

WHITE PAPER

BioFortis

Empowering Researchers Through Innovative Software

IS YOUR BIOBANK READY FOR THE CHALLENGE OF BIOMARKER-BASED RESEARCH?

Liberating the knowledge in your biospecimens to drive investigative research with Next Generation Biobanking

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INTRODUCTION

The vision of personalized medicine, the poor productivity of the pharmaceutical industry with respect to new drug approvals (NDA), and the drive to contain ever increasing healthcare costs is driving an unprecedented interest in biomarkers. As a result, biomarker-based studies are being adopted across the research and development process from early discovery through clinical research and clinical trials.

Fundamental to biomarker research is access to quality biospecimens that have been extensively annotated with clinical, molecular and patient data. While many organizations have invested heavily in the IT infrastructure of biospecimen management, or biobanking, such systems are facing challenges to effectively drive investigative biomarker-based research.

In this whitepaper we review the key drivers impacting “traditional” biobanking and detail the challenges such biobanks face in delivering new biomarker-based research. To facilitate the discussion of approaches to overcoming these challenges, we introduce the concept of Next Generation Biobanking and define the attributes an “ideal” Next Generation Biobank would need to drive effective biomarker-based research. Finally we demonstrate the benefits of adopting a Next Generation Biobanking approach, with a case study in cancer biomarker discovery.

The changing landscape

The true era of personalized medicine, while perhaps decades away, is impacting the pharmaceutical and healthcare industries today. Most notably, this vision is impacting the landscape of how clinical research and trials are conducted. Translational research, biomarker-based studies and careful patient segmentation in clinical trials, have led to successes such as new biomarker based drugs; drugs with companion diagnostics and highly targeted therapies. According to a Tufts Impact Report ¹, between 12% and 50% of current pipelines involve personalized medicines and biomarkers are commonly used in drug discovery. Indeed, over 100 FDA² approved drugs have some form of labeling that includes pharmacogenomic information, either

to identify responders or warn against side effects. (Table 1)

DRUG	GENE	INDICATION/ USE OF PGX
Herceptin	Her2	Breast Cancer/ Identify Drug Responders
Vectibix	EGFR	Colon Cancer/ Identify Responders
Iressa	EGFR Mutations	Lung Cancer/ Identify Responders
Ziagen	HLA-B*5701	Antiviral/Warning
Camptostar	UGT1A1	Colorectal Cancer/ Dose and Warnings
Celebrex	CYP2C9	Analgesic/ Target Dose Range
Zelboraf	BRAF	Melanoma/ Identify Drug Responders

TABLE 1: Popular FDA approved drugs with Pharmacogenomics labeling. Adapted from Table of Pharmacogenomic Biomarkers in Drug Labels².

At the core of this biomarker-based revolution is the need for biospecimens and the associated clinical, molecular and patient data. As a consequence, there is now a heightened awareness of the value of biospecimens, from collection, through biobank management, to the biobank acting as a driver of the clinical study. Hence, biobanks may be considered as the one of the key steps on the road to personalized medicine. (Figure 1)

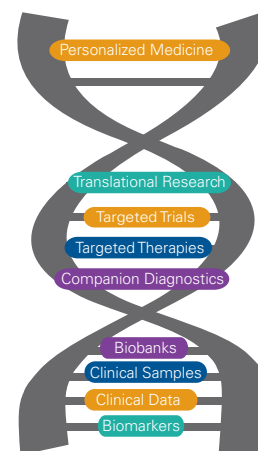


FIGURE 1: Biobanks are a key step in the path to personalized medicine.

There are two other drivers also impacting clinical research, one is less about the science and more about external trends, namely externalization of research. This shift to externalization at all stages of research and development is changing the way that research is performed and as a result biobanks are also under pressure to cope with this paradigm.

The other driver is the rise of so called “big data”, from new technologies, such as next generation sequencing (NGS), as well as large quantities of Electronic Medical Record (EMR)-based data and other real-world healthcare information. Traditional biobanks are not setup to leverage these

innovations, which have the potential to improve patient outcomes and provide for new therapies.

THE TRADITIONAL BIOBANK IS UNDER PRESSURE

Organizations have invested heavily in conventional biobanks, building out infrastructure in terms of hardware (freezers, automation, etc.) and developing or purchasing “first-generation” biobanking management software with an emphasis on operational efficiency in sample collection, storage and sample processing.

