Drug Metabolism and Pharmacokinetics Interest Group Report of the Interest Group Workshop
61st ASMS Conference, June 9th to June 13th, 2013, Minneapolis, MN

Have Recent LC-MS Techniques Advanced to Substitute AMS in Analyzing Microdose and other Low Level Clinical Studies for Metabolites and Drug Related Material?

The Drug Metabolism and Pharmacokinetics (DMPK) Interest Group Workshop was held on Monday June 10th from 5:45 to 7:00 pm. Coordinator Mustafa Varoglu led the meeting by introducing the session with overview slides prepared by Chandra Prakash and Don McKenzie. Approximately 75 scientists attended the workshop demonstrating interest in drug metabolism and pharmacokinetics. The active discussion and solid attendance were a good endorsement for continuing efforts by the DMPK-IG.

A brief business meeting was held at the end of the workshop to solicit ideas for future DMPK Oral Sessions and Workshops, as well as a call for nominees and volunteers for future DMPK-IG sessions.

1. Review of the DMPK IG Goals

The IG goals were reviewed: to provide a discussion forum to MS practitioners in drug metabolism, pharmacokinetics, qualitative and quantitative, non-regulated bioanalysis on:

1. Recent advances in techniques and methodologies for metabolite identification and pharmacokinetic bioanalysis
2. Interpretation of and application of related guidance documents (i.e. MIST, ICH M3, DDI, expl. IND)
3. Sharing of best practices across industry and academia
4. Provide input on ASMS conference program of interest to scientists working in DMPK
5. Reach out and coordinate with related groups to complement scope and broaden outreach to scientific community

2. Solicitation for nominations for 2014 and 2015 DMPK IG Coordinators

2013: Chandra Prakash, Mustafa Varoglu, Don McKenzie (CP and DM were unable to attend ASMS)
List of proposed DMPK-IG coordinators for 2014/2015:
Outgoing 2014: Chandra Prakash
New coming 2014: Don McKenzie, Mustafa Varoglu and alternate Kevin Bateman
New coming 2015: Kevin Bateman, Phil Tiller and alternate Natasha Penner
2016: Phil Tiller, Natasha Penner, alternate Sattanathan Paramasivan

3. Update on the DMPK Interest Group's Impact on the 2013 ASMS Program

Monday AM:	Integrated Qualitative and Quantitative LC-MS for Small Molecule Analysis
Monday PM:	Clinical Chemistry: Dried Blood Spot Analysis
	High Mass Accuracy in Drug Discovery and Development
Tuesday AM:	Imaging MS: Instrumentation and Ionization Sources
Tuesday PM:	Metabolites: Unusual and uncommon
Wednesday AM:	Quantitative Analysis by MS in Drug Discovery and Development: Novel Approaches
Wednesday PM:	Biomarkers of Drug Response, Efficacy and Toxicity: Novel MS Approaches
Thursday AM:	Regulated Bioanalysis and Diagnostics using High Resolution LC/MS
	Imaging MS: Pharmaceutical Applications

Thursday PM Biomarkers in Drug Discovery and Development

4. Suggestions on ASMS 2013 Oral Session Topics From DMPK-IG Attendees

The attendees agreed that the current topics were still of high interest and supported keeping them on the 2013 program. Additionally, attendees expressed additional interest in: Nano or Microflow Systems: Discovery Applications; Transgenic animals for human metabolite prediction; Accelerator Mass Spectrometry; Drug transporters in DMPK. Several of the talks in the drug metabolism sessions were not directly related to the topic and as an interest group we need to encourage people to submit DMPK focused abstracts for oral sessions at ASMS.

5. Discussion Topic: *"Have Recent LC-MS Techniques Advanced to Substitute AMS in Analyzing Microdose and other Low Level Clinical Studies for Metabolites and Drug Related Material?"*

The discussion started with feedback from a survey gauging DMPK-IG members' interest in conducting micro and radioactive dose studies in human ADME studies. Kevin Bateman (Merck and Co.) briefly presented on microdosing and accelerator mass spectrometry (AMS), including the changing utility, necessity, and role of microdosing and accelerator mass spectrometry for quantifying drugs and metabolites in clinical studies. In contrast, Phil Tiller (RMI Laboratories, Inc) summarized advances in sensitivity and specificity now available for identifying metabolites by non-radiolabeled LC-MS techniques. This background information allowed the audience to participate in robust discussion during which the following points were raised on these topics:

- AMS radiodetection provides universal and equal response in detection with a very low amount of original material
- AMS provides absolute bioavailability when dosed iv with a concurrent cold oral dose
- metabolism pathways may have some differences depending on the exposure level of drug in the system between microdosing and traditional dosing studies
- rank ordering multiple Phase 1 compounds is an advantage of microdose studies in humans (radiolabeled or cold)
- AMS is not currently used at its full sensitivity which allows traditional LC-MS to challenge it for low level quantitative analysis in clinical studies
- nano and microspray techniques are able to increase sensitivity of LC-MS and approach the sensitivity of AMS for compounds with high MS response
- while a microdose study can quickly evaluate a compound in man, if the compound proceeds, the necessity of starting a full Phase 1 trial results in a longer total timeline to advance compounds in the clinic.
- AMS will continue to play an important role in clinical development plans when issues such as synthetic feasibility, solubility and MS response are important

Presentations from the workshop will be uploaded to the DMPK-IG page on the ASMS web-site.

Current Officers for the ASMS DMPK Interest Group:

Chandra Prakash, Ph.D. (outgoing coordinator for 2013)
Biogen Idec
14 Cambridge Center, Cambridge, MA 02142
Phone: 617-679-3725
e-mail: chandra.prakash@biogenidec.com

Don McKenzie, Ph. D. (Proposed coordinator for 2014)
Covance Laboratories
Address: 3301 Kinsman Boulevard
Madison, WI 53704-2523
Phone: number 608-310-4023
e-mail: don.mckenzie@covance.com

Mustafa Varoglu
Cubist Pharmaceuticals, Inc.,
Address: 65 Hayden Avenue, Lexington, Massachusetts, 02421
Phone #.. 781-860-8660
e-mail: Mustafa.Varoglu@cubist.com