**MINI-OSMOTIC PUMP MODEL 2004**

0.25 µl PER HOUR, 28 DAYS (Actual specifications vary by lot)

**R E F E R E N C E  S O L U T I O N S**

- **CONTENTS**
  - One Mini-Osmotic pump
  - Ten flow moderators
  - Ten microsyringes (1.0 ml)
  - One sterile syringe-end filter (e.g., Sterile Millex® Syringe Filters, EMD Millipore, Billerica, MA, 01821, 978-715-4327)
  - One instruction/specification animals or for tests in vitro

**DURECT™**

DURECT Corporation, Cupertino, CA 95014

**ACTUAL LOT SPECIFICATIONS**

**LOT NO.**

<table>
<thead>
<tr>
<th>MEAN PUMPING RATE</th>
<th>MICROLITERS/HR.</th>
<th>STANDARD DEVIATION</th>
<th>MICROLITERS/HR.</th>
<th>TOTAL MEAN VOLUME</th>
<th>MICROLITERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>B. Components</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1. Performance (at 37°C)</td>
<td></td>
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<tr>
<td>Pumping Rate and Reservoir Volume: refer to Actual Lot Specifications at top of this instruction sheet.</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Dimensions, overall</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length</td>
<td>3.0 cm</td>
<td>Diameter</td>
<td>0.7 cm</td>
<td>Weight:</td>
<td>1.1 g</td>
</tr>
<tr>
<td>O.D. (tube)</td>
<td>0.04 cm</td>
<td>L.D. (tube)</td>
<td>0.05 cm</td>
<td>Weight (overall)</td>
<td>0.2 cm</td>
</tr>
<tr>
<td><strong>Flow Moderator</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length (overall)</td>
<td>2.4 cm</td>
<td>Gauge (tube)</td>
<td>21</td>
<td>Gauge (tube)</td>
<td>21</td>
</tr>
<tr>
<td>O.D. (tube)</td>
<td>0.08 cm</td>
<td>O.D. (tube)</td>
<td>0.05 cm</td>
<td>Weight (overall)</td>
<td>0.2 g</td>
</tr>
<tr>
<td>Material (Flange)</td>
<td>cellulose ester</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Pump Body Materials</strong></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Outer Membrane</td>
<td>cellulose easter blend</td>
<td></td>
<td></td>
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<tr>
<td>Drug Reservoir</td>
<td>thermoplastic hydrogel elastomer</td>
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</tbody>
</table>

**Instructions for Filling ALZET Mini-Osmotic Pumps**

If you desire the pump to start immediately, are working with a viscous solution, or at a rate faster than the pre-filled pump in sterile saline at 37°C for at least 40 hours. (Refer to Section VI, part B for instructions.)

When the environment in which the pump is used is different significantly from normal mammalian body temperature (37°C) and saline concentration, the flow rate of ALZET pumps may be affected. (To calculate the pumping rate under specific temperature and viscosity conditions, refer to the equation in Section IV.)

**ALZET Mini-Osmotic Pumps, Model 2004, should be removed upon completion of their delivery duration or by day 42 after implantation, if not used, due to continued after-dose delivery into the pump, it may swell and leak a concentrated salt solution, resulting in local irritation at the implantation site. Time the calculation based on nominal duration. Refer to the equation in Section V.)

**ALZET® MINI-OSMOTIC PUMP MODEL 2004**

**INSTRUCTION AND SPECIFICATION SHEET**

DURECT Corporation manufactures a miniature implantable pump for use in laboratory research. The ALZET Mini-Osmotic Pump 2004 delivers solutions continuously for at least 28 days without the need for further drug delivery. It is compatible with a wide range of drug concentrations and doses. This product is for use in experimental animals only. It is not to be used in humans, or in food or food products, or in humans. ALZET® MINI-OSMOTIC PUMP MODEL 2004 is for use only in laboratory research.

