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Best practices sharing: Setting up a professional clinical research unit in India

Abstract

The Drug Controller General of India has recently come up with very stringent laws to tighten the regulatory framework around clinical trials. One-way of improving the credibility of India and its researchers in the eyes of the regulators, sponsors and the general public is through professional site management team or setting up clinical research unit (CRU). The CRU acts as a bridge between the sponsor and the investigator. The CRU model has been better explained with the help of a good example of a clinical research institute. Since, a successful clinical trial needs high quality data, timeliness and clear communication between all parties, a professional CRU with a team of dedicated and trained professionals and infrastructure with written procedures and policies may be a solution to the pain and agony of poor site performance and investigator insufficiency and pressure.

Key words: Clinical research unit, clinical trial, investigator

BACKGROUND

For the past few years, India, as an emerging economy has been looked upon as a major center for clinical research because of its diverse patient pool, qualified investigators and clinical research professionals to conduct clinical trials. Further, our nation's clinical health research needs good quality, authentic and relevant research in the varied aspect of public health to progress.[1] An analysis carried out some years back reports unsatisfactory distribution of research topics and the quality of research reports and necessitates health policy to address these continuing deficits in public health research in order to reduce the very large disease burden in India.[2] However, attention needs to be paid to ensure that stringent quality checks are built in and that investigators conduct research in an impeccable manner.[3] Owing to some incidents in the past, the credibility of clinical trial industry in India is under question.[4] The result of this present situation is that the Drug Controller General of India has recently come up with very stringent laws to tighten the regulatory framework around clinical trials. In spite of enormous potential as a clinical research hub in India, the above scenarios are a warning sign. The data obtained from US trial registry shows that of the total global percentage of trial sites, the number of clinical trial sites in India has drastically decreased by approximately 50% (1.9-1.0%) in the last 2 years [Figure 1].

