# The use of Female Mice Implanted with Vascular Access Buttons<sup>TM</sup> (VABs) in Reproduction Studies

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## Introduction

Mice are frequently used in reproduction studies as a second rodent species in lieu of the rat. Reproduction studies in mice typically entail approximately 5 weeks of dosing for females and up to 8 weeks for males. As opposed to conventional routes of administration such as oral gavage, daily tail vein intravenous administration is not feasible in the mouse and requires the use of surgically catheterized animals. The use of Vascular Access Buttons<sup>™</sup> (VABs, Instech Laboratories), as opposed to conventional vascular access ports presents significant advantages. The access button is fitted with a light-weight magnetic cap that allows untethered access and permits gang-housing throughout the study. This study was conducted to evaluate the impact of surgical VAB implantation on female reproduction.



#### Materials and Methods

- □ Ten naïve CrI:CD1 female mice (approximately 7 weeks of age), surgically implanted with VABs with PinPorts<sup>™</sup> were obtained from Charles River Laboratories, Inc., Raleigh, NC. In addition, 10 naïve male mice (of the same strain and source) were ordered from the resident stock colony for breeding purposes.
- □ All animals were housed individually, and standard environmental, food and water conditions were maintained.
- □ VABs were flushed with saline and locked with heparinized saline (5 IU/mL). Animals were periodically checked for bi-directional catheter patency.
- □ The following parameters were evaluated:
  - Clinical Observations: Daily
  - Estrous Cyclicity: Daily beginning 10 days prior to breeding.
  - Body Weights: Twice Weekly (premating) and on Gestation Days (GD) 0, 3, 7, 10, 13 and 15.
  - Breeding & Reproductive Performance: VAB-Implanted females were mated overnight with naïve males (1:1, in the home-cage of the male) for 7 days.
  - Scheduled Necropsy: GD 15
    - Laparohysterectomy and macroscopic examination
    - Total number of corpora lutea
    - Total number of implantations
    - Viable and nonviable embryos
    - Early resorptions
  - Precoital intervals, and reproductive indices (mating, fertility and conception) were calculated
- The litter was considered the experimental unit, and intrauterine parameters were reported on a litter proportional basis.



**Figure 1.** Vascular Access Buttons<sup>TM</sup> and their use in implanted mice.

## Results

□ All animals survived to scheduled necropsy.

□ All females retained catheter patency for the duration of the study (15-19 days due to breeding stagger)

□ There were no remarkable clinical observations and female body weight gains during the premating and gestation periods were comparable to non-VAB implanted mice.

Animal	SD 0	SD 5	SD 9	Animal	Status	GD 0	GD 3	GD 7	GD 10	GD 13	GD 15
9133	31.3	30.8	32.5	9133	Gravid	30.7	32.9	34.7	36.8	43.7	51.1
9134	32	31.4	31.8	9134	Gravid	32.1	32.4	35.4	38.9	45.8	52.3
9135	29.8	29.3	29.7	9135	Gravid	29.2	30.3	33.2	35.8	43.7	51.9
9136	30.8	30.9	31.8	9136	Gravid	30.2	32	36.1	41.3	51.9	61.1
9137	27.1	27.1	28.2	9137	Gravid	29.2	29.3	32.4	36.7	45.5	53.3
9138	32.4	31.4	33.6	9138	Non-Gravid	32.8	33.8	35.8	32.8	35.3	37.0
9139	34.2	34	35.5	9139	Gravid	34.3	33.8	36.4	38.1	46.6	54.5
9140	28.5	28.5	29	9140	Gravid	28.9	30.2	34	36.9	43.7	49
9141	31.4	31	31.6	9141	Gravid	30.7	30.8	32.4	35.5	42	47.2
9142	28.4	27.4	29.3	9142	Gravid	28.5	30.1	33.4	36.3	43.2	50.7
Mean	30.6	30.2	31.3	Mean*		30.4	31.3	34.2	37.4	45.1	52.3
S.D.	2.1	2.1	2.3	S.D.		1.8	1.5	1.5	1.8	2.9	3.9

\* = mean and standard deviation was calculated with exception of the non-gravid female Table 2. Premating and Gestation Body Weights (grams).





Estrous cycle length could not be calculated for 2 of 10 females due to the lack of at least one return to diestrus (when cycle is considered complete) during the evaluation period. However, based on individual cycle data, both females were cycling based on the appearance of estrus/proestrus. Both females showed evidence of mating. □ All 10 females showed evidence of mating within 4 days of cohabitation; all 10 females were

□ Intrauterine and litter parameters were comparable to historical control data for non-VAB implanted mice.

Reproductive Performance	Non-VAB Historical Control Mean (Range)	VAB implanted Mice
Female Mating Index (%)	99.1 (95.0 - 100)	100
Female Fertility Index (%)	96.7 (88.0 - 100)	90
Female Conception Index (%)	97.2 (88.0 - 100)	90
Mean Estrous Cycle Length (days)	5.1 (4.4 - 7.0)	5.7
Mean Pre-Coital Interval (days)	2.7 (2.0 - 3.3)	1.9

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### Results (cont'd)

gravid (Pregnancy Rate 100%)

Table 3. Estrous Cyclicity and Reproductive Performance

Endpoint	Non-VAB Historical Control Mean (Range)	VAB implanted Mice		
lean Percent Pregnant	97.2 (88.0 - 100)	100		
Viable Fetuses/Dam (GD15)	12.4 (11.1 - 13.7)	13.8		
n Viable Fetuses (%/Litter)	94.6 (89.2 - 97.0)	97.8		
Post-Implantation Loss/Dam	0.9 (0.4 - 1.5)	0.3		
ost-Implantation Loss (%/Litter)	6.6 (2.5 - 10.8)	2.2		
No. of Corpora Lutea/Dam	14.0 (11.6 - 16.7)	14.9		
lo. of Implantation Sites/Dam	13.0 (11.4 - 14.6)	14.1		
Pre-Implantation Loss/Dam	1.0 (0.2 - 3.0)	0.8		
re-Implantation Loss (%/Litter)	6.4 (2.1 - 16.3)	5.3		

regnancy, Intrauterine, and Ovarian Parameters

#### Conclusions

ition of Vascular Access Buttons<sup>™</sup> had no observable effects on estrous cyclicity, eproductive performance, or intrauterine parameters and survival.

ation of males and VAB-implanted females had no adverse effect on the integrity of s or catheter patency, or reproductive performance.

lata support the use of VAB-implanted female mice in studies aimed at evaluation of and reproduction.