

#### **GENERAL ITEMS**

- ALZET Osmotic Pumps\*
- Homeothermic pad
- Sterile drape
- Sterile gauze, cotton swabs
- Hall Clippers (#40 blade
- Ethanol or chlorhexidine
- Betadine scrub
- Glass bead sterilizer
- Ocular Juhrican
- Svringe w/ sterile saline

#### **SURGICAL TOOLS**

- 7mm Wound Clips
- Reflex Wound Clip Applier\*
- Reflex Wound Clip Remover
- Scalpel handle #3, blade #15 (or Iris scissors)
- Moria forceps (smooth)
- Dumont forceps (#5-45)
- Hemostat (straight tip
- Syringe needle (22-20 gauge
- Scissors (fine Iris or Vannas spring)
- Sutures (non-absorbable, 6-0)
  - \* Available from DURECT Corp. (877-922-5938, <u>alzetcs@durect.com</u>)

# **Pump Preparation**

(refer to the package insert for complete filling instructions)

- Fill the empty ALZET pump with your vehicle or drug solution using a syringe and filling tube according to the procedure listed in the package insert included in your box of pumps.
- Insert the flow moderator into the filled ALZET pump until the cap or flange is flush with the top of the pump.
- Prime the filled pumps in sterile saline at 37°C.
- Refer to your package insert for the appropriate period of priming. Most pumps require at least an overnight priming period.

#### Anesthesia

Anesthesia is required for surgical implantation of ALZET pumps.

 Anesthetize the animal using either an inhalable (i.e., Isoflurane) or injectable (i.e., Xylazine® and Ketamine®, or sodium pentobarbital) anesthetic.

The use of inhalation anesthetics, such as Isoflurane, is highly recommended. It supplies supplemental oxygen during periods of respiratory depression and provides for rapid anesthetic recovery.

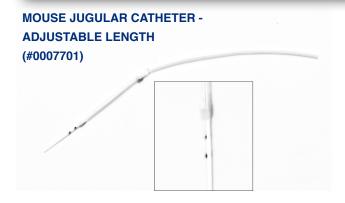
# **Surgical Preparation**

- Apply ocular lubricant in the eye.
- Remove fur from area centered over the ventral neck area. Loose hair can be removed with dry gauze, gauze dampened w/ ethanol or adhesive tape.
- Disinfect the skin first with 70% ethanol. Using a sterile swab apply the ethanol at the proposed incision site and work outward in ever widening circles over the entire hair removed area. With a new sterile swab, apply iodine at the proposed incision site and again work outward in ever widening circles. Repeat the ethanol and iodine scrub.
- Administer analgesic as directed by staff veterinarian

### **Surgical Procedure**

- Place the rodent in dorsal recumbency with the head secured, facing toward the surgeon. (For ease of manipulation during surgery, the animal can be placed in a sterile stockinette and the head and neck exposed for anesthesia administration and surgical access.)
- Place a small bolster beneath the animal's neck to expose the ventral neck more fully.





- Use a small, sharp scalpel blade or Iris scissors to make a single
   7-9 mm skin incision from the ramus of one side of the jaw to the clavicle just lateral to the trachea/midline.
- Gently dissect down through the adipose tissue and fascia to isolate the external jugular vein, which is superficial to most of the neck musculature. Tunnel under the vessel by gently lifting the vein with the Moria forceps and clean the jugular vein.
- Place one loose ligature around the cardiac end of the vein and another ligature around the cephalic end of the vein, approximately 3-4 mm apart. When passing ligatures under the vein, lift the vein with forceps to avoid abrasion. Tie off the cephalic suture with two knots, leaving ligature tails 4-5 inches long.
- Loosely tie the cardiac suture.
- Attach hemostats to both sutures to provide gentle counter-traction on the vein as needed.
- Use a fine 23-25 gauge needle bent at an approximate 90-degree angle to pierce the vessel. Alternately, a small incision can be made on the ventral aspect of the vessel with fine Iris scissors or Vannas spring scissors. Do not cut so much tissue as to weaken the vessel such that it breaks when traction is applied via the rostral ligature ends while passing the cannula.
- Once the vessel is pierced, control hemorrhage with gentle traction on the cardiac ligature ends.
- With your dominant hand, use Moria forceps to hold the free end
  of the catheter tip and with your other hand use Dumont forceps to
  gently grasp the jugular vein at the incision site.
- Insert the catheter into the lumen and advance gently at a 45 degree angle to the level of the heart (about 11 mm in an adult mouse). Tie the cardiac ligatures with two double knots snugly around the catheter, being careful not to crimp or occlude the catheter. The cephalic ligature should be tied around the catheter. Cut all ends of the ligatures close to the knots.
- Using a hemostat, tunnel over the neck, creating a pocket on the back of the animal in the mid-scapular region. Lead the pump into this pocket, allowing the catheter to reach over the neck to the external jugular vein with sufficient slack to permit free head and neck movement.
- Pass the caudal end of the pump through this tunnel into the pocket.
- Close the underlying fascial tissues with 6-0 non-absorbable sutures in a simple continuous or interrupted pattern.
- Close the skin with the same suture material, or wound clips.

# Alternate Method: Cannulation w/ Recovery

If a surgical recovery period after IV cannulation is desired prior to starting drug administration with ALZET pumps, two methods are available:

- 1. Use an ALZET pump to deliver vehicle solution during the desired surgical recovery period. Then, replace the vehicle-pump with a new drug-filled and primed ALZET pump.
- 2. Use a catheter lock solution to prevent blood clotting and maintain catheter patency during the recovery period.
- After cannulation, fill the catheter with a lock solution (i.e. 500 IU
  heparin and glycerol mixture), then plug the catheter to prevent
  leakage during the recovery period (catheter plugs from SAI
  Infusion, part #CP-21, are compatible with ALZET specialized
  catheters).
- The lock solution should be replaced every 3-4 days.
- Fill the ALZET pump with drug solution and prime.
- Prior to attaching the pump to the catheter at the end of the recovery period, withdraw a minimal amount of blood to ensure that the catheter is patent and flush with a small volume of saline.
- Attach the freshly filled and primed pump to the catheter.

### **Post Operative Analgesia**

 An analgesic can be give post-operatively as needed. Analgesic treatment should be provided under the direction of the staff Veterinarian.

# **Clinical Monitoring and Management**

- Animals should be monitored daily until the wound clips or sutures are removed then once to twice weekly until completion of the study. Clinical Monitoring and Management Clinical Monitoring and Management
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- Animals should be monitored daily until the sutures are removed then once to twice weekly until completion of the study.
- It is especially important to check the health of the animal the morning after surgery. Animals that reopen the incision site will typically do so after the first night.
- If any adverse effects are seen, the staff Veterinarian will need to be informed immediately for appropriate treatment. Potential adverse effects from this procedure are minimal, but may include:
  - Anesthetic-related respiratory depression: Adverse anesthetic effects can be minimized by proper dosing of anesthetic agents and careful monitoring of animals during the anesthetic period.
  - Infection of the incision site: ALZET Osmotic Pumps are provided sterile. Infection can be prevented or minimized if trained surgeons use aseptic surgical techniques and maintain the sterility of products being used. Administration of prophylactic antibiotics may be useful in minimizing the risk of infection, and this should be discussed with the staff Veterinarian.
  - Post-operative pain or discomfort as evidenced by: decreased activity, decreased food and water intake, weight loss, vocalizations, rough hair coat, hunched posture.

