I. Technical Description of the ALZET Micro-Osmotic Pump Model 1002

A. Complete Micro-Osmotic Pump System with Flow Moderator In Place

1. Nominal Performance (at 37°C)

- Pumping rate: 0.25 µl/hr
- Duration: 14 days
- Reservoir Volume: 100 µl

2. Flow Moderator

- Material (tube): stainless steel
- Material (flange): styrene acrylonitrile
- Material (lumen): polyethylene glycol
- Material (tablet): paracetamol

B. Components

1. Filling Tube

- Length (tube only): 11.1 cm
- Diameter: 0.27 cm
- O.D. (tube): 0.04 cm
- L.D. (tube): 0.02 cm

2. Flow Moderator

- Length: 13.1 cm
- O.D. (tube): 0.08 cm
- L.D. (tube): 0.06 cm
- Weight (empty): 0.05 g
- Weight (loaded): 0.25 g
- Material: aluminised acrylonitrile
- Material (tablet): paracetamol

3. Pump Body Materials

- Outertubes: polylysine
- Drug Reservoir: thermoplastic elastomer

II. Checklist for Satisfactory Performance of the ALZET Micro-Osmotic Pump

1. Use the mean pumping rate and fill volume information specific to this lot of pumps when making dose calculations.
2. A partially or completely discharged ALZET pump cannot be refilled or recharged.
3. All ALZET pumps are filled completely and all fill volumes have been calculated based on nominal duration. Refer to the equation in Section V for complete fill volume specifications to calculate the exact delivery duration and maximum possible dose for this lot of micro-osmotic pumps.
4. Use a catheter. ALZET pumps can be used to deliver substances into the venous or arterial circulation, into the brain, or into any organ, tumor, or solid tissue. The instructions on how to prepare the pump for these applications, refer to Section VI.
5. Verify correct operation of ALZET pumps by both monitoring blood levels and recording the course of the infusion, and determining the residual amount of solution remaining in the pump after expiration. Refer to Section VII for further information, including an in vitro verification method.

III. Instructions for Filling ALZET Micro-Osmotic Pumps

A.  Complete Micro-Osmotic Pump System with Flow Moderator In Place

1. Step 1. Weigh the empty pump together with its flow moderator.
2. Step 2. Filling the pump is accomplished with a small syringe (1.0 ml) and the provided blunt tipped, 27 gauge filling tube. Use of a larger syringe and filling tube, which introduce air bubbles into the reservoir, distorts the solution in the syringe and affects the flow rate. It is essential that the syringe and attached tube be free of air bubbles.
3. Step 3. With the flow moderator removed, hold the pump in an upright position and insert the filling tube through the opening at the top of the pump. This places the tip of the tube near the bottom of the pump reservoir.
4. Step 4. Push the plunger of the syringe slowly, holding the pump in an upright position. If the fluid begins to come out of the lumen, or solid tissue. (For instructions on how to prepare the pump and osmolality conditions, refer to the equation in Section VI part c, and the actual release rate and fill volume specified at the top of this instruction sheet.
5. Step 6. Weigh the filled pump. The difference in the weights obtained in Step 1 and 2 will give the net weight of the solution loaded. For most applications, volume (ml) is used as the unit of measurement (ml) for other aqueous salt solutions). The incorporation of cyclodextrins

IV. Solvent and Agent Compatibility With ALZET Micro-Osmotic Pumps

The pumps are compatible with aqueous solutions, dilute acids and bases, dilute or low concentrations of DMSO and alcohol, and up to 5% DMSO in most other solvents. ALZET pumps are not compatible with aliphatic and aromatic hydrocarbons, such as heptane, toluene, xylene, and other volatile solvents. Care should be taken to avoid air bubbles in the reservoir. If a pump contains contaminated, its surface may be wiped with an aqueous solution of 70% isopropanol. Do not soak the pump in 70% isopropanol.

If back pressure is encountered, the filling tube can be tilted at a slight angle during filling. The filling aperture can also be widened slightly by moving the filling tube back and forth, or by inserting and removing the flow moderator several times before inserting the filling tube.

