BRAINTREE SCIENTIFIC, INC.
LAB RESEARCH PRODUCTS

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Pump Selection

ALZET pumps are available in a variety of sizes, durations and flow rates to meet a wide range of research needs. While the pumping rate of each model is fixed at manufacture, the dose of agent delivered can be adjusted by varying the concentration of agent with which each pump is filled. Provided the animal is of sufficient size, multiple pumps may be implanted simultaneously to achieve higher delivery rates than are attainable with a single pump. For more prolonged delivery, pumps may be serially implanted with no ill effects.
When choosing a pump model, consider the following:

- Animal size: refer to our guidelines for pump implantation based upon animal size
- Route of compound administration for the desired target tissue and response
- Desired delivery rate
- Preferred duration of administration
- Compound characteristics* (solubility, cost)
- Dose
- Ambient Temperature & Osmolality (relevant to use in heterotherms or in vitro only)

***Note**: The molecular weight of a compound is not relevant in the use or selection of ALZET pumps, since it has no impact on the release rate or function of the pump.

Animal Considerations

ALZET pumps can be implanted subcutaneously or intraperitoneally following the animal size guidelines below. ALZET pumps may also be connected to a catheter to deliver the pump contents directly into the venous or arterial systems, the brain, or into any organ or tissue. We recommend use of the smallest size pump allowable for the solubility of the agent and duration of the experiment.

Estimated Minimum Animal Size For Implantation of ALZET Pumps

Note: The minimum animal size estimates are based on experience with male Sprague Dawley rats and Swiss Webster mice. When using the pumps with other types or genders of rats and mice, or with animals other than rats and mice, these guidelines should be modified accordingly. (N/A = not applicable)

Model Numbers	1003D, 1007D, 1002, 1004	2001D, 2001, 2002, 2004, 2006	2ML1, 2ML2, 2ML4
Mice			
Subcutaneous	10g	20g	n/a
Intraperitoneal	20g	n/a	n/a
Rats			
Subcutaneous	10g	20g	150g
Intraperitoneal	20g	150g	300g

The pumps have been used in animals across the age spectrum, and in many different species. Following are specific tips on using ALZET pumps in a few specific animal models:

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- Neonates
- Nude mice
- Species or applications in heterothermic animals
- Species or application at osmolalities other than mammalian

ALZET osmotic pumps have been used most extensively in mice and rats. However, references are available on the use of ALZET pumps in the following animals:

Bird	Gerbil	Pig
Cat	Goat	Primate
Cattle	Guinea pig	Rabbit
Chinchilla	Hamster	Rat
Chipmunk	Horse	Sheep
Deer	Iguana	Skunk
Dog	Kangaroo	Squirrel
Ferret	Mastomys	Mouse Toad
Fish	Mink	Vole
Frog		

This list is not meant to be comprehensive. If your animal model is not included, please contact ALZET Technical Support to inquire about references and specific guidelines (click here).

Route of Administration

ALZET pumps can be implanted either subcutaneously or in the peritoneal cavity, and these are the most common infusion sites. The choice between them is normally made based upon prior work with the test compound, compound absorption and clearance, and animal size. Uptake into the portal circulation can be more significant if a compound is administered intraperitoneally, so avoiding this route may be prudent for compounds cleared rapidly by the liver.
In addition, all pump models are easily attached to a catheter, such that a pump implanted either subcutaneously or intraperitoneally is used to infuse into a vessel, organ or tissue. Following are the major routes of administration via ALZET pump reported in the literature:

- Subcutaneous
- Intraperitoneal
- Intracavitary:
  - *Articular Cavity*
  - *Bladder*
  - *Cerebral Ventricles*
  - *Intestine*
  - *Stomach*
  - Uterus
- Intravenous
- Intra-Arterial
- Intraluminal
- Local Tissue Microperfusion:
  - *Arterial Wall*
  - *Bone*
  - *Brain*
  - *Ear*
  - *Eye*
  - *Muscle*
  - *Nerves*
  - *Ovary*
  - *Spinal Cord*
  - *Spleen*
  - *Testes*
  - *Tumor*

Delivery Rate

Selecting a pump with the optimal flow rate may be important for certain applications, such as when infusing into solid tissue. For example, lower flow rates (e.g., < 5 µl/hr) are typically preferred for administering compounds into brain parenchyma. Visit the ALZET bibliography or contact ALZET Technical Support for references indicating which pump models are preferred for solid tissue microperfusion.

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Duration of Administration

The nominal durations for ALZET pumps range from 1 day to 6 weeks depending upon the pump model. (List of pump durations) All pumps will deliver for longer than the nominal duration in order to ensure they last the full nominal duration and to allow for priming. (What is priming?) The actual duration of a particular lot can be estimated based on the mean pumping rate and fill volumes provided, together with statistical parameters, on the instruction sheet included in each box. (see example) Divide 95% of the average reservoir fill volume (µl) by the average pumping rate (µl/hr) to allow for a 5% residual which cannot be displaced from the pump. The mean pumping rate and mean fill volume are determined by in vitro testing performed by DURECT.

In fact, some pumps will deliver for longer periods depending upon the actual specifications of a given manufacturing lot. If your study calls for a particular duration not listed on our web site, please check with ALZET Technical Support for availability.

Longer durations can be achieved by serial implantation. For example, a 2 month infusion would be achieved by implanting a 4 week pump, removing it after one month, and replacing it with a fresh 4 week pump. You could also implant a 6 week pump model, followed by a 2 week pump model. A list of references on long-term administration with ALZET pumps is available (click here). This reference list includes published studies in which infusions of up to 18 months duration have been accomplished, and up to 36 serial implantations have been performed on a single animal. (Click here for a list of references on extended duration studies).

