eBook

ENSURE HIGH-QUALITY DATA AND FASTER SUBMISSIONS

Best practices guide for integrating expert data services in your clinical trial

FIRMA
CLINICAL RESEARCH
Expert Insights | Quality Outcomes

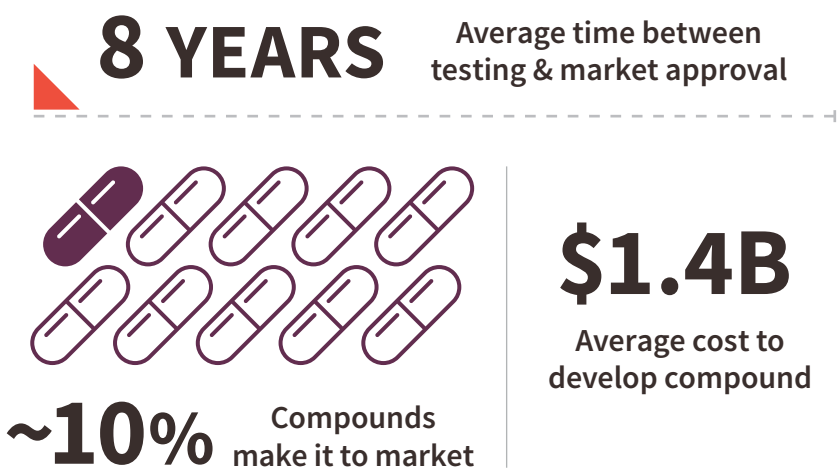
INTRODUCTION

Traditional drug development is an intense and resource-heavy process that takes years for drugs to get to market. While the FDA has developed an accelerated approval approach to speed the availability of drugs to treat some rare diseases,[1] the interval between initial safety assessment (Phase 1) and market approval is still estimated to take an average of eight years[2] and cost $1.4 billion,[3] with only 9.6% of compounds ever reaching patients in the healthcare treatment setting.[4]

How can these costs and timelines be streamlined?

One way to avoid costly delays and better position for development success in today's clinical trial landscape is through the proper implementation of expert data services. Beginning with responsive study designs that capture accurate and meaningful data throughout the drug development process, accelerating clinical trial database builds, and continually assessing data quality and analysis, drug developers can shorten trial timelines and reach investigational product submission dates more quickly.

In this eBook, you will learn how integrating data service support properly through your development lifecycle promotes timely response to protocol changes, efficient, high-quality data collection and, ultimately, speeds your time-to-approval submission.

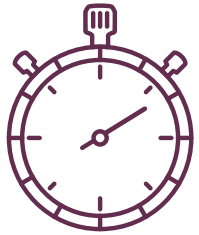


DATABASE BUILD

According to a 2017 study from Tufts Center for the Study of Drug Development, companies take an average of 68 days to build and release a clinical study database in an electronic data capture (EDC) system.[5] Delays in building and releasing a study database are associated with downstream delays for other data management processes such as:

- ▷ Patient data entry
- ▷ Time-to-database lock

What are common challenges associated with database build? What opportunities arise from optimizing the database design process with standards and systems that can anticipate and mitigate potential delays?



68 DAYS

Average time to build and release a clinical database

30+ DAYS

Downstream lag time for patient data entry and time to database lock[6] resulting from delays in releasing study database

DATABASE BUILD

CHALLENGES

Protocol Amendments

Protocol amendments pose one of the greatest obstacles to achieving rapid database build. Common protocol amendments include:

- Modifications made to the eligibility criteria and demographics of the patient population
- Availability of new safety information
- Adjustments in the number/types of safety assessment procedures
- Edits and revisions made to general protocol information[7]
- Revisions to the safety endpoints based on FDA's comments

OPPORTUNITIES

Early Clinical Data Strategy

Involve your biostatistics team from the beginning of a study to apply their expertise in:

- Study design considerations, including whether an adaptive trial design might be suitable
- Potential interim testing and analysis strategies
- Participating in and providing input to the Data Safety Monitoring Board (DSMB)
- Participating in regulatory meetings with you to defend your planned analysis of study data

Average protocol amendments for less complicated study protocols[8]

Average protocol amendments for more complex studies

Protocol amendments are implemented prior to the first patient visit

DATABASE BUILD

CHALLENGES

Database Release Can Cause Downstream Delays

Building and releasing a database quickly is important to maintain the larger project timeline. On average, clinical trial teams take 68 days to build and release a typical study database, risking downstream delays reaching regulatory submission and approval.[9]