**TABLE 1**

<table>
<thead>
<tr>
<th>LOT NO.</th>
<th>MEAN PUMPING RATE</th>
<th>MICROLITERS/HR.</th>
<th>STANDARD DEVIATION</th>
<th>MICROLITERS/HR.</th>
<th>TOTAL MEAN VOLUME</th>
<th>MICROLITERS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Flow Supplier</strong></td>
<td></td>
<td></td>
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<tr>
<td>DURECT Corporation, Cupertino, CA 95014</td>
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</tr>
</tbody>
</table>

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

A. Complete Mini-Osmotic Pump System with Flow Moderator in Place

1. **Performance (at 37°C)**

   - Pumping Rate and Reservoir Volume: refer to Actual Lot Specifications at the top of this instruction sheet.
   - Duration: 28 days (refer to Section VI, part C)

2. **Flow Rate Monitoring**

   - The release rate and reservoir volume published in ALZET marketing specifications represent the target for manufactured pumps. However, individual lots of pumps vary within acceptable limits. Each lot of ALZET pumps is tested under well-controlled conditions to determine its actual pumping rate and reservoir volume. These specifications are listed at the top of this instruction sheet. Always use the Actual Lot Specifications (Pumping Rate and Fill Volume) when calculating release rate and fill volume specifications, to calculate the exact delivery duration and maximum explantation date for this lot of mini-osmotic pumps.

3. **Verify correct operation of ALZET pumps by both monitoring blood levels of the drug solution and observing any changes in animal behavior.**

4. **Solutions should be at room temperature during filling.**

5. **ALZET® MINI-OSMOTIC PUMP MODEL 2004**

   - A. Performance (at 37°C)

   - Pumping Rate and Reservoir Volume: refer to Actual Lot Specifications at the top of this instruction sheet. When the environment in which the pump is used differs significantly from normal mammalian body temperature (37°C) and saline concentration, the flow rate of ALZET pumps may be affected. (To calculate the pumping rate under specific temperature and viscosity conditions, refer to the equation in Section IV.)

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I. Introduction

The above formula is useful in the range of $\pi = 0$ to 25 atm and $T =$ (0.054T) + 0.03.

II. Viability of the ALZET Mini-Osmotic Pump in Vivo

III. Determination of Average Pumping Rate

The reservoir volume of ALZET Mini-Osmotic Pumps is slightly larger than that required to assure pumping for the complete 28 days. As a result, at the end of 28 days the volume of the drug solution will remain in the pump. This solution can be aspirated from the pump by using a 27 gauge needle on an 1 ml syringe to calibrate the exact pumping rate. Recovery of the drug solution can be enhanced by flushing the reservoir with additional drug solution, typically 5 ml. The amount of drug solution which was recovered from the reservoir can then be assayed using an appropriate method to calculate the average pumping rate, the difference between the amount of drug initially loaded and the residual amount in the pump reservoir.

IV. Determination of the In Vivo Pumping Rate

ALZET pumps are supplied with a specified volumetric pumping rate determined in in vitro testing. However, it is not always possible to predict the pumping performance with any degree of certainty.

V. Calculating the Duration of Pumping

The formula for calculating the pumping duration is $D = (V / D_{O}) Q_{O}$, where $D$ is the duration in hours, $V$ is the pump reservoir volume in ml, $D_{O}$ is the pumping rate in ml/hr, and $Q_{O}$ is the pumping rate in ml/hr specified by the manufacturer at 37°C in 0.9% saline.

VI. Operation of the ALZET Mini-Osmotic Pump

A. Determination of Average Pumping Rate

This procedure is mandatory when the pump is being filled. After filling, each ALZET pump is submersed in 0.9% saline at 37°C for a period of 1 hour. To determine reproducibility, ALZET pumps are transferred to test tubes containing fresh saline at regular intervals through day 28. The output from each pump is collected and the mean pumping rate is calculated from the following expression:

$$\text{Average Pumping Rate} = \frac{\sum Q(t)}{T}$$

where $Q(t)$ is the pumping rate at time $t$, and $T$ is the total duration of pumping.

