

Priya Temkar

*Business Consultant,
Clinical Services - Life-Sciences,
Tata Consultancy Services, Mumbai,
Maharashtra, India*

Address for correspondence:

Mrs. Priya Temkar,
Clinical Services - Life Sciences,
Tata Consultancy Services, Plant
No.12, Godrej and Boyce Complex,
LBS Marg, Vikhroli West,
Mumbai - 400 079, Maharashtra, India.
E-mail: priya.temkar@tcs.com

Abstract

Clinical operations generation next... The age of technology and outsourcing

Huge cost pressures and the need to drive faster approvals has driven a technology transformation in the clinical trial (CT) industry. The CT industry is thus leveraging mobile data, cloud computing, social media, robotic automation, and electronic source to drive efficiencies in a big way. Outsourcing of clinical operations support services to technology companies with a clinical edge is gaining tremendous importance. This paper provides an overview of current technology trends, applicable Food and Drug Administration (FDA) guidelines, basic challenges that the pharma industry is facing in trying to implement such changes and its shift towards outsourcing these services to enable it to focus on site operations.

Key words: Analytics, clinical operations, cloud, current trends, electronic source, mobility, outsourcing, social media, technology

CLINICAL OPERATIONS-THE PIVOTAL PILLAR OF DRUG DEVELOPMENT PROCESS

Clinical operations is the backbone of the overall CT and is responsible and accountable for the performance of the trial, right from its initiation until the site close-out. In addition to the CT being steered by the pharma company and the Contract Research Organization, investigators and their sites/hospitals work alongside as key players for the successful execution of a CT. Ensuring that all the activities mentioned above are in compliance with International conference on harmonization of good clinical practices (ICH-GCP), applicable regulatory guidelines, protocol and standard operating procedures (SOPs) to generate high quality data for timely regulatory submissions, is a time

consuming and expensive affair. A study on CTs conducted by Gartner estimated that 1-day of drug development costs a sponsor \$37,000.^[1]

Hence targeting process improvements, via technological advances to reduce operational costs, increase productivity, and shrink timelines is the need of the hour.

THE CURRENT STATE OF THE CLINICAL TRIAL INDUSTRY

Outsourcing trends

Nearly 70% of total Research and Development (R&D) costs are spent on CTs.^[2] As per the latest report by the Association of Clinical Research Organizations, CTs

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Temkar P. Clinical operations generation next... The age of technology and outsourcing. *Perspect Clin Res* 2015;6:175-8.

Access this article online	
Quick Response Code: 	Website: www.picronline.org
	DOI: 10.4103/2229-3485.167098

which are outsourced are completed on an average 30% faster than those conducted by sponsoring companies or Academic Research Organizations in-house. This results in average time savings of 4–5 months, which is an invaluable period of time for the patients in need of treatments. This also translates to \$120–150 million in development cost savings.^[3]

Total pharma R&D spend was approximately \$137 billion in 2013 and is estimated to grow to approximately \$145 billion in 2016, 68% (\$93 billion) of which is attributed to drug development, inclusive of clinical and pre-clinical spend. Approximately 37% (\$19 billion) of total clinical development spend (\$51 billion) was outsourced in 2013, and the outsourced spend is expected to grow to \$23 billion by 2016.^[4] These figures not only predict the increasing demand for outsourcing of clinical research but also flag the need for delivery readiness to cope up with this increasing need.

India is a preferred destination for outsourcing, not only owing to the availability of a large pool of skilled manpower and the cost arbitrage, but also due to the increasing realization of pharma industry about the need to leverage technology in drug development which is undoubtedly India's core strength.

Technology trends

Current technology trends to name a few are social media, mobility, analytics, cloud, and electronic source (eSource), etc., More and more companies want to implement above technologies in their CTs, as this will revolutionize their business. The tremendous growth in these areas will have a significant impact on the pharmaceutical drug development industry and IT companies delivering CT services.

