Investigator Council presents: Insights

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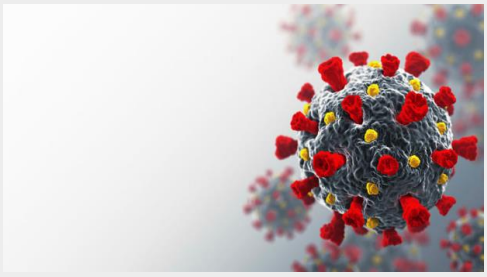
TRIAL MANAGEMENT IN THE TIME OF COVID-19

ISCR is continually focused on sharing relevant communications to help ensure everyone's health and wellbeing, and in keeping sites updated on recent guidance and practices in the conduct of clinical trials around the COVID-19 pandemic.

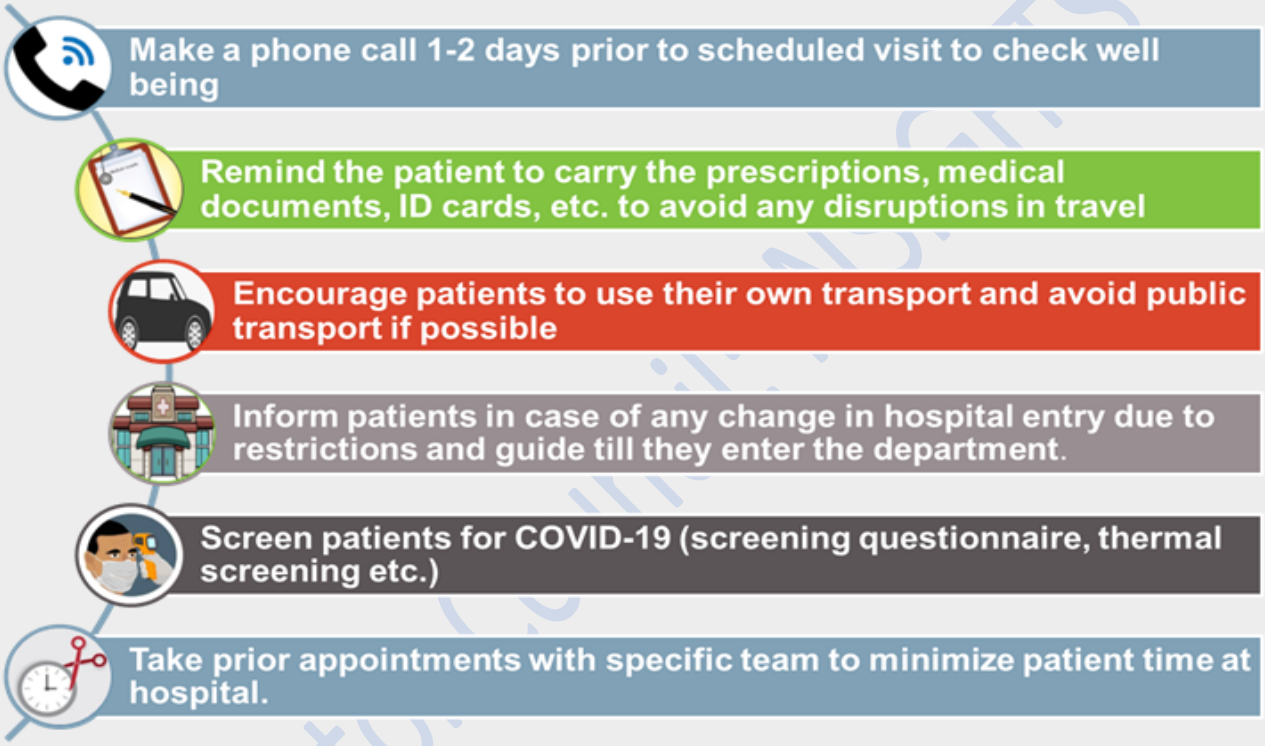
The situation around COVID-19 continues to evolve along with the approaches to effectively address the rapidly changing environment. We would like to share current developments and processes that are being implemented to address key challenges, in the efforts to minimize the impact of pandemic on various clinical trial programs that are being conducted across the country. Few approaches being adopted are as below:



