NEW FRONTIERS: THE CHANGING WORLD OF BIOSPECIMEN COLLECTION AND MANAGEMENT

Today's drug discovery and drug development is critically dependant on *biospecimens*, tiny samples of blood, tissue and proteins that form the essence of biological research. In the development of a drug or new procedure, a company may collect hundreds of thousands of these specimens from both humans and animals, beginning with basic research and continuing all of the way to post-approval Phase IV clinical trials. Traditionally, methods for collecting and storing biospecimens have been highly regimented and were very specific to purposes for which they were collected. However, this model has changed significantly in the past five years. As a result of the genomics and proteomics revolutions, researchers have begun widespread efforts to examine the link between the molecular and genetic basis of diseases and their potential treatments. This growth of biomarker research and personalized medicine has brought a radical shift in the way that companies collect and store specimens for research and development, calling for more unified and large-scale software systems to track their biological materials.

In past models, samples were either collected during discovery for the purpose of exploring a biological pathway that might lead to a drug, or during development to prove the safety and efficacy of a drug candidate to regulatory agencies. These two different drivers for biospecimen collection led to a number of fragmented approaches within pharmaceutical and medical research centers. Prior to large scale transcriptional profiling, genotyping and pharmacogenomics, discovery was limited to very specific assays on small populations of specimens that were banked in a local freezer for the limited duration of the particular research. On the development side, most clinical protocols applied a fairly fixed process of collecting materials from patients enrolled in a trial, testing those samples and then banked them only for a FDA-mandated holding period.

As a result of this legacy, many companies have applied painfully ad-hoc and informal systems to track, store and process these materials in pursuit of their research. The records for these materials proliferated in spreadsheets, access databases and laboratory notebooks on a lab-by-lab basis. As a consultant working in this industry, I have seen homegrown Microsoft Access databases written by research assistants in their spare time, and laboratory technicians trained to find specimens by flipping through a notebook placed next to a freezer. To the extent that commercial software was available to fulfill these needs, the industry provided highly localized "card catalogs" intended to fulfill narrow storage objectives within individual labs.

The recent focus on molecular medicine, genomics and biomarker research have changed this landscape considerably. The promise of genomic and personalized medicine lies in the ability to forge a connection between "phenotypic" clinical data (such as medical records, case reports, and other information about patient outcomes) and scientific measurements on collected specimens, such as the results of a SNP, transcriptional profile or sequencing assay. Research is shifting towards molecular profiling, where specific assays are conducted on large populations of diseased and normal specimens to aid the search for genetic, protein and transcriptional clues to the origin and pathways of disease. With the trend towards biomarker discovery and personalized medicine -- identifying the right drug for the right patient -- the need for the en-masse integration of clinical data with scientific results has become critical to identify the criteria for subpopulations that may best benefit from a new drug or treatment. Long term longitudinal studies (such as government-managed biobanks) where populations are followed for a long period of time to uncover population trends now require the ability to operationally track millions of

specimens. Many pharmaceutical companies are also creating patient "registries"; prospective banks of a large numbers of samples from particular patient populations in the hope of examining genetic or transcriptional trends that may yield clues to potential treatments or drug response profiles. Together, these trends have increased the number of discovery samples that are collected in a clinical context.

These industry changes have generated a significant new interest in maintaining organized centralized databases of biospecimens across an organization's entire drug discovery and development enterprise. This centralization is further driven by the need to better manage multifaceted patient consent and regulatory issues related to sample collection, and in recognition of the scale, expense, and longevity of biospecimen collection. Given that molecular profiling requires consented human samples, each material is governed by a complex intersection of a patient consent agreement, the collection site's institutional review board (IRB) requirements, and HIPAA or other privacy concerns. Materials may often only be used for certain purposes, or held for a certain amount of time. This drives the need for an organization to effectively monitor acceptable use for its samples, track consent agreements and process consent revocations when needed. Consent management is nearly impossible if a single sample is tracked within several different disconnected databases. Moreover, the aggregation of consented clinical and non-clinical samples requires greater regulatory scrutiny both from a privacy and FDA GLP/GCP compliance perspective, which is better assisted by a centralized database. Especially in pharmacogenomics, samples collected prospectively for pre-clinical discovery may later need to be assayed for FDA submissions, meaning that discovery organizations must retain the capacity to maintain materials for subsequent GLP research. This often leads to a desire to maintain segregation within a database between GLP and non-GLP materials. Given the large scale of collection and expense of rare samples, companies need cross-organization, accurate operational support during sample handling. In addition, the significant number of experiments that are duplicated from laboratory to laboratory, across various departments and throughout their global organizations would be eliminated by an enterprise approach to biospecimen management and results tracking.

