الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Management

of Clinical Trials during the COVID-19 (Coronavirus) pandemic

Table of Content

Introduction 2

Clinical Trials 3

I. Initiating new trials 3

II. Ongoing Trials 3

A. Policy and Procedures 3

B. Subject safety 4

C. Communication with authorities 5

D. Changes in the distribution of the investigational medicinal product (IMP) 6

E. Changes to monitoring 7

F. Changes to auditing 7

G. Protocol deviations 8

H. Test for COVID-19 8

References 9

INTRODUCTION

This guidance issued for parties involved in conducting clinical trials in Saudi Arabia (e.g. sponsors, Contract Research Organization (CROs), Investigator sites and Investigators) to assure the safety and well-being of trial participants, to support the continuity of clinical trials, and to maintain compliance with Good Clinical Practice (GCP) during the coronavirus disease 2019 (COVID-19) outbreak.

All the parties working in conducting clinical trials in Saudi Arabia should take into considerations that there might be other national regulations from Ministry of Health (MoH), Ministry of Interior, The National Committee of Bioethics (NCBE), Saudi Health Council and other relevant authorities, which can be used to complement this guidance in respect to particular matters that may take priority over these recommendations.

Clinical Trials

I. Initiating new trials

Applicants planning to submit new clinical trials should include additional or alternative considerations in the study protocol to cover the pandemic COVID- 19 challenges. The Saudi Food and Drug Authority (SFDA) will accept the electronic submission via the clinical trials department email (ct.drug@sfda.gov.sa), with the priority review process for COVID-19 clinical trials.

II. Ongoing Trials

A. Policy and Procedures

The sponsor should prepare and implement policy and procedures, or update the current policy and procedures, to add additional or alternative measurement to protect trial participants and manage study conduct during the COVID-19 outbreak. The new challenges raised by COVID-19 outbreak should be addressed in the policy and procedures, but not be limited to, impact on the informed consent process, study visits and procedures, data collection, study monitoring, adverse event reporting, and changes in investigator(s), site staff, and/or monitor(s) secondary to travel restrictions, quarantine measures, or COVID-19 illness itself. Policy and procedures should be compliant with applicable with the national policy and regulations for the management and control of COVID-19.

B. Subject safety

The participant's safety and well-being in clinical trials is the priority for the SFDA in all circumstances.

The applicant should consider the current circumstances, and modify the study protocol and procedure to ensure the safety of the participants in the trials in all trial aspect such as the participation of the patient or continue to participate and visit (remote or on-site), hold or maintain the Investigational Medicinal Product (IMP), safety reports according to the current situation and in collaboration with investigators and Institutional Review Boards (IRBs)/Independent Ethics Committees (IECs). The participants should be updated about the study changes that could affect them.

Since trial participants may not be able to come to the investigational site for protocol-specified visits, sponsors should evaluate whether alternative methods for the safety assessments (e.g., phone calls, virtual visit, alternative location for assessment, including local labs or imaging centres) could be implemented when necessary and feasible, and would be sufficient to assure the safety of trial participants. Sponsors should determine if in-person visits are necessary to fully assure the safety of trial participants (for example to carry out procedures necessary to assess safety or the safe use of the IMP appropriately); in making the decision to continue use or administration of the IMP, the sponsor should consider whether the safety of trial participants can be assured with the implementation of the altered monitoring approach. The sponsor, CROs, investigators should consider Saudi Arabia's local regulations or guidelines for in-person visits such as The Saudi Arabia Cancer Institute (SANCI) guideline: "Saudi National Cancer Institute COVID- 19 Caregiver and Facility Clinical Practice Guidelines".

The SFDA recommends implementing the modified study protocol after IRB approval and notification, but due to the current circumstances, the sponsor, CROs, investigators should document the proof of contacting the IRB (e.g., email) and send the IRB response afterward. In case the changes in the protocol based on eliminating immediate hazards the sponsor or investigator should initiate them prior written IRB/IEC approval/favourable opinion according to the GCP guidelines.

