

# Surgical Protocol

**Micro** SMP-300



## Recommendations for Intravenous Administration in Mice

### INTRODUCTION

iPRECIO® is a completely implantable, programmable micro-infusion pump system for experimentation in small laboratory animals. The pump has a built-in microprocessor which can be programmed to administer small volumes, in vivo, for extended durations. Additionally, the pump houses a septum designed for percutaneous access, through which filling and exchange of solutions is made possible. The iPRECIO® system's highly precise, in vivo-, capabilities uses a patented, high accuracy, mechanical pump technology, the "Rotary Finger Method", which was developed by Primetech.

Continuous intravenous administration (IV) is one of the most flexible methods for introducing drugs for bio-medical research. Rapid drug responses, good control on delivery and dose (high doses as well) is more easily obtained when performing IV administration. PK studies may be carried out without hepatic first-pass effects and oral absorption issues.

IV administration requires more specialized equipment and technique/skill as it is necessary to access a blood vessel and ensure reliability of catheterization. It is further necessary to use a funnel intravenous catheter to insert into the jugular vein in mice.

**WARNING : iPRECIO® Micro – Infusion Pump is not intended for human use.**

### REQUIREMENTS

#### Perioperative Care

- Antibiotics and the treatments
- Anesthetic agents and the techniques
- Heating Pad
- Surgical glove, mask, cap and gown
- 70% Isopropyl Alcohol
- Disinfectant Soap
- Sterile saline
- Electric shaver or Hair remover

#### Pocket and Tunnel Making

- Surgical scissors and forceps
- Sterile scalpel blade with handle
- Trocar Sleeve Kit (metal trocar with plastic sleeve)

#### Pump Fixation

- 5-0 non-absorbable suture with curved needle

#### Intravenous Catheter Fixation

- Cotton swab
- Microscissor or 23-gauge needle

- Intravenous catheter: FunnelCath™ PUFC-C30-20(3F to 2F) or PUFC-C30-10(3F to 1.2F) ; connect to 22ga swivel 7cm. (supplied by Access Technologies)
- Stainless coupler: Stainless steel tubing coupler 22ga x 8mm (supplied by Instech Solomon)

### Wound Closing

- Wound clips and wound clips applier

## METHODS

- 3M™ Vetbond™ Tissue Adhesive (supplied by 3M)

### 1. Perioperative Care

Careful attention to sterile techniques and the use of sterile equipment are crucial to successful surgery. Additionally, antibiotics are most effective to administer pre- and post-surgery in order to maximize blood levels during surgery and recovery. Primetech recommends the use of a heating pad to prevent decreased body temperature in the peri- and post-operative animal.

### 2. Anesthetize the Animal

Anesthesia must be used to ensure a reliable experimental result. General anesthesia should be maintained for around 20 – 30 minutes. Primetech recommends using an anesthetic method that supports prompt post-operative recovery.

### 3. Antenna fixing and Catheter Attachment...See Fig.1

1. Cut the outlet tube around 7cm under sterile conditions.
2. Suture the antenna to the pump tube.
3. Connect the coupler into the tip of the pump tube.
4. Cut the 7cm distal end of the intravenous catheter and connect to the pump tube with a coupler.

