ALZET® MICRO-OSMOTIC PUMP MODEL 1003D

INSTRUCTION AND SPECIFICATION SHEET

MODEL 1003D

ALZET® MICRO-OSMOTIC PUMP

1. Performance (at 37°C):
   - Pumping Rate and Reservoir Volume: Refer to Actual Lot Specification.
   - Duration: 3 days (refer to Section VI, part C).

2. Flow Moderator
   - The pump is evacuated under well-controlled conditions to establish a pumping rate and reservoir volume. These specifications are listed at the time of manufacture. Use the Actual Lot Specifications (Pumping Rate and Fill Volume information) when calculating drug concentration and dose.

3. Filling Tube
   - Length (tube) 1.1 mm
   - Gauge (tube) 27
   - O.D. (tube) 0.08 cm
   - Material (tube) stainless steel
   - Weight (empty) 0.4 g
   - Total Displaced Volume 0.5 ml

4. Components
   - Filling Tube
     - Length (tube) 1.1 mm
     - Gauge (tube) 27
     - O.D. (tube) 0.08 cm
     - Material (tube) styrene acrylonitrile
     - Weight (empty) 0.4 g
   - Pump Body Materials
   - O.D. Material (tube) styrene acrylonitrile
   - Material (tube) stainless steel
   - Drug Reservoir
     - polysulfone water resistant
   - Thermoplastic hydrocarbon 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 reused.
3. All ALZET pumps are filled completely and all 8 volumes have been removed, (Refer to Section V for filling technique).
4. The vehicle-drug combination to be delivered is compatible with the interior of the pump. (Refer to Section IV for vehicle compatibility guidelines).
5. The drug to be delivered is soluble and stable in the vehicle solution 37°C for the duration of the experiment.
6. The mass rate of drug delivery is calculated using the following equation:
   \[ \text{m} = \frac{Q}{C(1 + k)} \]
   \( Q \) is the volume delivery rate (µl/hr) of the solution from the pump, and \( C \) is the concentration (µg/ml) of the agent in the vehicle.
7. Good sterile technique is used during the filling, handling and subsequent implantation of the pumps. Use the filling procedure (Section V for filling procedure and Section V for implantation procedure). ALZET pumps have been exposed to a sterilizing dose of radiation from a 60Co source.

III. Instructions for Filling ALZET Micro-Osmotic Pumps

1. Fill the pump with the exact volume of solution that will be used and mix well. (Refer to Section VI, part D for an explanation date for this lot of micro-osmotic pumps.)
2. After this time, due to continued attraction of water into the pump, it may swell and leak a concentrated salt solution, resulting in local irritation around the pump. (Refer to the equation in Section VI, part C for an explanation date for this lot of micro-osmotic pumps.)
3. Perform the following steps when filling ALZET pumps:
   - Step 1. Weigh the empty pump together with its flow moderator.
   - Step 2. Fill the pump with a solution from a 1.0 ml syringe and fill it completely (i.e. discharge volume). Use a 0.5 ml syringe to fill a small portion of the reservoir to check for leaks. (Refer to Section V for fill volume information.)
   - Step 3. Push the plunger of the syringe slowly, hold the pump in an upright position and fill the syringe until it is full. The solution is then expelled from the flow moderator into the reservoir. (Refer to Section V for fill volume information.)
   - Step 4. Weigh the empty pump together with its flow moderator.
   - Step 5. The flow moderator removed, hold the pump in an upright position and fill it slowly and evenly using the filling technique. Use the flow moderator to direct fluid into the pump. (Refer to Section V for fill volume information.)
   - Step 6. Wipe off the excess solution and insert the flow moderator until it is flush with the valve housing. (Refer to Section V for a description of these verification techniques.)
   - Step 7. After this time, due to continued attraction of water into the pump, it may swell and leak a concentrated salt solution, resulting in local irritation around the pump. (Refer to the equation in Section VI, part C for an explanation date for this lot of micro-osmotic pumps.)

