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Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Tufts CSDD 20 YEARS Impact Reports

Impact REPORT

ANALYSIS AND INSIGHT INTO CRITICAL DRUG DEVELOPMENT ISSUES

eClinical data volume and diversity pose increasing challenges and delays

Data management cycle times are longer than those observed a decade ago

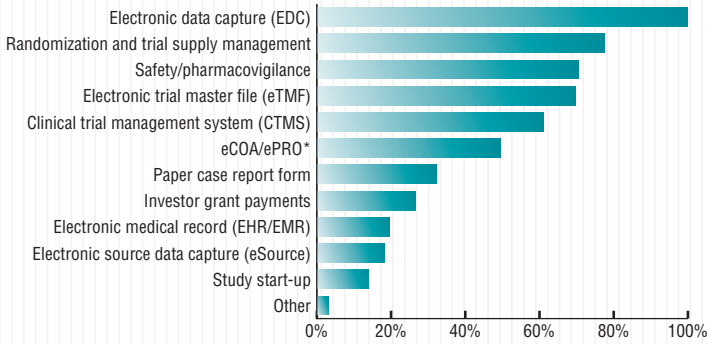
- Sponsors and CROs use an average of six applications to support clinical trial activities.
- 26% of sponsors and 52% of CROs report that they still use paper case report forms.
- Companies report taking 68.3 days, on average, to build and release a study database, with modest variation observed between companies.
- Protocol changes are the most common reason for delays in building study databases.
- Frequency of releasing the final study database after the first patient visit is associated with longer downstream delays and inefficiencies.
- Cycle time from last patient, last visit (LPLV) to database lock is 36 days on average, up from 33 days 10 years ago.
- 77% of sponsors and CROs cite difficulty loading data into their primary EDC system due to compatibility, technical demands, and integration challenges.

As the scope and complexity of global drug development programs continue to rise, data management functions must bear the burden of handling an ever larger amount of diverse clinical data. Electronic clinical outcome assessments, mobile devices, social media communities, and electronic health/medical records are but a few examples of new and diverse sources of data now captured during a clinical trial. The volume and diversity of data is presenting integration, compatibility, loading, and interoperability challenges that the pharmaceutical industry must address to optimize drug development performance.

To better understand the current data management operating environment, Tufts CSDD and Veeva Systems conducted a study including nearly 260 sponsor and CRO companies to obtain a baseline assessment of data management practices and experience, results of which are summarized in this report.

Sponsors and CROs use approximately six applications to support each clinical study

Share of companies using proprietary or commercial applications in clinical studies



- All study respondents reported using EDC applications in clinical trials.
- Approximately three-quarters reported using applications to manage randomization and trial supply management, safety and pharmacovigilance, and electronic trial master file data.
- 26% of sponsors and 52% of CROs reported that they still use paper case report forms to support their clinical studies.

** eCOA/ePRO = Electronic clinical outcomes assessment and electronic patient reported outcomes*

Source: Tufts Center for the Study of Drug Development

Sponsors and CROs use their primary EDC to capture traditional data types

Reported incidence of data collected and proportion captured in the primary EDC

Data type	Incidence	Proportion in primary EDC
eCRF	100%	77.5%
Local lab	59.5%	4.7%
Quality of life	59.5%	3.9%
Central lab	56.8%	4.8%
ePRO	34.2%	3.3%
Pharmacokinetic	33.9%	1.3%
Biomarker	28.0%	0.8%
Pharmacodynamic	21.4%	0.5%
eCOA	20.6%	1.1%
Medical images	20.2%	1.2%
Genomic	9.7%	0.4%
Mobile health	9.7%	0.3%

Source: Tufts Center for the Study of Drug Development

- All sponsors and CROs reported managing eCRF (electronic case report form) data in their primary EDC application, with eCRF data representing more than three-quarters (78%) of the information managed by that application.
- Only one out of five sponsors and CROs reported managing eCOA (electronic clinical outcomes assessment) and medical imaging data in their primary EDC.
- Less than one in 10 (9.7%) reported collecting mobile health and genomic data, but virtually none of that data are captured in the primary EDC.

Current data management cycle times are longer than those observed 10 years ago

Aggregate mean cycle times in days

		Company type		Company size			Primary EDC provider	
	Overall	Sponsor	CRO	Low volume	Medium volume	High volume	Industry leaders	All others
Time to build and release study database	68.3	73.4*	52.8*	72.8	60.2	71.4	72.8	60.2
Time from patient visit to entering patient's data into EDC system	8.1	8.4	6.8	8.2	7.7	8.4	8.2	7.7
Time from last patient, last visit to database lock	36.3	38.7*	27.7*	42.7	33.7	33.7	42.7	33.7

** Differences within subgroup are significantly different (p<.05)* *Source: Tufts Center for the Study of Drug Development*

- Time from last patient, last visit to database lock was an average of 36.1 days in 2017, up from 33.4 days in 2007, due in large part to the rapid growth in eClinical data volume and diversity of data captured.
- CROs, on average, reported building and locking study databases 20 days and 11 days faster, respectively, compared to sponsors.
- Companies using leading EDC applications, on average, experienced longer study database build cycles, compared to companies using other EDC applications.

