COVID 19 - Ongoing clinical trials - FAQ

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The COVID-19 pandemic has an immediate impact on the conduct of clinical trials. The availability of research site staff in the context of overcrowding must be taken into account, as must national containment rules.

The relevance of initiating new trials must be weighed, and priority must be given to trials related to the management of patients infected with SARS-CoV-2.

For ongoing trials, the situation is unprecedented and should lead all stakeholders to put in place all the necessary measures to ensure the safety of patients participating in research. Adaptation of follow-up conditions could be considered but also appropriate measure to guarantee, if necessary, the continuation of treatment when the clinical situation justifies it.

The continuation of inclusions may accordingly be considered in situations of unmet medical need, provided potential risks associated with the risk of concomitant SARS-CoV-2 infection are taken into account. For patients already included in a clinical trial with active ongoing treatments, risk evaluation should consider the risk associated with interrupting treatment on one hand, and the risk associated with continuing treatment in an epidemic context, as well as the strain on research teams on the other hand. Priority must also be given to patients with progressive, life-threatening pathologies.

In such cases, the sponsor, in coordination with the investigators, should assess the risks of any changes considered in the trial with regard to the safety of subjects and the integrity of the trial data, with priority given to the safety of subjects. This assessment should be made available upon request to the authorities.

The ANSM, in coordination with the French Ministry of Health, proposes practical solutions for implementing the necessary adaptations for ongoing clinical trials in the current situation. Questions relating to the continuation or not of the trials are taken into account here, as well as possible modifications in the conduct of research to respond to the new constraints resulting from the pandemic.

Those questions are the result of a dialogue with the sponsors and research teams and may be implemented by other issues if necessary. The solutions proposed by the authorities have been established in order to respond in the best way to the exceptional health situation that we are experiencing. Our common goal is to reach optimal efficiency and simplicity without ever threatening the safety of research participants.

These adjustments are considered on an exceptional basis and all clinical trials will be returned to the previous follow-up conditions after the end of the health crisis. Any modification that the sponsor intends to establish as permanent will have to be submitted for authorisation to the authorities (ANSM and/or ethic committe).

In a context of exceptional measures, it remains essential to ensure that good practices are respected. The importance of optimal traceability of possible protocol deviations induced by the epidemic context and of the adaptations put in place should be particularly emphasized.

The national recommendations for France are in line with the European proposals established collectively and published by the European Commission

https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/guidanceclinicaltrials_covid19_en.pdf

1. **May a trial be suspended because of the pandemic?**
2. **May a patient change his trial site in order to unburden a center in tension or in order to limit his journeys?**
3. **Is it possible to open quickly new trial sites in order to unburden centers under stress or to limit journeys for patient on treatment?**
4. **May patient follow-up visits be adapted?**
5. **Is the delivery of investigational products for longer durations allowed?** (update : 04/08/20)
6. **Is the delivery of investigational products to the patient's home allowed?** (update : 04/08/20)
7. **Are monitoring visits to trial sites possible?**
8. **What should be done if a patient included in a trial and under treatment becomes infected with SARS-CoV-2? -** (updated: 03/23/20)
9. **Safety reporting** (updated 03/27/20)

SM-A: Substantial modification for authorisation (MSA modification substantielle pour autorisation)
SM-I: Substantial modification for information ie notification (MSI: modification substantielle pour information)
USM: Urgent Safety Measure
EC: Ethics Committee

1/ May a trial be suspended because of the pandemic?

Yes

A decision to suspend inclusions may be justified by the context of the study and/or the unavailability of teams (sponsor or investigators).

The continuation or not of ongoing treatments must be specified and justified. A decision to discontinue ongoing treatments must be evaluated according to the clinical context of each patient and associated risks.

- **In case of suspension of inclusions:** inform the EC and the ANSM (SM-I)
- **In case of discontinuation of experimental treatments:** inform the ANSM and the CPP with an USM followed in a second step by a SM-A

2/ May a patient change his trial site in order to unburden a center in tension or in order to limit his journeys?

Yes

- Get the agreement of the patient and the investigators at both trial sites.
- Transfer case report forms and all patient information.
- Supply the new trial site accordingly.

3/ Is it possible to open new trial sites quickly in order to unburden centers under stress or to limit journeys for patient on treatment?

