Case Study: Business Benefits from Monitoring of Ongoing Studies

Monitoring ongoing studies can only be done effectively if the study monitors get access to data as it is being collected, or if data from assays done on bio-samples are made available in digital form for integration and analysis.

Unlike retrospective analysis of completed studies, sponsor monitors don't have the luxury of waiting until final reports are compiled and published in PDF. The need of a study monitor is to see the evolving signals as the data becomes available. In practice, there are blocks and delays in the logistics of the disparate data needed for interim monitoring such as the LIMS data is not readily available in an exchange format, or the Investigator may generate the data only in a PDF report or human readable tabulation such as for bio-analytics models.

Converting these sources into machine readable digital form, so as to continually generate the evolving, longitudinal view of each subject, shortens the time to data driven decisions by the study monitoring team while offering opportunities to reduce cost and better prepare for the final report.

The following four case studies demonstrate the immediate business benefits Sponsors realize from monitoring ongoing studies being conducted by their CROs. Their challenges are overcome by PointCross Life Sciences' data solutions, resulting in accelerated data-driven decisions prior to receipt of the final published reports.

CASE 1

Sponsor looks to use on-going studies to make tactical and strategic decisions on planned and future studies and their design sooner, rather than wait until the final study reports are published.

Challenge: Completed studies were previously not readily available to the Sponsor in a machine-readable digital form, and only PDF study reports were available in an unstructured repository in which findings were difficult to search and extract. Insights from findings must be published with substantiation and data along with the annotated insights, but searching across PDFs proved time consuming and challenging to structure.

PointCross DaaS Solution: The PDF reports for all the completed legacy studies of relevance were digitized by a combination of (a) Rapidly re-generating the Trial Design, (b) Extracting Study metadata that allows each of these studies to be reposed with context and provenance, (c) Extracting all the Summary Tables for all published cohorts and groups, (d) extracting all individual subject data from the tabulations and listings in the Appendices (e) Regenerating the summaries for the published summary tables -using only the extracted individual tables - and reconciling them to ensure that the data extraction is accurate and complete, and finally (f) Loading the legacy study into the Xbiom™ universal data model so they can be analyzed along with the ongoing studies.

This is done with a series of automation and machine learning tools that have aided in the processing of several thousand studies, many of which now serve as an indexed and searchable library unique to the respective Sponsor.

Toxicologists are now able to analyze the study data and visualize the data and statistics generated from the data. Figures, Tabulations, Listings and annotations about insights of interest are generated and saved as "TFL" objects for collation and publication. Sharing of the TFLs with colleagues and CRO investigators create a shared understanding of each study and their relationship with other studies – both legacy and future planned.

Business Benefits: Reduce time to IND filing by months, because key strategic decisions do not need to wait for a formal report to be published but rather when there is sufficient data to make a data driven decision. Sponsors see a reduced cost of conducting studies by avoiding unnecessary studies or re-designed the studies to be started.

Applicable services and technologies: Digital data extraction and Nonclinical Study Standardization from human readable tabulations in PDF by PointCross' Data Concierge service. Collaboration, saved TFLs with annotations, and messaging solutions in Xbiom to identify TFLs related to an insight of interest.

CASE 2

Delay in availability of Pharmacokinetic (PK) data from Bio-Analytics labs inhibits assessment of clinical pathology findings.

Challenge: Pharmacokinetic Concentration (PC) calculations of the treatment and metabolites are generated from biosamples sent to bio-analytics labs. The PK modeling and generation of PK parameters such as Cmax and Tmax, AUC (for various timepoints), and Cav, reported in PDF format or Excel is not available in standard machine-readable format. The Sponsor was losing considerable time waiting for the generation of these reports and then manually extracting and curating the data so that it could be integrated with the in-life clinical pathology data.

