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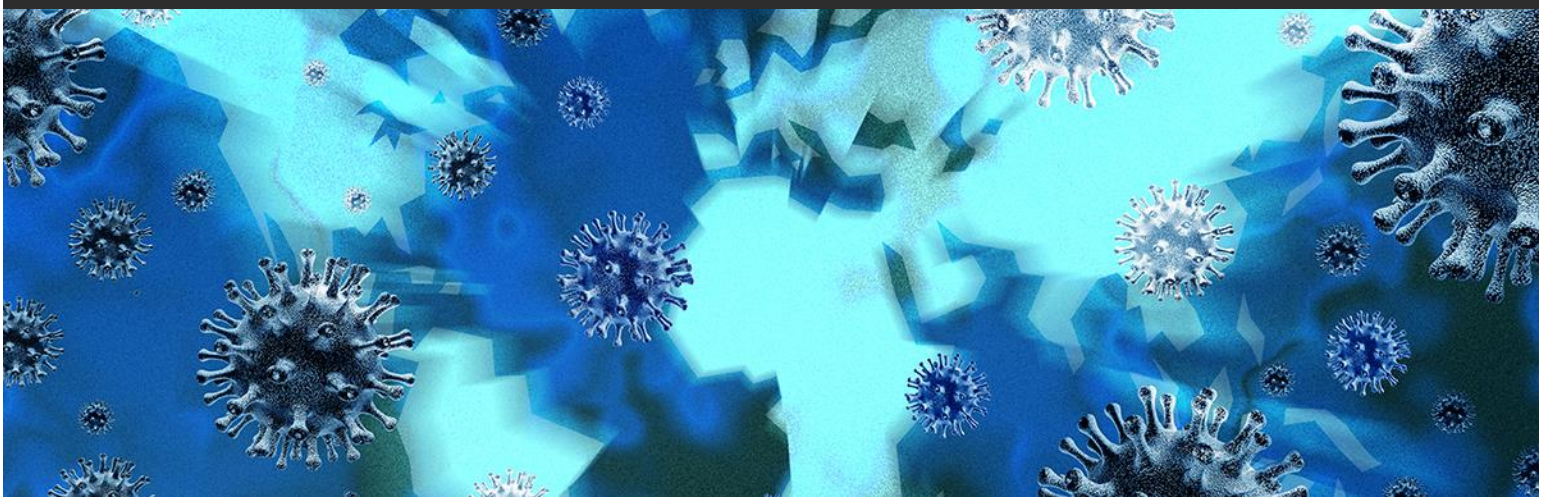
Alert | Health Emergency Preparedness Task Force: Coronavirus Disease 2019 — Focus on Italy



May 2020

The Management of Clinical Trials in Italy During the COVID-19 Emergency

Amid the Coronavirus Disease 2019 (COVID-19) pandemic, EU Member States are adopting extraordinary measures to address the challenges that the virus poses to the administration of clinical trials. Indeed, limited access to public places (including hospitals), restrictions on visits to health care facilities, self-isolation and/or quarantine of trial participants, as well as increased demands on the health service are affecting **ongoing trials**, impacting the completion of trial assessments and trial visits, and sometimes preventing the launch of new investigational initiatives.

On April 28, 2020, the EU Commission, the European Medicines Agency (EMA), and the Heads of Medicines Agency (HMA) published new guidelines on the management of clinical trials during the COVID-19 pandemic; the guidelines serve as a set of recommendations, harmonized across the EU, concerning the temporary changes and deviations from protocol that should be applied in conducting clinical trials during the pandemic. Indeed, the guidance provides Member States with flexibility and procedural simplifications which should be used during this global public health crisis for the safety of trial participants across the European Union, while **preserving the quality of the data generated by the trials**.

Individual Member States are encouraged by the EU Commission to issue specific national legislation with a view toward implementing the EU recommendations, while also building on related guidance provided by national medical and regulatory authorities, which in Italy is the Italian Medicines Agency (AIFA).

