CEIC Information about Clinical Trials or Intervention Studies with MD face to Covid19 current conjecture

The pandemic situation by the new coronavirus (SARS-CoV-2) may have an impact on the conduction of clinical trials and other clinical studies with regards to participants visits to trial sites, supply of the investigational medicinal product and monitoring activities, among other aspects.

During this period, participants may be advised by health authorities to not go to hospital establishments or can be under other movements restrictions (self-isolation, for example).

The Protocol should remain as the guideline document for all specific activities for each study, and, face to these constraints, measures should be made more flexible to allow minimize major deviations to it (distance consultations, sending instead of presential availability of the investigational medicinal product, remote monitoring, for example). Monitoring the safety of the participants already included and their access to investigational medicinal product should have priority on the recruitment of new participants.

It is therefore important to stablish some rules and procedures with regards to the notification or submission to CEIC, taking into account the various recommendations available in this matter and the several questions raised by the applicants.

Despite future recommendations, which can be harmonized by the European Commission, CEIC informs:

1. About participants visits to trial sites

i. As an alternative to face-to-face visits of the patients, it is possible to make telephone visits or through video call.

ii. For the start-up visits of the study, the appropriateness and opportunity of them and/or their realization by non-face-to-face, because of the current conjecture.

- Adoption of non-face-to-face patient visits should be reported to CEIC, as a non-substantial amendment (NSA).

2. About monitoring activities (quality)

i. These activities may be carried out by alternative and proportional mechanisms, remotely and/or centralized, such as telephone connections, video calls, etc., in order to ensure the continued safety and well-being of the participants;

ii. It must be always evaluated, by the Sponsor, the risk of the impact on monitoring deviations, considering the prioritization of critical activities, such as adverse reactions, safety reports, among others;

iii. Monitoring alternative routes and times shall be duly documented;

iv. For CRAs monitoring visits, monitors can be able to access remotely, as they often do, taking care of the audit trail and the confidentiality data of the participants.

- Monitoring is restricted to coded data that the participant has already consented to share out of the site.
- Remote monitoring does not include remote access to health records of the participants (unless the participant's privacy is taken care properly) or sending the source documents by fax (for remote review).

3. About Supply of investigational medicinal product (IMP)

It may be acceptable to send investigational medicinal product to patients through sites, in compliance with Good Clinical Practice and other applicable legislation and verifying the following:

i. Supply of the IMP to the participant, through sites, if they cannot go to Hospital (trial site), and when clinically appropriate/ necessary;

ii. It can be considered temporary and/or permanent discontinuation, if clinically appropriate/necessary;

iii. The direct supply to the patient, from the site trial, because it constitutes a change in the IMP circuit, in addition to being duly recorded in the documentation of the study, should be notified to the CEIC as NSA;

iv. The transport services of the IMP shall comply with good distribution practices issued by Infarmed, I.P., now applicable to the context of investigational medicinal product;

v. Always where the study medication, provided at home, requires administration by a nurse or other qualified person, these one must be included as a member of the study team.

- Always where the protocol already provides home nursing services, they may be extended to the provision and/or administration of the IMP, once the safety of the intervention is taken into account, simply notifying to CEIC as an NSA.
- Always where is not foreseen in the Protocol, or has not yet been approved by CEIC, this possibility should be submitted to the CEIC as PSA, notwithstanding the possibility of direct implementation, and further notification, provided that duly justified by the Principal Investigator (PI) and it must be ensure the security and the confidentiality of the participants.

4. About materials for participants and/or patients

i. The provision of explanatory leaflet(s) to the patient for the administration of medication, should be notified to the CEIC (NSA):

ii. Explanatory leaflets or other information dissemination materials for participants related with infection by the new coronavirus, should be given, preferably to the patient, by the investigator doctor, and notified to CEIC as NSA.

5. About protocol deviations

i. In order to allow an appropriate and expedite assessment (if applicable) each sponsor should ensure that deviations to the protocol are adequately documented, since it is expected an increase in these deviations;

ii. Deviations to the protocol, justified by Covid19, do not constitute, at the outset, a serious violation, unless the participants have been put at risk;

iii. Deviations to the protocol, for example in relation to the eligibility of participants for studies, justified by difficulties in the evaluation of subjects and in performing tests, are not acceptable;

iv. The Sponsor shall classify deviations to the protocol, and in this context, notify to CEIC, depending on the impact on the safety and well-being of the participants.

