BY ROBIN ROBINSON

PHASE IV: Technology Solutions

Technological solutions that integrate clinical research with clinical care are critical as the demand for data in a real-world setting accelerates.

According to John Hall, global medical affairs, epidemiology and outcomes research, at Quintiles, electronic health record providers are at the leading edge of new solutions, and are providing more effective ways to collect data while protecting physician relationships.

The industry faces several critical challenges when dealing with Phase IV and registry studies, which technology can help ameliorate, says Cynthia Verst, Pharm.D., senior VP, late phase research, i3 Innovus.

"First, when accommodating larger numbers of sites and patients, protocols and case report forms must be simple," she says. "Automated technology, including electronic data capture, interactive voice response, clinical trial management systems, optical character recognition, and electronic patient reported outcomes are integral and should be integrated for the effective and efficient management of any large late-phase study. Moreover, integrated and automated technologies are of paramount importance to render cost-efficient Phase IV and registry operational approaches. Simple and intuitive, zero-footprint EDC is an important tool for investigators to submit clean data."

DR. CYNTHIA VERST ■ *i3 Innovus*

Late-phase study results are often needed in realtime to provide an immediate signal of safety or effectiveness, to provide the sites with immediate results compared to the aggregate data, publication planning, and perhaps to fulfill post-authorization regulatory commitments."

She says effective site management can also help ensure the success of research-naïve sites.

"The study design and conduct must take into account the participation of community-based physicians/investigators, and they need to be simplified approaches that do not interfere with the routine daily practice of the physician," Dr. Verst says. "The use of site management centers and call centers is important to assist sites and ensure study participation success by removing the burden on the site."

Data collection, handling, integration, and cleaning must also reflect a simplified, targeted, and cost-sensitive approach.

"Late-phase study results are often needed in realtime to provide an immediate signal of safety or effectiveness, to provide the sites with immediate results compared to the aggregate data, publication planning, and perhaps to fulfill postauthorization regulatory commitments," Dr. Verst says. "An integrated, end-to-end technology solution provides the most immediate way to obtain real-time trial results."

According to David Selkirk, senior director at Clinimetrics, late-phase investigations, such as Phase IV, compassionate use, registries, and health outcomes, generally collect fewer efficacy endpoints than early-phase and pivotal trials.

"These studies also often involve quality-of-life measurements and patient-diary data," he says. "These patient-reported outcomes are generally not subject to strict data reconciliation as the source of the information is the patient directly, not the healthcare practitioner. Consequently, data collection and analysis systems for late-phase trials should be tailored to this setting in which the resource requirements for data processing are lower." ✦

STRATEGIES TO MAXIMIZE THE BRAND LIFE CYCLE

There are several strategies that pharmaceutical companies use to maximize the life cycle of a brand.

Options include:

- **Extended-release versions of the product:** During a drug's life cycle, innovator pharmaceutical companies may determine that they can get easier-to-use dosing regimens and resultantly better patient compliance by converting a product that is taken two to three times a day into a once-a-day product. Alternatively, some companies may choose to modify dosage forms that are used once a day and convert them into once-a-week products.
- **Use of isomers:** Innovator companies may determine that specific isomers of a product show better efficacy and fewer safety concerns than products that are not separated into their isomeric forms. These individual isomeric forms may be sold as new brands.
- **Use of pro drugs:** Innovator companies can extend a product's life cycle by creating pro drugs of an innovative product that may have some advantages over the already marketed product. With the appropriate marketing and pricing strategies, this new product could be a potential blockbuster drug since it not only provides prescribers the advantages of knowing the side-effect profile of the original innovator product (as may be applicable to the new drug), but may also afford the innovator company the additional advantages of associated patent and/or exclusivity rights.
- **Obtain additional exclusivity:** The FDA provides for additional periods of exclusive marketing rights in the event certain additional studies are carried out. Pharmaceutical companies that perform such studies may be able to obtain exclusive marketing rights and hence extend the life cycle of their product. Such additional periods of marketability may result from studies such as testing in the pediatric population.
- **Alternative uses of the product:** Products studied for one indication are often discovered to have other indications during the course of drug development. These products may hence later be rebranded and sold for another indication to extend the life cycle of the drug.

DR. DARSHAN KULKARNI

• **Pay generics to stay off the market** (Pay for delay): Innovator drug companies have, in the past, paid their generic competitors to delay entering the market. Such arrangements between the branded and generic companies are commonly referred to as pay for delay settlements. This is often a win-win situation for both parties since it provides both the brand and generic companies with additional revenue sources. However, detractors argue that such arrangements may cost the consumer several billion dollars a year. Accordingly, such arrangements have been targeted by the government as being potentially anticompetitive.

• **Create an OTC version of the drug:** Toward the end of the drug's life cycle, once the risk-benefit profile of the drug has been adequately studied and if an appropriate profile exists, it may be sufficient to convince the FDA to allow the sale of the product as a nonprescription, over-the-counter drug. Using such methods, brands that are often ineligible for third-party reimbursement may be able to maintain market share by being directly paid for by the consumer without the intervention of a physician.

• **Genericizing:** Pharmaceutical companies that believe that they cannot continue to market and manufacture the branded version of a product may choose to create and sell a generic version of their own product. This would allow the brand company to compete not only as a brand, but against the generics as a generic manufacturer.

Source: Darshan Kulkarni, Pharm.D., Esq., Kulkarni LLC.
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