IVIVE of Transporter-Mediated Clinical Drug-Drug Interactions in Industry –
An Update from the IQ Transporter Working Group

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on behalf of the IQ DMLG/CPLG Transporter Working Group

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Project Overview

Problem Statement:
Data from transporter DDI studies can be challenging to interpret due to poor in vitro to in vivo correlation as victims are frequently substrates of multiple transporters and inhibitors may inhibit multiple transporters/enzymes. Consequently, the need for and timing of clinical transporter DDI studies could benefit from additional scholarship.

IQ DMLG/CPLG Transporter Project Overview:
Collect in vitro and clinical transporter data on member company drugs and NMEs to:
(1) probe the in vitro to in vivo correlation of transporter drug interactions
(2) identify the overall magnitude of the interactions, their clinical implications, and evaluate the regulatory decision trees.
Data Collection

• **In vitro transporter studies**
  • Basic study design
  • Individual transporter assay results

• **Clinical transporter studies**
  • Reason for study initiation
  • Basic study design
  • Mean pharmacokinetic results
  • Clinical implications

• **Basic compound information** necessary for the interpretation of in vitro and clinical studies
Expected Results

The overall goal is to improve our understanding and risk management of clinical transporter-mediated DDIs, through:

• The evaluation of transporter decision trees and, if appropriate, suggest refinement(s).
• An improved understanding of predictability of clinically relevant transporter-mediated DDIs from in vitro data.
• The determination of the magnitude of transporter-mediated DDIs using clinical data for compounds from various companies, therapeutic areas/targets, and probe substrates/inhibitors.
• Understanding the clinical implications of transporter based drug-drug interactions.

Summary of results will be communicated in a white paper (expected: mid 2018)
Thank you!
Transporters of Interest

In alphabetical order

- BCRP
- BSEP
- MATE1
- MATE2K
- MRP2
- MRP3
- MRP4
- NTCP
- OAT1
- OAT2
- OAT3
- OAT4
- OATP1A2
- OATP1B1
- OATP1B3
- OATP2B1
- OATP4C1
- OCT1
- OCT2
- OCT3
- OST alpha/beta
- PEPT1
- P-gp