Mobility

The generation of smart phones and tablets has significantly changed our lifestyle and is now changing the face of drug development services as well, by improving the engagement of more and more patients in CTs, with trial information being available on their handheld devices coupled with an advantage of updating it on a real time basis. With 1.75 billion smartphones used globally, mobile health monitoring brings significant insights into clinical research organizations without adopting the cost of expensive monitoring systems.^[5]

Given the rapid expansion and broad applicability of mobile apps, the Food and Drug Administration (FDA) has issued a guidance document in February 2015, which focuses mainly on the functionality of the app rather than the platform and the FDA intends to apply its regulatory oversight to only those mobile apps that are medical devices

and whose functionality could pose a risk to patient's safety.^[6]

Social media

As more patients turn to online communities like Twitter, Facebook, etc., for support and information about available CTs, social media is already influencing CTs. Pharma companies need to develop their internal processes to bring in a streamlined approach to adopt social media in clinical research while ensuring compliance with current FDA guidance. As per the report published by the Tufts Centre for the Study of Drug Development, most companies began to use social media in clinical research in 2010 or later. In clinical operations, social media is being used for patient recruitment in an estimated 11% of all trials with usage largely limited to North American patient communities.^[7]

Social media has become a source of information for medical products. Irrespective of the type of social media used to publish information; the objective should be to convey correct, accurate, and nonmisleading information to patients and healthcare providers. With this objective in mind, the FDA had proposed two draft guidance in 2014. First one recommends that when using the internet/social media with character space limitations, either to communicate product information or while responding to medical queries on Google and Yahoo, due weightage should be given to risk and benefit information.^[8] The second draft guidance provides FDA's recommendations on the correction of misinformation from independent third parties, on the Internet and through the social media sites.^[9]

Websites like healthunlocked.com, patientslikeme.com, patientsknowbest.com, etc., are some of the patient health data websites used widely by patients to access and publish medical data.^[10]

Cloud

Benefits of cloud computing includes reduced costs, highly automated systems, remote access, and flexibility, together with good performance and data security and an online platform for CTs. Many life sciences organizations could save as much as 25% of their annual operating expenditure on clinical IT systems by using cloud computing.^[11]

Electronic source

eSource can become the electronic clinical trial record (eCTR), with the advent of direct data entry (DDE), which facilitates the direct collection of electronic data when a subject is being evaluated in a CT. This enables real-time monitoring, which in turn results in a significant drop in the number of protocol deviations and queries raised. In 2012, a phase II CT of 101 days was conducted under a US IND that used both DDE and risk-based

monitoring. The results, included data from 20 treated subjects and 4,562 electronic case report form (eCRF) pages entered into the database, demonstrated that there was only one on-site interim monitoring visit, and it took just 2 h. The clinical research site reported that DDE enabled more efficient collection and recording of data, allowing them to see more research subjects per day, thereby doubling productivity, and saving at least 70 h of data entry time.^[12]

In an effort to streamline and modernize clinical investigations the FDA has issued the E-source guidance (September 2013), which promotes capturing the source data in an electronic form, and assists in ensuring the reliability, quality, integrity, and traceability of data from eSource to electronic regulatory submission.^[13]

All the above technology trends, going forward will drive a change in the responsibilities held by key roles in CTs. Clinical Research Associate's (CRA) will be able to save time on extensive travelling and correcting transcription errors, leveraging risk-based monitoring (a transformational approach leveraging predictive analytics and centralized monitoring), and can focus on addressing core trial issues at the site. Biostatisticians will play an increased role in analyzing data trends, identifying outliers, predicting evolving risk patterns, and implementing adaptive designs. Data managers will also evolve from the data processors to central monitors, blending analytical and clinical expertise will come into picture quite early during the planning of the trial, predictive analytics will allow for the prediction of potential errors and responsiveness will be more proactive than reactive. Query management will become real-time and effective interactions between clinical operations and clinical data management, will enable immediate changes to be implemented in the eCRF data. With these changing roles and responsibilities, and evolving process improvements, the sponsor would predictably see significant time and cost savings.