Beyond sample centricity

As biomarker-based research becomes commonplace, there is growing pressure on traditional biobanks and traditional biobanking software to reach beyond this sample-centric and operational model. Processes and software that are perfectly able to cope with sample management are often challenged when, for example, there is a need to link specimens with clinical and molecular data in order to get a more holistic and scientific perspective on patterns and relationships.

Lack of flexibility to accommodate change

Biobanks are often built around limited data-models and institutional workflows. Conventional biobanking software often lacks the flexibility to accommodate changes in data sources and workflows demanded by biomarker research projects. The biobank can find itself unable to meet the demands of a wide variety of researchers, with different projects, data and research outcomes. This may result in fragmentation of the data and generation of silos that result in further inefficiencies.

The need to drive investigative research

Biobanks are increasingly being called upon to drive investigative studies; this demands both the ability to link rich data sets to the specimens, and simpler mechanisms to ask scientific and operational questions about this rich data.

Surviving the new research ecosystem

The trend to externalization and big data are also a challenge for traditional biobanking software, which often utilizes home-grown or commercial Laboratory Information Systems (LIMS) software.

Such software may work well enough within the local organization, but often lacks support for new complex research “ecosystem” of external collaborators, vendors and sponsors. (Figure 2)

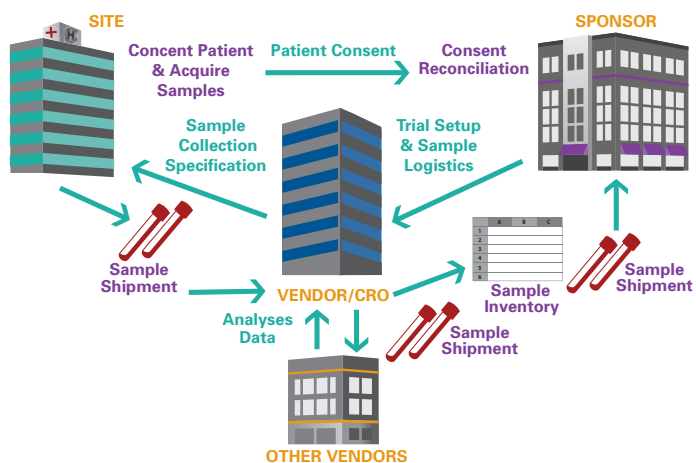


FIGURE 2: The new research ecosystem

Future use, consent and compliance

Biomarker-based studies, clinical trials and translational research projects are driving demand for samples; as a result, biobanks increasingly have to manage complex consent processes to ensure compliance and privacy. Timely response to regulatory questions about trial usage, unanticipated questions and post-marketing studies results in pressure on biobanks to have comprehensive consent reconciliation workflows. Conventional software often lacks such functionality.

THE CRITICAL BIOBANKING CHALLENGES

As discussed above, traditional biobanking faces a number of challenges as a result of the pressures of biomarker based research. To focus the discussion we have summarized these into three critical challenges. (Figure 3)

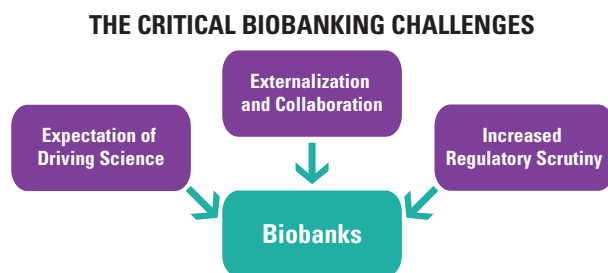


FIGURE 3: Critical biobanking challenges that need to be solved to enable effective biomarker-based research.

Biobanks are expected to drive science

Mining biospecimen data for scientific insights to drive biomarker-based research is key to realizing the full value of biobanking investments. To realize this potential, biobanks must shift from a focus on primarily operational and internal sample inventory management activities to driving scientific insight. Critical to these scientific insights is linking biospecimens with molecular and clinical information, coupled with tools to drive scientific inquiry to create a holistic view of a study, or even across studies.

