Mapped Out

Clinical research is evolving and adapting in order to glean more from the information collected during trials. Streamlined sample management planning and biorepositories are instrumental in achieving the best results

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The nature of clinical research has changed the way in which biological samples collected in clinical trials are valued, perceived and handled. Studies involving gene and cell therapies – as well as immunotherapies – are charting whole new areas for human health management, and the value inherent in a single patient sample has never been higher. Beyond their importance to proximate research, biological samples are also central to post-trial studies that examine the stratification of disease and its pathways and mechanisms.

To gain more value from the collected data, the industry has evolved from rudimentary laboratory information management systems (LIMS) that only worked within the lab environment, to today's sophisticated sample tracking systems that combine point-of-collection accessioning and global tracking with condition monitoring. These new systems track individually identified samples all the way from collection to biorepositories that guarantee the integrity and retrievability of each one in the distant future.

In addition to the way in which samples are handled, development teams are implementing novel techniques to gain more from the staggering volume of aggregate data produced during clinical trials. Information management enables verified data output from a wide variety of sources, and new visualisation software allows researchers to view them graphically to discover trends and anomalies that might otherwise pass unnoticed.

New Best Practices

Best practices in sample management continue to evolve as new avenues of research are developed. To be research-viable, samples must be controlled to a greater extent and surrounded by more data, with careful planning going into each step of their existence.

One of the leading ways to preserve sample and information integrity is to develop a comprehensive strategic plan that integrates the key elements of sample management and tracking; data management and statistics; data visualisation; and storage and retrieval. Sample management planning should be designed to help control pre-analytic variables that could compromise integrity or otherwise alter research outcomes. The procedure looks at every detail, including:

- What samples should be collected
- How they should be handled
- How they will be accessioned into a tracking system
- How they will be transported, tested, analysed and prepared for long-term storage

To guarantee integrity, every step in a sample's lifecycle must be monitored, recorded and carried out through meticulous adherence to standard operating procedures (SOPs) that are harmonised throughout the study. From collection through cold chain transport,

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to central lab testing and biorepositories, everything must be the same: collection tubes and shipping containers; lab equipment and cryogenic freezers.

Best practices involve preparing a comprehensive sample management plan that inspects facilities and carriers to ensure they have the capability and capacity to carry out programmes as intended.
The practical viability of individual samples for research may depend on being able to demonstrate due diligence in selecting resources to various regulatory agencies.

Data Management and Analysis

High-quality, reliable and statistically sound data from clinical trials are essential for good research. However, the amount of information available presents its own challenge, especially with the advent of electronic data collection and new wearable medical devices. This is further complicated when studies are international and development teams need to plan for data integration to coordinate complex, high-volume data collection and management from multiple sources. This process involves developing an infrastructure and coordinating logistics for programming, coding, cleaning and conditioning information that may come from a variety of platforms. By mapping sources, standardising formats and merging data, programmers can achieve improved consistency, accuracy and usability.

With the information in hand, the challenge now lies in interpretation and analysis. When sample and data management are combined with data visualisation software, complex information becomes more accessible and usable. An integrated data visualisation service will query sample databases in real time – enabling diverse, intuitive views of the most current information, automatic analyses and tracking and alert features for critical sample analytes.

Effective visualisation helps users evaluate data, using graphics to communicate a quantitative message such as making comparisons or understanding causality. The types of information that can be viewed more effectively using this approach in this way include:

- Time series – a single variable is captured over a period of time
- Ranking – categorical subdivisions are placed in ascending or descending order
- Part-to-whole – categorical subdivisions are measured as a ratio to the whole
- Deviation – categorical subdivisions are compared against a reference
- Frequency distribution – shows the number of observations of a particular variable for a given interval
- Correlation – a comparison between observations represented by two variables
- Geographic or geospatial – the comparison of a variable across a map or layout

Analysts reviewing a set of clinical data may consider whether some, all or a combination of the information and graphic types above are applicable to their task. The process of trial and error to identify meaningful relationships and messages is part of exploratory data evaluation.

Biorepository Facilities

Researchers have come to realise that ongoing and long-term access to properly managed, annotated samples is critical to developing new diagnostics and therapeutics. The availability of characterised biospecimens is essential in understanding disease pathways and facilitating biomarker and other research for future discoveries. In addition, because samples may have to be retested for compliance, data or safety reasons, a comprehensive biorepository plan must be part of integrated sample management planning.

A well-run biorepository should reassure clients that it is able to supply annotated biospecimens that have been maintained according to predefined controlled environmental conditions to help establish the validity of downstream analytics – whether they are histological, biomarker or molecular in nature. It also needs to ensure that biospecimens are kept safe and secure, the risk of damage or loss is minimised and that there are procedures in place to provide business continuity.

Facilities should follow Good Storage Practice guidelines and all biorepository processes should meet or exceed regulatory and ethical requirements, such as 21 CFR Part 11-compliant computer systems and unalterable audit trails for temperature monitoring. As studies are increasingly becoming globalised, clients benefit from harmonised SOPs across the lab and biorepository network, using the same instrumentation platform, technology and temperature monitoring systems. Many of today's facilities also provide sample processing on-site, extracting RNA and/or DNA from an original biospecimen, as well as the ability to separate these samples into multiple replicates to minimise freeze-thaw cycle damage and extend the utility of the original.

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Plan Ahead

Biological samples hold the potential to provide valuable insight at both individual and aggregate levels. Preplanning and integration are, therefore, key to maximising their value in today's clinical trials.

Modern drug development and the co-development of companion diagnostics emphasise the need for the strategic integration of sample management in study protocols. Comprehensive approaches are helping to increase the amount of new compounds being tested and the number of new therapeutics coming to market.

Eric Hayashi has more than 22 years' experience in the clinical trials industry. He is currently President and Chief Executive Officer of LabConnect, a leading provider of global central lab services, including routine and esoteric lab testing, kit building, sample management, biorepository and scientific support services for biopharmaceutical and medical device companies as well as CROs.
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