

# MINIATURE INFUSION PUMPS FOR MICE

ALZET<sup>®</sup> Osmotic Pumps are available in small sizes to enable continuous delivery of bioactive compounds to mice. With many inbred strains available, and new transgenic and knockout strains emerging rapidly, scientists have adopted the mouse as the premier mammalian model for *in vivo* research. To keep pace with this trend, laboratory equipment and research tools, including infusion devices, must be compatible for use in mice.

ALZET pumps are a practical and cost-effective method for administering test agents to unrestrained lab animals, including mice. Since the pumps are fully implantable (no need for external connections), mice are untethered and unrestrained during the entire dosing period. The lack of external connections minimizes infection and enables group housing of animals. Furthermore, ALZET pumps provide continuous infusion for prolonged periods of time, thereby reducing stress-related responses resulting from frequent handling and repeated dosing.

The use of ALZET pumps in mice has been documented since 1976 in over 8,400 published studies. Nine ALZET pump models, in a range of release rates and durations, are appropriate for use in mice. Continuous delivery for up to 6 weeks is feasible with a single pump, and even longer durations can be achieved through serial implantation.

## ROUTES OF ADMINISTRATION

ALZET pumps can be implanted SC or IP to enable systemic delivery of experimental agents to mice. They can easily be connected to a catheter for targeted delivery of compounds into vessels, brain tissues, cerebral ventricles, tumors, or other organs and tissues.

## IMMUNODEFICIENT MOUSE MODELS

Their automatic operation and small size make ALZET pumps an ideal infusion system for chronic dosing studies in immunodeficient mouse models, including nude and SCID mice. No researcher intervention is required during infusion, and animal handling is minimized to reduce the risk of infection and stress. ALZET pumps have been used in immunodeficient mice since 1980, and over 580 publications are available as evidence of their research value in these species. Additional information, including surgical implantation guidelines, is available upon request.



## HIGHLIGHTS

- 9 pump models available for use in mice
- Delivery rates ranging from 0.11  $\mu\text{l/hr}$  to 8  $\mu\text{l/hr}$
- Delivery durations ranging from 1 day to 6 weeks

## BENEFITS IN MOUSE RESEARCH

- Convenient and cost-effective method for chronic dosing
- Continuous and controlled delivery of test agents
- Minimize side effects and experimental variables
- Reduce animal handling and stress during dosing

## OPTIMUM MOUSE SIZES

ALZET pumps are suitable for subcutaneous (SC) and intraperitoneal (IP) implantation in mice according to the animal size guidelines described below.

Implantation Route	ALZET 100 $\mu\text{l}$ Models	ALZET 200 $\mu\text{l}$ Models
SC	10+ gram mice	20+ gram mice
IP	20+ gram mice	Possible via catheter

Although the 200  $\mu\text{l}$  pumps seem large, they are suitable for SC implantation in mice weighing at least 20 grams. This is supported by our studies in Swiss Webster mice which showed that pump implantation caused no additional stress or deviation from their normal weight gains. The 200  $\mu\text{l}$  pumps are widely used in mouse studies, as evidenced by 3,000+ publications in the scientific literature (publications and supportive quotes available upon request).

## INTRAVENOUS INFUSION

Compared to conventional infusion methods in which external catheters and swivels restrict animal movement and pose an infection risk, intravenous (IV) infusion with ALZET pumps presents a significant advantage in terms of animal welfare and experimental convenience. For IV infusion, the pump is fully implanted SC with the attached catheter leading into the target vessel. After pump implantation and vessel cannulation, mice can move freely around the cage, even in a group-housed environment.

## INTRACEREBRAL INFUSION

For compounds which do not cross the blood-brain barrier, local infusion directly into the brain is the only way to generate reliable data. The low flow rates and small size of ALZET pumps, used together with the Brain Infusion Kit 3, make an ideal combination for intracerebral delivery in mice. ALZET pumps have been used in hundreds of neuroscience studies to infuse agents, from neurotrophic factors to siRNA to psychoactive drugs and more.

### CSF Volume & Production Rate in the Mouse

**CSF Volume:** 0.035 ml (35  $\mu$ l)

**CSF Production rate:** 0.018 ml/hr (18  $\mu$ l/hr)

**Source:** Pardridge, W.M., *Transnasal and intraventricular delivery*. In "Peptide Drug Delivery to the Brain" (Table 4.2) Raven Press, 1991:112.

## CHRONIC INFUSION

ALZET pumps range in duration from 1 day to 6 weeks. However, animals can be dosed for longer periods by performing serial implantation of pumps. This procedure is generally well tolerated and enables steady state exposure of experimental agents over prolonged periods of time. The longest infusion study reported in mice using ALZET pumps is 9 months, with pumps replaced every 4 weeks (Guo *et al.* VCP recruitment to mitochondria causes mitophagy impairment and neurodegeneration in models of Huntington's disease. *Nature Communications*. 2016;7:12646). In contrast with other infusion devices, ALZET pumps contain no moving parts or batteries that can potentially fail during the course of a long-term study.



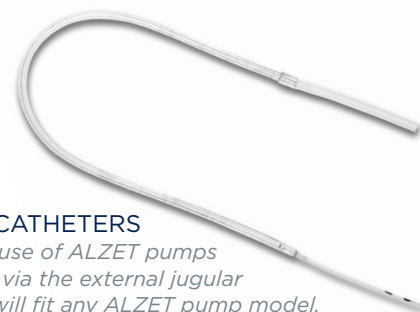
Pump Model	Reservoir Volume	Duration	Release Rate
1003D	100 $\mu$ l	3 days	1.0 $\mu$ l/hr
1007D	100 $\mu$ l	1 week	0.5 $\mu$ l/hr
1002	100 $\mu$ l	2 weeks	0.25 $\mu$ l/hr
1004	100 $\mu$ l	4 weeks	0.11 $\mu$ l/hr



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### MOUSE JUGULAR CATHETERS

*Designed to facilitate use of ALZET pumps for IV infusion in mice via the external jugular vein, these catheters will fit any ALZET pump model.*

### BRAIN INFUSION KIT 3

*The ALZET Brain Kit 3 is specifically designed for intraventricular and intraparenchymal infusion in the mouse. The fine gauge stainless steel cannula minimizes trauma to brain tissue during placement, and its 3 mm length is appropriate for targeting the lateral ventricles of adult mice. Uniquely designed depth adjustment spacers allow cannula length adjustment for targeting more superficial brain areas.*



## IN VIVO IMAGING APPLICATIONS

Bioluminescence Imaging (BLI) and Magnetic Resonance Imaging (MRI) techniques are powerful research tools enabling *in vivo* monitoring of ongoing biological processes over time in the same animal. ALZET pumps are increasingly being used in imaging studies, and they can easily be adapted for compatibility with MRI or BLI equipment. Please contact ALZET technical support for specific information.



Pump Model	Reservoir Volume	Duration	Release Rate
2001D	200 $\mu$ l	1 day	8.0 $\mu$ l/hr
2001	200 $\mu$ l	1 week	1.0 $\mu$ l/hr
2002	200 $\mu$ l	2 weeks	0.5 $\mu$ l/hr
2004	200 $\mu$ l	4 weeks	0.25 $\mu$ l/hr
2006	200 $\mu$ l	6 weeks	0.15 $\mu$ l/hr