Increased externalization and collaboration

Studies are increasingly externalized at multiple locations for both business and scientific reasons, creating a distributed research “ecosystem” of vendors, collaborators and partners. In such an ecosystem the biobank may be “virtual” where the emphasis is on the information linked to the sample rather than the physical sample itself and its management. This shift to increased externalization and collaboration also requires a high degree of flexibility to accommodate a wide variety of data sources, vocabularies, workflows and research goals.

Increased security and compliance mandates

The new distributed model of clinical research places new demands on biobanks to control potential privacy and regulatory issues both for trial and future-use samples. Furthermore as more clinical trials depend on specimen biomarker data, greater scrutiny is placed upon stringent adherence to compliance standards. While traditional biobanks may manage sample security they may not meet these enhanced regulatory compliance requirements for samples and their molecular and clinical data.

NEXT GENERATION BIOBANKING – BIOBANKS FOR THE PERSONALIZED MEDICINE ERA

We have conceived the term Next Generation Biobanking to describe the attributes required to solve the critical challenges of biomarker-based discovery.

Next Generation Biobanking has four key attributes;

- Harmonization of biospecimens with clinical and molecular information
- Generation of Scientific Insights
- Support for externalized collaborative studies
- Enhanced security and compliance

Harmonization of biospecimen data with clinical and molecular data

In order to gain scientific insights from biobank samples, Next Generation Biobanking tightly links the biospecimen with the plethora of molecular and clinical data that is collected in the course of a study to create an information “hub”(Figure 4). Investigators across the research ecosystem can then access this dynamic information hub and have a holistic view of the data. It is also key that this information hub be as flexible as possible, allowing disparate data sources to be integrated and multiple new studies, each with different scientific goals, workflows and data models to be easily setup and administered. The LIMS software favored by traditional biobanks often lacks this flexibility. Furthermore, Next Generation Biobanking provides tools to mine this information to rapidly generate or test scientific hypotheses and develop the knowledge to drive successful research outcomes.

Support for externalized, collaborative studies

Next Generation Biobanking provides the critical information infrastructure to effectively manage a distributed research ecosystem and its network of collaborators, partners and vendors, and to link this ecosystem to internal sample-centric workflows of traditional biobanking software. Since the research ecosystem is a dynamic, distributed system, next generation biobanking requires a high degree of flexibility to meet the demands of a wide variety of studies occurring in the research ecosystem. Indeed the comprehensive, physical biobank with hardware, software and samples, may not actually

exist within this externalized, collaborative paradigm. So Next Generation Biobanking allows organizations to effectively manage highly distributed “virtual” biobanks. Here samples may be held in multiple locations, with each location sending samples out for analyses as managed by a CRO for example. The data and the results of the analyses on the samples, are then made available in this virtual biobank. (Figure 4)

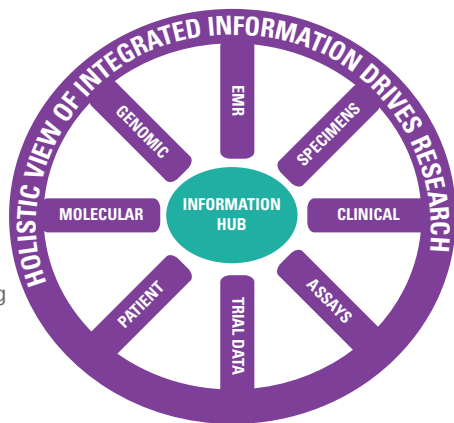
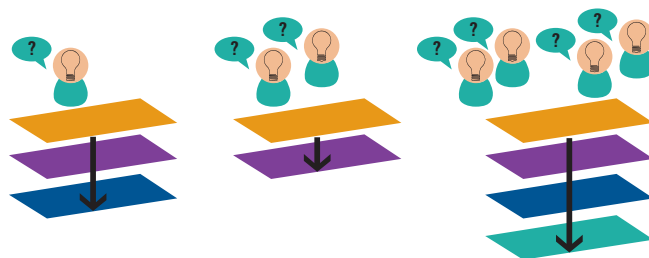


FIGURE 4: Next Generation biobanking creates a dynamic information hub

Gain scientific insights

Next Generation Biobanking puts powerful, “deep collaboration” tools in the hands of the researcher/ domain experts, and ensures that hypothesis-driven research can be carried out without the need to program, or call an IT professional or informatician. Indeed, Next Generation Biobanking recognizes that scientists may need to make *ad hoc* queries of the data, in order to perhaps search out samples for a particular study, delve into a new biomarker hypotheses or stratify patients for a clinical trial based on their sample information.