OPPORTUNITIES

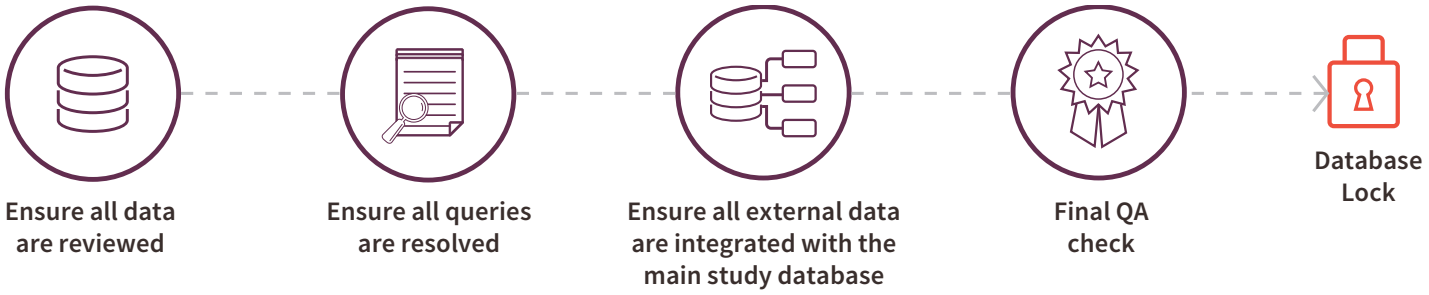
Database Release Prior to FPFV

Create a timeline with your data services team to ensure database release occurs prior to first patient, first visit (FPFV). This includes:

- ▷ Production of all EDC screens
- ▷ Finalization of all validated screens
- ▷ Production of edit check document
- ▷ Finalization of all validated edit checks
- ▷ Finalization of user acceptance testing (UAT)
- ▷ Completion of all data-processing requirements

What needs to take place before a database can be locked?

A well-planned and executed database lock is critical for high-quality and thorough biostatistical analysis of your trial data. Here are the steps to take to ensure a timely and successful database lock.

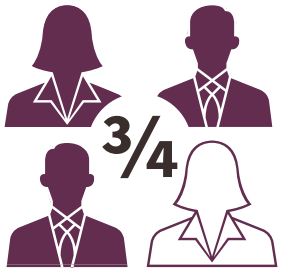


DATABASE BUILD

CHALLENGES

Data Entry and Integration

In a recent survey, more than three-quarters of industry professionals noted they have issues loading data into their EDC application and most (66%) claimed that EDC system or integration issues are the primary reasons they are unable to load study data,[10] especially since researchers collect data from many different sources, such as wearable technology, handheld devices, and social media platforms.[11] Loading data from multiple applications can be challenging to complete in a timely manner leading to greater delays and costs.



Industry professionals with issues loading data into their EDC[12]

Industry professionals unable to load study data because of EDC system or integration issues[10]

OPPORTUNITIES

Experienced Data Services Teams

Ensure your data services team has the appropriate experience by asking them:

1. What EDC platform should your study implement? What advantages does that platform provide compared to others?
2. Will all desired data be captured and easily integrated with the EDC platform?
3. Can the team ensure a CDISC-certified SAS database for regulatory submission? What is the strategy for implementing the requirements?
4. Will the database be US 21 CFR Part 11 and EU Annex 11 compliant upon completion?

DATA QUALITY

Estimates show that up to one in six compounds fail first approval in part because of data integrity issues. Poor data quality and integrity issues are leading contributors to deficiencies in clinical trials.[11]

CHALLENGES

Siloed Biostatisticians

Neglecting to include experienced biostatisticians during protocol and study design can lead to:

- ▷ Choosing inadequate study endpoints[13]
- ▷ Insufficient sample size to demonstrate efficacy

CRFs and Queries

Case report forms (CRFs) should be protocol-driven, robust in content, and used to collect study-specific data.[14]

Data quality issues arise when CRF data entry contains erroneous or missing data, and queries are resolved infrequently or in bulk at the end of a study, instead of throughout. This leads to expensive and timely delays with database lock.