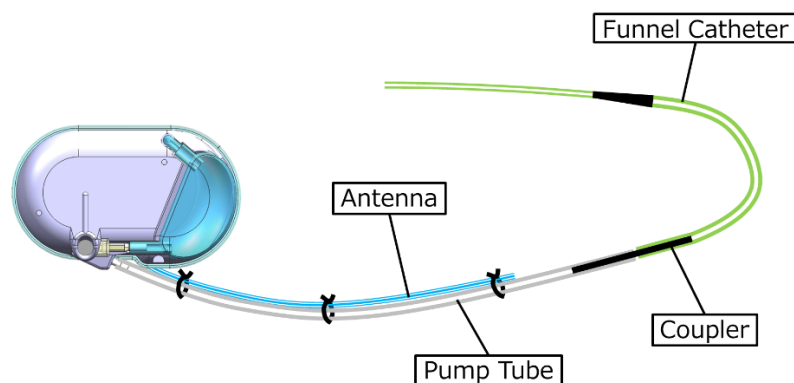


Fig.1 Antenna fixing and intravenous catheter connection

### 4. Pocket Making ...See Fig.2

1. Put the animal in prone position on the heating pad.
2. Remove the hair from the incision site and scrub with disinfectant soap and isopropyl alcohol. A series of three scrubs with both the disinfectant soap and alcohol is recommended.
3. Using a scalpel blade, make a 3cm midline incision through the skin on the thoracic vertebrae.

4. Using blunt dissection, create a pouch under the skin from the point of the incision to the caudal area by separating the skin from the underlying tissue with scissors.

The pocket should be the appropriate size (not too large and not too small) for pump fixation, low-stress implantation for a successful long-term infusion.

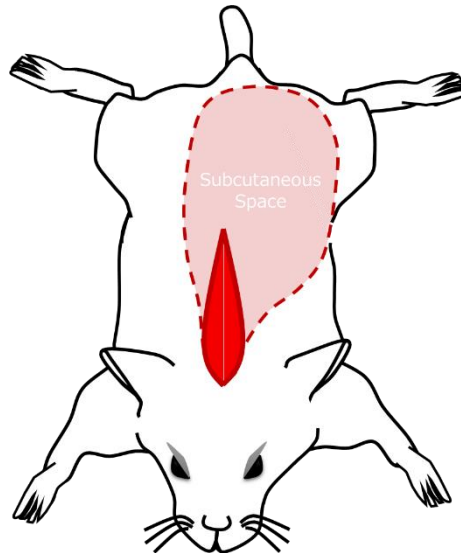


Fig.2 Subcutaneous pocket

#### 5. Tunnel Making ...See Fig.3

1. Put the animal in supine position on the heating pad.
2. Remove the hair from the incision site and scrub with disinfectant soap and isopropyl alcohol. A series of three scrubs with both the disinfectant soap and alcohol is recommended.
3. Using a scissors, make a 1cm midline incision through the skin on the neck. Gently separate the skin from the muscle by blunt dissection with a scissors.
4. Put the animal in lateral position on the heating pad.
5. Using the metal trocar sleeve kit, tunnel subcutaneously from the dorsal pocket to the neck skin incision.
6. Tunnel the pump tube subcutaneously from the dorsal pocket to the neck incision via/through the trocar sleeve.
7. Return the animal in supine position on the heating pad.

