Editorial

Theme: Ligand Binding Assays in the 21st Century Laboratory
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Ligand Binding Assays in the 21st Century Laboratory—A Call for Change

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OVERVIEW

In June 2009, a group of ligand binding assay experts met in Seattle, WA to discuss the need for greater efficiency in bioanalytical laboratories. The central premise was increased utilization of technological innovation will lead to increased quality, throughput, and efficiency. Currently, there are very few laboratories that have reached the ideal or utopian level desired. The biggest challenge currently facing the ligand binding community is a reliance on manual processes and paper-based systems, ineffective integration, and a lack of standardization in many areas. In order to address these gaps, we identified speakers who had developed solutions to parts of the overall problem. The event spanned 2 days with participation from three distinct groups: biopharmaceutical companies, contract research organizations, and research equipment providers. The goal was to share best practices, identify gaps, and define next steps. The outcome of the meeting was the development of four sub-teams that included: reagents, instrument platforms, automation, and electronic solutions. Each sub-team was given the task of identifying the most achievable and high-impact facets to change or improve.

WHY CHANGE?

Drug development costs have increased at a logarithmic pace and the number of new molecular entities has remained relatively flat over the same span of time. DiMasi *et al.*

estimated that the cost of drug development for each new drug was 800 million dollars [1], and recently, Adams and Branter updated the estimate to be one billion dollars [2]. As a consequence, nearly every biopharmaceutical company is looking for ways to reduce costs and increase the likelihood of technical success. The proposed mechanisms include: better use of efficacy biomarkers, early identification of toxic molecules, more efficient clinical trial designs, modeling and simulation, better data integration and knowledge management, and outsourcing of non-core competencies. A number of these solutions have a laboratory component. Therefore, if we can build more efficient laboratories that effectively use technological innovations, then it is feasible that more high-quality answers will be available for decision making at a reduced cost.

The goal seems very simple, so why have we not seen the development of state-of-the-art laboratories that are fully integrated from sample collection through knowledge management? The reasons are multifactorial, but the simplest explanation is that the time and resources needed to develop a revolutionary laboratory can be prohibitive. How can the 21st Century Bioanalytical Initiative lead to disruptive change? We believe that the solution is composed of a three-stage process that we are calling the three Ps.

PERSUASION

A grassroots discussion in Toronto was initiated at the 2008 American Association of Pharmaceutical Scientists (AAPS) Biotechnology Conference and was formalized as a 2-day workshop in Seattle. The representation was diverse, and all parties agreed that most laboratories could utilize the twenty-first century technology advancements more effectively. The conference was divided into four major areas of emphasis that correspond to the sub-teams described earlier (reagents, instrument platforms, automation, and electronic solutions). We identified successful attributes of a twenty-first century

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laboratory and also discussed gaps that need to be addressed. The goals of our reports are to provide recommendations for reagents, describe characteristics for an ideal ligand binding platform, discuss the challenges and opportunities that exist for automation, and examine the need for a ligand binding automated data interchange.

It is often said that an assay is only as good as the reagents. The experts on the reagent sub-team agree that critical reagents are essential components of ligand binding assays (LBAs), and their characteristics can determine reproducibility and performance of LBAs [3]. Therefore, clearly defined responsibilities pertaining to their management should be assigned to assure reagents are well characterized and that the supply chain, knowledge database, and inventory are appropriately maintained. Recommendations are described for a basic reagent characterization profile, expiration assignments, and storage conditions. Best practices are also provided for the life cycle management and supply of critical reagents used in these LBAs. Once the reagents are defined and appropriately characterized, the next step is to select an appropriate platform.

The platforms sub-team considered attributes of existing platforms and made recommendations for the future [4]. In order to deliver on those recommendations, the sub-team encourages the formation of a consortium to facilitate collaboration between platform development and the end users because there is a great opportunity to leverage the experience of diagnostic platform manufacturers. The hope is to collaborate and create robust, high-throughput platforms and instruments for the research and development industry. We hope that, as a community, it will be possible to harness the collective knowledge to enhance throughput, quality, and value through better products.