OPPORTUNITIES

Biostatistics Integration

Involve biostatisticians early in the clinical process to plan to:

Optimize study design by:

- ▷ Maximizing the probability of showing efficacy
- ▷ Minimizing the probability of a failed study

Cross-Functional Data Services

Data services team members — including both data managers and biostatisticians — an be involved in the development of eCRFs to ensure the collection and entry of pertinent data for analyses. Robust cross-functional training of data services team members allows for better identification and resolution of queries in real-time, instead of at the end of a study.

HOW CAN FIRMA HELP YOU SUCCEED?

With our ability to achieve database build in an average of 4 weeks, **Firma's Data Services team is more than 2x faster** than industry standard. Our team ensures a rapid start to your clinical trial, maximizing your ability to shorten your overall trial timelines. **Contact us** today to discuss how we can support your trial needs.

DATA QUALITY

CHALLENGES

Inflexible Trial Design

Classic study designs do not offer enough flexibility to make use of continuously emerging knowledge that is generated as the trial progresses and can lead to trial failure.[13]

To ensure data quality and expertise, choose a data services team led by PhD- and MS- level professionals with extensive knowledge of pharmaceutical development.

OPPORTUNITIES

Adaptive Trial Design

Adaptive trial design allows for modifications to the trial and statistical procedures of the trial after its initiation without undermining its validity and integrity. The purpose is to make clinical trials more flexible, efficient, and fast.[15] An experienced data services team can assist in the development of an adaptive design by collaborating with the sponsor to define:

- ▷ Inclusion-exclusion criteria
- ▷ Treatment duration
- ▷ Dose and study endpoints
- ▷ Evaluation criteria
- ▷ Randomization
- ▷ Study design
- ▷ Sample size
- ▷ Study hypothesis
- ▷ Statistical analysis plan

When compared to conventional designs, such flexibility:

- ▷ Creates an efficient study with fewer subjects and a shorter duration
- ▷ Increases likelihood of study objective success
- ▷ Yields improved understanding of treatment effect[16]

REGULATORY SUBMISSIONS

While some new drug applications (NDAs) fail due to lack of efficacy or safety concerns, many others fail to achieve approval because of a lack of data quality provided to regulatory authorities. In addition to providing clean, quality data throughout a study's lifecycle, additional regulatory support from your data services team ensures accurate and timely submissions.

CHALLENGES

Resubmission Delays and Incomplete Applications

Resubmitting failed applications is costly and timely, and ultimately delays approval. On average, one resubmission delays approval by 546 days.[17] Common reasons for resubmission include:

- ▷ Uncertainties related to dose selection
- ▷ Choice of study endpoints that failed to adequately reflect a clinically-meaningful effect
- ▷ Inconsistent results when varied endpoints were tested
- ▷ Inconsistent results when multiple trials or study sites were compared
- ▷ Poor efficacy when compared with standard of care[18]

When the FDA considers an NDA to be incomplete, the organization may issue a "Refusal to File" decision. Refuse-to-file actions are taken to alert sponsors as quickly as possible of deficiencies to help companies correct issues, instead of delaying a response with a complete response letter.[19]

OPPORTUNITIES

Data Services and DSMB Collaboration

Prepare for your FDA submission by selecting a biostatistician from your data services team to serve as a non-voting member of your DSMB, and as an independent statistician to generate unblinded tables for the DSMB. This individual can also support the independent data monitoring committee for interim analysis to ensure high-quality data collection and evaluation throughout the study lifecycle.

One method of support includes a two-level team comprised of:

- ▷ A blinded team tasked with writing SAS codes to generate and validate summary tables using dummy randomization
- ▷ An unblinded team that includes a statistician to run all analysis tables using the real randomization codes once SAS programs are ready

Firma Data Services team has contributed support to 50 drug approval filings (FDA, EMA, CFDA) - with 48 approvals

CONCLUSION

FDA commissioner, Scott Gottlieb, and other FDA officials have emphasized the need to rethink standards of evidence and the reliability of information used to make regulatory decisions.[20] It's more important than ever for sponsors to provide reliable evidence in support of innovative drug development.

Including your data services team early in the study design process is an important strategy to increase operational efficiency and promote high-quality data submission and analysis. Relying on an experienced team can help ease the burden of sponsors and study team members, speed a drug to market, and, ultimately, reach patient populations in need.

DATA SERVICES

Schedule a call with our Data Services Leadership team today for a free protocol evaluation or study concept document review, **info@firmaclinical.com** or visit **firmaclinical.com**.