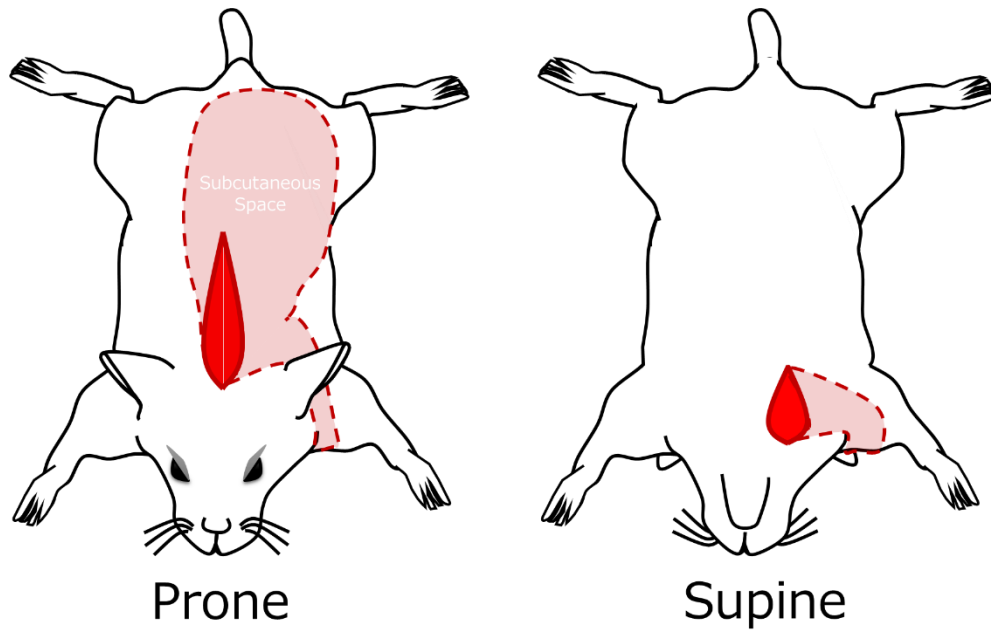


Fig.3 Subcutaneous tunnel

#### 6. Pump Activation...See Fig.4

1. Fill the solution to the tip of the tube.
2. (Optional) If you want to confirm a backward flow, you can activate the pump after placement of the intravenous catheter.
3. Activate the pump.

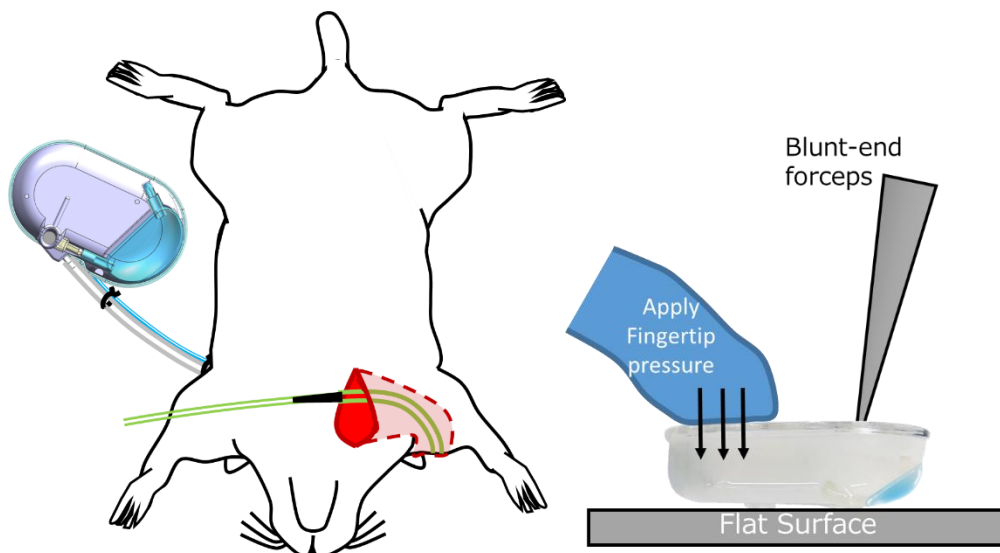


Fig.4 Pump placement for the activation

#### 7. Access to Intravenous...See Fig.5

1. Isolate the right jugular vein from the peripheral tissue using forceps or a cotton swab.
2. Pass three surgical sutures (A, B, C) around the jugular vein. The cranial suture (A) will be used to completely occlude blood flow. The middle suture (B) will be used to hold the catheter in place after cannulation. The caudal suture (C) will be used to temporarily occlude blood flow.