Focusing on the Italian framework, by means of two communications issued March 12 and April 7, 2020, AIFA introduced an extraordinary regime addressing the criticalities raised in connection with the management of clinical trials due to the spread of COVID-19. The new regime, which is temporary and limited to the emergency, entitles sponsors and Contract Research Organizations (CROs) to implement measures diverging from ordinary procedures for the execution or management of clinical trials outside clinical trial sites, subject to prior notification to the ethics committees of the involved sites, which are required to accurately track all deviations. Simultaneously, with a view to **ensure the maximum protection of trial subjects**, investigators and sponsors must draw up a risk assessment plan and implement a risk-proportionate action plan related to the extraordinary measures adopted, taking into account the provisions set forth by the Italian government to address the epidemiological emergency.

Some of the significant departures from ordinary procedures authorized by AIFA include: the **direct delivery** of the investigational medicinal products (IMP) **from hospital pharmacies** or warehouses **to patients' home**, the sponsoring of **home health care activities** to be performed with the support of trained professionals and third-party providers, and the **direct involvement of sponsors** in the management of trials.

AIFA's framework for implementation of the extraordinary measures and procedures is described below.

Delivery of investigational medicinal product (IMP)

If the patient is authorized and able to visit the investigational site, IMP should be provided, if feasible, with a larger amount to cover a longer period of time, under the supervision of the investigator.

With respect to other cases, investigators may arrange **direct deliveries** of IMP through dedicated couriers:

- from the hospital pharmacy to trial participants, upon indication of both the hospital pharmacy Director and the Principal Investigator, or
- from the warehouse where the IMP is stored to the trial participants, under shipping conditions specifically agreed with the experimental sites.

With delivery of IMP, adequate remote communication mechanisms with interested parties should be guaranteed.

Sponsoring home health care activities and direct involvement of sponsors in the management of trials

To minimize physical contact between patients and investigational staff, and to avoid overloading health care facilities, AIFA recommends that investigators and sponsors limit visits to only those strictly necessary. AIFA further recommends that sponsors arrange with investigational sites alternative measures to manage the trials' subjects in these exigent circumstances.

Among such alternative measures, sponsors/CROs may also consider carrying out certain health care activities like non-self-administering therapies (e.g., infusions) and other clinical procedures such as documentation of adverse events or vital signs directly at the patient's home, with the support of experimental site staff or third-party providers.

Therefore, deviating from FAQ 11 of EMA's "*Q&A: Good clinical practice (GCP)*", sponsors are now permitted, under the principal investigator's supervision, to enter into service agreements with third-party providers for the performance of activities related to clinical management of patients.

Management of clinical trial activities outside investigational sites

In this regard, AIFA provides that:

- the clinical and/or medical tests essential for the participants' safety should be performed in public laboratories located near patients' home. In the absence of viable alternatives, sponsors may also take into consideration the use of private sites;
- if a site is "closed" to the public for COVID-19 containment measures, or trial staff is unable to support and supervise patients enrolled in the trial, the study should be temporarily halted or, where feasible, patients should be transferred to the closest active trial site;
- on-site monitoring visits may be postponed or replaced by the introduction of procedures of enhanced centralized monitoring. Source Data Verification may be conducted through alternative means such as telephone calls or video-calls with the trial site staff, while guaranteeing compliance with applicable personal data protection laws. The use of other remote monitoring methods is subject to agreement with all subjects involved (e.g., CRO) and the consent of the Data Protection Officer.

Submission of clinical trials and substantial amendments

Regarding management of administrative procedures, AIFA expressly allows sponsors to:

- postpone submission of paper documentation and the CD-ROM related to the authorization requests and substantial amendments submitted through AIFA's online system (National Monitoring Centre for Clinical Trials, "OsSC");
- submit authorization requests for clinical trials concerning the treatment of COVID-19 by email, if filing via OsSC is not possible.

In addition, AIFA ethics committees are permitted to hold their meetings for the evaluation of clinical trials and substantial amendments via videoconferences or other remote means.

In conclusion, the exceptional regime established by AIFA – that remains valid until further notice issued by AIFA – explores alternative trial initiatives by allowing the use of simpler procedures to maintain the integrity of the trials and to ensure the safety of trial participants and staff, but which could also represent, in the future, innovative solutions for the execution and management of clinical trials.

* *This GT Alert is limited to non-U.S. matters and law.*

For more information and updates on the developing COVID-19 situation, visit GT's Health Emergency Preparedness Task Force: Coronavirus Disease 2019.

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