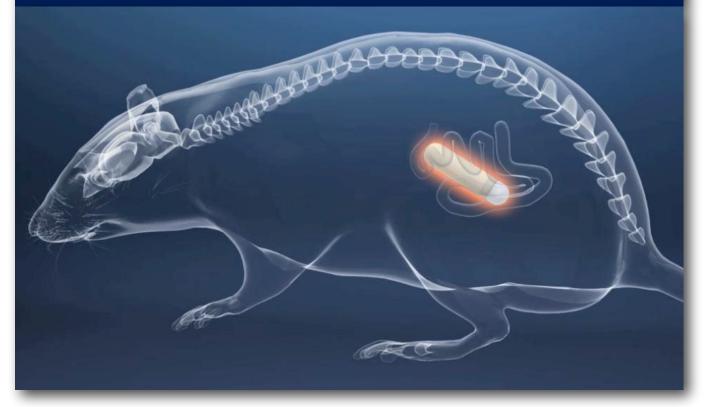
INTRAPERITONEAL IMPLANTATION

ALZET SURGICAL INSTRUCTION SHEET



GENERAL ITEMS

- ALZET Osmotic Pumps*
- Homeothermic pad
- Sterile drape
- Sterile gauze, cotton swabs
- Hair clippers (#40 blade
- 70% ethanol
- Betadine solution
- Glass bead sterilizer
- Ocular lubricant

SURGICAL TOOLS

- Wound Clips (7mm for mice, 9mm for rats)*
- Wound Clip Applier*
- Wound Clip Remover'
- Scalpel handle #3
- Scalpel blade #15
- Brown Adson forceps
- Hemostat (straight tip)
- Sutures (absorbable, 4.0)
- * Available from DURECT Corp. (877-922-5938,<u>alzetcs@durect.com</u>)

ALZET pumps can be implanted intraperitoneally in animals with sufficiently large peritoneal cavities. With any substance administered intraperitoneally, whether by injection or by infusion, a majority of the dose may be absorbed via the hepatic portal circulation rather than by the capillaries. For substances that are extensively metabolized by the liver (i.e., have a high "first pass effect"), the intraperitoneal route of administration may produce highly variable concentrations of agent in plasma and consequently highly variable effects. Therefore, the intraperitoneal route should probably be avoided with agents that have a significant first-pass effect.

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.



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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 to the eye.
- Shave the area centered over the site chosen for pump placement.
- Using a sterile swab, disinfect the incision site with 70% ethanol by working outwardly in ever widening circles. With a new sterile swab, apply iodine over the proposed incision site in a similar fashion.
 Repeat the ethanol and iodine scrub one more time.

Surgical Procedure

- Make a midline skin incision, 1 cm long, in the lower abdomen under the rib cage.
- Using forceps, carefully tent up the musculoperitoneal layer to avoid damage to the bowel.
- Incise the peritoneal wall directly beneath the cutaneous incision.
- Insert a filled pump, delivery port first, into the peritoneal cavity
- Close the skin incision with 2 or 3 wound clips or interrupted sutures.

Post Operative Analgesia

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

Clinical Monitoring and Management

- Depending on the size of the animal relative to the pump, intraperitoneal implantation can disrupt normal feeding and weight gain for a day or two thereafter. Allow 24 to 48 hours for the animal to recover after intraperitoneal implantation.
- Animals should be monitored daily until the wound clips or 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 the following:
 - 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.
- Wound clips must be removed 7-10 days post procedure.