B. Start-Up Time

If an ALZET pump is loaded at room temperature (23°C) with a drug solution that is not highly temperature sensitive, the drug will be the basis for the pumping rate calculation. Therefore, the indicator solution should be compatible with the drug and be easy to analyze. The concentration of indicator should be determined from a Working Standard curve available from SeraCare, 2515 N. Jefferson St., St. Louis, MO 63144-1498.

C. Determination of Pumping Duration

The following equation can be used to predict the pumping rate in heteromorphic animals or in those whose body fluids are isotonic with mammals:

$$Q = 0.135 T^{0.5} + 0.040 + 0.03$$

Here $Q$ is the specified pumping rate of the pumps at 37°C in 0.9% saline, T is the time in hours, and $Q_{O}$ is the pumping rate in ml/hr specified by the manufacturer at 37°C in 0.9% saline. The pumping rate will not reach steady state for several hours. If your results are not consistent with those given here, you should place the perfused animals in a 37°C incubator to ensure that the pumping rate is reproducible.

D. Selecting the In Vivo Pumping Rate

For a period of 12 months from date of shipment, DURECT warrants each ALZET pump to be free from defects in material and workmanship and will, at its own expense, exchange or repair the pump at any time during the 12-month period if such defects are found. DURECT is not responsible for any indirect or consequential damage, including damage to equipment. The sole and exclusive remedy for any breach of warranty shall be the replacement, at no cost to the customer, of those units of Product giving rise to such liability. DURECT shall not be liable for any special, incidental, indirect or consequential damages of any kind, or any other damages, including lost profits, arising from this Product or its use.

VII. Use of the ALZET Mini-Osmotic Pump With a Catheter or Brain Infusion Kit

VIII. Determination of the Average Pumping Rate

The above formula is useful in the range of $\pi = 0$ to 25 atm and $T =$ (0.054T) + 0.03. This expression is applicable only to the Model 2004. Note that as $Q$ decreases in proportion to the environmental temperature, the pumping duration increases.

IX. Technical Information About ALZET Mini-Osmotic Pumps

A. Technical Information Manual

A video of commonly used implantation procedures is available from DURECT. Use of this video requires the purchase of a Video Use Authorization (VUA) form. For further information regarding any of the other items listed, contact ALZET Technical Support.

B. Information about ALZET Brain Infusion Kits, ALZET Catheters, and other ALZET Products

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

ALZET Technical Support
DURECT Corporation
10240 Bubb Road
Cupertino, CA 95014

877-922-5238 (toll free in the U.S. and Canada)
408-367-4036 (Outside the U.S.)
888-880-4198 (fax)
408-367-4036 (voice)
408-387-4036 (Outside the U.S.)
408-367-4036 (fax)
408-880-4198 (FAX)
877-922-5238 (toll free in the U.S. and Canada)

X. Warranty

A warranty for a period of 12 months from date of shipment, DURECT warrants that each ALZET pump to be free from defects in material and workmanship and will, at its own expense, exchange or repair the pump at any time during the 12-month period if such defects are found. The pump and catheter can be used at the customer's option, after the pump is filled. The sole and exclusive remedy for any breach of warranty shall be the replacement, at no cost to the customer, of those units of Product giving which have been shown to DURECT's reasonable satisfaction have to be made.

This warranty is in lieu of all other warranties, expressed or implied, and with the exception of the express warranty herein, DURECT makes no warranty of merchantability, fitness for a particular purpose, or non-infringement. In no event shall DURECT be liable for any direct, indirect, incidental, or consequential damages, regardless of theory of liability. DURECT shall not be liable for any special, incidental, indirect or consequential damages of any kind, or any other damages, including lost profits, arising from this Product or its use.

DURECT Corporation
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