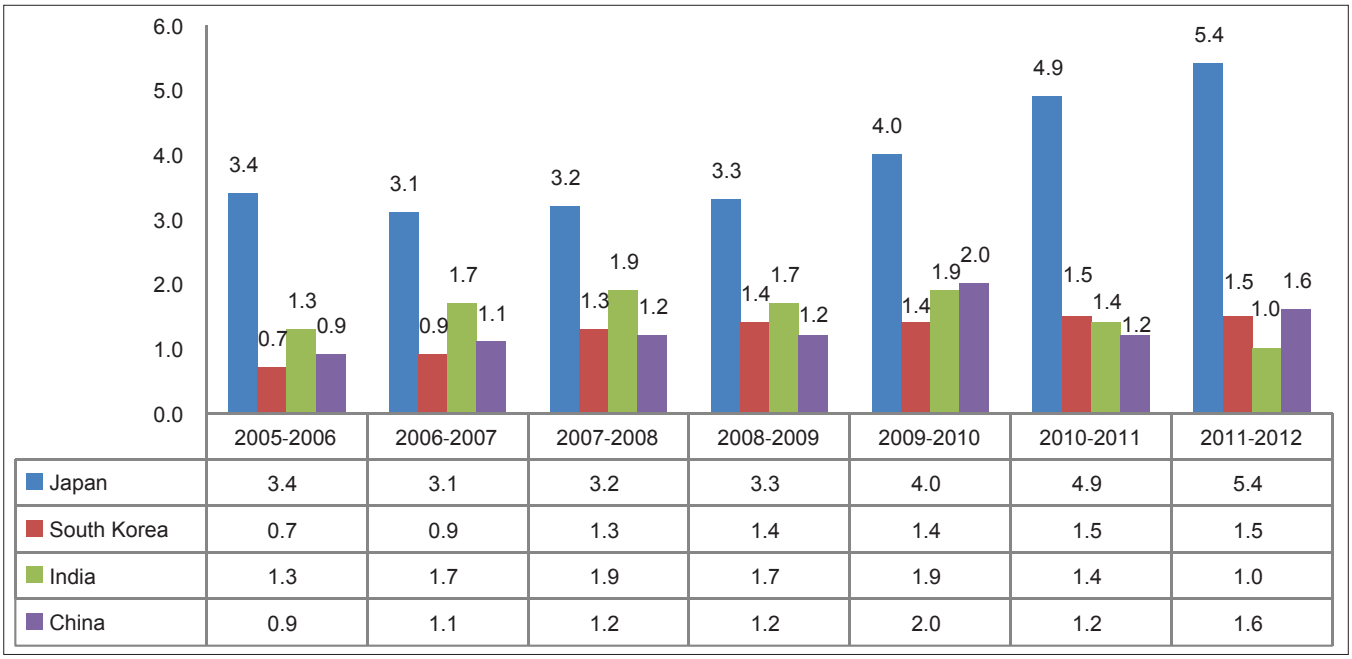
Access this article online

Quick Response Code:

Website: www.picronline.org

DOI: 10.4103/2229-3485.124570

This state may be overcome by a professional site management team, which acts as a bridge between the sponsor and the investigator. It is difficult for an individual investigator to manage clinical trials as medical practitioners in India do not have enough time to focus on research. Secondly, being good in clinical practice may not warrant that one is good in research practices. And lastly, clinical research encompasses enormous documentation, logistics and administrative skills and involves a large amount of non-medical tasks.



	2005-2006	2006-2007	2007-2008	2008-2009	2009-2010	2010-2011	2011-2012
Japan	3.4	3.1	3.2	3.3	4.0	4.9	5.4
South Korea	0.7	0.9	1.3	1.4	1.4	1.5	1.5
India	1.3	1.7	1.9	1.7	1.9	1.4	1.0
China	0.9	1.1	1.2	1.2	2.0	1.2	1.6

Figure 1: Percentage of clinical trial sites as per US trial registry

Investigators mostly dislike or are inadequate to perform all of these tasks independently. A number of factors contribute to the success of a clinical trial, including organization, communication, use of technology and support for patient recruitment. According to a 2005 Thompson Center Watch survey[5] of 612 investigative sites in the US, the most important factors responsible for study delays were categorized as contract and budget negotiation and approval (52%), patient recruitment (45%), protocol amendment and refinement (37%), Institutional Review Board (IRB) review and approval (35%) and informed consent form review and approval (28%).

Effective organization and communication are needed to develop and maintain a positive relationship among the sponsor, site and trial subjects. Such a relationship typically results in a higher level of satisfaction on the part of investigators and study participants. Moreover, sponsors increasingly expect use of electronic data capture programs, which can decrease the amount of time required to clean study databases as it allows certain tasks to be performed remotely and permits timelier data checks. Lastly, an organization can suggest effective ideas to aid in subject recruitment and provide support for implementation.

A SHIFT TO EXPLORING THE NEED FOR A CLINICAL RESEARCH UNIT MODEL

To establish a world class investigator site, the CRU needs to be a separate business unit with good governance. This implicates dedicated and accountable senior management supervision. The other essentials include careful and meticulous selection of investigators who have the required patient pool and have a research oriented mind set. Both investigators and the CRU management must be co-operative to the work flows, regulatory guidelines as well as written standard operating policies towards better execution of clinical research related procedures. The model CRU should be comprised of a panel of experienced investigators, dedicated and trained staff, drug and archival storage, quality assurance (QA) management, Institutional Ethics Committee (IEC)/IRB, information technology infrastructure and most importantly hospital access.

THE RIGHT PRESCRIPTION

An ideal CRU may be beneficial to all the parties involved. The investigator can concentrate on his core competence, i.e., handling and care of the research subjects and leave the administrative tasks and logistics to the CRU. This in turn is far more satisfactory to the investigators as they can benefit from the quality data produced in a faster manner. The research participants or the patients get focused and constant medical supervision and care through clinical trial, which in normal circumstances may not be available to them. The institution/hospital gets national and international recognition, as well as its patients are offered various/newer treatment options. The sponsor is benefitted because the CRU ensures better communication channels and that quality data is delivered within the prescribed timelines.

