Communication

Management of clinical studies in Italy during an emergency COVID-19 (coronavirus disease 19)

In light of the numerous requests received from the various parties involved in the Clinical Trials Office / Pre-Authorization Area and the GCP Inspections Office, the Italian Medicines Agency provides indications regarding the management of clinical studies and substantial amendments in Italy during the period emergency COVID-19 (coronavirus disease 19), valid until further notice.

Procedures for submitting clinical trials and substantial amendments

Considering the recent precautionary measures adopted by the Council of Ministers and the Ministry of Health and acknowledging that, as a consequence of the aforementioned precautionary provisions, many pharmaceutical companies, non-profit Sponsors and CRO have consequently applied or extended the smart-working mode in order to not to interrupt the activities related to clinical trials and at the same time to guarantee the maximum possible protection of the personnel involved, the following is communicated.

For applications for authorization of clinical trials and substantial amendments submitted through OsSC, the sending of the paper documentation and the CD referred to in the AIFA press release of 01.08.2019 is allowed (https://www.aifa.gov.it/- / updating-letters-for-the-authorization-of-clinical-trials-and-related-substantial-amendments).

We recommend, however, where possible, the payment of stamp duty on the transmission letter in virtual mode (excluding cases of exemption from said tax pursuant to art. 17 of Legislative Decree 460/1997 and art. 82, paragraph 5, of Legislative Decree 117/2017) and the affixing of the digital signature to the same uploaded in OsSC.

The paper documentation and the CD must be sent to the Clinical Trial Office as soon as possible.

In cases where submission via OsSC is precluded and it is therefore necessary to resort to the paper transmission method according to the provisions of the AIFA press release of 02.10.2018 (https://www.aifa.gov.it/-/attivazione-nuova-piatplatta -ossc-update-02-10-2018-), the transmission by e-mail cannot be accepted.

By express derogation from the above, it is permitted, for the sole submission of clinical trials concerning the treatment in general of COVID-19 (coronavirus disease 19), that the submission of authorization requests takes place through the apa @ pec mailbox. aifa.gov.it, and that the documentation supporting the aforementioned requests is sent via Eudralink or similar methods within the same e-mail.

Please note that, in this case, the entire authorization process of the aforementioned authorization requests will be continued by e-mail and the Applicant will proceed to return to OsSC as soon as possible, as foreseen for the paper transitory management (AIFA press release dated 06.08.2018: https://www.aifa.gov.it/documents/20142/871583/comunicazione_OsSC_06.08.18.pdf/20bdd0c0 -d754-817c-93ac-ca7b0476f1e5).

Expression of the opinions of the ethics committees on clinical trials / substantial amendments

Without prejudice to the current legislation and internal procedures of the individual ethics committees, the sessions of the same may also be held in web-conference mode or through other telematic types, with the frequency appropriate to manage the emergencies of the current emergency.

Possibility of managing clinical trial activities outside the experimental center

In the event that, to limit the risk of contagion from coronavirus, in the face of difficulties in moving patients to the experimental centers, or suspension of outpatient activities by some clinical centers, it is necessary - where feasible - to make the drug available to patients without them having to go to the hospital (thus ensuring therapeutic continuity), or carry out other activities related to clinical trials at the patient's home or facility other than the experimental clinical center (for example, visits and tests, reaction management adverse), a substantial amendment for immediate implementation must be sent for notification only to the Ethics Committees of reference, indicating the urgency related to the emergency in question.
In this regard, the Sponsors / CRO, taking into account the indications relating to the urgent measures regarding the containment and management of the epidemiological emergency from COVID-19 and the specific Ordinances of the different Regions, are invited to draw up a risk assessment plan and to implement an action plan in the pre-eminent protection of the subjects under experimentation and in view of the urgent need to minimize the contacts between patients and experimental staff in order not to overload the healthcare facilities.

In particular, the following exemptions are provided limited to the coronavirus emergency period:

1. Experimental drug management (IMP)

Where possible, if the patient comes to visit the experimental center, it may be useful to provide a quantity of drug that covers a longer period of time than that normally estimated.