Protocol changes are the most common reason for delays in building clinical databases

Top causes of database build delays

	Share of total (N=257)	LPLV to DBL* (Days)
Protocol changes	45.1%	31.8
User acceptance testing (including review and approvals)	16.7%	34.2
Database design functionality	15.2%	50.4
Study database move from development into production	8.2%	39.0
Standards management	4.3%	37.5
Ethics committee approval delays/ changes	1.2%	33.3
Overall		36.3

** Average for Phase II and III trials for study's last patient, last visit (LPLV) to database lock (DBL)*

Source: Tufts Center for the Study of Drug Development

- Protocol changes accounted for 45.1% of database build delays reported by sponsors and CROs.
- Companies citing protocol changes, on average, achieved LPLV-to-database lock five days faster than the overall average, indicating that protocol changes did not lead to downstream data management cycle time delays.
- While database design functionality was cited by only one out of six companies as a top cause for build delays, this cause was associated with an LPLV-to-database lock cycle time that was 39% longer than the overall average.

Longer data management cycle times are tied to releasing the study database after FPFV

Frequency of EDC release after first patient, first visit and downstream impact

Frequency	Percent	Patient visit to data entry* (Days)	LPLV to DBL* (Days)
Never (N=39)	15.2%	5.4	31.4
Rarely (N=135)	52.5%	7.8	34.4
Often (N=70)	27.2%	10.1	41.7
Always (N=7)	2.7%	10.2	53.8

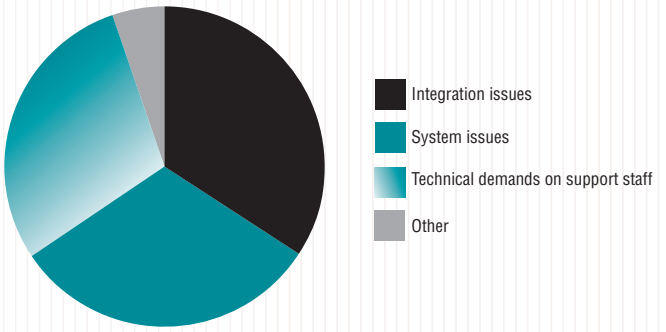
** Average for Phase II and III trials*

Source: Tufts Center for the Study of Drug Development

- More frequent study database releases after starting patient enrollment (first patient, first visit, or FPFV) are associated with longer downstream data management cycle times, including time to enter data after patient visits and time from LPLV to database lock.
- Companies that reported always releasing the study database after FPFV experienced significantly longer data management cycle times, compared to those that reported never doing so.
- Longer cycle times may result from poor site motivation, lower levels of study staff trust and confidence in a data management system, and ongoing database functionality issues.

77% of sponsors and CROs cite challenges loading data into their primary EDC system

Distribution of data loading challenges



Source: Tufts Center for the Study of Drug Development

- The majority of companies reported technical challenges in loading the data into, and problems stemming from the limitations of, the primary EDC system.
- One-third (32%) of issues are related to EDC system limitations, and nearly as many (29%) are related to technical demands on support staff.
- The remaining 34% of data loading issues are related to challenges associated with integrating disparate data sets into an EDC system.

About this study

Data for this analysis were developed from a Tufts CSDD study conducted between May and July 2017, resulting in completed surveys from 257 unique and verified companies (77% drug sponsors and 23% CROs). In terms of annual clinical trial volume managed by the responding companies, 84 initiate fewer than five trials per year, 80 typically initiate five to 15 trials per year, and 93 initiate more than 15 trials per year. Leading primary EDC providers include Medidata Solutions and Oracle. Respondents had an average of 16.5 years of experience managing data, and 87.9% of respondents were located in the U.S. but had global data management responsibility. Statistical significance was determined using multiple regression and Pearson's chi squared tests ($p<.05$).

This study, supported in part by an unrestricted grant from Veeva Systems, was conducted by Michael Wilkinson, Research Analyst, Tufts CSDD; Beth Harper, Consultant, Clinical Performance Partners; and Ken Getz, MBA, Associate Professor and Director of Sponsored Research at Tufts CSDD.

Definition of terms

Clinical trial — A specific type of clinical study in which a medical intervention is tested against a placebo or an active control in human subjects. Clinical study is a broader term that includes other forms of human participatory research, such as pharmacokinetic, epidemiologic, and behavioral studies.

Database lock — Point at which data collected in a clinical trial is deemed final, ready for analysis.

eCOA — Electronic clinical outcome assessment. Use of technology, such as smartphones, by patients, clinicians, and caregivers to report clinical trial outcomes

eCRF data — Electronic case report form data. Patient clinical data that is usually recorded, either electronically or on paper, and saved in an electronic case report form.

EDC — Electronic data capture system. Software that stores patient data collected in clinical trials. Data may be collected via a paper form and then transcribed to an eCRF, or collected electronically.

ePRO — Electronic patient-reported outcome. A patient-reported outcome collected by electronic methods.

About the Tufts Center for the Study of Drug Development

The Tufts Center for the Study of Drug Development at Tufts University provides strategic information to help drug developers, regulators, and policy makers improve the quality and efficiency of pharmaceutical development, review, and utilization. Tufts CSDD conducts a wide range of in-depth analyses on pharmaceutical issues and hosts symposia, workshops, and public forums.

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