The Role of Contract Research Organizations in Supporting the Development of Companion Diagnostics

By: Mark Roberts, PhD, Director, Diagnostics Development

Introduction

The ‘promise’ of personalized medicine is quickly becoming a reality, as the biopharmaceutical industry increasingly turns its focus to discovering and delivering targeted, personalized therapeutics. Companion diagnostics are at the core of this personalized medicine shift, helping provide more effective and efficient treatments in smaller numbers of patients. In fact, indications are that a companion diagnostic will accompany up to half of all future drug launches, boosting the worldwide companion diagnostics market to an estimated $3.45 billion by 2015 (www.visiongain.com).

Contract research organizations (CROs), which are uniquely positioned to span the gap between pharmaceuticals and their companion diagnostic partner assays, have a critical role to play in the process of drug and companion diagnostic co-development.

The Promise of Personalized Medicine

The drug development process is undergoing a major transformation. With the disappearance of the blockbuster, one-size-fits-all treatment model, the biopharmaceutical industry is moving from a drug discovery process that is focused on discovering the right drugs to one that is focused on targeting the right patients.

The benefits of this personalized medicine approach are clear: 1) it shifts the emphasis from reaction to prevention through the tailoring of medical treatment to the individual characteristics of the patient; 2) it enables the selection of the therapy most likely to be successful in a specific patient cohort; and 3) it minimizes or reduces the risk of adverse drug reactions.
The New Drug Development Paradigm: Companion Diagnostics at the Core

So what is a companion diagnostic?

The official definition of a companion diagnostic is “an in vitro device that is essential for the safe and effective use of a drug.” In its simplest definition it is a test that improves the outcomes of drug therapy — one that when used correctly will determine whether a particular patient will show a positive response to therapy with a certain drug, whether there is an increased likelihood of an adverse drug reaction, or if the dosing needs to be adjusted to achieve optimal blood levels.

Working in the diagnostics field for over 15 years, I’ve witnessed firsthand an evolution in how simple companion diagnostic tools such as therapeutic drug monitoring are perceived. Initially the industry considered such tests an encumbrance to adoption of a drug, one that increased the cost of therapy and posed questions around the drug’s safety profile. Overall, these perceptions hindered the widespread adoption of such diagnostic techniques.

Fast-forward ten years and the perceptions have dramatically changed. A better understanding of the genetic causes of disease and the response of patients to therapy has resulted in some notable success stories, especially in the oncology field. Consequently, there has been an evolution in thinking around the entire field of companion diagnostics. The industry now sees it as it truly is: a suite of techniques that when used correctly can improve outcomes — of drug development, of patient treatment, and of healthcare strategy.

FDA: Drug and Companion Diagnostic Co-Development

Over the past few years, the FDA has become increasingly visible as it moves to tighten its oversight of the companion diagnostics development process. In its 2011 Guidance Document, it reaffirmed that “if use of an in vitro companion diagnostic device is essential for the safe and effective use of a therapeutic product, the IVD companion diagnostic device and therapeutic product should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product labeling.”

The FDA cites several benefits of co-development, including: 1) it allows drug and device to be evaluated in the same trials, eliminating the need for additional trials for the companion diagnostic; 2) it produces real-time validation of the companion diagnostic’s performance and clinical utility; 3) it improves the safety/efficacy profile of the drug.

So what we have now is a changing marketplace where more stakeholders are involved; not only the biopharma and diagnostic companies, but also physicians, patients, regulatory authorities, and the payers who are investing heavily in medical outcomes research to ensure patients only receive therapy from which they will benefit. Although developing a companion diagnostic is not without cost or risk, co-developing the drug and diagnostic has the potential to both reduce cost and shorten drug development timelines.

Voice of the Client: CROs Role in Developing Companion Diagnostics

In an effort to gain a better understanding of the whole companion diagnostics arena, we surveyed experts from leading biopharma and in vitro diagnostic companies on how they were currently implementing their companion diagnostics strategies. We enquired as to their general needs around the companion diagnostic space, their strategy for building internal capabilities versus engaging external collaborators, and ultimately asked them what role, if any, they felt CROs could play in their drug/companion diagnostic co-development strategy.
As expected, all of the companies involved had some form of companion diagnostic strategy and all were looking to established external partnerships to support their strategy. Their needs were clear — they wanted partners with wide-ranging, fully integrated technical capabilities, who were flexible and agile, had a global footprint, and who possessed a detailed knowledge and vision around developing companion diagnostics.

Although most had not yet considered CROs as a companion diagnostic development partner, they quickly recognized that CROs were indeed highly experienced in the development and validation of diagnostic assays for use in clinical trials and clearly appreciated the efficiency of retaining a CRO to develop both the drug and the companion diagnostic assay. They verbalized the benefits as:

1. **A one-stop-shop**, where everything gets done together. The drug and device may be developed in collaboration, removing problems with sample availability and/or the need for additional device trials.

2. **A reduced time to market for the drug** by coordinating better communication between divisions of the FDA, providing clarity on optimal use of drug, and ensuring drug approval is not delayed by the lack of a companion diagnostic.

3. **Providing clarity** on optimal use of a drug, as well as the potential for differentiation in an increasingly crowded market.

**Commercialization Considerations**

One important aspect of the companion diagnostic development process that many biopharma companies overlook, particularly in the early stages of development, is that of commercialization of the companion diagnostic. By its very definition, for a companion diagnostic to be an essential part of safe and effective drug use it needs to be accessible — i.e.; the physician needs to be able to obtain the test result in the time frame required for the result to be meaningful.

When choosing both the optimal commercialization partner and the optimal technology platform, the biopharma company should consider a number of factors that will influence not only the type of testing to be performed, but also the location of testing;

1. The nature of the marker:
   - its concentration
   - the sample type
   - its stability

2. The required turnaround time of the result:
   - minutes?
   - same day?
   - one to two weeks?

In choosing the correct commercialization partners the biopharma company should review the partner’s channel to market: is it direct to end-user through a lab-developed test (LDT) strategy, or through the global launch of a regulatory cleared kit? If the latter, does the partner have a global commercial reach or will they need to engage a distribution network?
Finally, the importance of market economics cannot be overstated. A high-quality product will always be adopted but in this emerging field the question of who pays for the companion diagnostic often arises. Many payers reject coverage for companion diagnostics because they don’t understand their intended use, so engaging the payers upfront is critical for access to and commercial success of the companion diagnostic.

**CROs: Filling a Needed Gap Between Drug and Companion Diagnostic**

As the pace of companion diagnostic innovation accelerates, CROs are in a unique position to leverage the non-competitive nature of their business model to help their biopharma and diagnostic partners fill a void in the drug/companion diagnostic co-development process.

**A LESSON FROM REAL-TIME EXPERIENCE**

Covance’s Director of Diagnostics Development Mark Roberts shares an example of one CDx development project that illustrates how the CRO helps put its clients and their products on the right path to approval.

“Recently we were approached by one of our long-standing clients that had a biomarker that had potential applicability to patient stratification. The client needed a CRO partner that could implement a specific assay globally in order to meet tight sample processing timelines. We already had the required equipment operational in Indianapolis and were able to quickly operationalize the same equipment in our facilities in Geneva, Singapore, and Shanghai to support the client’s needs.”

**About Covance**

Covance, with headquarters in Princeton, New Jersey, is one of the world’s largest and most comprehensive drug development services companies, with annual revenues greater than $2.2 billion and more than 11,000 employees in over 60 countries. Covance has the people, processes, client service, and global resource capabilities to respond to the toughest drug development challenges.

For more information about Covance, visit us online at [www.covance.com](http://www.covance.com).