250 High Pressure Syringe has a glass liner hidden inside. The outside of the syringe is smooth and slippery. If it is accidentally dropped, the glass liner inside of it can crack and will be damaged beyond repair.

7. Users must test the feasibility of aerosolizing their own formulations prior to experimental use

This technology has been cited in hundreds of peer-reviewed published studies in which it was used successfully to aerosolize a wide range of pharmacologic and biologic materials and toxicological agents, including nanoparticles, viral and bacterial agents, liposomes, proteins, peptides and oligonucleotides. In general, many studies have demonstrated that the MicroSprayer® technology does not exert shear stresses on the viability of biologic materials as do systems dependent on compressed air. However it is the responsibility of the user to test their own formulation with this technology prior to use in an *in vivo* or *in vitro* model. Users are responsible for determining the feasibility of aerosolization of their particular formulation at the dose volume, composition and frequency they wish to use. In particular, researchers must:

- Test the effect upon their own formulation when it is aerosolized with this technology and
- Test their ability to aerosolize the same formula repeatedly in the MicroSprayer[®] Aerosolizer without clogging (blocking) of the tip.
- 8. Users must practice *in vivo* use with imaging agents or dye *before* use with their formulation Even when users have done intubation in past, it is important allow time to practice *in vivo* use of the MicroSprayer® Aerosolizer BEFORE working with your test formulation to confirm that the tip of the MicroSprayer® was correctly positioned. Some materials used for validating deposition include dye, radioopaque contrast or imaging materials such as Technetium-99m, or fluorescent particles in suspension. This permits the user to observe if the test formulation was uniformly distributed in the lungs, or was mostly deposited in the trachea or swallowed. If a dye is used, we recommend very dilute (< 1%) solution of laboratory dye, such as Methylene blue or Evans blue, or similar. (We strongly discourage using India ink for this purpose, as it may contain carbon particulates or shellac that can clog the sprayer tip over time.) If the solution is not sufficiently diluted, it can clog the tip of the sprayer. Be sure to flush the device fully after use.
- 9. We offer helpful accessories. Penn-Century also makes several helpful accessories, including a Small Animal Laryngoscope and a Mouse Intubation Platform to help users quickly and easily visualize the epiglottis and insert the tip of the MicroSprayer® Aerosolizer more rapidly, safely and easily for optimal results.
- 10. Before starting, users must have a plan how they will determine and measure dose deposition and dose response. This device has been designed to permit rapid, precise, efficient and safe pulmonary administration of aerosols. Use of this equipment for intratracheal applications requires understanding of correct intubation and anesthesia techniques in experimental animals. The ability to do this depends entirely on the skill of the user. As manufacturers, we cannot advise on these methods. Once the animal has been correctly anesthetized, the user must practice insertion of the MicroSprayer® and operation of the syringe in a manner that will result in consistent, uniform deposition of the aerosol in the lungs without injury to the animal.
- 11. Mastering the variables leads to more reproducible and relevant data. The use of this intratracheal technology requires mastering many different variables for correct use. Until these variables are mastered and the researcher can operate and maintain the devices consistently as intended, they will have no way to distinguish if the data they obtain was the result of their formulation and dose size or was caused by incorrect insertion or care of the equipment. Once the user has mastered the ability to insert and operate the device in a reliable, safe and consistent manner, they must have a plan for how they will determine and quantify dose deposition and dose response in the lungs. As manufacturers, Penn-Century cannot advise users on these methods, but examples can be found in the more than 1,300 scientific publications citing our liquid and dry powder devices.

CAUTIONS FOR INTRATRACHEAL IN VIVO USE

<u>Use of liquid or dry powder Penn-Century devices for intratracheal applications is a form of intubation</u>. Familiarity with intubation and anesthetized animal prep is a prerequisite for use of these devices. Unlike other forms of intubation, intratracheal aerosol administration with these devices requires some hand motion for to produce an aerosol. When using any Penn-Century intratracheal aerosol device – whether liquid or dry powder, the user must push the plunger of the syringe fast to aerosolize the material inside. For optimal lung deposition, the tip of the delivery tube must be positioned near to, but not touching the carina. <u>Therefore, the user must</u> <u>exercise care and attention to minimize any forward motion of the hand while pushing quickly and firmly on the plunger, to prevent trauma or injury to the animal.</u>



Correct placement in the trachea is essential. For obtaining the best results for intratracheal use, the placement of the very tip of the delivery tube is critical. In published studies, optimal lung deposition from Penn-Century intratracheal aerosol devices is obtained when the very tip is carefully positioned in the trachea so that the very tip is near to <u>but not touching the carina</u> (first bifurcation) of the anesthetized animal. If the tip of the MicroSprayer[®] Aerosolizer is inserted only halfway down the trachea, it is possible that the aerosol will only impact against the walls of the trachea, turn to large droplets and be coughed or swallowed. If the tip is too close to the carina, injury can result when the plunger is pushed with sufficient force to generate an aerosol.