If, after a second filling, the fill volume is less than 90% of the reservoir volume indicated in the lot specifications at the top of this instruction sheet, call ALZET Technical Support for assistance at 800-692-2990 (U.S. and Canada).

List of Solvents Compatible with the Reservoir Material for ALZET Micro-Osmotic Pumps

(For solvent compatibility with ALZET Catheters, please contact Durect)
V. Implantation of the ALZET Micro-Osmotic Pump in Vivo

The ALZET Micro-Osmotic Pump can be implanted subcutaneously in an animal weighing at least 5 grams within 24 hours of its opening. To ensure that there is no visible incision, a small incision is made in the skin below the rib cage of an animal weighing at least 20 grams. Another small incision in the abdominal muscle is made directly under the cutaneous incision. The pump is inserted, flow moderator first, into the subcutaneous tissue and the skin is closed with a suture to allow an estimated delivery duration of 14 days. The pump is inserted, flow moderator first, into the subcutaneous tissue and the skin is closed with a suture to allow an estimated delivery duration of 14 days. The pump is inserted, flow moderator first, into the subcutaneous tissue and the skin is closed with a suture to allow an estimated delivery duration of 14 days. The pump is inserted, flow moderator first, into the subcutaneous tissue and the skin is closed with a suture to allow an estimated delivery duration of 14 days. The pump is inserted, flow moderator first, into the subcutaneous tissue and the skin is closed with a suture to allow an estimated delivery duration of 14 days.

D. Predicting Pump Performance Outside Mammalian Environment

The rate of diffusion of drug into solution from the reservoir of the implantable osmotic pump is dependent on the viscosity of the drug solution and the temperature at which the pump is submerged. The viscosity of the drug solution is determined by the properties of the drug and its concentration, and the temperature at which the pump is submerged is determined by the environmental temperature. The relationship between the rate of diffusion and the environmental temperature is given by the following equation:

\[ \frac{V}{\pi t} = \frac{V_{0}}{\pi (t_0)} \]

where \( V \) is the volume of drug solution remaining in the reservoir at time \( t \), \( V_{0} \) is the initial volume of drug solution in the reservoir, and \( t_0 \) is the ambient temperature of the environment. The equation can be used to predict the pumping rate of the implantable osmotic pump in vivo.

VI. Operation of the ALZET Micro-Osmotic Pump

1. To operate the pump with a catheter, perform the following steps:
   a. Using a pair of scissors or pliers, break the white flange from the pump.
   b. Attach the stainless steel tube to a piece of polyethylene or vinyl catheter tubing with an inside diameter (I.D.) of 0.58 mm-0.76 mm (0.02 - 0.03 inches). The catheter tubing with the replacement, at no cost to the customer, of those units of Product
   c. This step is mandatory in all catheter
   d. This step is mandatory in all catheter
   e. This step is mandatory in all catheter
   f. This step is mandatory in all catheter
   g. This step is mandatory in all catheter
   h. This step is mandatory in all catheter
   i. This step is mandatory in all catheter
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   t. This step is mandatory in all catheter
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   v. This step is mandatory in all catheter
   w. This step is mandatory in all catheter
   x. This step is mandatory in all catheter
   y. This step is mandatory in all catheter
   z. This step is mandatory in all catheter
   AA. This step is mandatory in all catheter
   BB. This step is mandatory in all catheter
   CC. This step is mandatory in all catheter
   DD. This step is mandatory in all catheter

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X. Technical Information About ALZET Micro-Osmotic Pumps

A wealth of information on ALZET osmotic pumps and their uses is available through a variety of resources. To obtain any of these materials, or if you desire additional information, contact ALZET Technical Support.

ALZET Technical Support

DURECT Corporation
10280 Bulb Road
Cupertino, CA 95014
408-367-4036 (Outside the U.S.)
408-865-1406 (Facsimile)
408-367-4036 (Outside the U.S.)
408-865-1406 (Facsimile)

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This Warranty is in lieu of all other Warranties, express or implied, including warranties of merchantability or fitness for a particular purpose, which are hereby excluded. In no event shall DURECT be liable for any incidental, special, indirect, or consequential damages, whether caused by the negligence of DURECT or otherwise, of those arising out of or in connection with this Warranty, and in no event shall DURECT be liable for such damages.

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