Fast and comprehensive assessments of drug–drug interaction risk

An interview with senior researchers at a global biopharmaceutical company
The PharmaPendium DMPK module now includes a new, advanced Drug–Drug Interaction Risk Calculator (DDIRC), which builds on the analytic power of the first version of this tool. Developed in collaboration with seven pharmaceutical industry partners, the new DDIRC is designed as a user-friendly tool that supports more effective prediction of potentially harmful drug–drug interactions (DDIs).
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— Senior research scientist at a global pharmaceutical company

We interviewed two key scientists at one of those industry partners: a senior research scientist responsible for in vitro DDI studies and a senior research investigator who leads the in vitro screening team for DMPK. They discussed their work, their impressions of the new DDIRC, and their plans for building a workflow that incorporates DDIRC data.

They explained that DDI risk assessment is a key part of their drug discovery and development process: “For example, if we had a candidate molecule causing CYP450 inhibition or induction, it is critical to understand the potential impact on pharmacokinetics of the victim or perpetrator drug. Depending on many factors, we may need to assess risk among a class of drugs or drugs specific to a metabolic pathway. Many traditional methods for quick investigations utilizing existing data can be very time-consuming.”

They also stated that the company policy is to investigate early and thoroughly mitigate risk: “We are conservative regarding potential DDIs; spending extra effort in attempting to address them while we are designing the molecule. For any hint of DDI from in vitro or in vivo investigations, we employ modeling and other tools to understand completely any potential risk. DDIRC helps us to expedite this process.”

PharmaPendium was already in use at the company: “We have toxicology colleagues who regularly use PharmaPendium to retrieve information for responses to regulatory authorities and data on key parameters.”

Incorporating the new DDIRC in their workflow was an attractive proposal: “Our previous DDI risk assessment strategy used traditional methods, such as PBPK modeling, which requires extensive amounts of data and a high level of expertise. Requesting a modeling assessment typically requires involving colleagues from another group as well as a lengthened timeline. The idea of an easy-to-use calculator without need for extensive clinical data appealed to us.”

The DDIRC proved itself a valuable asset: “The DDIRC gives us autonomy, helping us evaluate potential DDI within our group quickly, confidently and on our own time.”

The DDIRC harmonizes with the existing risk assessment workflows: “The DDIRC complements our existing in vitro and in silico tools. The calculator quickly provides information about parameters of interest, such as area under the curve ratio (AUCR) relating to specific drugs and/or drug classes. We have compared clinical outcomes to DDIRC predictions and for our dataset a good correlation was observed giving us greater confidence in the tool.”

They are also complimentary about the features of the new DDIRC: “We appreciate the new functionality of saving input for later review versus having to export and save during each assessment. The data visualization options have always been great and we are happy to see it is maintained in this upgraded DDIRC version. For example, the AUCR color-coding makes it very easy to hone-in on a result quickly. We also value having all input and calculation data captured in export from the DDIRC.”

In summary, the interviewed DMPK scientists are both very satisfied with the DDIRC and will be happy to continue using it: “PharmaPendium’s new Drug–Drug Interaction Risk Calculator is quicker and more comprehensive than other tools in our toolbox that can we can easily utilize ourselves.”
PharmaPendium informs critical drug development decisions on safety and efficacy, risk assessments and mitigation and study designs with fully searchable FDA and EMA drug approval documents and FAERS data, a drug-drug interaction risk calculator and comparative safety, pharmacokinetic, efficacy, and metabolizing enzyme and transporter data.

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