SUMMARY OF KEY FEATURES:





MicroSprayer® Aerosolizer Model IA-1C

- Materials: Based on flexible, 23-gauge stainless steel tubing and other chemically resistant components
- **120-degree bend:** All standard devices made with a 120-degree bend to make it easier to see around one's hand when trying to view the epiglottis. (Straight custom devices can be ordered.)
- Length of intratracheal portion: 1.25"
- **Hub:** 1/4-28 tpi
- Tip is rounded to avoid harm to delicate tissues during insertion.
- Operates only with: Penn-Century's patented FMJ-250 High Pressure Syringe (REQUIRED)
- Dose range: When used with FMJ-250 High Pressure Syringe, can administer dose volumes up to 250 microliters, or multiple smaller doses of 25 to 50 microliters or combinations of those dose volumes, using dosing spacers provided.
- Outer diameter: .025" (0.64 mm), except at the very tip which is .028" (0.71mm)
- Inner diameter: .017" (0.43 mm) (NOTE: Liquid passes through patented aerosol components at the very tip. The diameter of these passageways in the Model IA-1C is approximately 60 microns in diameter.)
- **Re-usable/Sterilizable:** Can be cleaned and sterilized with very hot (filtered or distilled) water, organic solvents, by autoclave or ultrasound.

FMJ-250 High-Pressure Syringe

Required for use with MicroSprayer® Aerosolizer – Model IA-1C

- **Description:** Unique patented air-free, gas tight syringe. Made of stainless steel outer layer with a borosilicate glass liner, a PCTFE seal and other chemically resistant components, and designed to be sterilized and re-used. It is subject to breaking if dropped on a hard surface.
- Pressure: Operates at up to 3000 psi.
- Hub: 1/4-28 tpi (Note: <u>Not</u> a luer hub)
- **Materials:** Constructed of stainless steel and chemically-resistant components with a replaceable plunger with a Teflon[®] tip. May be used with any length Model IA-1C.
- Maximum Capacity: 250 µl (microliters).
- Dose increments: The syringe is opaque and has no external measurement marks. A set of dose volume "spacers" is provided with each to device to permit accurate measurements of doses of either 25 or 50 microliters, or combinations of those amounts. These are attached to the plunger, and removed one by one, per instructions provided, to permit precise single doses of either 25-µl or 50-µl, or combinations of those amounts. Syringe can used for administration of multiple doses.
- Re-usable/Sterilizable: Can be cleaned and sterilized with hot water, organic solvents, or by autoclave or ultrasound.

Removing air bubbles from the syringe

When loading the FMJ-250 High Pressure Syringe for the first time, air bubbles will typically become trapped inside that are not visible to the eye. Any air that is trapped inside of the syringe or in the MicroSprayer[®] will degrade the uniformity of the aerosol and lead to streaming. <u>All air bubbles must</u> <u>be "purged" or eliminated before the MicroSprayer[®] is attached and the device is used, using the Air Purge Kit provided by Penn-Century, according our instructions below.</u> After first purging the air, the syringe can be refilled again and again without introducing more air into it.

- <u>The Penn-Century MicroSprayer® Aerosolizer is an air-free aerosol system.</u> Air bubbles may on occasion become attracted to the hydrophobic Teflon® tip of the plunger in the FMJ-250 syringe while you are filling it causing the quality of the spray to degrade. One sign of air in the syringe is that when you use it to spray, you may observe hair-like streams or partial streaming instead of a uniform cloud of aerosol. In order to deliver discrete sprays of small doses (no streaming at the beginning or end of the spray cycle), the FMJ-250 syringe must be completely free of air bubbles. Users must practice loading and spraying with water and with the solution to be used to assure they have eliminated all air.
- If the spray quality indicates the presence of air bubbles, the user must eliminate these by using the special Air Purge Kit provided. This kit has a soft white dispensing tip that will not scratch the syringe or damage the Teflon[™] tip of the plunger.



