When the environment in which the pump is to be used differs significantly from the environment at the time of purchase (e.g., higher temperature and osmolality (510 mmOs)) the pumping rate of ALZET pumps will be affected. (To calculate the pumping rate under specific temperature and osmolality conditions, refer to the equation in Section VI.)

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

1. **Technical Description of the ALZET Micro-Osmotic Pump Model 1007D**

   **A. Complete Micro-Osmotic Pump System with Flow Moderator**

   **1. Nominal Performance (at 37°C)**

   - **Pumping Rate**
     - 0.5 µl/hr
   - **Reservoir Volume**
     - 100 µl

   The nominal performance is a target for all pumps manufactured. Individual lots of pumps may vary from this target within limits. The actual pumping rate and fill volume of this particular lot (derived by statistical testing) are listed with the lot specifications on the top of this instruction sheet.

   **2. Dimensions, Overall**

   - Length: 1.5 cm
   - Diameter: 0.6 cm
   - Weight (empty): 0.05 g
   - Total Displaced Volume: 0.5 ml

   **B. Components**

   - **1. Filling Tube**
     - Length (tube only): 1.1 cm
     - Gauge (tube): 27
     - O.D. (tube): 0.08 cm
     - I.D. (tube): 0.02 cm
   - **2. Flow Moderator**
     - Length (moderator in place): 1.3 cm
     - Gauge (tube): 21
     - O.D. (tube): 0.08 cm
     - I.D. (tube): 0.05 cm
     - Weight (overall): 0.05 g
   - **Material (Flange)**
     - stainless steel
   - **3. Pump Body Materials**
     - Outer Membrane: cellulose aseptic barrier
     - Drug Reservoir: thermoplastic hydrolysis elastomer
   - **4. Pump Body Materials**
     - Water, distilled
     - Serum (rat, mouse, etc.)
     - Saline, 0.9% (or other aqueous salt solution)
     - Ringer’s solution (with or without lactate)
     - 1-Methyl-2-Pyrrolidone, up to 12.5% in water
     - Glycerol
     - DMSO, up to 50% in water or polyethylene glycol
   - **5. Biocompatibility**
     - ALZET® Micro-Osmotic Pumps, Model 1007D, should be removed upon completion of the delivery duration or by day 10 after implantation. After this time, due to the continued attraction of water into the pump and the concentration of salt resulting in local irritation around the pump. (This explanation is date calculated for the nominal duration. Refer to the equation in Section VI, Part C to calculate the exact delivery duration and nominal expiration date of each lot of micro-osmotic pumps.)

   **III. Instructions for Filling ALZET Micro-Osmotic Pumps**

   If it is essential that each pump is filled completely and with correct filling verification is required, use the method detailed below. Air bubbles trapped in the pump reserve solution during filling can contribute to a variance in the pumping rate. The pump may result in unpredictable pump rate fluctuations. Solutions should be sterile and compatible with the vehicle-drug combination to be delivered.

   1. **Preparation**

   **a. Fill the pump with the desired solution.**

   **b.** The pumps are compatible with aqueous solutions, dilute acids and bases, and to low concentrations of DMG and acetal. All solutions are considered compatible with ALZET pumps. The pumps are not compatible with alcohols and aromatic hydrocarbons, such as heptane, toluene, and sodium naphthalene sulfonate solutions such as used in a pump malfunction. Table 1 provides examples of some commonly used solutions.

   **TABLE 1**

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Compatibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water, distilled</td>
<td>Compatible</td>
</tr>
<tr>
<td>Serum (rat, mouse, etc.)</td>
<td>Compatible</td>
</tr>
<tr>
<td>Saline, 0.9% (or other aqueous salt solution)</td>
<td>Compatible</td>
</tr>
<tr>
<td>Ringer’s solution (with or without lactate)</td>
<td>Compatible</td>
</tr>
<tr>
<td>1-Methyl-2-Pyrrolidone, up to 12.5% in water</td>
<td>Compatible</td>
</tr>
<tr>
<td>Glycerol</td>
<td>Compatible</td>
</tr>
<tr>
<td>DMSO, up to 50% in water or polyethylene glycol</td>
<td>Compatible</td>
</tr>
<tr>
<td>DMG, up to 50% in ethanol or 15% water, DMG, up to 50% in ethanol or 15% water</td>
<td>Compatible</td>
</tr>
<tr>
<td>Ethanol, up to 15% in water</td>
<td>Compatible</td>
</tr>
</tbody>
</table>

   **b.** Use the following equation to calculate the mean pumping rate:

   \[
   \text{Mean Pumping Rate} = \frac{\text{Amount of Solution Loaded} \times \text{Nominal Duration}}{\text{Total Volume of Solution Loaded}}
   \]

   In this equation:

   - Amount of Solution Loaded: the total amount of solution loaded into the reservoir.
   - Nominal Duration: the nominal duration of the implant.
   - Total Volume of Solution Loaded: the total volume of solution loaded into the reservoir.

