



John Kolman (JK): There will always be some stragglers, but most drug developers want to stay ahead of the curve and have already made a commitment to pharmacogenomic and pharmacokinetic analysis in one form or another. They're looking for an assay that includes the PharmaADME core list and delivers high-quality results, and are very anxious to see the VeraCode ADME Core Panel offered by service providers.

**Q. How will pharmaceutical companies use the VeraCode ADME Core Panel assay?**

MG: The genes in the ADME core panel were chosen because they are believed to be the most indicative of what could cause variations in patient response. The VeraCode ADME Core Panel assay will help pharmaceutical developers to better structure each clinical trial to select the ideal patient population, one that is going to respond best to the drug, or to understand why they have variable responses.

MP: Pharmaceutical companies will want ADME assay results pretty early in the process, especially in Phase I trials where speed is essential. For Phase I trials, you'll have inclusion and exclusion criteria for the makeup of that patient group. Say it's a 2D6 metabolized drug, they want 50 patients and only want to include those that will be good metabolizers. You have a short period of time to make this decision, maybe a week, so you need to turn around assay results on a dime. The VeraCode ADME Core Panel allows you to refine the patient group and perform that analysis very quickly.

JK: Because the VeraCode ADME Core Panel assay will be used to collect information about what could impact patient outcomes, the data will be used to stratify potential patients at all stages of a trial. That's why it's become pretty standard practice to collect blood samples throughout a clinical trial and either process them immediately or archive them for later pharmacogenomic analysis. In fact, the European Medicines Agency recently released guidance to all pharmaceutical manufacturers that they will need to collect and bank material for DNA testing going forward. Then it's available for retrospective analysis using the VeraCode ADME Core Panel assay, if needed.

MP: For example, if you find bimodal response distributions, the VeraCode ADME Core Panel assay will enable you to go back and identify a metabolic effect or other factor that might be influencing that response. That information will allow you to better stratify or target your Phase II and Phase III trials by limiting the people who won't respond, or those people who might have a toxic response. Basically, pharmaceutical developers will use these types of assays to make better decisions early, to kill drugs if there are problems, or to better target the population so that they can increase their efficacy and improve their safety profile.

**Q. There has been a lot of discussion about potentially using pharmacogenomic assays to study older drugs that benefited only small segments of a patient population. Could the VeraCode ADME Core Panel assay be used to identify patient segments where these drugs are effective?**

JK: That's certainly an option. Many drug compounds failed because there was a lack of understanding about exactly the kind of genetic underpinning that makes a drug effective or toxic.

MP: Even today, pharmaceutical companies are cutting their portfolios and focusing on only key markets. That doesn't mean that the drugs they cut are bad, just that they might not be as specific as they'd want them to be. Pharmaceutical companies are outsourcing those compounds and letting other companies invest in identifying the biomarkers that will determine the responder patient profile, if there is one.

MG: Usually these are drugs that have some adverse side effect profile that was unacceptable. Companies will want to see if they can identify the patient population that was susceptible to that side effect profile and basically resuscitate the drug by creating a test that becomes a companion diagnostic for that drug.

**Q. From a process standpoint, what makes the VeraCode ADME Core Panel different from other ADME tests?**

MG: The test as it's run on the BeadXpress platform is fast and easy to use. We feel comfortable that our staff is more than capable to take it on with a modest amount of training. We see it as a very good fit and valuable addition to our services.

JK: For ADME testing, you need an assay that you can turn around in short order. You really can't have a test that drags over days and might be impacted by multiple technicians. That's a non-starter. In developing the VeraCode ADME Core Panel assay, Illumina has made some clever technology modifications to reduce it to a single day's work flow. That really has an impact on our ability to apply quality compliance measures to the performance of the assay.

“With the BeadXpress, the end result is very clean calls using the SNPs in which we have the most confidence. Having core markers that are well reported is the key.”

MP: Less hands-on time is essential. The fact that the VeraCode ADME Core Panel assay doesn't require restriction cutting and a lot of manipulation makes our process development simpler and more straight forward, with less of an opportunity for errors. When you have a simplified process with less hands-on time, your data tend to be very consistent across batches and across operators. That's important when you're operating in a very strict GLP or CLIA regulatory environment.

**Q. What benefits do the technologies behind the VeraCode ADME Core Panel assay provide?**

JK: The big difference with the BeadXpress Reader is improved signal-to-noise ratio. Competing technologies cover the same markers, but that's not the issue. The real issue is how well a system reports the distinctions of two different genotypes at the same marker. By virtue of having a more robust analysis system, the BeadXpress makes those calls more reliably. Other technologies compensate for their reduced signal-to-noise ratio by requiring additional SNP targets to make a robust call. Adding more markers with weak signal-to-noise actually becomes more confusing, not clearer. With the BeadXpress, the end result is very clean calls using the SNPs in which we have the most confidence. Having core markers that are well reported is the key.

The triallelic discrimination is very powerful and that's helpful. For non-binary SNPs, the BeadXpress Reader provides a clear null, one, and more than one result. Copy number is also well supported.

MP: What's more important to me than just having informative markers is having highly accurate and highly reproducible results, and that's what the VeraCode ADME Core Panel provides. The VeraCode