6. About recruitment of new participants and/or continuation on the study

i. No participant may be included in a study if it is not possible to verify the necessary procedures for the full compliance of the inclusion and exclusion criteria provided in the Protocol;

ii. New participants should also not be included if there is no guarantee that there are conditions to comply with the study protocol;

iii. Always where the safety of a participant is at risk, because he/she cannot conclude the main assessments or follow the critical mitigation steps, it should be discussed the possibility of discontinuing it from the study;

iv. Urgent safety measures shall remain available to any investigator and/or sponsor for mitigating the risk of participants, as well as the tools for temporary interruption of study and/or recruitment;

v. It shall be equated/weighted the suspension of the activation of trial sites for new approved studies, as well as the temporary suspension of recruitment;

vi. If it is necessary to transfer a patient from one trial site to another, it should be notified to CEIC as NSA;

- Any temporary interruption of the study, including for logistical reasons, such as the unavailability of the study team, should be considered as urgent safety measure, and then notified to CEIC (NSA).
- The waiver of compliance with the protocol remains unacceptable.
- Major changes to the protocol with an impact on the safety and well-being of participants should be submitted as PSA, which will be evaluated in an expeditious manner.

7. On the risk/benefit of conducting certain clinical trials

Clinical trials that may have an additional risk of infection without possible benefit for the participant, should be carefully re-evaluated on their initiation and/or maintenance, such as clinical trials with

medicinal products that act as a immunosuppressants in healthy volunteers, where there is no therapeutic benefit for the Volunteer.

- CEIC should be notified (NSA) of these decisions.

8. About validity and signature of CEIC documents

It may be not possible for CEIC to sign the approval documents in an expeditious and timely manner, as well issue documents on letterhead. Thus:

i. The Sponsors/Applicants shall consider as valid the alternative methods of communication, such as a confirmation by email and/or information/communication through RNEC, of CEIC's deliberations.

ii. All documentation (letters requesting additional information and/or approval, or others), once signed, it will then be sent, by the means of usual.

9. About contingency plans from Sponsors

The contingency plans developed by the sponsors should be notified to CEIC (NSA), respecting the applicable general guidelines, as well as the specific procedures requested by CEIC and/or Infarmed in this context.

10. About participants in CT infected with the new coronavirus

i. The infection of participants in clinical trials by the new coronavirus should be considered as an adverse effect and reported to CEIC (NSA);

ii. It should be followed the guidelines from the health authorities with regards to the infection by the new coronavirus;

iii. In case the patient maintains, as far as possible, the compliance with the procedures of the study, all records should be kept, and the risk-benefit assessment of the patient should remain as a priority.

- CEIC should be notified (NSA) of the decision to keep the patient in the study.

11. About the evaluation of Clinical Trials with new medications for the disease Covid19

CEIC will give priority to the evaluation of new clinical trials aimed to treat or prevent the disease by the new coronavirus (SARS-CoV-2).

- Applicants should submit the study through RNEC, clearly identifying in the subject the scope of Covid19 disease, and send an email to CEIC (ceic@ceic.pt) in order to expedite the process with a view to expeditious approval.

All requests for **substantial amendment**, as a result of a change in procedures in relation to Covid19, **will be evaluated expeditiously by CEIC**, and it is necessary for this, at the time of submission by the usual routes, **communication via e-mail to ceic@ceic.pt.**

All the amendments to the procedures of previously approved clinical studies, in **which do not require submission to CEIC as PSA**, according with this information, **should be** duly documented, and **notified to CEIC**, for monitoring of the clinical trial by this Commission.

The adoption of these procedures of direct implementation; that is, without prior approval by CEIC shall respect their proportionality and serve the best interests of the participants (patients or not) from clinical trials.

Where deemed appropriate, CEIC will continue to request amendment and/or suspension of procedures, of adaptation to the Covid19 context, adopted by the sponsors and/or applicants.

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