If you desire the pump to start immediately, are working with a viscous solution, or if you wish to attach a catheter, incubate the pre-filled pump in sterile saline at 37°C for at least 48 hours. (Refer to Section V for complete instructions.)

When the environment in which the pump is used differs significantly from normal mammalian body temperature (37°C) and osmolarity conditions, the pumping rate of ALZET pumps will be affected. (To calculate the pumping rate under specific temperature and osmolarity conditions, refer to the equation in Section V part D.)

ALZET micro-osmotic pumps, Model 1004, should be removed upon completion of their delivery duration or by day 42 after implantation. After this time, due to continued absorption of water into the reservoir, it may not be possible to dissolve the salt solution, resulting in local irritation around the pump. (Thisexpiration date is calculated based on the lot specification to calculate the exact delivery duration and maximum expiration date for this lot of micro-osmotic pumps.)

Via a catheter, ALZET pumps can be used to deliver substances into the brain or arterial circulation, into the brain, or intraperitoneal. It is not essential that the sheath and attached tube be free of air bubbles.

Perform the following steps when filling ALZET pumps:

1. Fill the pump tubing completely with the fluid to be delivered. Confirm compatibility with ALZET catheters by placing the tubing into the water bath. If the tubing does not swell, it is compatible. (Refer to Section V for a description of these verification techniques.)

2. With the flow moderator removed, hold the pump in an upright position and slowly fill the reservoir by applying gentle pressure to the pump until it can no longer accept fluid. This places the tip of the tube near the bottom of the pump reservoir.

3. Stop filling when the plunger of the syringe is level with the pump outlet. When using a syringe, the plunger should be visible through the tube filling opening.

4. With the flow moderator removed, hold the pump in an upright position. With the solution appearing at the outlet, stop filling and carefully remove the tube. (Rapid filling can introduce air bubbles into the delivery system.)

5. Disconnect the syringe and insert the flow moderator until the white flange is flush with the top of the pump. The insertion of the flow moderator is confirmed when the flow moderator is seated in the reservoir body. This should be visually observed or confirmed by the presence of a clear line moving through the flow moderator.

6. Filling the pump is accomplished with a small syringe (1.0 ml) and a 0.22 µm syringe-end filter (e.g., Sterile Millex® Syringe Filters - eMD Laboratories, Inc., Billerica, MA 01821, 978-715-4321).

7. To prevent back pressure, the pump should be fitted with a fitting tube, which can be placed in a variety of outlets. (For solvent compatibility with ALZET catheters, please contact ALZET Technical Information Services for assistance at 400-352-2290 (U.S. and Canada).)

8. ALZET micro-osmotic pumps are filled with sterile water for injection, USP grade, or 0.9% saline. If a solvent other than water is used, the volume indicated in the lot specifications at the top of this instruction sheet must be used. (Refer to Section II for complete filling instructions.)