One of the major advantages of CRU structure is an improvement in research credibility, which can be achieved by protecting human research subjects through accreditation programs. The unique point of CRU model is the integrative nature of the system wherein, the trial sponsors, the investigators, IRB members, clinical trial participants and the institution work towards the protection of the research participants. It is well said that research organizations, IRBs and IECs can benefit by accreditation in bringing its procedures and policies in line with international standards. Involvement in accreditation is a world-wide accepted essential aspect in internal activities pertaining to quality improvement, which brings credibility to the research activities.

CRU organization usually works under the umbrella of IRBs/IECs, which can directly govern ethical conduct of the research studies. An internal independent QA team evaluates and continually improves the integrity of clinical research activities, promotes compliance to regulations and Organizational policies and procedures by conducting regular internal audits and inspections, identifies areas for improvement and develops strategies to enhance efficiencies. As a result, root cause analysis of deviations is performed in real time much before the sponsor monitoring visits. Thus, involvement of an internal QA team ensures delivery of quality data right from the beginning of the trial.

Although the principal investigator (PI) has the ultimate responsibility for the entire study, the CRU helps in sharing the burden of the responsibilities. Essential responsibilities still remain with the PI, i.e., patient recruitment, informed consent administration, patient care and medical management including adverse events/serious adverse events and overall management of protocol adherence. The CRU assists the PI in informed consent process and its documentation, case report form (CRF) completion, coordination with PI, patient and sponsor, logistics such as courier, sample management, infrastructure upkeep (calibration etc.), drug accountability and investigational product management, protocol adherence, compliance with timelines, archival management and financial tracking.

THE JOURNEY OF A MODEL CRU

The CRU model can be better explained with the help of a good example of a clinical research center formed with the ultimate aim of improving health-care research. A CRU is faced with initial challenges such as convincing the hospital for a dedicated space for operations. It is also necessary to persuade the investigators regarding the importance and value addition of the CRU. Finally, the sponsors need to understand and accept the legalities and benefits of the model.

This center has bagged a couple of accreditations including the ISO 9001:2008 certification and the prestigious Association for Accreditation of Human Research Protection Program accreditation. One of the studies conducted at this center has also been audited by US Food and Drug Administration with no findings.

PRACTICES

In this framework, three constructs are considered absolutely essential for the successful execution of research into practice: Continuous evaluation, reporting and training. Continuous evaluation includes management review meetings to assess site performance. The CRU management reviews patient recruitment rates; customer and patient satisfaction indices based on collected feedbacks; protocol and standard operating procedure (SOP) deviations along with the root cause analysis; set timelines for study initiation from qualification visit and CRF completion and query resolution. A useful tool for managing operations is the use of cloud based clinical trial management system for the real time reporting and recording of study activities and events. The third practice, which helped maintain the quality standard is continuous trainings and best practice sharing.

KEY TO SUCCESS

The most important factor for achieving the targets is to involve and work with the right people. The second factor is to define all the detailed processes in place as SOPs. Allocation of specific roles and responsibilities to the study team increases work efficiency. Periodic trainings and knowledge sharing helps to constantly remind the study team regarding the regulatory guidelines and also keeps the staff abreast of new developments. Apart from these factors, there is a constant effort to imbibe a culture of quality and discipline in the research team. As a case study, it is interesting to note that post the setting up of this dedicated CRU, the average number of study initiations at the center has doubled.

CONCLUSION

To conclude, a successful clinical trial needs high quality data, timeliness and clear communication between all parties. Hence, a professional CRU with a team of dedicated and trained professionals and infrastructure with

written procedures and policies may be a solution to the pain and agony of poor site performance and investigator insufficiency and pressure.

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How to cite this article: Divate U, Das S, Bhosale N, Divate P. Best practices sharing: Setting up a professional clinical research unit in India. Perspect Clin Res 2014;5:37-40.

Source of Support: Nil. **Conflict of Interest:** None declared.