CLINICAL OPERATIONS-BASIC CHALLENGES AND MITIGATIONS

Time spent on administrative support work

When you need your clinical operations project team to speed up on core trial/protocol activities, they probably end up spending a significant amount of their time on support work. Some examples include, time invested on financial disclosure reconciliation, updating CT systems, ensuring safety reports reach all intended recipients, complying with stringent safety reporting timelines, processing drug shipment records reconciliation/approvals, updating CT registries, and CT document tracking for IND submissions,

managing electronic Trial Master Files (eTMF) etc., Outsourcing these activities to a vendor, who can provide these services and complement the same with automation, thus driving process optimization, can yield long-term cost benefits, improving productivity, while allowing CRAs and study teams to focus their time and energy on critical trial aspects. Not only does outsourcing reduces the CapEx and allows an organization to focus on its core activities, technology-enabled companies develop tools to automate processes, and achieve faster turnaround time. For example, tools/applications are developed to screen multiple state board websites and identify investigators with a debarment/sanction. This would not only speed up the manual process, but would also ensure accuracy, which becomes critical when it's a matter of regulatory compliance while completing investigator debarment checks and/or State Medical Board Sanction Checks for hundreds of investigators.

Selection of appropriate investigators and trial sites

Inexperienced or trial naïve sites can be a nightmare for the CRA. However, quite often site selection is the most underrated process, mainly on large global trials involving hundreds of sites and investigators, which are selected over a short span in an attempt to speed up trial start-up. The selection of sites which meets the criteria for conducting a trial is critical to the success of a CT and a well-designed feasibility questionnaire which addresses multiple criteria such as qualification, relevant experience, patient recruitment rate, infrastructure and site accreditation, etc., makes a lot of difference to this process.

Building up a robust web-based feasibility system, coupled with a comprehensive investigator database along with incorporating a detailed feasibility questionnaire covering all trial aspects, with fields for uploading site documents wherever appropriate for review and an integrated algorithm with automated site risk scoring tool to allow the rating of sites providing real-time feasibility data, can prove extremely beneficial. Thus, successful feasibility studies can be conducted by leveraging technology, complemented by a team with strong clinical expertise.

Clinical trial records maintenance

In order to comply with regulatory requirements, pharma companies involved in CTs have to maintain and store certain documents, images, and contents related to the CT for a duration specified by the country specific regulations. This information is maintained in the eTMF and archived at the end of the study.

Processing of CTRs (scanning, indexing, compilations, reconciliation, review, and maintenance) has always been a daunting task for any sponsor in order to achieve appropriate

quality standards for complying with any audit/inspection and for regulatory submissions. Outsourcing different studies to different vendors, also many a times leads to the use of different CT systems of the service providers. The study team needs to spend time on completing the training on different systems in order to gain access and to finally use them effectively. The possibility of errors and noncompliance remains high until the study team becomes proficient in the use of these systems. Flow of records/data through different CT systems creates barriers to the ease of end-to-end data visibility and also creates nuances in analyzing the missing gaps in trial records. Developing a comprehensive CT management system integrated with an organized eTMF can be an effective solution to manage CTRs and have a complete visibility of available trial records for periodic review and to be prepared for any audit or inspection.

CONCLUSION

Identifying the opportunities for leveraging technology and automations in a CT process and choosing the best technology options along with the most appropriate services/technology partner to streamline these processes can facilitate faster turnaround times for getting drug to the market ensuring high quality data, complemented by cost efficiencies.