- Implementation of telemedicine practices and remote capture of patent data (e.g. Patient Reported Outcomes (ePRO), patient apps, Home Health Care including home nurses).
- Adopting a risk-based monitoring approach including digital monitoring technologies as in person activities are restricted.
- Additional Trial Documentation considerations during the COVID-19 Pandemic (e.g. COVID-19 risk assessment forms).
- Adapting trial execution to evolving local EC & Regulatory guidance (IP Distribution, protocol deviation management).
- Vendor engagement to include COVID-19 challenges and mitigation strategies (e.g Direct to Patient IP supply (DTP).
- Informed Consent Adaptions to the COVID-19 pandemic as per local regulations.
- Additional criteria for patient recruitment during the COVID-19 pandemic e.g. including SARS-CO-2 test as selection criteria to avoid enrolment of infected subjects in the study.
- Recommendation to the patients to keep hygiene measures recommended by WHO, social distancing and use of personal protection equipment (masks and gloves), also monitoring closely signs and symptoms (Temperature, O2 saturation etc.) depending on the stage of the pandemic.
- Implementing eConsenting which is a system that allows for the electronic consenting and signature from the subject.
- Clinician Outcomes Assessments (eCOA) Assessments done on mobile devices, COA can be administered and captured by a third party (e.g.-rater for scales assessments, patients for daily activities).

These efforts are to mitigate risks and to minimize patient and site burden while maximizing commitment to research during these unprecedented times.

RECOMMENDED BEST PRACTICES WHILE RESUMING PATIENT AND TRIAL MANAGEMENT



INVESTIGATOR SITE SOP TEMPLATES

Purpose of this Initiative:

- Investigators and Clinical Research Sites are pivotal to "Clinical Trial" conduct to bring innovative drugs to market. As we move towards an era of highly controlled Clinical Trial management, standardized methodology of conducting trials at Investigator sites is a key expectation from Indian Regulators and Indian Regulations. We at ISCR would like to support them by providing templates for preparation of Standard Operating Procedures which can be adapted as per site's need.

- This is particularly essential and helpful when we want new clinical sites to be developed as well as when some of the well-established ones want to keep themselves updated with some of the best practices used across the industry.

- The current available templates have been carefully drafted and reviewed by wide range of Industry Experts including investigators and auditors to ascertain most acceptable practices and needs and to align with most recent regulations governing clinical research in India.
    - Preparation, maintenance and review of SOPs.
    - Audio Visual recording of Informed Consent.
    - Informed Consent Process.
    - Source Documentation at site.
    - Safety reporting & management by site.
    - Site Communications (EC, Sponsor & Regulatory).
    - Training of Clinical Study Staff.
    - Archival of completed studies.
    - SOP on subject compensation.

**Please contact us at info@iscr.org for more information or to request for these SOP templates and to provide feedback on the templates.

INVESTIGATOR'S COLUMN

Patient Participation in Clinical Research and Trials

Clinical Trials are important to evaluate the efficacy and safety of new therapies and can provide the opportunity to receive new and effective medicines. Conducting a meaningful Clinical Trial requires cooperation among different stakeholders, which includes, Sponsors (e.g. pharmaceutical industry), Clinical Investigators, Patients, Physicians, and Regulators. Study participants are the critical stakeholders for any Clinical Trial. Without their proper participation even the best of the best designed studies fail to answer the research question. Patient participation in Clinical Trials is one of the important challenges faced by investigators. The Statistical power of the study depends on the adequate number of participants enrolment. The inability to recruit an adequate number of participants reduces the statistical power of the study and often leads to inconclusive results. Attitude of the public towards participation in Clinical Trials has been studied since many years. Results of such studies are not encouraging. A survey in Germany showed that only 25% of the surveyed population were willing to participate in a clinical research. A cancer center survey conducted in The United States showed that only 35% of Americans were ready to participate in a Clinical Trial.

