

Preserve the Value of Yesterday's Study Data in Today's World of eSubmissions

As regulatory agencies around the world rapidly adopt Clinical Data Interchange Standards Consortium (CDISC)-standardized data for submissions, you are likely facing the challenge of how to work with legacy databases. Quintiles Biostatistics can successfully convert data that are inconsistent in structure and content — even data sourced from multiple sponsors and vendors — to create fully consistent databases that adhere to Study Data Tabulation Model (SDTM) specifications.

By working with Quintiles on this complicated and daunting task, you can avoid what is potentially a critical rate-limiting step for the successful completion of your submission. We provide formal CDISC SDTM Theory and Application training for all of our Biostatistics staff — and with more than 320 employees with CDISC expertise, located in 14 offices worldwide, Quintiles has the dedicated resources to handle any size CDISC conversion in a timely and cost-efficient manner.

A RECENT CASE STUDY

Quintiles Biostatistics worked closely with three co-sponsors to convert data from more than 30 studies into CDISC-standard formats in support of an eNDA application. The studies were conducted over a period of more than 10 years, and there was wide variation in the data collection standards. We developed a data standardization plan specifying which SDTM domains would be created, and imputation and formatting rules to be applied. Included in our efforts were substantial FDA interactions. Submission of these CDISC-compliant data files resulted in the FDA's acceptance of the entire CDISC database for all legacy studies without any requests for changes or further information.



Experience in Database Conversion

Through the successful completion of numerous submissions for a variety of sponsors, Quintiles Biostatistics has gained the experience and knowledge required to convert databases to CDISC SDTM format. We have a solid understanding of the expectations of regulatory agencies with respect to submission of data and all associated documentation.

Consistency and Accuracy

We can develop a complete strategy for the conversion process by drilling down to the details of each database. Our programming expertise allows us to apply an efficient and systematic process to ensure consistency and accuracy of the final product.

In-Depth Understanding of CDISC

Quintiles has provided leadership in the development of the CDISC standards — including being the first global provider of the full range of drug development and marketing services to be certified as a CDISC Registered Solutions Provider. Our involvement provides us a unique and beneficial perspective to assist sponsors in compiling CDISC-compliant deliverables.

Flexible Solutions

We collaborate with our customers to get results. Quintiles can provide either a standard CDISC solution or our staff can work with you to tailor a solution to meet your needs.

CONSIDER THESE LEGACY DATABASE ISSUES:

- > What study data are required for the submission [CRF vs analysis] and in what format?
- > The timing of the study database conversion. This work can be done as studies are completed and can be independent of other submission work.
- > What will be the basis of the integration process — the CDISC converted data or the original data?
- > Which version of CDISC SDTM requirements will you follow? It is expected that the CDISC SDTM Version 3.1.2 will be available during 2009.

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We Understand the Dynamic Needs of Biotech

The key elements for a successful biotech company are not the same as for a typical pharma company. Because Quintiles started out as a small group of biostatisticians, we fully appreciate the challenges that a smaller organization can face in a large industry. We know that you need a customized, tailored approach when considering a partner for your statistical needs.

Quintiles Biostatistics has the tools to help you succeed. We offer strategic consulting in protocol design and planning to help you make optimal decisions on study design, sample size, study planning, analysis methods, and precise interpretation and presentation of results. Our internal Center for Statistics in Drug Development (CSDD) group consists of highly experienced statisticians who bring a wealth of knowledge and first-hand experience in the clinical trials arena. We can also tap into our expert external consultants from both the academic and drug development industries to bring an even bigger and broader level of knowledge to your specific statistical challenges.



CASE STUDIES

On one pivotal trial, our Center for Statistics in Drug Development (CSDD) was able to decrease an originally proposed sample size by almost 50%.

This was accomplished by:

- > Taking a different approach to the sample size calculation
- > Modifying the interim analyses set-up, and
- > Incorporating relevant covariates in the analysis

This proposed approach was fully accepted by the FDA reviewer.

In a recent very large Phase III trial, our CSDD group proposed an unblinded sample size re-assessment near the end of the study. The protocol was approved by the FDA and saved the sponsor two months in the expected duration of the study.