Saudi Arabia's national and local restriction for COVID-19 may affect the ongoing clinical trials in many ways that led to implement alternative considerations and process accordingly the sponsor, CROs, and the investigators should document and explain the impact of restrictions on conducting the clinical trial. The alternative considerations and process should be in line with the study protocol as possible.

The Sponsor, CRO, and the investigator should document and explain in the case report form any changes in study visit schedules, missed visits, or patient discontinuations whether related to COVID-19 or not based on the site source data.

C. Communication with authorities

When a new event is likely to have a serious effect on the benefit-risk balance of the trial, it is possible that immediate actions are required by the sponsor and investigator to protect the subjects against immediate hazard. These, urgent safety measures may be taken without prior notification, but the information needs to be provided to the SFDA as soon as possible. In this communication, the sponsor is expected to provide adequate information on the cause, the measures taken and the plan for further actions;

If changes are likely to affect the safety or well-being of the participants and/or the scientific value of the trial, but do not require immediate action from sponsor or investigator, it should be possible to submit them as substantial amendment applications. Sponsors are encouraged to take into account the limited capacity of assessors, and submit only high quality, complete applications containing only the necessary changes. Over-reporting should be avoided

SFDA encourages sponsors and investigators to work with NCBE and local IRB prospectively define procedures to prioritize reporting of deviations that may affect the safety of trial participants.

D. Changes in the distribution of the investigational medicinal product (IMP)

The Sponsor, CRO, and the investigator should prepare and implement plans with the investigator sites to assure the IMP continuity for the trial participants with respect to national or local restrictions and alternative measures (e.g., Hospitals who work under the MoH deliveries medications to patient's home).

Additional alternative measures could be used:

- Provide the participants with extra IMP, to avoid non-critical visits to the site.
- Secure delivery methods for self-administration IMP to the participants.
- Home nursing or alternative sites by trained but non-study personnel recommended for IMP administered at the investigational site.

The alternative measures should be managed according to the IMP characteristic, storage condition, trial participant's health status, and safety.

The IMP accountability should be maintained according to the GCP regulations and should be addressed and documented.

E. Changes to monitoring

When the monitoring visits are no longer possible for sponsor, CRO, and investigator due to national or local restriction, they should optimize temporary alternative measures could include:

- Cancelling or postponing of on-site monitoring visits and extending of the period between monitoring visit;
- Implementing phone and video visits (according to the investigator site capability and taking into account trial participant integrity and privacy);
- Remote site selection visits and investigator training for trials.

The Sponsor, CRO, and the investigator should take into account the site staff and facilities for the alternative measures.

The remote source data verification, such as sharing copies of participant's medical records with the sponsor and CRO would breach the participant's confidentiality and should be avoided.

Results of adjusted monitoring/review measures should be reported to the sponsor in monitoring reports and in the clinical study report.

F. Changes to auditing

According to Saudi Arabia's national regulations from the MoH and the Ministry of Interior for social distancing restrictions, the audits should be postponed unless the restrictions were removed or suspended. For on-site visits and remote audits can be considered, after agreement with the investigator and if the audits are assessed as essential.

G. Protocol deviations

The sponsor, CRO, and the Investigator who are conducting clinical trials in Saudi Arabia should manage, document, and minimize the protocol deviations that occurred due to COVID-19 according to standard procedures, GCP and/or national regulation to guarantee the participants safety and study data integrity.

H. Test for COVID-19

According to the nature of SARS-CoV-2 that consider as one of the highly contagious viruses, regular screening for COVID-19 may be required based on national regulations. In case the test was performed on the participants, the test should not be reported as an amendment to the protocol even if done during clinical study visits unless the sponsor is incorporating the data collected as part of a new research objective or according to other national regulations.

References

1- European Medicines Agency (EMA). 2020. Version 2, Guidance on the Management of Clinical Trials during the COVID-19 (Coronavirus) pandemic. [Online]. Netherlands: European Medicines Agency (EMA), [Accessed 28 Mar. 2020]. Available from: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/guidanceclinicaltrials_covid19_en.pdf

2- Food and Drug Administration. 2020. FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic. [Online]. United States: Food and Drug Administration, [Accessed 3 Apr. 2020]. Available from: https://www.fda.gov/media/136238/download

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