IV. Solvent and Agent Compatibility With ALZET Osmotic Pumps

The pumps are compatible with aqueous solutions, dilute acids and bases, dilute or low concentrations of DMSO and alcohol, and up to 100% glycerol. They are compatible with aliphatic and aromatics hydrocarbons, such as heptane, toluene, and xylene, but not with alcohols or ketones which may cause pump malfunction. Table 1 provides examples of some commonly used solvents known to be compatible with the pump.

Table 1: List of Solvents Compatible With the Reservoir Material

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Compatibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>Compatible</td>
</tr>
<tr>
<td>70% isopropanol</td>
<td>Compatible</td>
</tr>
<tr>
<td>Ethanol</td>
<td>Compatible</td>
</tr>
<tr>
<td>DMSO</td>
<td>Partially compatible</td>
</tr>
<tr>
<td>Glycerol</td>
<td>Compatible</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>Compatible</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>Compatible</td>
</tr>
</tbody>
</table>

Note: The solvent shown above the line is compatible with the reservoir material of the pump. The caution must be taken to ensure solvent is also biocompatible with tissues and fluids at the site of implantation.
V. Implantation of the ALZET Micro-Osmotic Pump in Vivo

The ALZET micro-osmotic pump can be implanted subcutaneously in an animal or transcutaneously in a human. With the former method, a small incision is made in the skin below the rib cage of an animal weighing at least 20 grams. Another incision is made directly over the injection site between the two initial incisions. The pump is implanted, first the flow moderator, then the catheter tubing with an inside diameter (I.D.) of 0.58 mm-0.76 mm (0.02-0.03 inches). Polyethylene tubing, commonly called PE-60 (I.D. = 0.03 mm), is often used. Leave the syringe attached to the distal part of the catheter. The pump and catheter can now be implanted. Leave the syringe attached to the distal part of the catheter. The pump and catheter can now be implanted.

VI. Operation of the ALZET Micro-Osmotic Pump

ALZET pumps are precision drug administration tools. This section details the specifications for Model 1003D pumps that you received, and the method by which the reproducibility of the rate is calculated. For a period of 12 months from date of shipment, DURECT warrants that ALZET pumps are supplied with a specified volume pumping rate with the sole and exclusive remedy for any breach of warranty shall be the replacement of the pump unit. As a result, the pump imbibes water during operation. Likewise, cutting open a spent pump is not a reliable means of verifying pump performance.

A. Determination of Average Pumping Rate

The duration of pumping can be computed from the following equation.

\[ \text{Volume pumped} = \frac{\text{Volume of reservoir}}{\text{Pumping rate} \times \text{Duration}} \]

B. Determination of the In Vitro Pumping Rate

The pumping rate of subcutaneously or intraperitoneally implanted osmotic pumps is within 5% of the pump's theoretical rate.

C. Determination of Pumping Duration

The duration of pumping can be computed from the following equation.

\[ \text{Duration} = \frac{\text{Volume of reservoir}}{\text{Pumping rate}} \]

D. Vitrino Test Qualification

A random sample of 20 ALZET pumps is selected from the same lot as the product which you have received. These pumps are filled with a dye solution according to the method described in Section III. The values for the Mean Fill Volume, including standard deviation, appear in the filling specifications for each lot. The Mean Fill Volume can be used as an indicator of the rate at which the pump imbibes water during operation. Likewise, cutting open a spent pump is not a reliable means of verifying pump performance. As a result, the pump imbibes water during operation. Likewise, cutting open a spent pump is not a reliable means of verifying pump performance.

IX. Additional Technical Information About ALZET Osmotic Pumps

A wealth of information on ALZET osmotic pumps and their uses is available from ALZET Technical Support. Through this complimentary service you can request:

- A Technical Information Manual
- A video of commonly used surgical implantation procedures
- Custom searches of the ALZET osmotic pump bibliography of publications
- Presentation materials for authors presenting their work on ALZET Brain Infusion Kits, ALZET Catheters and other products

To obtain any of these materials, or if you desire additional information, contact ALZET Technical Support.

ALZET Technical Support
Direct Contact:
10240 Bubb Road
Cupertino, CA 95014
800-800-2990 (U.S. and Canada);
408-387-4038 (Outside the U.S.)
alzet@durect.com (e-mail)
www.alzet.com