Compound Characteristics

Because of its mechanism of operation, the ALZET pump is well suited for administering a wide range of compounds regardless of their molecular weight. The molecular weight has no impact on the delivery or function of the pump. How does the pump work? Successful delivery of an enormous range of compounds has been reported in the literature (Click here for a list of all agents that have been delivered using ALZET pumps).

Solubility

For poorly soluble compounds, a larger pump with a faster flow rate (allowing for a lower drug concentration), may be required to administer the required dose. (List of pump models and reservoir volumes) (Tips on selecting a vehicle)

Cost

When working with compounds that are expensive, or in limited supply, the driving factor in choice of pump may be small reservoir capacity. Volumes smaller than the reservoir capacity of a single pump can be administered successfully via catheter. (Method)

Dose

Depending on the solubility of the compound, administering a larger dose quickly will require a pump with a relatively higher flow rate. Some studies have a daily dose as the goal. Use the following equation or our interactive calculator to determine the daily dose delivered by a particular pump:

$$K = C \times Q$$

K = compound delivered per hour, in µg

C = concentration of solution, in µg/µl

Q = release rate of pump, in µl/hr

Depending upon the size of the animal (e.g., adult rat or larger) multiple pumps may be implanted simultaneously to deliver a larger dose than would be possible with a single pump.

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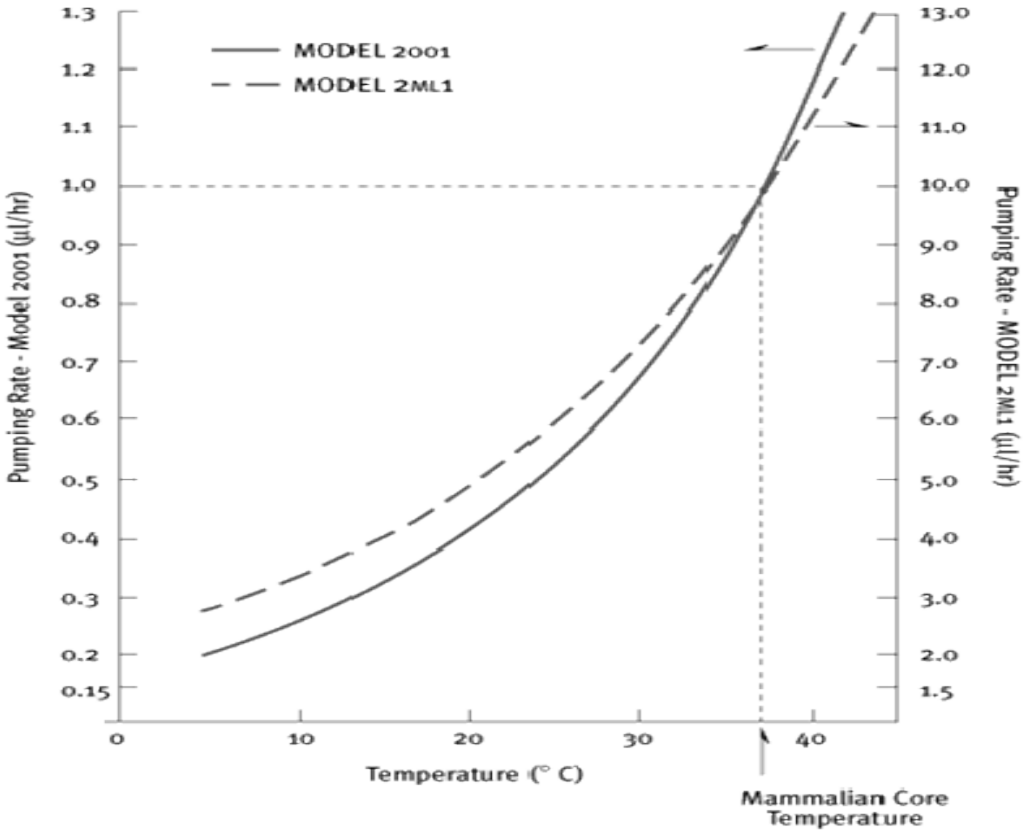
Ambient Temperature & Osmolality

Rates and durations listed for ALZET pumps are based on use in vivo in mammals unless otherwise specified. In alternate settings, such as in vitro or in other species, the pumping rate and duration may differ since they are affected by temperature and osmolality. Both temperature and osmolality affect the rate at which water crosses the semi-permeable membrane and enters the osmotic sleeve.



The pumping rate of ALZET osmotic pumps varies in direct proportion to temperature. The graph on the left shows the representative pumping rates for two pump models from 4 degrees to over 40 degrees in 0.9% saline.

Use the following equations, or the interactive calculator , to predict the pumping rate in heterothermic animals or in those whose body fluids are hypertonic relative to mammals.

Models

2001, 2002, 2004, 2006, 2001D, 1004, 1003D, 1007D, 1002, and 1004

$$Q_T = Q_0 (0.135\, e^{(0.054T)} - (0.004\pi) + 0.03)$$

2ML1, 2ML2, and 2ML4

$$Q_T = Q_0 (0.141\, e^{(0.051T)} - (0.007\pi) + 0.12)$$

- Q_T = the pumping rate at temperature T
- Q_0 = the specified pumping rate at 37°C in µl/hr
- T = temperature in degrees Celsius
- π = osmolality of the solution outside the pump (atm)

These formulae are useful in the range of π = 0 to 25 atm and T = 4°C to 42°C. The equation is predictive within +/- 10%. At normal mammalian osmolality of 310 milliosmoles/l, the osmotic pressure is 7.5 atm. Environmental temperatures above 42°C have been found to cause fluctuating delivery rates and are not recommended.