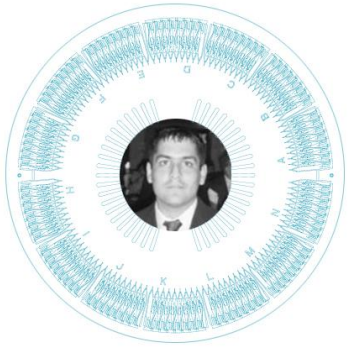
One Mouse, One PK…the Magic of Capillary Microsampling and Gyrolab

Case Study

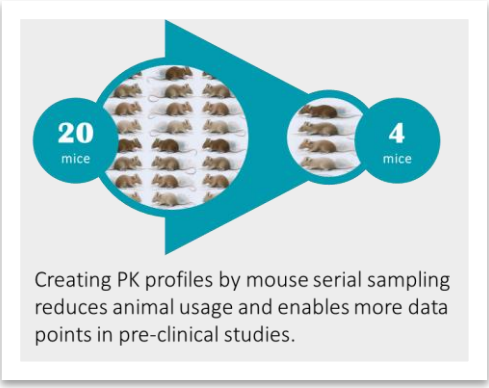


"If you don't have the right platform then you would struggle to analyze the samples. At MedImmune we were fortunate to have an assay in place using Gyrolab".

Sufyan Maqbool is an Associate Scientist in Clinical Pharmacology and DMPK at MedImmune, in Cambridge, UK. His recent work has focused on developing capillary microsampling (CMS) methodologies for PK assays. On June 2, 2014 he presented his work at the Gyrolab User Seminar in Copenhagen, Denmark.

Better science with fewer animals

Over the past 40 years the 3Rs (Reduce, Refine, Replace) have become widely accepted ethical principles to be incorporated into animal-based science, with the aim of reducing the numbers of animals used, and refining techniques to minimize pain and distress. Now, thanks to a combination of refined small-volume sampling techniques and sensitive immunoassay methods, the 3Rs are being implemented to a greater extent than previously possible.



Creating PK profiles by mouse serial sampling reduces animal usage and enables more data points in pre-clinical studies.

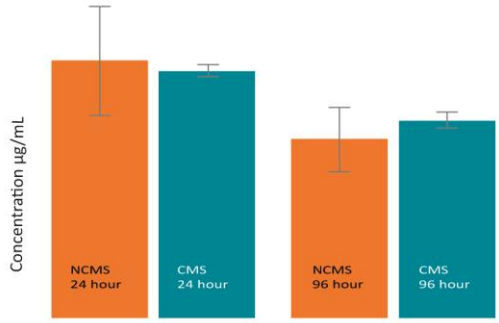
Animal use in scientific research in the UK alone runs at 3.7 million per year, with 78% in rodents (Home Office, 2011). The UK restricts blood drawn from rodents to no more than 15% of total blood volume in 28 days, meaning that with conventional sampling methods, only two 150 µL blood samples can be taken from an individual mouse in a four-week study. Sufyan set out to develop CMS methodologies for MedImmune that would ensure compliance with the UK restrictions, reduce animal stress and also improve data quality.

More data points from fewer mice

The CMS technique, originally developed at AstraZeneca and seamlessly transferred to MedImmune, typically involves preparing 8–10 µL of plasma or serum samples from exact volumes of 16–20 µL blood samples, which are taken from tail to ice within 30 seconds. The technique requires minimal technology and is relatively easy to learn and implement, as long as in-life personnel are properly trained and understand the importance of extracting an exact volume. In an example Sufyan presented, these small volumes enabled sufficient blood to be drawn from just four individual mice yielding nine data points each during a 28-day study. In contrast, conventional sampling techniques required 20 mice, each of which yielded only two data points.

CMS with Gyrolab yields better results for MedImmune

But, as Sufyan says, "If you don't have the right platform then you would struggle to analyze the samples. At MedImmune we were fortunate to have an assay in place using Gyrolab. The system routinely delivers a dynamic range of 70 – 50 000 ng/mL, is high throughput, uses small sample volumes, and requires only a few steps, thus minimizing variability. Assay development often takes no more than three days."



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

He tested CMS using a Universal PK assay to detect human immunoglobulin G (IgG) in mice. The CMS data for the two data points made possible with non-CMS, gathered at 24 and 96 hours after intravenous injection of IgG, revealed comparable signal levels but with a much lower standard error of mean.

A magical combination of technique and technology

In these studies, CMS indeed drastically reduced the number of animals required, and also enabled repetitive sampling from each individual to produce more data points for more precise PK/TK data. Gyrolab allows great flexibility when limited sample is available, such as with CMS, and also facilitates the analysis of several analytes in one sample.

Thus, the "magic" of CMS isn't really magic at all, but rather a perfectly matched combination of refined sampling methods and high-performance assay technology. The real magic comes in the many potential gains: less stress on the animals, fewer animal procedures required by in-life staff, more sampling points per animal and better data quality due to less animal variability. And all of these benefits lead to significant cost savings. Sufyan's studies support ongoing interest in CMS in MedImmune, and the method may well be implemented across the organization.