9. Drug reservoir Volume 100 µl

10. Reservoir Weight (empty) 0.4 g

11. Length (tube only) 1.1 cm

12. Diameter 0.04 cm

13. O.D. (tube) 0.02 cm

14. Gauge (tube) 21

15. Material (tube) Stainless steel

16. Flow Moderator Length (tube only) 1.3 cm

17. Gauge (tube) 23

18. O.D. (tube) 0.08 cm

19. L.D. (tube) 0.06 cm

20. Material (tube) nylon

21. Material (flange) polyethylene

22. Drug Pump Body Materials Outter Membrane cellulose easter brick

23. Drug Reservoir thermoplastic hydrocarbon elastomer

24. Table 1: List of Solvents Compatible with the Reservoir Material of ALZET Osmotic Pumps

<table>
<thead>
<tr>
<th>Solvent</th>
<th>ALZET compatibility with reservoir material</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acids, with pH greater than 1.8</td>
<td>Not compatible</td>
<td>Refer to Section Vll for a description of these verification techniques.</td>
</tr>
<tr>
<td>Bases, with pH less than 14</td>
<td>Not compatible</td>
<td></td>
</tr>
<tr>
<td>Cremophor EL</td>
<td>Not compatible</td>
<td>Refer to Section Vll for a description of these verification techniques.</td>
</tr>
<tr>
<td>Cyclodextrins</td>
<td>Not compatible</td>
<td></td>
</tr>
<tr>
<td>Dextrose, up to 5% in water</td>
<td>Compatible</td>
<td>Refer to Section Vll for a description of these verification techniques.</td>
</tr>
<tr>
<td>Dextran</td>
<td>Up to 5% in water or polyethylene glycol</td>
<td></td>
</tr>
<tr>
<td>Diethyl ether</td>
<td>Up to 5% in water or polyethylene glycol</td>
<td></td>
</tr>
<tr>
<td>DMSO, up to 50% in water or polyethylene glycol</td>
<td>Compatible</td>
<td>Refer to Section Vll for a description of these verification techniques.</td>
</tr>
<tr>
<td>DMSO, up to 50% in ethanol</td>
<td>Compatible</td>
<td></td>
</tr>
<tr>
<td>Ethanol, up to 15% in water</td>
<td>Compatible</td>
<td></td>
</tr>
<tr>
<td>Glycerol</td>
<td>Up to 30% in water</td>
<td></td>
</tr>
<tr>
<td>Glyceryl 1,2,3-tri-Methoxy</td>
<td>Up to 25% in water</td>
<td></td>
</tr>
<tr>
<td>Glyceryl 1,2-Pyridine, up to 12.5% in water</td>
<td>Compatible</td>
<td></td>
</tr>
<tr>
<td>Glyceryl Butyrate</td>
<td>Up to 12.5% in water</td>
<td></td>
</tr>
<tr>
<td>Phosphate buffer</td>
<td>Up to 10% in water</td>
<td></td>
</tr>
<tr>
<td>Proteins, up to 10% in water</td>
<td>Compatible</td>
<td>Refer to Section Vll for a description of these verification techniques.</td>
</tr>
<tr>
<td>Serum (rat, mouse, etc.)</td>
<td>Compatible</td>
<td>Refer to Section Vll for a description of these verification techniques.</td>
</tr>
<tr>
<td>Saline, 0.9% (or other aqueous salt solution)</td>
<td>Compatible</td>
<td>Refer to Section Vll for a description of these verification techniques.</td>
</tr>
<tr>
<td>ringer's solution (with or without lactate)</td>
<td>Compatible</td>
<td>Refer to Section Vll for a description of these verification techniques.</td>
</tr>
<tr>
<td>ringer's solution (with or without lactate)</td>
<td>Compatible</td>
<td>Refer to Section Vll for a description of these verification techniques.</td>
</tr>
<tr>
<td>triclopropane, up to 5% in water</td>
<td>Compatible</td>
<td>Refer to Section Vll for a description of these verification techniques.</td>
</tr>
<tr>
<td>triacetin, up to 5% in water</td>
<td>Compatible</td>
<td>Refer to Section Vll for a description of these verification techniques.</td>
</tr>
<tr>
<td>Solutol, up to 30% in water</td>
<td>Compatible</td>
<td>Refer to Section Vll for a description of these verification techniques.</td>
</tr>
<tr>
<td>Water</td>
<td>Compatible</td>
<td>Refer to Section Vll for a description of these verification techniques.</td>
</tr>
<tr>
<td>Water, distilled</td>
<td>Compatible</td>
<td>Refer to Section Vll for a description of these verification techniques.</td>
</tr>
</tbody>
</table>
Note that the solvents listed above are known to be compatible with ALZET osmotic pumps. Durect strongly recommends that ALZET pump users verify the biodist of drug at several periods during the course of the experiment and ensure that the biodist is not critical. If the biodist is not possible or is technically undesirable, users should measure peak drug levels and use them as indicators of drug delivery. Use a blunt-end filling tube attached to a syringe to aspirate the remaining solution from the reservoir. This will allow the pump to deliver the agent at its designed rate.

