

Founded in 2004, Pharmaron is a global life science service provider that offers a broad spectrum of research, development and manufacturing service capabilities throughout the entire drug discovery, preclinical and clinical development process across multiple therapeutic modalities, including small molecules, biologics and CGT products.



Driven by Science to Help Our Partners Succeed



Laboratory Services



Chemistry, Manufacturing & Control



Clinical Development



Biologics & CGT

pharmaron.com  bd@pharmaron.com



AGENDA

Time	Event	Speaker
9:00	Arrival and Registration	
10:00	Welcome and Framing the DMPK Core Challenge	Barry Jones and Scott Summerfield
10:20	Below the Bar - The Limbo of Low Turnover Assays	Helen Rollison
11:00	Morning Break and Poster Breakout	
11:20	Measuring What Matters: Reliable Fraction Unbound at the Extremes	Mike Bestwick
12:00	Pushing the Sensitivity Limit with Modern MS Technologies	Adrian Pereira and Adam Hughes
12:40	Lunch and Poster Breakout	
13:40	Radiolabelling for all Modalities: Are Two Labels Better Than One?	Ray Cooke
14:20	Open Discussion: One Small Step for DMPK, One Giant Leap for NAM-kind	Simon Taylor and Scott Summerfield
15:00	Networking and Close	

Meeting Agenda:

DMPK Challenges: From the Normal to the Extreme

Objective:

To explore DMPK challenges at the extremes of chemical space and modality, focusing on assay adaptability, analytical sensitivity, and emerging investigative models across Rule of Five (Ro5), beyond Ro5 (bRo5), and biologics.

REGISTER HERE



9:00 – 10:00

Arrival and Registration

10:00 – 10:20

Welcome & Framing the DMPK Core Challenge

Barry Jones & Scott Summerfield (20 minutes)

An introduction to Pharmaron and the session; framing what “normal” versus “extreme” means in contemporary DMPK, as drug discovery moves beyond traditional small molecule Ro5 space. We will discuss how strategies and standard DMPK assays must be modified or extended and consider the relevance of these approaches across Ro5 and bRo5 chemical space.

10:20 – 11:00

Below the Bar - The Limbo of Low Turnover Assays

Helen Rollison (40 minutes, incl. Q&A)

Designing molecules characterised by low metabolic turnover is frequently an important strategy when trying to improve the PK properties of novel drugs. For DMPK scientists, these low turnover molecules have driven a range of tactics to ensure the *in vitro* and bioanalytical methodologies provide reliable and reproducible results, with experimental design guided by the physico-chemical properties of the modalities of interest. Current approaches rely on *in vitro* systems that are viable over longer timeframes than are traditionally feasible with suspension hepatocytes and other *in vitro* metabolic models. Analytical sensitivity becomes important as does the determination of potential biotransformation pathways. This presentation highlights the key considerations required to generate robust and meaningful information for chemical entities characterised by low metabolic turnover.

11:00 – 11:20

Morning Break – Poster Breakout (20 min)

11:20 – 12:00

Measuring What Matters: Reliable Fraction Unbound at the Extremes

Mike Bestwick (40 minutes, incl. Q&A)

The increasing prevalence of highly protein bound compounds in modern drug discovery has renewed the need for robust measurement of extremely low fraction unbound (F_u) values. Low F_u is often associated with properties frequently falling outside the traditional bRo5 chemical space. Advances in analytical sensitivity and experimental design now enable reliable measurement of F_u well below previously accepted thresholds that defaulted to an assumed minimum F_u value of 1%. Methodologies such as flux dialysis and modified equilibrium dialysis methods, when implemented with appropriate controls, can generate robust and reproducible data for highly bound compounds. We will discuss a structured, fit for purpose workflow that considers how orthogonal methods can produce accurate measurements and interpretation of very low F_u , supporting confident decision making in this increasingly relevant chemical space.

12:00 – 12:40

Pushing the Sensitivity Limit with Modern MS Technologies

Adrian Pereira and Adam Hughes (40 minutes, incl. Q&A)

Quantitative analytical measurements require the combination of high selectivity and sensitivity to ensure measured concentrations accurately reflect those circulating in the subject at the time of sampling. The demand for higher sensitivity never ceases as modern drug design searches for novel chemical modalities and higher potency therapeutics agents, be this in drug discovery (*in vitro* and PK) or drug development (regulated bioanalysis and ^{14}C -labelled ADME studies). Mass spectrometry combined with high fidelity separations provide exquisite selectivity for the quantitative measurements in biofluids, and here we will discuss how modern instruments, such as accelerator mass spectrometry (AMS) and hi-res MS, are continuing the push to measure low level concentrations with sufficient throughput for both discovery and development support.

12:40 – 13:40

Lunch and Poster Breakout (60 min)

13:40 – 14:20

Radiolabelling for all Modalities: Are Two Labels Better Than One?

Ray Cooke (40 minutes, incl. Q&A)

The establishment of the commercial supply of radioisotopes dates back to 1940s with the forerunner of the organisation that became “Amersham”. Nowadays, the main isotopes of choice within drug discovery and development are tritium (^3H) and carbon 14 (^{14}C). The choice of isotope depends on:

- the objectives of the investigation
- where the study sits on the drug discovery/development process
- the nature of the molecule/modality
- the ease of isotope incorporation (radiosynthesis)

As molecules become more complex and climb the molecular ladder (bRo5 MW 500), radiolabels still remain a useful tool for DMPK scientists. We will discuss the strategies available, the need to consider multiple labels, and the considerations required when approaching radiolabelling at the extremes.

14:20 – 15:00

Open Discussion: One Small Step for DMPK, One Giant Leap for NAM-kind

Chaired by Simon Taylor & Scott Summerfield (10 min intro, 30 min discussion)

This open discussion focuses on how we, as a DMPK community, can rethink investigative models to reduce reliance on *in vivo* studies while still generating robust, decision-enabling data. Case studies will be presented for discussion, and we will explore how advances in modelling and complex biological systems are enabling a shift toward more predictive, mechanistic, and translational approaches. This interactive session will allow for discussion on practical strategies, current challenges, and future opportunities for transitioning away from traditional *in vivo* paradigms while strengthening scientific confidence in DMPK decision making.

15:00

Networking and Close