NEUROSCIENCE PRODUCTS & APPLICATIONS

ALZET® Osmotic Pumps and Brain Infusion Kits have been used in cutting edge neuroscience research for over four decades. Their ability to circumvent the blood-brain barrier and administer agents directly to the central nervous system (CNS) has enabled new and exciting discoveries in the study of neuropathic pain, cerebral ischemia, neurodegenerative diseases, and more.

Gathered here is a selection of CNS infusion tools and applications to help you achieve reliable and reproducible results.

alzet®
OSMOTIC PUMPS

BENEFITS OF ALZET PUMPS IN NEUROSCIENCE RESEARCH

- Small size for use in mice and young rats
- Direct delivery across the blood-brain barrier
- Continuous and controlled delivery of neuroactive compounds
- Ideal for behavioral studies — no animal handling required during infusion
- Easy attachment to a catheter for delivery to the brain, spinal cord, or peripheral nerves
- Well-established method with over 18,500 publications
- Improved bioavailability of short half-life peptides and proteins
- Convenient & cost-effective for chronic dosing of lab animals
- Automatic nighttime and weekend dosing
- Simple design and easy to use
- Improved animal welfare

Subcutaneous placement of an ALZET pump and brain cannula enables automatic and continuous delivery of agents to the CNS of unrestrained lab animals.

ALZET BRAIN INFUSION KITS

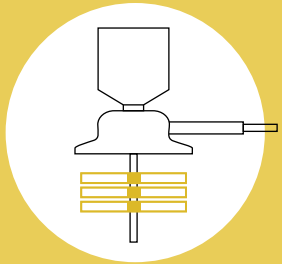
ALZET pumps and brain infusion kits are a reliable and convenient tools to deliver agents across the BBB, and directly to their site of action in the brain. They enable continuous delivery of a precise drug dose, and ensure that sufficient levels are maintained at the target location to elicit their effects.

ALZET Brain Infusion Kits can be used in two ways:

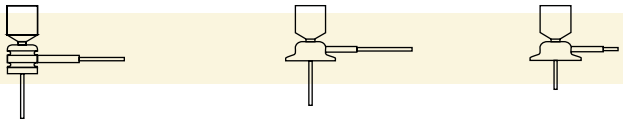
- Infusion into the cerebral ventricles, exposing a wide variety of brain regions to the infusate via the cerebrospinal fluid.
- Direct microinfusion of discrete brain structures, resulting in localized distribution of infusate in the target tissue.

Each ALZET Brain Infusion Kit includes materials for 10 brain infusions:

- 10 Brain Infusion Cannulae
- 10 Vinyl Catheter Tubes
- 40 Depth-Adjustment Spacers
- 1 Instruction Sheet



Depth adjustment spacers allow the penetration of the cannula tip to be reduced in 0.5 mm increments

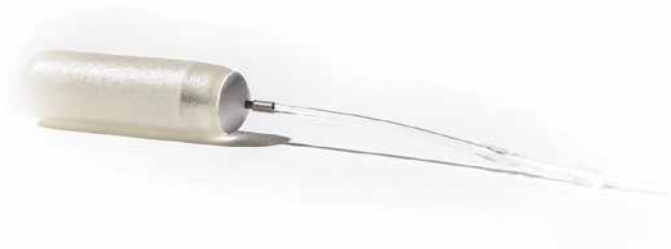


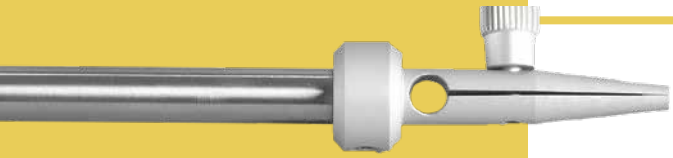
Brain Infusion Kit (BIK)	BIK1	BIK2	BIK3
Order number	0004760	0008663	0008851
Material (tube)	Stainless steel		
Gauge (tube)	28 Gauge		30 Gauge
Dimensions (tube)	ID = 0.18 mm; OD = 0.36 mm		ID = 0.16 mm; OD = 0.31 mm
Penetration depths	3-5 mm		1-3 mm
Material (elbow stop, tab)	Polycarbonate		
Side connector (for catheter attachment)	0.71 mm (21 Gauge)		
Cannula Design	Narrow diameter with suture grooves		Low profile and wide base for skin closure and stability
Features	Compatible with all ALZET pump models; optimum for delivery to lateral ventricles of rats (BIK1 & 2) and mice (BIK3); easily customized for delivery to different brain regions or animal sizes; fine cannula minimizes trauma to the brain during placement; provided sterile		

INTRATHECAL CATHETERS

Specifically designed for use with ALZET pumps, these catheters are constructed with high quality materials for increased patency and reduced tissue trauma. They incorporate useful features, such as flexible and secure catheter junctions to minimize kinking and leaking, and a teflon-coated, stainless steel wire to facilitate placement. They are available sterile and individually packaged.