1. Dry the inside and outside of the FMJ-250 Syringe with compressed air: Be sure all liquid is removed from the FMJ-250 Syringe barrel before proceeding. This can be accomplished by removing the plunger and blowing a small amount of compressed air through the FMJ-250 Syringe using compressed air in a can such as is available for cleaning computer keyboards or camera lenses. It should be possible to see clearly from one end to the other when holding the syringe barrel to the light.

2. <u>Re-insert the plunger until it is almost, but not fully, pushed in</u>.

- 3. <u>Find and fill your Air Purge Syringe.</u> Locate the Air Purge Kit provided with your devices. Remove the protective blue tip from the 1 cc plastic syringe. Attach the special red plastic (polypropylene) dispensing tip to the plastic syringe and fill the assembly with test formula or water.
- 4. <u>Eliminate all air bubbles from the plastic Air Purge syringe</u> by holding it in a vertical position and tapping and flicking the sides of the plastic syringe vigorously with your fingernails to drive the bubbles upwards to the tip. Push the plunger to squeeze out all air. Immerse the tip of the Air Purge syringe in water or your formulation to assure that no air is in the syringe or dispensing tip.

- 5. Use the Air Purge Syringe to fill the FMJ-250 Syringe until air bubbles are released. Grasp the FMJ-250 Syringe vertically with the tip facing upward, and pull back the plunger to a distance about equal to the length of the white dispensing tip of the Air Purge syringe. Insert the white dispensing tip into the open end of the FMJ-250 Syringe and begin to fill the FMJ-250 Syringe from the plastic syringe, (as shown on previous page photo on far right). Observe as you do this that bubbles of air may escape from the tip of the FMJ-250 Syringe. You may need to refill the plastic Air Syringe 2-3 times and reinsert in the FMJ-250 Syringe and keep filling until there are no more air bubbles escaping from it.
- 6. When there are no more air bubbles escaping the FMJ-250 Syringe, slowly withdraw the white dispensing tip of the Air Purge syringe, so that by the time the white dispensing tip is almost completely removed, you see a "bulge" of excess water a "meniscus" that has formed at the distal tip of the FMJ-250 Syringe. Now, set aside the plastic Air Purge syringe. Immerse the distal tip of the FMJ-250 Syringe in either water or in the solution to be administered, and push the plunger to expel the small amount of liquid that remains inside of the FMJ-250 syringe. Pull back on the plunger of the FMJ Syringe and fill it to capacity. If the distal tip of the FMJ-250 Syringe is maintained below the liquid you use to fill it, you can avoid reintroducing air into it. Attach the MicroSprayer® Aerosolizer, push some of the liquid through it to eliminate any air in side of the MicroSprayer®. Detach the MicroSprayer®, load the syringe as noted below and the system is ready to operate.
- 7. **NOTE:** Nothing prevents the plunger of the FMJ-250 from being pulled out completely! Be careful to observe how far you can pull the plunger up without pulling it out completely. If the plunger is pulled out completely, air can be reintroduced into the FMJ-250 Syringe.
- 8. Another method to rid the system of air bubbles is to remove the plunger from the FMJ-250 barrel and, using the Air Purge syringe, inject liquid into the proximal end of the FMJ-250 barrel (where the plunger is inserted) while holding the barrel in a horizontal position. A meniscus or curve on the surface of the liquid will appear at the mouth of the FMJ-250 barrel. If there is difficulty in getting the meniscus or bulge to appear, hold the FMJ-250 barrel so that the mouth (proximal end) is pointing slightly downward. Place a drop of your test formula or water on the FMJ-250 Teflon plunger tip and bring the tip into contact with the meniscus. Push the plunger all the way in and proceed as above.