Acknowledgments

The author would like to thank and express deep gratitude to Dr. Nimita Limaye, VP, Risk-Based Monitoring, CDM, Medical Writing and Clinical Service, TCS, for her review and insight on this white paper.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Rozwell C. Case Study: Boosting the Predictability of Clinical Trial Performance. Gartner G00147214; 27 March 2007. Available from <https://www.gartner.com/doc/502840/case-study-boosting-predictability-clinical>. [Last cited on 2015 Apr 12].
2. Amalia R, Balbinot A, Bhagianadh D, Bontempo C, Jesús D, Dallari GS. Putting Contract Research Organizations on the

3. Radar: An Exploratory Study on Outsourcing of Clinical Trials by Pharmaceutical Companies to Contract Research Organizations in Non-traditional Trial Regions. SOMO Centre for Research on Multinational Corporations; February 2011. Available from: http://www.somo.nl/publications-en/Publication_3615. [Last cited on 2015 Apr 12].
4. Clinical Research. A Legacy of Innovation, a Future of Transformed Medicine. Washington: Association of Clinical Research Organizations; 2014. Available from: <http://www.acrohealth.org/wp-content/uploads/2014/10/acro-white-paper-tah10.pdf>. [Last cited on 2015 Apr 12].
5. Stanton D. Quintiles Talks R&D Spend and Outsourcing Trend in Second Public Offering. Outsourcing pharma.com; 10 March, 2014. Available from: <http://www.outsourcing-pharma.com/Clinical-Development/Quintiles-talks-R-D-spend-and-outsourcing-trend-in-Second-Public-Offering>. [Last cited on 2015 Apr 12].
6. Worldwide Mobile Phone Users: H1 2014 Forecast and Comparative Estimates. eMarketer; 16 January, 2014. Available from: <http://www.emarketer.com/Article/Smartphone-Users-Worldwide-Will-Total-175-Billion-2014/1010536>. [Last cited on 2015 Apr 12].
7. FDA Guidance for Food and Drug Administration Staff on Mobile Medical Applications. U.S. Department of Health and Human Services Food and Drug Administration; 9 February, 2015. Available from: <http://www.fda.gov/downloads/MedicalDevices/.../UCM263366.pdf>. [Last cited on 2015 Apr 12].
8. Lamberti MJ, Stergiopoulos S, Naik P, Getz KA. Industry Usage of Social and Digital Media Communities in Clinical Research. A Tufts Center for the Study of Drug Development White Paper. Boston: Tufts University; 2014.
9. FDA Draft Guidance for Industry on Internet/Social Media Platforms with Character Space Limitations-presenting Risk and Benefit Information for Prescription Drugs and Medical Devices. U.S. Department of Health and Human Services Food and Drug Administration; June, 2014. Available from: <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm401087.pdf>. [Last cited on 2015 Apr 12].
10. FDA Draft Guidance for Industry on Internet/Social Media Platforms: Correcting Independent Third-party Misinformation about Prescription Drugs and Medical Devices. U.S. Department of Health and Human Services Food and Drug Administration; June, 2014. Available from: <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm401079.pdf>. [Last cited on 2015 Apr 12].
11. Al-Ubaydli M. How Social Networks Enable Patients to be More Involved in their Healthcare. The Guardian; 17 April, 2012. Available from: <http://www.theguardian.com/healthcare-network/2012/apr/17/patients-social-networks-new-technologies>. [Last cited on 2015 Apr 12].
12. Uehling MS, Hines C. Ahead in the Cloud – A New Home for Clinical Trial Data. Pharmaceutical-technology.com; 31 January, 2012. Available from: <http://www.pharmaceutical-technology.com/features/featureahead-in-the-cloud-a-new-home-for-clinical-trial-data/>. [Last cited on 2015 Apr 12].
13. Mitchel JT, Markowitz JM, Yin H, Gittleman D, Cho T, Kim YJ, et al. Lessons learned from a direct data entry phase 2 clinical trial under a US investigational new drug application. Drug Inf J 2012;46:464-71
14. FDA. Guidance for Industry on Electronic Source Data in Clinical Investigations. U.S. Department of Health and Human Services Food and Drug Administration; September, 2013. Available from: <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm328691.pdf>. [Last cited on 2015 Apr 12].