The automation sub-team provided a comprehensive evaluation of the current state of automation and offered a look into the future [5]. The sub-team believes that automation in the twenty-first century laboratory should take advantage of recent advances in electronics, instrumentation, and programming. In order to be successful, laboratory automation should copy the “plug-n-play” technology found in the computer industry where various devices from disparate manufacturers are put together. The authors highlight multiple ways to reduce the barrier to entry for automation such as: access to universal scripts for system validation and standardize scripts that provide not only instrument integration but integration of user identification and data transfer. Some of the more forward thinking recommendations included: system security based on biometric data that is linked to the investigator’s training records and facility access. They also discuss the use of RFID tags to better control chain of custody.

The electronic solutions sub-team had the difficult task of defining the scope for a seemingly infinite set of possible topics. They were able to focus the efforts around an automated data interchange [6]. This sub-team recommends the development of an automated data interchange that will benefit end users by reducing the resources required to support data management and the adoption of new technology. This same automated data interchange will benefit vendors of LBA data systems and laboratory instruments by providing end user electronic data requirements. Ultimately,

this consistency will benefit the LBA community by yielding in-demand electronic solutions that improve the end users’ experience. The sub-team is actively recruiting interested end users and vendors to participate in the development of the automated data interchange.

Our intermediate goals for this stage of the initiative are continued dialog in these four critical areas. In addition to the reagents white paper, we hope to see an automated data interchange, better platforms, a plug-and-play system, and integration between all of these facets of the laboratory.

PARTNERSHIP

A truly meaningful outcome of this initiative will be a new paradigm in laboratory workflow and more importantly a shift in the way that people think. It is unacceptable that in the twenty-first century, an innovative industry in biopharmaceuticals has tools that are a decade behind the consumer market. We now live in a society in which adolescents use mobile devices that are more sophisticated than the tools that we use in the research environment. In the near future, our initiative plans are to make available tools to easily integrate systems (plug-and-play) and devices that will allow scientists to make more measurements with fewer resources, thus ultimately generating higher-quality results. The end product of this effort will be a seamless transition of data from collection all the way to data review. The best way to achieve this goal in a reasonable time frame is through partnership. The partnership began in 2008 when the cross-functional working group was formed and has extended across industries to include all parties involved. It is clear that this problem is larger than one company or one industry. Our initiative brings the collective thoughts of all parties involved from manufacturers to end users with the goal of better performance.

Partnerships can come in many forms including: fee-for-service, consortiums, and risk sharing. The main advantages that partnership offers are expertise, diluted risk, and information sharing. There are several examples of successful partnerships in the bio-pharmaceutical industry, including the Alzheimer’s Imaging Initiative [7], Asian Cancer Initiative [8], and Women’s Health Initiative [9]. These are precompetitive ventures that share the cost of basic science research associated with the disease pathology. Other industries, such as the aerospace industry, semiconductor industry, and green energy technology, have also successfully partnered to build better products and advance ideas. A recent example of a precompetitive technical partnership is the US Drive which was formed with a central goal of making more affordable and fuel-efficient vehicles enter the market sooner. There are definite similarities to the present initiative, including multi-industry representation, exchange of technical precompetitive information, and consumer market driving change. The results of this initiative are still in the early stages, but the 78-page document describing the scientific output in 2010 is impressive [10]. We are in the planning stages of tools that will facilitate a community of practice and continued programming within the AAPS.

PROFIT

The final stage and ultimate success will be realized when the free markets force change. Profit will be the food source that will drive the ecosystem of the future. The current ecosystem has rewarded isolationism, status quo thinking, and incremental evolution. Our hope is that this initiative will create a paradigm shift in the ecosystem so that survival is predicated on being better, faster, and more integrated. The twenty-first century laboratory ecosystem will be composed of companies that invest in technology, build better quality products, and consistently look for more integrated solutions. We believe that companies that make these commitments will be rewarded by growth through enhanced value. The suppliers of products will see value enhancement through increased product sales. The end users will create greater value through enhanced knowledge, better quality, and reduced cycle time. The only way to make this change a reality is to demand these improvements through a market selection process.

CONCLUSION

We believe that the 21st Century Bioanalytical Laboratory Initiative is an essential step in the long-term viability of our discipline. Everyone is being asked to do more with less in order to remain competitive. We believe that this is the first step in the transformation to create a more effective bioanalytical laboratory for the future.

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