<u>NEVER load the syringe through the</u> <u>MicroSprayer® Aerosolizer as it may make it</u> <u>more likely to become blocked or clogged.</u>

How to fill the FMJ-250 High Pressure Syringe with your formulation



Method 1: Fill syringe directly

Method 2: Use Air Purge Kit syringe

Method 3: Attach Luer Adapter and any standard needle

You have a choice of three methods for loading the FMJ-250 High Pressure Syringe. The maximum dose capacity of the FMJ-250 High Pressure Syringe is 250µl. Once it is filled, it can be used to administer either one complete dose of 250 microliters or multiple smaller doses, using the volume spacers provided. (See below). There are three standard methods for filling the device. <u>NEVER load the syringe through the MicroSprayer®</u> <u>Aerosolizer. NEVER insert a sharp object or needle down into the syringe tip, as this may scratch or damage the syringe seal or the white Teflon™ tip of the plunger. Depending on the material being used, you may use any of the following methods to fill the syringe:</u>

- Method 1: Remove the MicroSprayer[®] Aerosolizer from the syringe and immerse the distal end of syringe into the solution to be delivered. Pull back on the plunger. <u>Note: If you pull too far, the plunger will come all the way out.</u>
- Method 2: Your FMJ-250 High Pressure Syringe comes with an Air Purge Kit that can be used to eliminate air bubbles that may become trapped inside the syringe. The 1 ml plastic syringe supplied with the kit can also be used to fill the FMJ-250 Syringe. This syringe comes with a soft dispensing tip (red) that can be attached to the plastic syringe and inserted into the distal end of the FMJ-250 Syringe to fill it. The red plastic tip is soft and will not scratch the seal of the FMJ-250 syringe or the Teflon™ tip of the plunger. If this method is used, remove the plunger of the FMJ-250 syringe completely, hold it in an almost horizontal position with the distal end slightly higher, and begin to fill the device from the distal end until the liquid wells up as a bulge or meniscus at the proximal end. Then, gently insert the plunger into the proximal end. Remove the air purge syringe and attach the MicroSprayer[®].
- Method 3. You may fill the syringe from a sterile glass vial or other reservoir by attaching a hypodermic or blunt dosing needle to the FMJ-250 syringe. <u>Note that the tip of the FMJ-250 Syringe does not have a standard luer fitting</u>. If you wish to attach a needle with a standard luer screw thread to the FMJ-250 Syringe, you must first attach the <u>red</u> Luer Adapter that was provided with your equipment to the FMJ-250 Syringe. Then, attach any standard hypodermic or blunt dosing needle to the Luer Adapter. Then, insert the tip of the needle directly into the test material, or through the septum of a glass drug container, and pull back on the plunger to fill the syringe fully. Remove both the needle and adapter after filling. Attach the MicroSprayer® Aerosolizer.

Attaching and using the dose volume measurement spacers ("stops")

Each FMJ-250 High Pressure Syringe is supplied with a set of five 25-µl and five 50-µl dose volume spacers to precisely administer doses of those sizes or combinations of the two. These volume spacers are easily attached to the plunger of the syringe, pushed tightly together and carefully removed one by one. The gap or space that remains defines one dose of that particular volume. In this way, multiple doses can be administered with one full syringe.





Pull the plunger out far enough to make room for the spacers you wish to use. Attach dose volume spacers as desired to the plunger rod. Press down on the thumb button of the plunger until spacers are pushed tightly against the plunger handle. Remove one by one for precise individual aerosol doses.

- While filling the syringe, pull back on the plunger so there is enough space to attach the appropriate spacers to the plunger rod. This will require practice and attention. <u>Note: If you pull back on the plunger</u> of the syringe when the tip of the syringe is exposed to the open air, you will introduce more air into it that will need to be eliminated. If you pull the plunger too far, the plunger will come all the way out. This can cause air to enter the syringe.
- Select the dose volume you wish to administer. You may administer individual doses of 25 or 50 microliters, or combinations of those volumes by using more than one spacer.
- **3.** The volume spacers will snap onto the plunger rod with a clicking sound.
- 4. When all spacers are attached, push in the plunger firmly until the all the volume spacers are pushed tightly together against the top of the syringe, with no gaps. Some test formula may be ejected as you do this. This is desirable as it will help assure accurate dosing and eliminate any air that may remain.



5. The system is now ready.

- 6. To administer Dose #1, carefully remove the spacer or spacers closest to the thumb button of the plunger that equal the dose volume desired. <u>BE CAREFUL NOT TO CHANGE THE POSITION OF THE PLUNGER as you do this.</u> After one dosing spacer is removed, the gap or space that remains equals the volume of that dose.
- Push in the plunger with quick, sharp, firm and fast motion to produce a uniform puff of aerosol spray. If the motion is too slow or gradual, you will produce only a stream.
- Then, remove the next spacer and repeat.
- In this way, a series of doses (for example, five 50 µl doses) can be delivered sequentially, one after the other, from one animal to the next, before the syringe needs to be refilled.