Description (Order No.)	Material	Length	General Features
Rat Intrathecal (0007740)	Polyurethane	23.7 cm	Optimum for occipital insertion; includes 10 cm of very fine tubing (28G; 0.36 mm OD); teflon-coated, stainless steel wire stylet.
Rat Intrathecal-Short (0007741)	Polyurethane	15 cm	Shorter length for lumbar insertion; includes 10 cm of very fine tubing (28G; 0.36 mm OD); teflon-coated, stainless steel wire stylet.
Mouse Intrathecal (0007743)	Polyurethane	6 cm	Includes 2.5 cm of very fine tubing (32G; 0.23 mm OD); teflon-coated, stainless steel wire.





Features a narrow, non-intrusive tip

Order No. 0008860

Cannula positioned horizontally away from the stainless steel rod for easier visualization during cannulation.

Order No. 0008861

CANNULA HOLDERS

Designed to hold the removable tab on all ALZET brain infusion cannulae, these devices facilitate stereotaxic placement of brain cannula to the skull of laboratory animals.

CYANOACRYLATE ADHESIVE (LOCTITE 454)

Loctite 454 (Order No. 0008670) is an instant adhesive gel for use with ALZET Brain Infusion Kits and other brain cannulae. It offers a convenient alternative to dental cement, and researchers have found it to be ideal for brain cannulation in mice and other small animals. One 3 gram tube is enough for 10 brain cannulations.

WOUND CLOSURE SYSTEMS

The AutoClip & Reflex wound closure systems provide a fast and effective alternative to sutures for closing incisions made for ALZET pump implantations. The components are available separate, or as a kit containing the Applier, Remover, and stainless steel wound clips (7 mm or 9 mm). The 9 mm AutoClips are ideal for use in rats, while the 7 mm Reflex clips are optimum for use in mice and young rats. Visit www.alzet.com, or contact us for a complete list of wound closure products available.

ALZET OSMOTIC PUMPS: RATES & DURATIONS

ALZET pumps are available in 3 different sizes, durations ranging from 1 day to 42 days, and various release rates to meet your experimental needs.

Pump Model	1003D	1007D	1002	1004	2001D	2001	2002	2004	2006	2ML1	2ML2	2ML4
Reservoir Vol.	100 µl	100 µl	100 µl	100 µl	200 µl	200 µl	200 µl	200 µl	200 µl	2 ml	2 ml	2 ml
Duration	3 days	1 week	2 weeks	4 weeks	1 day	1 week	2 weeks	4 weeks	6 weeks	1 week	2 weeks	4 weeks
Release Rate	1.0 µl/hr	0.5 µl/hr	0.25 µl/hr	0.11 µl/hr	8.0 µl/hr	1.0 µl/hr	0.5 µl/hr	0.25 µl/hr	0.15 µl/hr	10 µl/hr	5.0 µl/hr	2.5 µl/hr
Order No.	0000289	0000290	0004317	0009922	0000294	0000292	0000296	0000298	0007223	0000323	0000325	0000327

NEUROSCIENCE RESEARCH APPLICATIONS

Models of Neurodegenerative Disease

ALZET pumps have been used to facilitate the development of animal models of neurodegenerative disease, including Alzheimer's, Parkinson's and Huntington's. The ability of ALZET pumps to provide a slow, continuous and chronic dose is favorable for sustaining a stable disease state over prolonged periods. *In vivo* models of Parkinson's have been produced by continuous administration of 6-hydroxydopamine (6-OHDA) into the striatum of rats, systemic infusion of the neurotoxin MPTP to mice or monkeys, and systemic rotenone dosing in rats. A rat model of Alzheimer's, the FAB rat, is induced by ICV infusion of a solution containing amyloid peptide, ferrous sulfate, and buthionine sulfoximine over 4 weeks using ALZET pumps. A model of Huntington's is chemically-induced via continuous infusion of the mitochondrial toxin 3-nitropropionic acid in rodents and nonhuman primates. These established models display biochemical, behavioral and morphological characteristics of neurodegenerative disease states and facilitate the study of disease mechanisms and potential neuroprotective therapies.

Intrathecal delivery

Targeted delivery via the epidural or intrathecal space circumvents the blood-brain barrier, and can provide a means of delivery for analgesics or other compounds without the side effects associated with systemic administration. ALZET pumps are commonly used for intrathecal infusion of agents at low and constant rates to study axonal regeneration, hyperalgesia, antinociception, and other aspects of pain. A large body of work is also focused on the development of tolerance related to opiate treatment.

