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## Vascular Access Port (VAP) Usage in Rats

The repeated intravenous (bolus) administration of fluids to rats via the tail vein often results in vascular damage. This damage can range from subcutaneous hemorrhage and mononuclear cell infiltration to severe necrosis of the blood vessel and tail, depending on the duration of the study, injection frequency and irritancy of the test article formulation. In an effort to prevent these problems, fluids are often injected through a larger blood vessel like the jugular or the femoral vein via a surgically implanted catheter that is exteriorized at the nape of the neck and connected to an infusion pump. Physiological fluids must be continuously administered to the animals between doses in order to maintain the catheters patency. Although quite effective and reliable, this technique is quite labour intensive and costly. A second, less labour intensive and less costly alternative consists of subcutaneously implanting a vascular access port (VAP) again connected to one of the larger blood vessels noted above. As such, a validation study was conducted at ITR Laboratories in order to assess the utility and reliability of these vascular access ports (VAP) for long term intravenous (bolus) injection in rats.

A total of 20 female Sprague-Dawley rats were randomly assigned to 2 dose groups as described in the table below:

Group Numbers	Group Designation	Location of Catheter Implantation	IV Catheter Lock Solution	Dosing Frequency	Dose Volume (mL/kg)	No. of Animals (Females)
1	VAP*	Femoral Vein	Saline	3X Weekly	5	10
2	VAP*	Femoral Vein	Heparin/Saline	3X Weekly	5	10

\* Surgically implanted with a Vascular Access Port (Model ROP™ V-A-P by Access™ technologies).

Animals of Groups 1 and 2 were administered 0.9% Sodium Chloride for Injection, USP 3 times weekly by intravenous injection via the VAP for 26 consecutive weeks.

In order to evaluate the effectiveness of 2 different lock solutions in preventing occlusion of the IV line, the VAP and IV catheter of animals from Group 1 were locked with Saline only, while for Group 2 a 100 IU/mL Heparin/Saline solution was used from completion of surgery for implantation of the VAP until initiation of treatment and between successive administrations.



For the animals of Groups 1 (Saline only, used as lock solution), 97% of the doses were injected via the VAP with ease, while approximately 3% of the doses were injected with difficulty. Similarly, for the animals of Group 2 (Heparin/Saline used as lock solution), 87% of the doses were injected via the VAP with ease, approximately 12% of the doses were injected with difficulty, while on 4 occasions the dose could not be administered due to occlusion of the intravenous catheter. In all 4 cases the dose was administered on the subsequent dosing occasion.

There were no noteworthy clinical signs and body weight gains were unaffected over the course of the 26 week study.

Macroscopically, pale firm material, sometimes adhering to the venous intima was observed at the infusion site (catheter tip and caudally along the catheter tract) in the majority of the animals from both dose groups without a clear difference in the incidence or severity of the findings between dose groups. The skin and muscle surrounding the VAP were also examined and no remarkable findings were found in any of the animals from both dose groups.

In conclusion, the 3 times weekly intravenous (bolus) administration of 0.9% Sodium Chloride USP via a surgically implanted Vascular Access Port (VAP) to Sprague-Dawley rats over a period of 26 consecutive weeks was well tolerated. The VAP remained patent throughout the 26-week treatment period in the vast majority of animals. ITR Laboratories is therefore pleased to offer this reliable and cost effective alternative to conventional externalization of catheters for longer term intravenous injection studies in rats, particularly those involving intermittent dosing.

## OTHER NEWS:

**RESTRUCTURING:** After ending 2008 with a positive balance sheet, ITR Canada this week announced an internal restructuring program. The program, in part a result of our investment in data collection automation in 2008 and also a reaction to the current uncertain economic climate, sees the amalgamation of a number of technical departments and the introduction of an enhanced cross training effort to allow ITR greater flexibility among its workforce. The changes unfortunately resulted in a small reduction in staff numbers (primarily junior staff) but ensures ITR will continue to operate efficiently through 2009 and beyond.

**ITR CANADA will be present at SOT from March 15-19, 2009  
Come drop by our booth # 2957  
We look forward to seeing you there!**