- Practice first with water. It is best to practice use of the volume spacers with water to get a sense of the thumb pressure that is required. Pressure should be quick and firm not tentative, gradual or slow to create a full plume of aerosol, especially at small volumes.
- Be mindful of air bubbles in the syringe. Particularly when trying to administer small doses, any air bubbles trapped in the syringe when it was filled will impair performance. When you practice using the device, if you observe streaming, or small, hair-like streaks in the aerosol, or a large droplet at the end of pushing, may indicate that there are air bubbles that are trapped in the syringe that must be forced out or "purged."





Determining the dose response curve and optimal dose range for in vivo use

Once it is filled, the FMJ-250 High Pressure Syringe can be used to administer precise multiple doses up to 250 microliters, in aliquots of either 25µl or 50µl, or combinations of those (i.e. 75 or 50 microliters. Typical delivery volumes for mice are 25µl and 50µl and 50-100µl for rats. However, far higher volumes have been reported in those animals and others. Research with these devices has successfully demonstrated a far broader dose range is not only possible with MicroSprayer[®] Aerosolizer but safe and effective.

Intratracheal aerosol administration with our technology has been shown to permit more efficient use of smaller volumes and the administration of far larger dose volumes than would be safe or feasible by air-driven, nebulizer type systems targeting the nose or by liquid droplet instillation methods. It is the responsibility of the researcher to perform feasibility studies prior to administering their formula – proceeding stepwise in small increments if necessary – to determine the safest and most effective dose and get an accurate picture of dose response. This dose range will vary according the *in vivo* model being used, the potency and volume of the drug – and will also be affected by the skill of the user. There is no universal dose volume that applies to all drugs or animals. Approaching the question of dose volume with an open mind may yield valuable information.

Care of MicroSprayer® Aerosolizer – Model IA-1C

<u>The MicroSprayer® Aerosolizer must be cleaned immediately and thoroughly after use to</u> <u>maintain it in good working condition.</u>

Basic guidelines for cleaning

The MicroSprayer[®] Aerosolizer_consists of stainless steel and other chemically resistant components and can be subjected to any standard sterilization or autoclaving procedure: gas, liquid, wet, dry, heat, cold, *dilute* acids, *dilute* bases, etc. In addition, the MicroSprayer[®] Aerosolizer can be heated as high as 500 degrees Fahrenheit. To avoid damage to the device, if you are uncertain about use of a particular method or material, PLEASE CONTACT US FIRST.

It is essential to fully clean, test, dry and properly store your device after use to insure that it performs as it should. Solutions and suspensions used in the device are forced under pressure through patented atomizing components at the tip of the MicroSprayer® Aerosolizer. Over time, if the device is not fully flushed out and cleaned after use, there may be a build-up of residual material that hardens and clogs the tip. Users must also be mindful not to place the device on dirty or dusty surfaces when not in use.

- <u>To minimize clogging, solutions should be filtered before spraying</u>. Some suspensions of particles may need to be filtered to avoid a larger particle that blocks the tip.
- **Reasonable care should be taken to avoid dust and dirt which can foul the sprayer tip**. For instance, when placing the assembled system or individual components on a surface, it is best to avoid surfaces from which the device might pick up dirt or lint. A large, clean Petri dish works well for this purpose.
- <u>ALWAYS clean and fully flush the MicroSprayer® Aerosolizer after use with very hot distilled or filtered</u> water. You may also use any organic solvent, such as ethanol, xylene or acetone to dissolve any materials that may be inside. If you wish, you can soak the devices in any of these as well, to soften any material that has become hardened in it, and then flush it out with the same solution using the syringe. You may fill the syringe with solvent and spray it into an enclosed container. (ALWAYS USE CAUTION WHEN SPRAYING ANY SOLVENT OR HAZARDOUS CLEANING AGENT TO FOLLOW SAFETY INFORMATION PROVIDED AND AVOID CONTACT OF THE SPRAY WITH EYES, FACE OR SKIN.
- The MicroSprayer[®] Aerosolizer is best sterilized with solvents known to be effective in dissolving whatever has been used for the test article or formulation. Preferred cleaning agents are non-alkaline, non-phosphate, non-acid and non-detergent based.
- The MicroSprayer[®] Aerosolizer <u>may also be autoclaved at standard sterilization temperatures.</u>
- It is best to <u>avoid</u> cleaning the device with undiluted acid or base solutions, or bleach (Clorox[™]/Clidox[™]), as these can be corrosive. If you have questions, contact us before using.
- Never use a flame or high heat to clean the MicroSprayer[®] Aerosolizer as this may damage it beyond repair.
- Do not subject the MicroSprayer[®] Aerosolizer to extreme changes of temperature.