Deep collaboration is therefore key to leveraging the full potential of the knowledge in biospecimens and extends beyond simple data mining (Figure 5), to encompass all steps of the data exploration workflow. Deep collaboration allows all the stakeholders in the research ecosystem to work together to create queries and get answers in a transparent way. Since the research ecosystem may contain less than perfect data, deep collaboration allows these issues to be uncovered and effectively managed.



A single researcher in a silo often can go deep into the data, but maybe limited by their domain expertise. Small groups of researchers may be able to collaborate on asking questions but can't go very deep with the tools they have today. Deep Collaboration is when multiple groups of researchers can collaborate in asking questions. Shared domain knowledge allows deeper insights into the layers of data.

FIGURE 5: Next Generation Biobanking enables deep collaboration to drive scientific insights.

Enhance Security and Compliance

The consequences of a chain-of-custody problem, or donor consent issue on trial or future-use samples could be potentially disastrous for a study. Next Generation Biobanking software is designed with extremely fine-grained access and security controls that extend to all the data linked to a biospecimen, ensuring compliance with all regulatory guidelines. Comprehensive consent and biospecimen reconciliation processes ensure that both trial use and future use of samples can be managed effectively.

NEXT GENERATION BIOBANKING IN ACTION

BioFortis has a wealth of experience and domain knowledge in empowering researchers involved in biomarker-based clinical and translational research, who need to safely and effectively conduct externalized, science-driven collaborative studies. The BioFortis Next Generation Biobanking software platform harmonizes biospecimen data with clinical and molecular data in a collaborative environment that emphasizes scientific insights, while ensuring security and compliance to leverage the knowledge in biospecimens.

Enabling the search for prostate cancer biomarkers Translational Research Scientists at a major European molecular medicine center are utilizing BioFortis Next Generation Biobanking technology for their study of prostate cancer. Currently, approximately 15-20% of patients diagnosed with prostate cancer develop bone cancer sometime in the ten years following treatment of the primary cancer. Hence, researchers are attempting to identify detectable biomarkers in serum that could be markers for invasive cancer.

A complex research ecosystem and a wealth of clinical and molecular data

The research consortium consists of a clinic that sees prostate cancer patients, records medical histories and clinical parameters. Biospecimens (serum, urine, tissue biopsies) from these patients are also stored in a tissue biorepository along with biospecimens from hundreds of other patients with a variety of diseases. The clinic is affiliated with universities with state-of-the-art proteomics, metabolomics, and gene expression core facilities, where analyses of patient samples are routinely carried out. Data from these different platforms is stored locally on dedicated servers associated with the instrumentation and dedicated software, limiting access and utility of the processed data.

Real outcomes from BioFortis technology

BioFortis software interfaces with the clinical, biorepository, and core facilities data sources and provides a common exploratory research environment with which to access integrated information and cross-query the various data sets to fuel discovery. BioFortis' deep collaboration tools uncovered key scientific insights that enabled identification of protein biomarkers;

- To differentiate high grade vs. low grade prostate cancer
- Predictive of bilateral disease and distant site metastasis
- To distinguish invasiveness to lymph nodes vs. proximal urethra

The BioFortis Next Generation Biobanking software platform enabled researchers to access and explore a combination of different data sets on both the clinical and molecular analytical sides. Exploration of the data within the deep collaborative environment enabled the discovery of proteomic biomarkers of prostate cancer and led to patent filings by the

organization. Furthermore these biomarkers formed the foundation for development of new blood-based molecular diagnostics and targets for therapeutic intervention.

CONCLUSIONS

We conclude that Next Generation Biobanking bridges the gap between existing biobanking software and processes and empowers researchers to meet the demands of biomarker-based research. (Figure 6) The BioFortis Next Generation Biobanking software platform has been designed based on these Next Generation Biobanking attributes and represents an ideal solution for organizations as they strive to deliver on the vision of personalized medicine.



FIGURE 6: Next generation offers a bridge to enable biomarker-based discovery

For information about how BioFortis can bring your existing biobanking into the Next Generation, or help you build a Next Generation Biobank for your biomarker-based clinical and translational research projects, connect with us today, for a free, no obligation consultation.

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