Broad Therapeutic Area Experience

Whether your indication is oncology, CNS, infectious disease, cardiovascular or one of the other critical areas of need, we will assign a specialized team that has the therapeutic experience you require and the professional expertise that you want.

Committed to Biotech

Quintiles has a dedicated group of project managers who work only with biotech companies. This group brings to your project invaluable knowledge and leadership that is critical to your success. Our proactive statisticians bring the flexibility, efficiency, teamwork and responsiveness you need.

Beyond Standard Analysis Services

Quintiles Biostatistics also offers:

- > Strategic consulting
- > Drug Development Plans
- > Adaptive Clinical Trials
- > Feasibility analyses
- > Due diligence
- > Event rate analysis to predict LPLV

- > Safety and Adjudication committee support
- > Periodic safety reporting
- > Data mining algorithms for protocol deviation and event detection
- > Site fraud detection analysis
- > Automated patient narratives
- > Pre-lock production strategies to decrease time from database lock to final CSR
- > Submission strategies and analysis
- > Statistical representation at regulatory agencies

CASE STUDIES (CONTINUED)

One of our CSDD statisticians worked closely alongside a sponsor to develop their Phase III strategy and program. By re-evaluating the sponsor's original study design strategy, the Phase III confirmatory studies were redesigned to meet – with fewer patients – a shorter timeline that still met efficacy requirements and size of safety database. Our statistician also supported the sponsor at the end of the Phase II meeting with the FDA when the redefined plan was accepted. This collaborative approach resulted in a cost savings of \$8 million.

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Increase Efficiency, Accelerate Timelines and Produce a Superior Quality Submission

In recent years the Quintiles Biostatistics team has completed more than 20 submissions globally for sponsors varying from emerging biotechs to large pharma companies. We provide formal CDISC SDTM Theory and Application training for all of our Biostatistics staff. We also have a large network of medical and regulatory experts who will collaborate with you and our statisticians in order to deliver the most effective submission possible.

Whatever your therapeutic area or regulatory requirements, our statisticians will work closely with you to make key strategic decisions — what studies should be included, which endpoints to analyze, and how best to present your data in the submission. These decisions are fully documented in an integrated Statistical Analysis Plan and a Data Integration Plan. We also understand the requirements for electronic Common Technical Documents (eCTDs) and how to successfully build your electronic submission.

CASE STUDY

We recently teamed with three co-sponsors to convert, integrate, analyze, report and submit data from 30 studies in support of their first eNDA.

- > Quintiles Biostatistics handled the integration of legacy and current study data, conversion of data into CDISC SDTM standards (including PK data), creation of the eNDA submission, production of reviewer aids and training materials, and post-submission support.
- > Our strategic, multi-team approach reduced the timeline from end of Phase III to completed integrated analysis by nearly 50%.
- > Quintiles delivered the CDISC SDTM-compliant data files for all 30 studies with no requests from the FDA for changes or further information.



Strategic Planning

We offer innovative thinking to develop your optimal statistical approach, detailed knowledge of regulatory requirements, and proactive planning of appropriately-timed regulatory meetings to start your submission on the right track.

Efficient Data Analysis

Quintiles Biostatistics provides a proactive analysis strategy for integrated summaries utilizing a cumulative integration approach with ongoing analysis runs and systematic and collaborative reviews. Our goal is to achieve a shorter turnaround time from the end of last study to a completed submission.

Complete Data Package Solution

From the start, we specialize in preparing your data to CDISC SDTM standards, with the thorough documentation that is required. Before actual submission, we engage in test data transfers to ensure any technical issues related to data acceptance are resolved.

Post-Submission Strategy Planning

Our job does not end with your submission. We continue to support you with a “rapid response team” to address any questions or ad hoc requests from the regulatory agency, produce your post-submission safety updates and provide advisory committee support.

CONSIDER THESE SUBMISSION ISSUES:

- > Did you know that Integrated Summaries of Safety and Efficacy may not be required if certain criteria are met by your submission?
- > How will you handle converting non-CDISC compliant legacy study data to meet CDISC SDTM standards?
- > Will recoding of adverse events, medications and medical histories be needed for your submission to ensure consistency across studies?
- > Do you have studies that need translation, and have you planned to handle the task concurrently with submission analyses to avoid any delays?

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