Always test the MicroSprayer® Aerosolizer after cleaning

ALWAYS TEST THE MICROSPRAYER® AEROSOLIZER AND FMJ-250 HIGH PRESSURE WITH WATER

AFTER CLEANING and before storing to observe that the sprayer continues to deliver a full, uniform plume of spray that looks as good as it did when the device was new.



1: After testing, blow air to remove excess liquid 2: Clean and reattach protective cap 3: Store in box

- <u>After testing the devices with water and determining they are work as normal, blow air through the</u> <u>MicroSprayer® Aerosolizer fully before storing to expel all remaining liquid inside</u>. Direct a small stream of compressed air into the threaded sprayer hub of the MicroSprayer® Aerosolizer until all fluid remaining in the sprayer tip is expelled. Products such as "DUST-OFF" or similar for cleaning computer keyboards are also suitable.
- 2. Do not blow compressed air through the device without testing it first with water. If the tip is partly clogged, drying it with air will may further harden any partially dissolved material in the tip or drive a piece of dirt or dust further into the tip.
- 3. <u>ALWAYS clean and blow dry the white protective plastic end cap that came with the MicroSprayer®</u> <u>Aerosolizer and screw it back on before storing it to remove any dust or grit that has gotten on it</u>
- 4. Always store the MicroSprayer[®] Aerosolizer and FMJ-250 Syringe in the original boxes in which they were shipped to prevent it from getting dropped or bent.

What to do if MicroSprayer® Aerosolizer becomes blocked or clogged



If the MIcroSprayer[®] tip starts to become partially blocked, you will notice an increase in the force required to depress the syringe plunger. IF SO, STOP PUSHING!

In general, it does not help at this point to increase the force on the plunger as this may only serve to further drive the offending material into the small passages of the sprayer tip or cause damage to the plunger or syringe. If this occurs:

- 1. Remove the MicroSprayer[®] Aerosolizer and soak it in very hot, boiled dionized or distilled or filtered water, or soak in organic solvent and draw back on the syringe plunger, holding it in the fully retracted position for 15 seconds.
- Reattach the MicroSprayer[®] Aerosolizer to the FMJ-250 Syringe. With the tip of the MicroSprayer[®] Aerosolizer in very hot water or organic solvent, attempt to pull back on the plunger of the syringe. Then remove the MicroSprayer[®] Aerosolizer, eject the contents of the syringe and flush it thoroughly with water. Repeat.
- 3. It is perfectly safe to clean the device with stronger organic solvents (It is safe to push through any organic solvent methanol, ethanol, even acetone, chloroform, Trichloroethylene).
- 4. NEVER insert a pin or needle into the hole at the tip of the MicroSprayer[®] Aerosolizer to clear it. This could crack or damage the aerosolizing components.
- 5. USE CAUTION when using ultrasound cleaners with the MicroSprayer[®] Aerosolizer. It is possible to immerse the MicroSprayer[®] Aerosolizer in an ultrasound with water or solvent to try to remove blocked material. AVOID placing the tip of the MicroSprayer[®] Aerosolizer directly on the bottom surface of the ultrasound as the vibration may alter or damage the components in the tip. We do not know if repeated use of ultrasound will affect the device. This should be used as a last resort only.
- 6. The following method has been successful for some users: SDS (sodium dodecyl sulfate) 5% NaHO (NaOH Sodium hydroxide) 2%; then Ultrasound; then Autoclave.
- 7. If that doesn't work, and the MicroSprayer[®] Aerosolizer is completely blocked and is not letting any liquid pass through at all, contact Penn-Century, Inc. for additional recommendations.
- 8. Recently, Penn-Century has introduced a new tool for unblocking the tip of the MicroSprayer[®] Aerosolizer that uses the pressure of the FMJ-250 High Pressure Syringe to push solvent or hot water in reverse from the tip to hub of the sprayer. **Contact us for details about this "Reverse Cleaning Adapter."**

Care of the FMJ-250 High Pressure Syringe



The FMJ-250 High-Pressure Syringe is made of stainless steel outer layer with a borosilicate glass liner, a PCTFE seal and other chemically resistant components. It is designed to be sterilized and re-used.

