

Long-Term Administration of Agents in Mice

ALZET[®] Osmotic Pumps range in duration from 24 hours to 6 weeks. However, mice can be dosed for longer periods by performing serial implantation of pumps. This procedure is generally well tolerated and enables continuous delivery of experimental agents for periods which exceed the duration of a single pump. Chronic delivery of agents to mice is now even easier with the introduction of the new ALZET Model 1004, the smallest pump available for mice. The model 1004 pump delivers continuously for 4 weeks at a rate of 0.11 ul/hr, and can be implanted in mice as small as 10 grams.

The ALZET bibliography contains over 139 published studies reporting the pump replacement procedure to extend duration of drug administration in mice. Currently, the longest duration study reported using ALZET pumps in mice, is 7 months, achieved by serially implanting pumps every 28 days.

The pump replacement procedure is undemanding, requiring only a minor surgical procedure for subcutaneous replacement of pumps in the anesthetized animal. Researchers often use the same location of the spent pump for placing the new pump. If the drug or solvent is known to cause irritation to local tissue, it is recommended to choose a different location for implantation of the new pump in order to allow for proper healing of the original site. The pump replacement procedure is also generally well tolerated by the animal. A number of publications attest to this, as described in the following study quotes:

"The treatment was always very well tolerated without the occurrence of any side effects." Bello L, et al. *Clinical Cancer Research* 2004; 10(13):4527-4537 **5-month duration study with Model 2004 pumps, replaced every 28 days**

"All mice that entered the study recovered from the surgical procedure and appeared to have no adverse effects." Feeney SJ, et al. *Cytokine* 2003; 23(4-5):108-118 **13-week duration study with Model 2004, pumps replaced every 4 weeks**

"...mice did not show any reaction on the subcutaneously installed ALZET diffusion pumps" Eder IE, et al. *Cancer Gene Therapy* 2003; 9(2):117-125.; **7-week duration study, pumps replaced every two weeks**

Note: Because of their mechanism of operation, ALZET pumps can only be used a single time. Since the reservoir chamber of the pumps cannot be decompressed, or re-inflated once they have compressed to their full capacity, it is NOT physically possible to refill them. In addition, leaving expired pumps in situ is not recommended as these pumps will swell and can leak concentrated salt solutions.