Please note that, in accordance with current legislation (article 7 of the Ministerial Decree of 21 December 2007), the medicines needed for the trial must be sent by the Sponsor to the pharmacy of the health facility where the trial is held, which will provide for their registration, appropriate storage and delivery to the experimenter. Therefore, given the serious emergency COVID-19, even if the priority route remains the delivery to the hospital pharmacy which then proceeds to the subsequent delivery to the experimental center, on the indication of the director of the hospital pharmacy and the principal investigator (PI) direct deliveries can be agreed Hospital pharmacy to subjects also through dedicated couriers, without prejudice to the supervision of the process by the hospital pharmacy and the constant information of the same Pharmacy and the IP of the delivery in the manner imposed for the correct conduct of the experimentation and the aforementioned risk plan which must take into account the type of IMP, the methods of administration, storage and transport. Suitable remote communication mechanisms with interested parties must be guaranteed in order to replace information that will no longer be provided in person. Depending on the case, the telephone and / or video call can be used where deemed necessary to inform the patient. Adequate tracking of what is being implemented in this emergency situation is recommended. The conditions set out in FAQ 10 of the EMA document "Q&A: Good clinical practice (GCP)" - GCP Matters (https://www.ema.europa.eu/en/human-regulatory/ research-development / compliance / good-clinical-practice / qa-good-clinical-practice-gcp).

If the CRA of the study cannot proceed to carry out the control of the final accounting of the drug for the purposes of reconciliation, it is believed that this operation, if indifferent, can be carried out by a pharmacist of the hospital Pharmacy or by the appropriately trained study coordinator / data manager. The IMP can be returned to the Sponsor directly from the hospital pharmacy.

2. Clinical tests

With regard to carrying out hematological tests, in the awareness of the need to be able to have the tests performed in laboratories near the patient's home, these tests must be performed in public facilities. The use of private facilities not in possession of the recognition of suitability pursuant to Ministerial Decree of 19 March 1998, must be carefully evaluated and traveled only if it represents the only possibility to protect patient safety, the use of such data for regulatory purposes will have to be discussed when submitting data.

3. Closure of the centers

If a center is "closed" to the public for COVID-19 containment measures, it should be carefully assessed whether the experimental staff is able to guarantee the continuity of the experiment. If the center is unable to follow the patients in the trial, the study should be temporarily suspended or, if possible, patients transferred to the nearest experimental center among the active ones. Of course, the exchange of information between the PIs and the transmission of clinical documentation and other material (e.g. IMP) of the experimentation between one center and another must be guaranteed. The contracts between the Sponsor and the healthcare structures involved must be updated in accordance with the new agreements.

It is not considered practicable to use as a back-up an unauthorized center to conduct the specific clinical study, as the center is not active, does not know about the trial and could not ensure a correct therapeutic continuation for the patient.

4. Monitoring of clinical trials

In analogy with what expressed in the previous paragraph, the Sponsors are invited to draw up a risk assessment plan and to implement an action plan that takes into account the need to reduce unnecessary contacts in this period of epidemiological emergency from COVID-19. First it should be assessed whether the monitoring visits in situ can be replaced by a strengthening of centralized monitoring or if such local visits can be deferred.

Exceptional methods such as telephone contacts or, better, video conferences with the staff of the experimental site for the purpose of source data verification can be implemented. These methods must be described in the appropriate POS of the Sponsor / CRO and must be assessed and approved by the Personal Data Protection Officer of the experimental center.

Other unusual monitoring methodologies that involve more risky methods of accessing sensitive data, such as through video recording of source documents or making available for monitors the original documents in shared electronic areas, must always be agreed with the Head of Protection of the hospital structure data, but it is considered appropriate that a specific opinion of the Privacy Authority be obtained.

5. Possibility for the Sponsor to enter into direct contracts with agencies / specialized service companies (eg home nursing services) to conduct activities related to the clinical management of patients who fall under the responsibility of the principal investigator (PI)

In reiterating that these measures must be understood as extraordinary and limited to the strict coronavirus emergency period, in derogation from FAQ 11 of the EMA document "Q&A: Good clinical practice (GCP)" - GCP Matters (https: //www.ema.europa. eu / en / human-regulatory / research-development / compliance / good-clinical-practice / qa-good-clinical-practice-gcp) the Sponsor is allowed to

directly enter into contracts with these specialized agencies / companies. All other indications of the aforementioned FAQ remain applicable, such as:

 the need for supervision to be maintained by the PI

 efficient communication lines are established between the staff in charge and the PI

 that the staff in charge is properly trained and the related duties and responsibilities are indicated in the contract and / or delegation log

 that the protection of data confidentiality is guaranteed.

6. Possibility of reimbursement of exceptional expenses

Taking into account the exceptional nature of the contingency, if in order to implement urgent measures for the protection of the subjects participating in a clinical study, expenses are expected to be borne by such subjects, similarly to what is already allowed in extraordinary cases (for example studies on rare diseases), the Sponsor is allowed to reimburse these expenses directly to the subjects, keeping appropriate supporting documentation.