EMERGENCY MEASURES RELATED TO CLINICAL TRIALS IN BUILDING 'A', DEPARTMENT OF INTERNAL MEDICINE, UNIVERSITY OF DEBRECEN

I. History

Dr. Miklós Kásler, Minister of Human Capacities commanded the implementation of the following measures forthwith on 14th March 2020.

'All non-emergency or non-urgent interventions in accordance with Point i. of Section 3 of Act CLIV of 1997 on Health must be postponed from the 16th March 2020 to the end of emergency. '

(Medical emergency: a sudden change in health which, in the absence of urgent medical care, would endanger the patient's life, or result in a severe or permanent health impairment. Public Health Law)

II. General Principles of the Regulation

Regulations for emergency related to clinical trials must be created observing the guidance of the authority in power (OGYÉI).

Decisions must be made per trial according to the substantial risk assessment of the Sponsor/CRO and the PI. The PI is not allowed to diminish the conditions with regard to the Sponsor's decision but may make stricter decisions keeping patients' safety by considering the given situation. After having informed patients, their decisions - considering the above - must be accepted.

III. Concrete Measures of the Regulation

Thanks to the fact that our study team is committed to prevent the spread of COVID'19, the team intends to conduct visits by phone for as long as possible instead of visits in person.

If a patient participates in a study but does not take the investigational medical product anymore, we will apply visits by phone in all cases instead of visits in person.

III.A. Mandatory In-person Site Visits

If the PI in conjunction with the Sponsor decides that an in-person site visit in a trial is necessary (medical emergency), in-person site visits may be conducted. Participants' risk of COVID'19 must be assessed by phone before in-person visits in all cases, patients' may be asked to come for an on-site visit in case of low risk for infection, otherwise they must remain in compulsory or voluntary home quarantine. Patients must avoid public transport during their travel to the site. Duration of site visits and number of contacts must be minimized. Hygiene regulations for general medical attendance must be applied in these cases as well. Particular questions must be asked, and answers must be acquired before on-site visits preferably by phone. If a patient is at high risk for COVID'19 infection, the Sponsor must be informed, and it is necessary to take the case into reconsideration. It is the PI's responsibility to make the decision and take special measures after reconsideration.

III.B. Non-mandatory In-person Site Visits

If in-person site visits are not mandatory or the patient is not able to come to the site personally, the PI and the Sponsor must consider if additional tests (laboratory, imaging, ECG) planned for on-site visits are necessary or may be postponed. It is necessary to consider patient safety when making decision about treatment continuation. If these tests are indispensable, treatment can only be continued considering test results. If critical tests are impossible to do, the patient must stop using the investigational product, and the Sponsor/CRO must be informed forthwith.

Simpler diagnostic tests (e.g. blood test) may be performed at the patient's home after agreement and having the Sponsor's permission. If the Sponsor grants permission, tests may be performed at another supplier's laboratory (e.g. local laboratory).

If the actual visit does not include additional tests mentioned above or the Sponsor grants permission to postpone them, it is advisable to deliver the investigational product from the site to the patient's home under controlled circumstances in the interest of continuing the trial.

The concrete process must first be agreed upon with the Sponsor of the given trial and documented in detail later on.

In case of the Sponsor's permission our study team prefers delivery by the team members. As long as the present members should not be able to perform the delivery, we are planning to expand the group. Additional members educated by the PI are going to be registered for the delivery process on the Delegation Log. We intend to have the patients receive the investigational products at his/her home personally.

In case of the Sponsor's request patients may receive the investigational product at the entrance of the site or receive it at their home by a licensed courier, but we will allow these methods only in exceptional cases after careful consideration and if the Sponsor requires it.

Prof. Dénes Páll MD
Department of Internal Medicine, University of Debrecen
Head of the Department of Clinical Pharmacology

22 March 2020, Debrecen

REGULATION OF THE DELIVERY OF INVESTIGATIONAL PRODUCTS CONCERNING CLINICAL TRIALS IN BUILDING 'A', DEPARTMENT OF INTERNAL MEDICINE, UNIVERSITY OF DEBRECEN

I. Preliminary Telephone Conversation with the Patient

1. Contact the patient by phone.
2. Inquiry about the way he/she feels considering SAE, AE.
3. Inquiry about the medicine he/she is taking, incidental alteration.
4. Inquiry about the patient's risk for COVID'19 infection, if he/she is in compulsory or voluntary home quarantine. Investigational medical product may only be delivered if the patient's risk for COVID'19 is low. Risk assessment of COVID'19 is carried out under separate questionnaire.
5. In case of high or extremely high risk for COVID'19 infection reconsideration and repeated agreement with the Sponsor are needed. The PI is responsible for the final decision.
6. Informing the patient about the opportunity of IMP delivery to his/her home.
7. In case of patient's request for home delivery place (exact address), time of delivery and deliverer's identity need to be discussed.
8. The patient is asked to pack the IMP he/she has in his/her home, because the team member is going to bring it back at the time of delivery of the new IMP.
9. Answering the patient's further questions.
10. Recording the telephone conversation in writing.

II. Preparation of the Investigational Medical Product

1. Calling IWRS, asking for IMP.
2. Choosing the IMP that is going to be delivered, checking markings on it again.

III. Investigational Medical Product Delivery

1. Preparation of the box suitable for delivery, bag, cooler box (cooler block), placing it onto the vehicle paying maximal attention to the protocol and the Trial Material Manual.
2. The member of the study team delivers and hands the IMP over the patient in his/her home choosing the shortest and fastest route. In this case acceptance in writing is not necessary.
3. A person named by the patient in advance may take the IMP over only in exceptional cases. In this case the name, personal data of the person must be recorded, and his/her signature is necessary. Another location that differs from the patient's permanent or temporary address may be accepted only in exceptional cases. These cases must be recorded.
4. Delivery between the site and the patient's home is done in accordance with the temperature requirements defined in the protocol and the Trial Material Manual. We do

not feel temperature monitoring necessary, as the IMP is distributed at the site. IMP delivery to the patient's home is done by the patient's request as it formerly was.

If the Sponsor insists on temperature monitoring, we will measure the temperature by min-max. thermometer.

5. It is documented when the IMP left the site, who delivered, what type of instrument was used, the time when the patient received it. If someone else who was named by the patient received the IMP, the register of acceptance needs to be archived.

6. At the time of delivery of the new IMP the team member brings the IMP given previously and transports it to the site.

7. If the delivery of the IMP is not possible (the patient or his/her representative is not available despite the previous arrangement), the IMP must be transferred to the site at the earliest possible time. The failure of delivery and the time of return must both be recorded.

8. If the patient is available later, redelivery will be attempted.

9. In case of missed redelivery detailed documentation is needed and the Sponsor/CRO must be informed.

10. Detailed documentation is of great importance considering the fact that the patient agreed upon and requested home delivery.

IV. Post-arrangement with the Patient by Phone

1. Inquiry about the patient's experiences up to the present and keeping to the therapy.
2. Inquiry again about AE, SAE.
3. Relevant patient duties must be explained and confirmed considering the medication.
4. Informing the patient about the therapy, and the medication method.
5. Answering the patient's relevant questions.
6. Recording the above in the source document.

Regulation above is to be applied in a clinical trial if and only if the sponsor has approved it. The regulation shall be repealed if the authority (OGYÉI) reveals a recent recommendation that contains conflicting information.

Prof. Dénes Páll MD
Department of Internal Medicine, University of Debrecen
Head of the Department of Clinical Pharmacology

22 March 2020, Debrecen