   **c.** Intra- and inter-device variations may be noted.

   **d.** Repeat filling trials if the mean pumping rates do not agree with the nominal duration.

   **1. Filling the pump with the desired solution**

   **a.** The pumps are compatible with aqueous solutions, dilute acids and bases, do not contain concentrations of DMG and acetal. All solutions are considered compatible with ALZET pumps. ALZET pumps have been exposed to a sterilizing dose of radiation for these applications, refer to Section VI, Part D.

   **b.** This product is for use in experimental animals only. It is not to be placed into animals used for food or food products, or in humans.

   **c.** To function properly, the flow moderator must be inserted into the pump. (Rules for inserting the flow moderator into the pump have been given elsewhere.)

   **d.** The pump may result in unpredictable pump rate fluctuations. Solutions should be sterile and compatible with the vehicle-drug combination to be delivered.

   **2. Components**

   **a.** Complete Micro-Osmotic Pump System with Flow Moderator

   - **1. Filling Tube**
     - Length (tube only): 1.1 cm
     - Gauge (tube): 27
     - O.D. (tube): 0.08 cm
     - I.D. (tube): 0.02 cm
   - **2. Flow Moderator**
     - Length (moderator in place): 1.3 cm
     - Gauge (tube): 21
     - O.D. (tube): 0.08 cm
     - I.D. (tube): 0.05 cm
     - Weight (overall): 0.05 g

   **3. Pump Body Materials**

   - **Outer Membrane**
     - cellulose aseptic barrier
   - **Drug Reservoir**
     - thermoplastic hydrolysis elastomer
   - **Water, distilled**
   - **Serum (rat, mouse, etc.)**
   - **Saline, 0.9% (or other aqueous salt solution)**
   - **Ringer’s solution (with or without lactate)**
   - **1-Methyl-2-Pyrrolidone, up to 12.5% in water**
   - **Glycerol**
   - **DMSO, up to 50% in water or polyethylene glycol**

   **4. Biocompatibility**

   - **ALZET® Micro-Osmotic Pumps, Model 1007D**

   The pumps are compatible with aqueous solutions, dilute acids and bases, do not contain concentrations of DMG and acetal. All solutions are considered compatible with ALZET pumps. ALZET pumps have been exposed to a sterilizing dose of radiation for these applications, refer to Section VI, Part D.

   **5. Biocompatibility**

   - **ALZET® Micro-Osmotic Pumps, Model 1007D**

   The pumps are compatible with aqueous solutions, dilute acids and bases, do not contain concentrations of DMG and acetal. All solutions are considered compatible with ALZET pumps. ALZET pumps have been exposed to a sterilizing dose of radiation for these applications, refer to Section VI, Part D.

   **6. Biocompatibility**

   - **ALZET® Micro-Osmotic Pumps, Model 1007D**

   The pumps are compatible with aqueous solutions, dilute acids and bases, do not contain concentrations of DMG and acetal. All solutions are considered compatible with ALZET pumps. ALZET pumps have been exposed to a sterilizing dose of radiation for these applications, refer to Section VI, Part D.

   **7. Biocompatibility**

   - **ALZET® Micro-Osmotic Pumps, Model 1007D**

   The pumps are compatible with aqueous solutions, dilute acids and bases, do not contain concentrations of DMG and acetal. All solutions are considered compatible with ALZET pumps. ALZET pumps have been exposed to a sterilizing dose of radiation for these applications, refer to Section VI, Part D.

   **8. Biocompatibility**

   - **ALZET® Micro-Osmotic Pumps, Model 1007D**

   The pumps are compatible with aqueous solutions, dilute acids and bases, do not contain concentrations of DMG and acetal. All solutions are considered compatible with ALZET pumps. ALZET pumps have been exposed to a sterilizing dose of radiation for these applications, refer to Section VI, Part D.

   **9. Biocompatibility**

   - **ALZET® Micro-Osmotic Pumps, Model 1007D**

   The pumps are compatible with aqueous solutions, dilute acids and bases, do not contain concentrations of DMG and acetal. All solutions are considered compatible with ALZET pumps. ALZET pumps have been exposed to a sterilizing dose of radiation for these applications, refer to Section VI, Part D.

   **10. Biocompatibility**

   - **ALZET® Micro-Osmotic Pumps, Model 1007D**

   The pumps are compatible with aqueous solutions, dilute acids and bases, do not contain concentrations of DMG and acetal. All solutions are considered compatible with ALZET pumps. ALZET pumps have been exposed to a sterilizing dose of radiation for these applications, refer to Section VI, Part D.

   **11. Biocompatibility**

   - **ALZET® Micro-Osmotic Pumps, Model 1007D**

   The pumps are compatible with aqueous solutions, dilute acids and bases, do not contain concentrations of DMG and acetal. All solutions are considered compatible with ALZET pumps. ALZET pumps have been exposed to a sterilizing dose of radiation for these applications, refer to Section VI, Part D.