Note that the weight of a partially empty or discharged pump cannot be accurately determined because the pump imbibes water during operation. Likewise, calibrating an empty pump is not a reliable means of verifying pump performance.

A. Predicting Pump Performance Outside Mammalian

B. Start-Up Time

V. Implantation of the ALZET Micro-Osmotic Pump

In Vivo

A random sample of 20 ALZET pumps is selected from the same lot of micro-osmotic pumps. This lot of micro-osmotic pumps.

For intraperitoneal placement, make a small midline incision in the skin at the back of the animal. Carefully make a small incision in the skin between the scapulae. Another small incision is made in the skin adjacent to the incision; this incision is used to remove the pump from the pump reservoir. This incision is made in the skin adjacent to the incision; this incision is used to remove the pump from the pump reservoir. Post-operatively, the animal must be handled carefully to prevent the catheter from being pulled out. The animal must be handled carefully to prevent the catheter from being pulled out.

B. Start-Up Time

VI. Operation of the ALZET Micro-Osmotic Pump

ALZET pumps are precision drug administration tools. This section details the actual operating parameters and tolerances of Model 1004 pumps that you should consider when using this pump. The Model 1004 pumps are designed to operate under conditions that are specified in the pump's specifications.

C. Determining Pumping Duration

The volume pumped by each pump is determined from the lot specifications on the other side of this instruction sheet.

D. Predicting Pump Performance Outside Mammalian

Ranges of Temperature and Osmolality

The variation in pump performance due to temperature and osmolality is predictable within ± 10% of the pump's nominal value. The pump's performance can be predicted by using the following equation:

\[ Q = \frac{2.5}{V} \left( 1 + 0.05 \Delta T \right) \]

Where:

- \( Q \) is the pumping rate in µl/hr
- \( V \) is the volume of the pump (µl)
- \( \Delta T \) is the temperature difference between the environmental temperature and the pump temperature (°C)

This equation is predictive within ± 10% of the pump's nominal value.

E. Determining Pumping Duration

The amount of indicator pumped out of the pump reservoir.

Note: This equation is predictive within ± 10% of the pump's nominal value.

F. Determining Pumping Duration

The method Durect uses to estimate the pumping rate of osmotic pumps is relatively simple.

G. Determining Pumping Duration

The amount of indicator pumped out of the pump reservoir.

Note: This equation is predictive within ± 10% of the pump's nominal value.

H. Determining Pumping Duration

The amount of indicator pumped out of the pump reservoir.

Note: This equation is predictive within ± 10% of the pump's nominal value.

I. Determining Pumping Duration

The amount of indicator pumped out of the pump reservoir.

Note: This equation is predictive within ± 10% of the pump's nominal value.

J. Determining Pumping Duration

The amount of indicator pumped out of the pump reservoir.

Note: This equation is predictive within ± 10% of the pump's nominal value.

K. Determining Pumping Duration

The amount of indicator pumped out of the pump reservoir.

Note: This equation is predictive within ± 10% of the pump's nominal value.

L. Determining Pumping Duration

The amount of indicator pumped out of the pump reservoir.

Note: This equation is predictive within ± 10% of the pump's nominal value.

M. Determining Pumping Duration

The amount of indicator pumped out of the pump reservoir.

Note: This equation is predictive within ± 10% of the pump's nominal value.

N. Determining Pumping Duration

The amount of indicator pumped out of the pump reservoir.

Note: This equation is predictive within ± 10% of the pump's nominal value.

O. Determining Pumping Duration

The amount of indicator pumped out of the pump reservoir.

Note: This equation is predictive within ± 10% of the pump's nominal value.

P. Determining Pumping Duration

The amount of indicator pumped out of the pump reservoir.

Note: This equation is predictive within ± 10% of the pump's nominal value.

Q. Determining Pumping Duration

The amount of indicator pumped out of the pump reservoir.

Note: This equation is predictive within ± 10% of the pump's nominal value.