ENDNOTES

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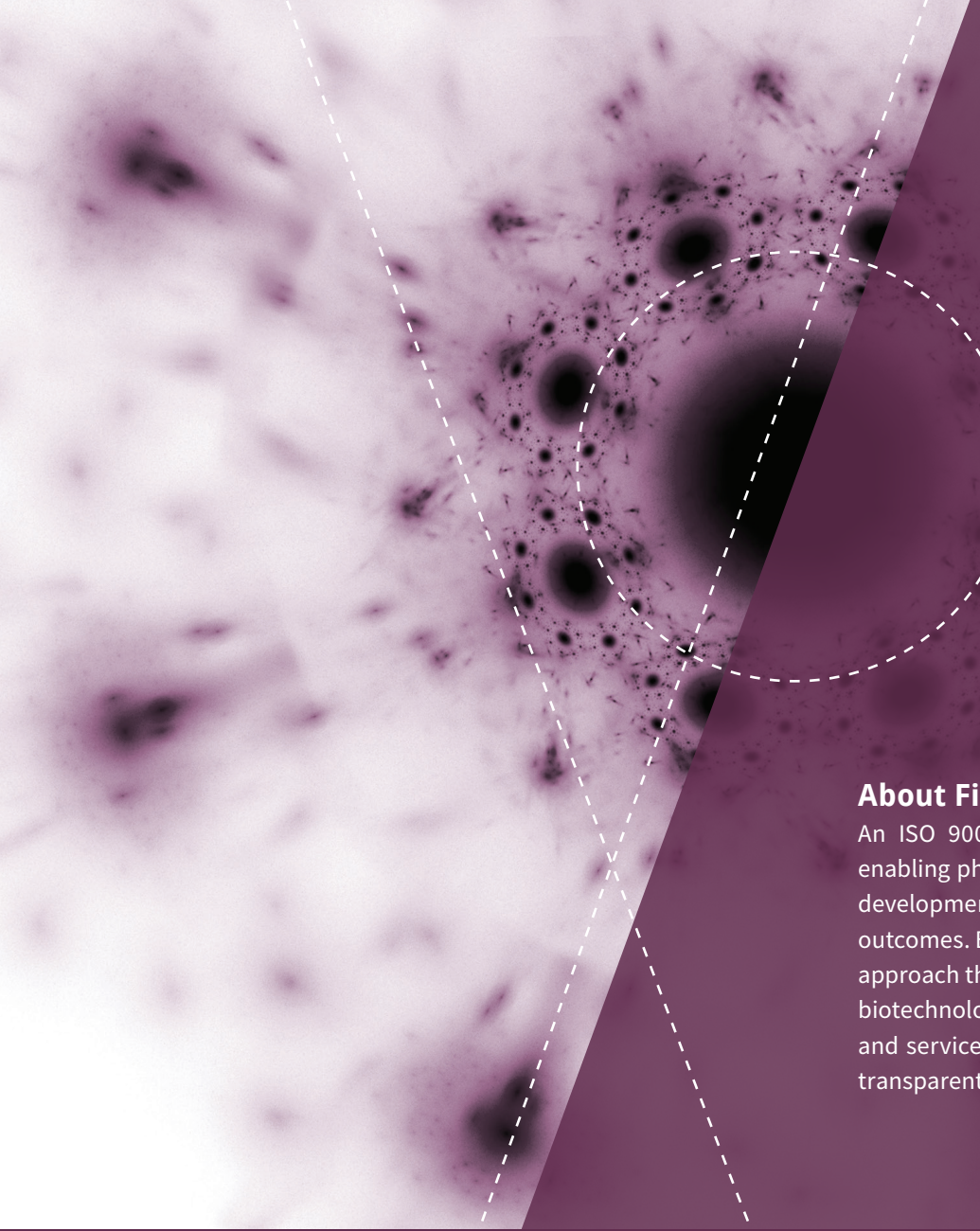

About Firma Clinical Research

An ISO 9001:2015 quality-certified organization, Firma Clinical provides focused CRO services enabling pharmaceutical and biotech clients to plan for and advance research in the dynamic drug development landscape. This support enables clients to make informed decisions that lead to better outcomes. Built on decades of clinical leadership and expertise, Firma is dedicated to a collaborative approach that accelerates the development of safe and effective treatments for the pharmaceutical, biotechnology, and medical device industries. The company offers a wide array of tailored processes and services across all phases of clinical development, strategically focusing on flexible solutions, transparent communication, and on-time deliverables.

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