

## Overview

For efficacy and PK studies researchers often rely on terminal blood sampling in mice, where each mouse provides only a single blood draw. With NoAb's cannulated mouse model, our highly skilled surgeons implant cannulae in the jugular vein and carotid artery of the mouse. Using state-of-the-art automated blood sampling equipment, blood samples are collected serially from each freely-moving mouse, without the use of swivels or anaesthesia, and with volume replacement at each time point.

## Benefits

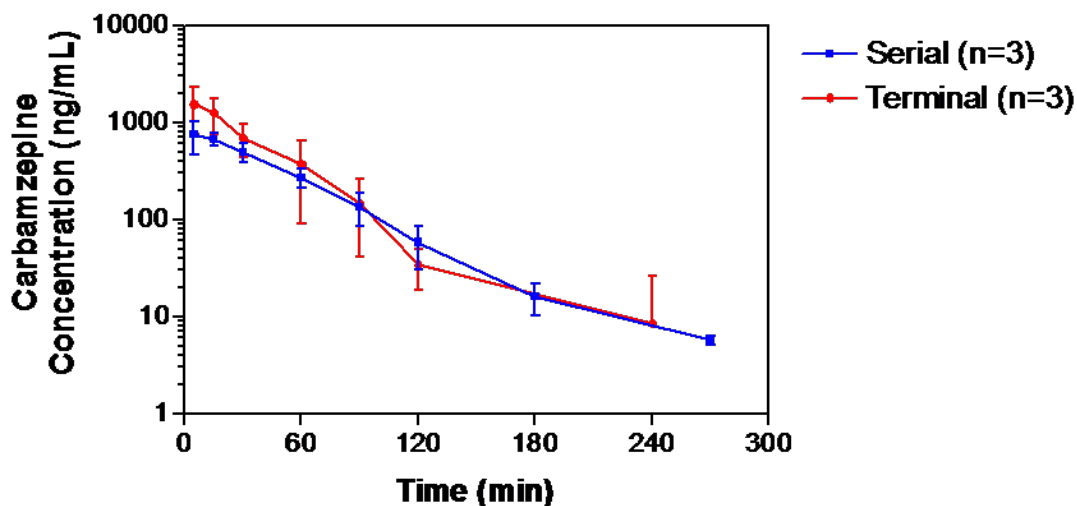
- ❖ A blood/plasma concentration vs. time curve from each individual mouse
- ❖ Reduced inter-animal variability versus traditional parallel sampling
- ❖ Automated sampling, reducing stress on the animals and eliminating the possible confounding effects of anaesthesia
- ❖ 80-90% less compound and animals used per study (assuming 6 cannulated mice = 48 terminal collection mice)

## Typical Study Design

- ❖ Six mice (three for each of *i.v.* & *p.o.* dosing) are catheterized in the jugular vein and carotid artery, and connected to the automated blood sampling system (BASi Culex)
- ❖ Animals are dosed with the test article, and blood samples are collected over 9 time points within 24 hrs. Sample volume is replaced with heparinized saline
- ❖ The number of samples and volume collected can vary depending on bioanalytical requirements and while observing a maximum blood loss volume of approximately 15%
- ❖ Diluted whole blood or plasma samples are analyzed by LC-MS/MS and a summary data report is generated

## Sample Results

### 2 mg/kg CBZ *i.v.*



Mean ( $\pm$ S.D.) estimated PK parameters for carbamazepine following 2 mg/kg *i.v.* bolus administration to mice. Samples were taken by terminal blood draws (n=3 mice/time-point) and serial automated blood draws (n=3 mice).

Parameter	Units	Terminal Blood Draws <sup>a</sup>	Serial Blood Draws <sup>b</sup>
$C_0$	ng/mL	680	823 $\pm$ 343
Terminal $t_{1/2}$	min	45.0	49.5 $\pm$ 22.6
$AUC_{0-inf}$	min <sup>2</sup> ng/mL	36505	42661 $\pm$ 8075
CL	mL/min/kg	54.8	48.1 $\pm$ 9.45
$MRT_{0-inf}$	min	46.8	49.5 $\pm$ 6.59
$V_{ss}$	mL/kg	2562	2414 $\pm$ 778

<sup>a</sup> Estimated from the mean plasma concentration versus time profiles.

<sup>b</sup> Estimated from individual whole blood concentration versus time profiles for each animal. Blood/plasma concentration ratio  $\approx$  1.

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