3. Tie a secure knot around the vein using suture (A) to ligate the vessel.
4. Apply tension to suture (A) and tape the suture tails to the surgery table.
5. Make a loose knot on suture (B), and tape the suture on one of the tails.
6. Make a loose knot on suture (C), and clamp the suture tails with hemostat.
7. Gently apply tension to suture (C) using a hemostat to occlude blood flow.
8. Using a microscissor or 23 gauge needle, catheterize caudally;
  - I. Using a microscissor
    - i. Make small “V” cut into top of vein.
    - ii. Lift up “V” flap to open hole for easier insertion.
  - II. Using a 23 gauge needle
    - i. Prepare a catheter introducer by bending the beveled tip of a 23-gauge syringe needle. Hold the syringe needle with the beveled side facing up. Grasp just the beveled area of the needle with a needle holder and bend the tip downward to an angle of approximately 90°. The syringe needle may be placed onto a 1 cc syringe to be used as a handle to hold onto the needle and allow for a clear view of the surgical area.
    - ii. Using the 23-gauge needle as an introducer, pierce the vessel just proximal to the ligation suture (A) and insert the catheter caudally. Once the catheter is inserted into the vessel, withdraw the catheter introducer.
9. Secure the catheter to the jugular vein with suture (B) by gently pulling the loose suture tail.
10. Once the catheter is secured, release the tension on suture (C) and advance the catheter around 12mm beyond suture (C).
11. Tighten suture (B) and (C) around the catheter.
12. Release the tension on the ligation suture (A) and tie the loose ends around the catheter to help anchor it in place.
13. Trim all suture tails as short as possible.
14. Close the skin incision with 5-0 non-absorbable suture or wound clips. Once closed, seal the incision with Vetbond™ tissue adhesive.

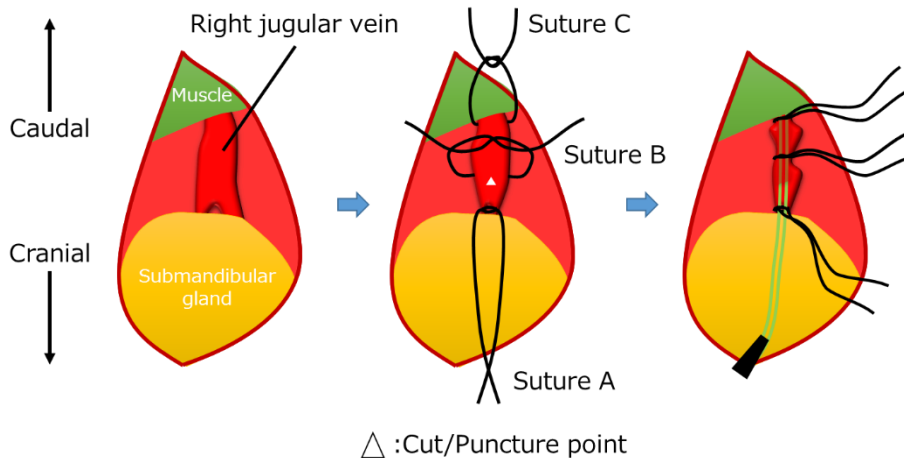


Fig.5 Access to the right jugular vein

#### 8. Pump Placement and Wound Closing ...See Fig.6

1. Place the pump into the pocket.
2. Close the skin incision near the pump with 5-0 non-absorbable suture or wound clips.
3. Seal the incision with Vetbond™ tissue adhesive.

Proper pocket closing will help in wound healing and helps to prevent infections.

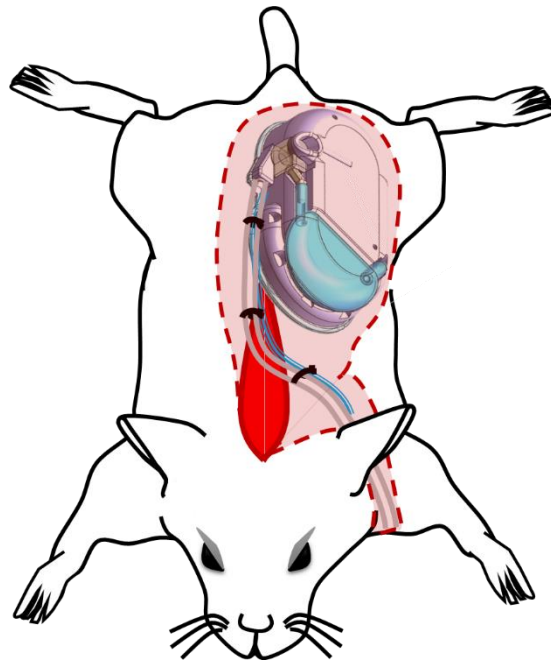


Fig.6 Connect the antithrombotic catheter

Innovative drug infusion technology for laboratory animals.



Primetech Corporation