Targeting Peripheral Nerves

With relative ease, ALZET pumps can be connected to a catheter to enable continuous delivery of solutions directly to a nerve cuff or chamber. The ability to deliver peptides and other compounds to the desired site can amplify their effects, while minimizing widespread systemic side effects. The targeted delivery of tetrodotoxin with ALZET pumps blocks nerve conduction temporarily, which is useful when studying innervations and neuromuscular development. Controlled and localized administration of neurotrophins is also critical when studying nerve regeneration following injury.

Delayed CNS Delivery

ALZET pumps can be adapted to allow for a recovery period following surgery, such as after implantation of brain cannulae. In this method, the pump is filled with drug solution and attached to a length of catheter tubing filled with a vehicle control solution. A spacer substance, such as oil or sterile air, is placed between the control and drug solutions to prevent mixing. Upon implantation, the pump releases drug solution from the pump reservoir into the catheter tubing, displacing control solution from the catheter into the animal. Once all of the control solution is released, the drug solution reaches the end of the catheter and drug dosing begins.

Chronic Delivery

Chronic administration of several months or longer may be necessary to evaluate the long-term effects of test compounds *in vivo*, or to establish a stable animal model of disease. ALZET pumps offer a reliable and convenient alternative to frequent injections for chronic dosing of lab animals. Steady-state levels of therapeutic agents can be maintained in tissues or plasma for up to six weeks with a single pump, and the treatment duration can be extended for multiple months through serial implantation.

Selecting an Optimum Vehicle

Vehicle selection is an important consideration in compound administration to the CNS. Ideally, the vehicle should be biologically inert and have no toxic effect on the animal. Other factors to consider include compound solubility and stability, tissue compatibility, pH, viscosity, and sterility. Artificial cerebrospinal fluid (aCSF) is commonly used for administration of test agents to the CNS. A method for the preparation of aCSF is available on request. This solution closely matches the electrolyte concentrations and physiological compatibility of endogenous CSF.

CSF VOLUMES AND PRODUCTION RATES IN MICE & RATS

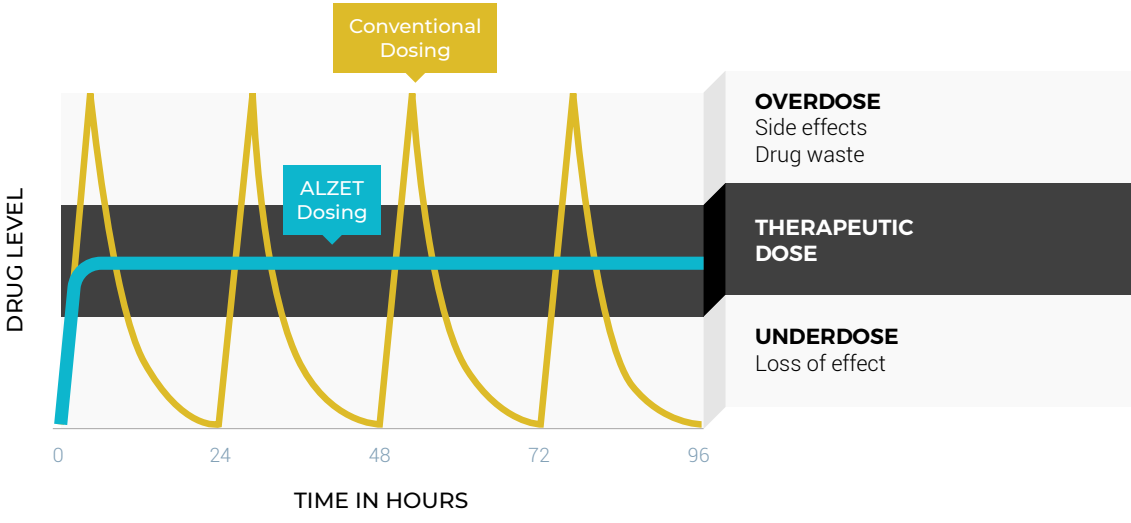
Species	Volume	Production Rate
Mouse	35 µl	18 µl/hr
Rat	150 µl	180 µl/hr

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

Access ALZET surgical implantation videos online!
Visit our channel: www.vimeo.com/channels/alzet

THE POWER OF CONTINUOUS DELIVERY

Injections can result in great variations in serum and tissue concentrations. Immediately after injection, compound concentrations commonly exceed effective levels, resulting in overdosing and toxicity. Rapid clearance causes periods between injections wherein the compound is absent from serum and tissues, resulting in underdosing and lack of drug effect. ALZET pumps deliver compound solutions at controlled and predictable rates, ensuring that constant and optimum levels of test agents are maintained throughout the study duration.



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