There are published systemic reviews to understand the barriers for participation in Clinical Research. One such study identified the following as the important barriers.

(1) Additional demands of a study, including procedures, appointments, travel problems, and cost;
(2) Preferences of patients regarding a particular treatment or no treatment;
(3) Worry caused by uncertainty of treatments or trials; and
(4) Concerns of patients about information and consent.

An Indian study revealed, complexity of study protocol along with lack of awareness about study among participants and sociocultural issues of subjects related to clinical trial participation are the main barriers for participating in Clinical Trials. Participants also reported that patient's fear of side effects, negative publicity by media, and large geographical distance with the study site were the factors that influenced recruitment at sites.

On the other hand, patients also face many challenges to get enrolled in Clinical Research. Often patients and treating doctors are ready for participation but are unaware of the opportunity to enroll. The doctor–patient relationship has been the cornerstone of medical care, especially in Indian scenario. Switching from their regular doctor to a new one because of participation in a CTs might cause patients to face difficulties in accepting an unfamiliar doctor and a new environment. Only few hospitals in the world qualify for even very large CTs. So, number of hospitals conducting CTs are very less. Being conducted in very few centers poses challenges of non-accessibility for many patients in remote places. Apart from identifying the clinical research sites, the need for frequent visits, cumbersome repeat of similar investigational procedures, often invasive procedures like blood withdrawals, pose challenge for patients. Many a times patients are discontinued from study by giving a reason which may not be convincing from the patients' point of view. Informed Consent process is a vital stage of any biomedical research. But extensive paperwork and multiple signatures by participants related to informed consent process that too

under audio-visual recording creates an uneasy environment to the patients. And because of previous alleged incidents of malpractice, there is a mistrust of drug trials among the public. This mistrust can influence the decision about whether to join a trial or not.

Traditionally Clinical Trials are researcher centric and the patients come into picture only during recruitment phase of the study. So conventionally, the research is done on patients, not with patients. To overcome this fact and make patients participate equally during whole process of research, the guidelines have been formulated by international agencies for patient and public involvement (PPI) to improve the clinical research quality. PPI is defined as a research being carried out 'with' or 'by' patients and members of the public rather than 'to', 'about' or 'for' them.

Presently there are several ways the patients can contribute to the process of drug development at different levels. There are many initiatives to engage patients during the development of Clinical Trials. The Patient-Centered Outcomes Research Institute in the United States and the James Lind Alliance in the United Kingdom have come up with an initiative where patients participate in identifying priorities in the area of research. Similarly, patients associations like "PatientsLikeMe" (www.patientslikeme.com) have been involved during the process of study designs. This can help the participating patients to clearly understand the risk and benefits of enrolment. Also, through this, patient can suggest amendments in the protocol which may address their concerns. Flexible and convenient patients' visits can be one of such examples. Involvement of patients in preparation of ICF (Informed consent Form) clears many questions and doubts among the patients regarding the protocol. Getting advice from the patients during the process of ICF development helps in preparation of more acceptable and patient friendly consent forms. The patients feel more comfortable to participate in a Clinical Trial if they meet and listen to an actual patient who was once enrolled and has completed a study. Oxford University's Healthtalkonline (http://healthtalkonline.org/), initiative include videos of clinical trial experiences of actual patients. Organizations like NIH (National institute of Health, United States) and www.clinicaltrialsregister.eu, European Union are helping to enhance knowledge of patients about Clinical Trials and also help them to locate specific Clinical Trials for the patients.8

Researcher and patient partnership is vital for successfully carrying out any clinical research. International authorities encourage involving patients at various steps of preparation and implementation of the study protocol. Participation of the actual patients in the process of development of protocol makes the study more acceptable and patient friendly, in turn helping better recruitment and retention of participants in the study.

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