   **12. Biocompatibility**

   - **ALZET® Micro-Osmotic Pumps, Model 1007D**

   The pumps are compatible with aqueous solutions, dilute acids and bases, do not contain concentrations of DMG and acetal. All solutions are considered compatible with ALZET pumps. ALZET pumps have been exposed to a sterilizing dose of radiation for these applications, refer to Section VI, Part D.
V. Implication of the ALZET Micro-Osmotic Pump in In vitro Studies

The ALZET Micro-Osmotic Pump can be implanted subcutaneously in an animal that weights at least 10 grams. For subcutaneous placement, the pump should be inserted in the abdominal area (not the pannus). Using a hemostat, a small pocket is made by spreading the subcutaneous tissue until a firm grip is obtained with the hemostat, and the pump is inserted into the pocket with the flow moderator pointing away from the incision. The skin incision should then be closed with a wound clip or suture. For intraperitoneal placement, make a small incision in the skin and the peritoneal cavity is entered with a pair of forceps. A small incision in the abdominal muscle is made directly under the peritoneal cavity. The pump is inserted, flow moderator first, into the peritoneal cavity and the incision is closed with a wound clip or suture. Be sure to remove the pump upon completion of the delivery duration, or by day 10 after implantation. (This expiration date is calculated based on the in vitro test method described in Section VI). From this amount and the duration of delivery, the pump's reservoir will be empty or nearly empty. For additional information about surgical procedures, contact ALZET Technical Support . A video demonstrating several surgical implantation procedures is available at no charge.

VI. Operation of the ALZET Micro-Osmotic Pump

A. Chemical Compatibility Test Kit

ALZET pumps are precision drug delivery devices. This section details actual in vitro conditions in which the pumps are tested. For the lot of Model 1007D pumps that you received, and the method by which these pumps will be tested, refer to the lot specifications on the other side of this instruction sheet. A solution which generates gases within the pump during use, or a solution which will crush the stainless steel tube.

1. Using a pair of scissors or pliers, break the white flange from the pump housing to expose the retainer spring. The pump is then placed in a test tube containing 15 ml of isotonic saline at 37°C. The rate of the agent is calculated from the in vitro test method described in Section VIII. In Vitro Pumping Rate. The duration of delivery.

B. Start-Up Time

To order an ALZET test kit, call 877-922-9338 (toll free in the U.S. and Canada). A video of commonly used surgical implantation procedures is available at no charge.

1. Using a pair of scissors or pliers, break the white flange from the pump housing to expose the retainer spring. The pump is then placed in a test tube containing 15 ml of isotonic saline at 37°C. The rate of the agent is calculated from the in vitro test method described in Section VIII. In Vitro Pumping Rate. The duration of delivery.

C. Determination of Pumping Duration

The reservoir volume of ALZET Micro-Osmotic Pumps is slightly larger than that required to assure pumping for the complete 7 days. As a result, at the end of the pumping duration some of the drug solution will still be present in the pump, even if the delivery rate has reached zero. The method DURECT uses to estimate the pumping rate of micro-osmotic pumps is to measure their pumping rate in vitro at 0.9% saline at 37°C (± 0.5°C). These pumps are transferred to test tubes containing fresh saline at 37°C (± 0.5°C). This test solution should be compatible with the pump and be easy to analyze in isotonic saline. (One such indicator is FD&C Blue #1 dye, see note). The pumping rate highly unpredictable. Also, solutions with precipitated materials.

1. When the solvent you wish to use does NOT appear in Table 1, an ALZAID® Chemical Compatibility Test Kit is available to allow you to assess agent compatibility. If the solvent you wish to use is not listed in Table 1, contact ALZET Technical Support . A wealth of information on ALZET Micro-Osmotic Pumps and their applications.

2. A solution which generates gases within the pump during use makes the pump imbibes water during operation. Likewise, cutting open a spent pump is not a reliable means of verifying pumping performance. Lastly, measuring blood levels of drug solely at the exit of the catheter may not reflect the actual pumping rate and dose delivered while representing circulation.

Note that a partially emptied or discharged pump cannot be recharged with a new agent because the pump imbibes water during operation. Likewise, cutting open a spent pump is not a reliable means of verifying pumping performance. Lastly, measuring blood levels of drug solely at the exit of the catheter may not reflect the actual pumping rate and dose delivered.

1. When the solvent you wish to use does NOT appear in Table 1, an ALZAID® Chemical Compatibility Test Kit is available to allow you to assess agent compatibility. If the solvent you wish to use is not listed in Table 1, contact ALZET Technical Support . A wealth of information on ALZET Micro-Osmotic Pumps and their applications.

IV. Additional Technical Information About ALZET Micro-Osmotic Pumps

A wealth of information on ALZET Micro-Osmotic Pumps and their uses is available through ALZET Technical Support . Through this comprehensive technical support plan, you will receive:

- A Technical Information Manual
- A video of commonly used surgical implantation procedures
- ALZET Micro-Osmotic Pump Bibliography
- Literature materials for authors presenting their work
- Information about ALZET Brain Infusion Kits, ALZET, and other ALZET products.

To order any of these materials, or to receive additional information, contact ALZET Technical Support .

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