

One Mouse, One PK.....The Magic of Capillary Microsampling and the Gyrolab™ Assay Platform

Sufyan Maqbool, Jo Goodman, David Fairman, Dominic Corkill, BSU & Bioanalytical Sciences, Clinical Pharmacology & DMPK (CPD) Ove Jonsson, Michael Spreadborough, Christopher Smith

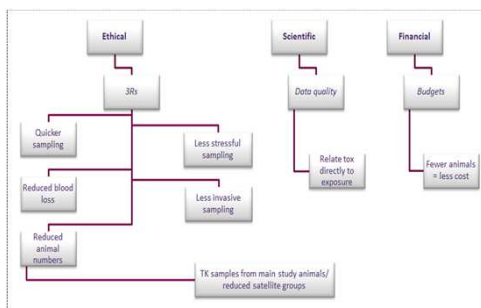
Introduction

Capillary Micro sampling (CMS) is a flexible technique for collection and handling of small exact volume of liquid matrices (plasma and or serum).

The CMS technique can be scaled down to enable repeated pharmacokinetic (PK) sampling of plasma and serum from mice, to determine drug exposure of the 150 KDa antibody.

A PK assay on Gyrolab™ immunoassay platform can be used to measure the concentration of drug in different matrices. Thus enabling construction of concentration-time profiles

3R (Reduce, Refine, & Replace)



Why Use Capillary Micro Sampling (CMS)

... is a flexible technique for collection and handling of small exact volumes of liquid matrices, such as blood, plasma or serum.

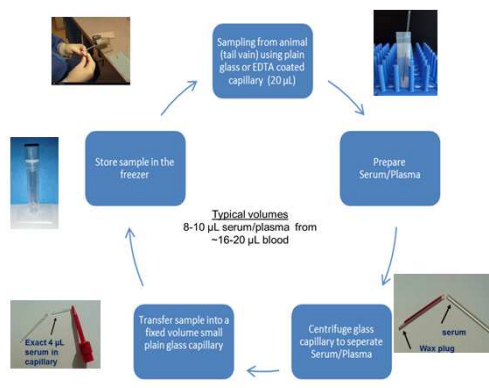


From tail to ice in 20-30 seconds

Fastest sampling method and smallest volume (Without surgery)



CMS a Step by Step Approach



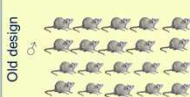
Study Design

Animal Groups & Numbers	Sampling time point in hours							
	1	5	24*	48	72	96* (Terminal bleed Non-CMS only)	192	240
Group 1 Non-CMS (Animals 1, 2, 3 & 4)			X			X		
Group 2 CMS (Animals 5, 6, 7 & 8)	X	X	X	X	X	X	X	X

- Only 24 & 96 hour time points compared for both CMS & Non-CMS

- Number of Mice: 4 in each group
- Dose: 10 mg/kg
- Route of administration: Intravenous
- Mice: Male C57BL/6
- Molecule: Control Antibody (IgG)
- Matrix Serum

Non-CMS



To obtain a complete profile to match CMS sampling 20 mice will be required

CMS



Complete profile with 9 time points using 4 animals (<15% total blood volume in 28 days)

Reduce and refine animal use

- Maximize scientific value
- Increase productivity
- Reduce costs

CMS is low-tech and easy to implement!

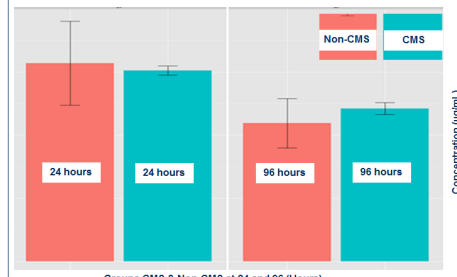


However, proper training of the in-life personnel and understanding the importance of the exact volume is crucial.

The Gyrolab™ Immunoassay Platform

- Nano litre scale technology with streptavidin-coated column structures for instant capture binding
- Flow through sandwich ELISA format: Biotinylated Capture-Analyte-Alexa 647 labelled detection
- Reduced reagent use
- Robustness (less operator dependent)
- Increased throughput
- PK assay on Gyrolab™ utilises reagents to detect human immunoglobulin G (IgG) in any animal matrix

Equivalence between CMS & Non-CMS



Groups CMS & Non-CMS at 24 and 96 (Hours)

Group	Time	MeanResponse	StdError
NCMS	24	94.200	19.917873
NCMS	96	65.650	11.751135
CMS	24	90.725	2.254763
CMS	96	72.600	2.799107

Conclusion



- Animal numbers can be drastically "REDUCED"
- Sampling from main study animals will "REFINE" PK/TK data
- CMS can be used to collect small blood volumes
- The Universal PK assay on Gyrolab™ eliminates the need for antibody pair screening
- Gyrolab™ allows a lot of flexibility in the CMS setting where limited sample is available
- Possibility of multiplexing by using Gyrolab™ all from one sample