Yes

- Derogation from sending a SM-A to the EC Information by a SM-I
- A contact with the DGOS is possible for information on the selected research sites: DGOS-PF4@sante.gouv.fr

4/ May patient follow-up visits be adapted?

Yes

The collection of information by teleconsultation is recommended on an exceptional basis, with a focus on safety data and primary objective endpoints.

Any data that cannot be assessed remotely will be noted as missing.

The failure to complete a protocol visit will not be considered as a reason for study discontinuation and, beyond the necessary documentation, will not be considered as a major deviation that must be notified to the ANSM according to GCP § 5.20.

Deviations shall nevertheless be reported and evaluated in the final study report (see ICH guideline E3).

- Document any protocol deviations for subsequent analyses.
- USM if modification of follow up procedures are needed, followed in a second step by an SM-A

5/ Is the delivery of investigational products for longer durations allowed?

Yes in compliance with safety instructions, patient information and traceability.

If visits during which the investigational medicinal products or devices should have been delivered to patients are skipped, arrangements must be made to assess the tolerability of the treatment and to adjust the treatment if necessary, for example by teleconsultation.

- Notification to ANSM (SM-I) including additional measures on follow-up.

Caution : narcotic products are excluded from this measure.

6/ Is the delivery of investigational products to the patient's home allowed?

Yes in compliance with all safety instructions, patient information, traceability and sponsor's instructions, established if necessary in conjunction with the manufacturer, in agreement with the research site.

➡ USM then SM-A specifying the conditions for delivery, monitoring and information of participants.

Te delivery to the patient of the products necessary for the research remains the responsibility of the investigator and, if available at the research site, of the site's pharmacy.
The sponsor provides the research site with logistical support for the transport to the patient of the products necessary for the research.
If requested by the research site/pharmacy, the sponsor provides packaging and labels. In all cases, the promoter finances the transport.

Industrial sponsors will simplify as much as possible their procedures for transporting the products needed for the research. The chosen solutions, including financial support, must limit as much as possible any additional workload for the research site and pharmacy, and must take into account the situation of each research site.
For more details on the requirements to be met and the possible circuits : see the complementary document drawn up by ANSM / DGS / CNRIPH / CNIL (in French)

https://www.ansm.sante.fr/Activites/Essais-cliniques/COVID-19-Essais-cliniques-en-cours/COVID-19-Essais-cliniques-en-cours-Quel-est-le-circuit-preconise-en-cas-de-delivrance-a-domicile

The current version of these recommendations does not apply to the implementation of home delivery of non-self-administered investigational drugs.
If such modalities should exceptionally be considered, a SM-A must be submitted to the ANSM to ensure that all safety conditions for parenteral administration in the patient's home are met .

7/ Are monitoring visits to trial sites possible?

Existing containment guidelines must be followed. Postponement of site visits should be considered according to national recommendations and local constraints.

The sponsor is encouraged to contact the investigators in order to adapt to the constraints of each trial site.

Centralised monitoring remains possible with sponsor/site contact subject to the availability of the research teams in tense situations. Sending copies of medical records, even pseudonymised, is not authorised.

- ➡ Compliance with national regulations
- ➡ Contact investigators to adapt the modalities according to the availability of the trial sites.

8/ What should be done if a patient included in a trial and under treatment becomes infected with SARS-CoV-2?

The continuation or suspension of investigational products should be evaluated by the investigator in liaison with the sponsor based on the clinical context.

Testing strategy for clinical trials patients have to be in line with national recommendations.

- Documentation on file
- Update on 23MAR20: COVID-19 :

Infection should not be declared as a new event except in the case of specific measures taken by the sponsor.

However, if this event corresponds to the definition of SUSAR, that is suspicion of an unexpected serious adverse effect, or of a serious adverse event that may be linked to the act of implementing the medical device, it should be declared to the ANSM according to the current requirements.

9/ Safety reporting

Should the investigator report serious adverse events to the sponsor?

Yes
The investigator must immediately report serious adverse events to the sponsor according to the current regulation except those mentioned in the protocol or in the brochure for the investigator as not requiring immediate notification.

If the sponsor is unable to assess the events declared, may he postpone his declaration to SUSARs?

No
The sponsor is requested to continue to declare the SUSARs as well as all the immediate vigilance notifications in accordance with the French regulation in force.

