1. Nominal Performance (at 37°C)

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

The performance of a pump is determined by the mass delivery rate (µg/hr) and the duration (days) of delivery. The mass delivery rate is given by the equation:

\[ ko = Q \cdot cd \]

Here, \( ko \) is the mass delivery rate (µg/hr), \( Q \) is the volume delivery rate (µl/hr), and \( cd \) is the concentration of the drug in the vehicle (µg/µl).

Pressure Rate 0.25 µl/hr

Duration 14 days

Reservoir Volume 100 µl

Residual Amount of Drug Remaining in the Pump at the End of the Delivery Period

The residual amount of drug remaining in the pump at the end of the delivery period can be calculated using the following equation:

\[ M = ko \cdot (1 - e^{-\frac{t}{\lambda}}) \]

where \( M \) is the residual amount of drug remaining in the pump, \( ko \) is the mass delivery rate, \( t \) is the duration of delivery, \( \lambda \) is the inverse of the exponential rate constant, and \( e \) is the base of the natural logarithms.

The residual amount of drug remaining in the pump at the end of the delivery period is approximately equal to the concentration of the drug in the vehicle solution at 37°C.

2. Flow Moderator

Flow moderators are essential components of the ALZET Micro-Osmotic Pump System. They are designed to control the rate of drug delivery by regulating the flow of the vehicle-drug combination through the pump. The flow moderator must be fully inserted into the body of the pump to ensure correct operation. The following steps should be followed when filling ALZET pumps:

Step 1. Weigh the empty pump together with its flow moderator.

Step 2. Filling the pump is accomplished with a small syringe (1.0 ml) and the provided blunt-tipped, 27 gauge fitting tube. Use of a larger syringe tends to plug the tube, which can introduce air bubbles into the reservoir. Draw the solution into the syringe and attach the fitting tube. It is essential that the fitting tube be free of air bubbles.

Step 3. With the flow moderator removed, hold the pump in an upright position and insert the fitting tube through the top of the pump. Be sure to go no further. This places the tip of the tube near the bottom of the pump reservoir.

Step 4. Push the plunger of the syringe slowly, holding the pump in the same orientation. Ensure that the solution appears to fill the outlet, stop filling, and carefully remove the tube. (Rapid filling can introduce air bubbles into the system.)

Step 5. Wipe the excess solution and insert the flow moderator until the white flange is flush with the top of the pump. The insertion of the flow moderator after filling the pump may result in unpredictable pumping rate fluctuations. Table 1 provides examples of some commonly used vehicle-drug combinations.

3. Pump Body Materials

The pumps are compatible with aqueous solutions, dilute acids and bases, dilute or low concentrations of DMSO and alcohol, and up to 15% in water. They are incompatible with propylene glycol, ethanol, up to 15% in water, and DMSO, up to 50% in ethanol. The pumps are compatible with alcoholic and hydrophobic substances, such as heparin, phospholipids, and hormones, up to 25% in water. The pumps may be affected by such substances as iso-osmotic solutions. Table 1 provides examples of some commonly used vehicle-drug combinations.

4. 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 15% in water. They are compatible with propylene glycol, ethanol, up to 15% in water, and DMSO, up to 50% in ethanol. The pumps may be affected by such substances as iso-osmotic solutions. Table 1 provides examples of some commonly used vehicle-drug combinations.

5. Instructional Sheet for Filling ALZET Micro-Osmotic Pump Model 1002

ALZET pumps have been exposed to a sterilizing dose of radiation from a 60Co source. The pumps have been exposed to a sterilizing dose of radiation from a 60Co source. The correct operation of ALZET pumps is verified by monitoring blood levels of drug during each experiment, by determining the residual amount of drug remaining in the pump at the end of the experiment, and by testing in vivo (refer to Section VII for a description of these verification techniques).
In Vitro, the ALZET Micro-Osmotic Pump in Vivo

The ALZET micro-osmotic pump can be implanted subcutaneously in an animal at the desired site. After the incision is made and the subcutaneous tissue dissected, a small incision is made in the skin between the scapulae. Using sterile technique, the pump is inserted with the plunger attached, and the subcutaneous tissue is closed with sutures. The pump is placed into the pocket made in the skin to allow for expansion away from the incision site. The incision is then closed with a wound clip or sutures.

For intraperitoneal placement, a small incision is made in the skin below the rib cage of an animal weighing at least 20 grams. Another small incision is made in the abdominal muscle between the rib cage incision and the umbilicus. The pump is inserted, first moderator into the peritoneal cavity, and then the incision is closed with either a wound clip or sutures. The pump is then connected to the administration line. The fluid is delivered to the animal at a constant rate until the drug solution is depleted. The pump is removed at the end of treatment period or by day 21 after treatment. (This equation is calculated based on nominal duration. Refer to the equation in Section V, Part C, and the actual release rate and fill volume specifications to calculate the expected pumping duration and maximum expiration time for this lot of osmotic pumps.)

Additional technical information about surgical procedures, contact ALZET Technical Support at 800-692-2990 (U.S. and Canada). A video demonstrating several surgical implantation procedures is available at no charge.

Operation of the ALZET Micro-Osmotic Pump

ALZET pumps are precision drug administration systems. This section details the actual pumping rate and fill specifications for the lot of Model 1002 pumps described in this document. As shown by these figures were determined. After a 4- to 6-hour start-up period, the Model 1002 pump delivers at a constant rate over a predictable range within all but about 5% of the reservoir contents have been removed. This characteristic is not affected by fluid viscosity, temperature, or the presence of precipitating substances. The equation method DURECT used to estimate the pumping rate of osmotic pumps is:

\[ Q = \frac{C}{	ext{tH}} \]  

where \( Q \) is the specified pumping rate of the pump in \( \mu \)l/h, \( C \) is the concentration of drug in the pump reservoir in milligrams, and \( \text{tH} \) is the time in hours to deliver 1 milliliter of solution from the pump reservoir.

The pump is delivered as a solution which generates gases within the pump in use makes the pump operate at slightly higher than optimum rate. The following equation is used to calculate the rate at which the pump operates:

\[ Q_{\text{p}} = Q_{\text{O}} \times \left( \frac{C_{\text{O}}}{C} \right) \]  

where \( Q_{\text{p}} \) is the pumping rate in \( \mu \)l/h, \( Q_{\text{O}} \) is the specified pumping rate of the pump at 37°C in 0.9% saline solution, \( C_{\text{O}} \) is the concentration of the drug solution in the pump reservoir, and \( C \) is the concentration of the drug solution being administered.

The equation is used to determine the pumping rate of osmotic pumps to be expected in homeothermic animals for which the following assumptions are made:

1. The animal’s body temperature is maintained at 37°C.
2. The animal’s body temperature is stable over the treatment period.
3. The drug solution is administered at a constant rate.
4. The drug solution is delivered at a constant rate.

The equation is used to calculate the pumping rate of osmotic pumps to be expected in homeothermic animals for which the following assumptions are made:

1. The animal’s body temperature is maintained at 37°C.
2. The animal’s body temperature is stable over the treatment period.
3. The drug solution is administered at a constant rate.
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