These critical changing drivers necessitate a new class of "enterprise biobanking" software systems, such as the Sapphire™ BioBanking Solution available from LabVantage Solutions, Inc. (www.labvantage.com). These systems maintain centralized records of an entire organization's biological material assets, as well as the by-products of the experimental process, such as aliquots and derivatives. These systems serve as a consistent platform for their storage and handling, allowing an organization to take advantage of sophisticated chain of custody features, such as electronic signatures and shipping and receiving functionality. These systems provide a place for a company to centralize their consent and study management records. By providing a standard infrastructure for the storage, data capture, retrieval and processing of samples throughout an organization, each individual lab can leverage a robust infrastructure to manage workflow and maintain accurate sample records. Moreover, these solutions are able to be validated to manage both GLP/GCP and non-GLP materials, allowing for the consistent production of regulatory filings, scientific experimental reports and validated clinical development records.

The toolset for sample storage, handling and shipping is only the first part of the solution. An important aspect of enterprise-grade systems is the ability to address the needs of multiple laboratories around the world, so that it can truly serve as a single operational and logistical point of record for an organization's samples. Secondly, it has broad and robust features for integrating with existing laboratory information management systems (LIMS) and clinical trial management systems (CTMS), and other systems to

fulfill their promise of integrating clinical datasets with research results. Integration is essential to avoiding re-entry of data (e.g., when a particular target platform LIMS receives a sample, it can accession information directly from these solutions). Thirdly, it is capable of global deployment and management, so that it can be accessed throughout the enterprise. Finally, the systems is flexible enough to allow for a variety of different business processes to be configured and deployed so that it can assimilate with the particular procedures and business practices that may already be in place at a company.

For example, Sapphire's thin-client technology enables enterprise wide access and visibility to the solution simply through an Internet Explorer browser. This also reduces total cost of ownership and enables rapid deployment with little end user training. It offers robust features for intricate data capture, compliance, chain of custody, and location management functionality on a global basis across virtually unlimited repositories. Through Sapphire's Evergreen configuration tool, the solution is extensively meta-data configurable, and easily adapted to a customer's particular biobanking processes, while maintaining the ability to upgrade the configuration to future versions of the software. Its open architecture allows for easy integration with internal systems, public and private databases, and instrumentation. The module is part of LabVantage's Sapphire platform, so it is seamlessly integrated with its laboratory information management solution (LIMS) for Life Sciences R&D as well, providing an advantage to companies that want to standardize their sample and data collection software across laboratories.

Finding enterprise biobanking solutions on the market today is challenging. Outsourced ASP solutions make tight integration with in-house systems difficult to achieve and raise a number of concerns about information security and the ability to add features. Smaller scale, inventory or freezer management products have very little integration capacity and are not designed to be enterprise-grade systems. These available out-of-the-box products appear to be designed mainly for individual labs and do not have the ability to capture the complex information collected during receipt or sample processing. Custom commercial frameworks serve too much as "starting codebases" rather than configurable products, and are not upgradeable, leading to significant future costs. Although off the shelf laboratory information management systems
(LIMS) have strong sample tracking features, most lack the location management and logistics functionality required in an enterprise biobanking solution.

The changing dynamics of discovery are forcing companies to think differently about biospecimen management, as new discovery models are becoming more de facto in the process of finding the next blockbuster or "niche-buster" drug. It is fortunate that the software tools are now becoming available to meet these important needs.

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