May confirmed cases of COVID 19 be considered "expected" if viral infections are described in the Reference Safety Information (RSI) of the investigational medicinal products?

No
The expected serious undesirable effects mentioned in the RSI should correspond to a specific preferential term (PT) of the MedDRA classification in force.

Is it possible to submit annual safety reports (ASR/DSUR) without a handwritten signature?

Yes

It is possible to send annual safety reports (also named DSUR for drugs) with a scanned signature or a simple mention in the email specifying the name of the person who validated the document.

May the deadline for submitting annual safety report (ASR) be extended?

Yes

A maximum period of 2 additional months may be granted after informing the ANSM by email on its usual mail boxes. Note that the sponsor already has 2 months to submit the report after the end of the period covered by the ASR .

May the meetings of the safety committees be postponed due to the lack of monitoring and / or the non-availability of members?

Yes

If it is impossible to set up the planned meetings of the safety committee, the sponsor may consider postponing after assessing the consequences for the safety of participants. As appropriate, the sponsor may also take measures, for example the suspension of inclusions pending the next meeting.

Documentation

- Postponement decision : communication to the members of the supervisory committee and to the investigators as well as to the ANSM and the CPP (substantial amendment for information)
- Other measures: documentation and transmission to the ANSM and the CPP according to their nature as previously detailed : i.e. substantial amendment for information in case of suspension of inclusions and substantial amendment for authorization if urgent safety measures are taken.

Submission to ANSM for adaptation in ongoing trials when related to COVID-19

National recommendation are available on ANSM website

Modifications put in place specifically for the pandemic period can be presented in an addendum and a modified version of the protocol is not required.

Substantial Modification and notification

- e-mail submission to : ams-essaiscliniques@ansm.sante.fr

Caution: it is **mandatory to name the e-mail** as follows :

- "**MSA-COVID-19** / Type d'essai / N° Phase d'essai / N° EudraCT / Domaine thérapeutique"
  or
- "**MSI-COVID-19** / Type d'essai / N° Phase d'essai / N° EudraCT / Domaine thérapeutique "

Urgent Safety Mesure

- e-mail submission to : vig-essaiscliniques@ansm.sante.fr

Caution: it is **mandatory to name the e-mail** as follows **: COVID-19_MUS** EudraCT_code substance

For Medical Device trials

- e-mail : EC.DM-COS@ansm.sante.fr

Modalities for the evaluation of clinical trials related to the management of the pandemic COVID-19

Accelerated procedures for the initial assessment of applications for authorisation have been put in place by ANSM, DGS and all ECs.
In order to ensure the proper follow-up of these dossiers, contact should be made in order to prioritize the clinical trial, guide the evaluation and determine whether additional information is needed.

Submission of an initial clinical trial application

➦ ANSM

- e-mail submission to : aec-essaiscliniques@ansm.sante.fr
  according to national recommendation

Caution : it is **mandatory to name the e-mail** as follows **: " AEC-COVID-19 /** Type d'essai **/** N° Phase d'essai **/** N° EudraCT **/** Domaine thérapeutique**"**

- For Medical Device trials: use the following email address : **EC.DM-COS@ansm.sante.fr**

➦ Simultaneous contact with ccs-pole-recherche@sante.gouv.fr to organize ethics committee's evaluation

As requested by the WHO, sponsor must ensure that the WHO official acronym for the coronavirus disease (COVID-19) is entered in the title field of the trial registration data set.

A contact with Ministery of Health (DGOS) is possible for information on the selected research sites: DGOS-PF4@sante.gouv.fr .

Similarly for the vigilance statements (individual cases, news events and annual safety report) relating to these tests, add at the beginning of the naming of the usual emails the mention "COVID-19".

It should be noted that the developers of medicines or vaccines are invited to contact EMA as soon as possible with information about their proposed development by emailing 2019-ncov@ema.europa.eu .
EMA provides a full fee waiver and a fast-track procedure for scientific advice.

https://www.ema.europa.eu/en/news/covid-19-developers-medicines-vaccines-benefit-free-scientific-advice

For any question related to clinical trials, you may contact :

ANSM submission: questions.clinicaltrials@ansm.sante.fr please mention "COVID-19" in the subject of your message

Ethics Committee submission: ccs-pole-recherche@sante.gouv.fr