PointCross Solution: For PK reports provided in the PDF report, the PK parameters were extracted and un-pivoted to a machine-readable, columnar form for loading and integration into the remaining study in Xbiom. We further reduced the time and cost for the sponsor monitors by directly calculating the Pharmacokinetic parameters from the Concentration data from the assays.

Business Benefits: PK parameter calculations traditionally took the Sponsors' CRO between two weeks to a month to generate. PointCross is able to generate these within two business days, at no additional charge to Data Concierge customers. This saved the Sponsor over three weeks and thousands of dollars in modeling service charges by the CRO. This allowed the Sponsor to assess the treatment effects closer to real time, while reducing thousands of dollars in cost for obtaining the Pharmacokinetic parameters.

Applicable software and service deployed: Digital data extraction from PDF reports from DaaS service; Ability to standardize and normalize to SEND-IG CT using Terminology Harmonizer and Standards Management. Pharmacokinetic modeling and regression fits of subject data using statistical and mathematical techniques.

CASE 3

Sponsor conducting Xenograft studies on a tumor growth antagonist drug candidate needs to estimate the IC50 on a nonclinical study with multiple trial arms and treatment compounds.

Challenge: The study design is an involved lattice with multiple trial arms and with multiple CROs involved. Standard trial designs such as those in SEND are not sufficient. Tumor growth values are provided very frequently by multiple CROs. Sponsor-provided plasma concentration values are provided in Excel sheets. A method for estimating the inhibitory concentration for halving tumor size (IC50) is needed, each time new tumor growth and concentration data is received.

PointCross Solution: Over the course of 1 week, a trial design was developed using the study protocol. Furthermore, the biologics and data science team at PointCross developed a tumor growth model for the IC50 calculations, while the data modeling team generated automated data extraction and integration schema for incremental data provided by a constellation of CROs on daily or multiple loads per week. The Sponsor is now able to visualize the trends and analyze a number of parameters around the evolving progress of the tumor data in near real-time, and consider any protocol amendments in quasi-real time.

Business Benefits: Significantly quicker scientific and strategic decisions on the progress of the study, and the comparative performance of the tumor antagonist against other available standards of care. Normalizing and harmonizing multiple disparate data sources into a single coherent data time line for each subject.

Applicable services and technologies: Digital data extraction from human readable tabulations in Excel; Pharmacokinetic modeling and regression fits of subject data using statistical and mathematical techniques; Tumor growth modeling, end-point analysis and IC50 calculations developed using statistical and mathematics scripts.

CASE 4

Incorporating Histopathology data of organs and tissues for terminal subjects from a draft PDF report

Challenge: Necropsy data and histopathology results were available only as a PDF report after the study's conclusion. The CRO-provided LIMS data for pathology was not available until a conversion to SEND had been done, well after the final PDF Study Report was generated. This prevented pathology findings and incidence counts from being cross-assessed against in-life and clinical pathology findings by sponsor toxicologists.

PointCross Solution: PointCross extracted the digital data for all subjects and their organs and tissues within 7 days of receipt of the draft PDF report, and loaded the digital data into the Sponsor customers' site on Xbiom's universal data model and repository. This enabled the Sponsors' pathologists and toxicologists to analyze and observe incidence counts for cohorts being assessed against the in-life data.

Business Benefits: The Sponsor was able to save 4-6 weeks by having access to the digital histopathology data, and avoided a fee of between $8,000 - $10,000 by the CRO for digital pathology data provisioning from the LIMS. Data discrepancies and tentative observations were available for disclosure to study team and report writers. The Sponsor was able to summarize incidence counts, and was able to access digital pathology data against other ongoing or concluded studies.

Applicable software and services deployed: Digital data extraction from PDF reports; Standardization and normalization to SEND-IG CT using Terminology Harmonizer and Standards Management, conversion to universal data model with Smart Transformation module for Digital Data representation and repurposing for analysis and visualization in the Xbiom platform; Automated generation of SEND data domains for submittable SEND from the UDM data in Xbiom.