NOTE: The FMJ-250 High Pressure Syringe is very durable and will withstand normal use. There is a borosilicate glass liner (bore) inside the syringe that can crack, however, if the syringe is subjected to temperatures higher than standard autoclave temperatures, or to sudden temperature contrasts, or is dropped on the floor or forcefully strikes a hard surface. If this occurs, the syringe may leak or the plunger may no longer move smoothly up and down in the glass bore of the syringe. If the glass liner is cracked, the syringe will not function properly and the device will not be repairable.

Cleaning Syringes

- The FMJ-250 High Pressure Syringe is best sterilized with solvents known to be effective in dissolving whatever has been used for the test article or formulation. Preferred cleaning agents are non-alkaline, non-phosphate, non-acid and non-detergent based.
- Rinse the syringe after use with an appropriate solvent or cleaning agent. Following the use of a cleaning agent, rinse the syringe with deionized water. Remove the plunger and blow excess liquid from the inside of the syringe and the plunger. Be sure that there is no residual cleaning agent in the syringe before using or storing the syringe. ALWAYS clean, blow off and put on the protective the black end cap back on the syringe before storing and in the original protective plastic box provided on shipment

Sterilizing, Autoclaving, and Disinfecting

- Avoid use of bleach! Do not soak or submerse the entire syringe in any cleaning agent as this may weaken bonding materials over time. The FMJ-250 Syringe and plunger <u>should never be soaked in</u> <u>bleach</u> (Clorox[™] or Clidox[™]) as this may cause permanent corrosion and/or staining.
- **Sterilizing**. The FMJ-250 Syringe may be sterilized with appropriate sterilizing agents such as ethylene oxide.
- Cautions about Autoclaving. FMJ-250 Syringes may be autoclaved, at autoclave temperatures up to 115 °C. However, please be aware that over time autoclaving may shorten the syringes' life expectancy. Stainless steel expands faster than glass upon heating, so, autoclaving may cause strain to glued surfaces and may eventually lead to adhesive deterioration. BEFORE AUTOCLAVING, ALWAYS REMOVE THE PLUNGER FROM THE SYRINGE.

Replacement plungers for FMJ-250 High Pressure Syringe

After long use or from over-pressuring the system, the white Teflon[®] tip of the syringe plunger may become worn. One symptom of this is that the plunger may feel loose, or may leak from its proximal end (around the plunger rod). If this happens, a replacement plunger may be purchased from Penn-Century, Inc. without having to replace the entire syringe. Contact us for details.

Reminder: ALWAYS test both the MicroSprayer[®] Aerosolizer - Model IA-1C and FMJ-250 High Pressure Syringe with water if they have been stored and not used for a long period of time.

For a full summary of the company's repair and warranty policies, please review the Penn-Century Terms and Conditions.

As manufacturers, Penn-Century, Inc. can offer:

- Product knowledge
- Operation of our devices
- Familiarity with published studies related to use of the same device and, if possible, similar drugs
- Familiarity with customer feedback about them

IMPORTANT NOTICE: Requirements for references to Penn-Century devices in publications, abstracts and presentations

As a condition of sale, the Buyer agrees that upon publication or presentation of any research conducted using a Product, <u>the Penn-Century name as the</u> <u>manufacturer</u> ("Penn-Century. Inc. Wyndmoor, PA") and the name of the Products must be correctly spelled and cited, and include Penn-Century's registered trademark and model number as follows and as applicable: "MicroSprayer® Aerosolizer – Model ____", "FMJ-250 High Pressure Syringe", "Dry Powder Insufflator™ - Model ____" or "Small Animal Laryngoscope – Model LS-2". A breach of this section shall result in immediate harm to Penn-Century, and in addition to any and all rights available to Penn-Century, Penn-Century shall be entitled to an injunction or other equitable relief as a remedy for such breach.

For any questions, contact us at Penn-Century, Inc. – info@penncentury.com or 215-753-6540.

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