**EMEA guidelines:**

Due to the urgency, the guidance was published without prior public consultation. The aim of the guidance is to serve as an EU-level harmonised set of recommendations. National legislation can be used to complement this guidance, but may take priority over these recommendations.

To summarize:

1. Initiating new trials: the feasibility of starting a new clinical trial or including new trial participants in an ongoing trial should be critically assessed by sponsors.
2. Ongoing trials: the sponsor should consider in a risk assessment which measures are appropriate:
   * Conversion of physical visits into phone or video visits, postponement or complete cancellation of visits to ensure that only strictly necessary visits are performed at sites;
   * A temporary halt of the trial at some or all trial sites;
   * Suspension or slowing down of recruitment of new trial participants;
   * Extension of the duration of the trial;
   * Postponement of trials or activation of sites that have not yet been initiated;
   * Closing of sites;
   * If unavoidable (it should be justified that this is a truly exceptional situation based on the personal risk-benefit ratio for the individual trial participant), transfer of participants to investigational sites away from risk zones, or closer to their home, to sites already participating in the trial, or new ones could occur;
   * Patient safety laboratory tests, imaging test or other diagnostic tests may be done in local labs. Local analysis can be used for safety decisions. If this is a trial endpoint and the samples cannot be shipped to the central lab, analysis should be performed locally and then explained, assessed and reported in the clinical study report following ICH E3.
3. Risk assessment: all decisions to adjust clinical trial conduct should be based on a risk assessment by the sponsor. This should be documented. In addition, the sponsor should reassess risks as the situation develops. The investigator should perform a risk assessment of each individual participant.
4. Communication with authorities: priority will be given to trial applications for the treatment or prevention of COVID-19. In ongoing trials, urgent safety matters may be taken without prior notification, but the information must still be communicated to the RA and EC after the fact.
5. Changes to ICF: sponsors should be mindful of the current pressure on the medical profession and should carefully assess the pertinence of adding new subjects in ongoing clinical trials. There may be a need to re-consent already included trial participants. However, avoid the need for trial participants to visit investigator sites for the sole purpose of obtaining re-consent. If re-consents are necessary for the implementation of new urgent changes in trial conduct (mainly expected for reasons related to COVID-19), alternative ways of obtaining such re-consents should be considered during the pandemic e.g. contacting the trial participants via phone or video-calls and obtaining oral consents supplemented with email confirmation.
6. Changes in the distribution of the IMP:
   * In case of urgent shortage of IMP at some sites or transfer of trial participants from one site to another clinical trial site, there might be a need to potentially re-distribute the IMP between sites in accordance with GMP annex 13 (section 47);
   * Delivery of IMP to the homes of participants is expected, this may be done from the site to the home of the participant (so not from the depot to the participant);
   * Direct from sponsor to trial participant IMP delivery is accepted in a few member states under this emergency situation.
7. Changes to monitoring: Certain sponsor oversight responsibilities, such as monitoring and quality assurance activities need to be reassessed and temporary, alternative proportionate mechanisms of oversight may be required. Possible temporary, alternative measures could include:
   * Cancelling of on-site monitoring visits and extending of the period between monitoring visit;
   * Implementing phone and video visits (without unnecessarily increased burden to the investigator site and taking into account trial participant integrity);
   * Adapting the on-site monitoring plan when it is impossible to follow, supplementing it with (additional/increased) centralised monitoring and central review of data if possible and meaningful.

It is essential that robust follow-up measures are planned and ready to be implemented when the situation is normalised. So-called remote source data verification (e.g. providing sponsor with copies of medical records or remote access to electronic medical records) is currently not allowed in most member states as it might infringe trial participants’ rights.

1. Protocol deviations: An increase in protocol deviations in relation to the COVID-19 situation will in itself not trigger the actions required by GCP § 5.20. They will however need to be assessed and reported in the clinical study report, following ICH E3.

The full text can be read here: <https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/guidanceclinicaltrials_covid19_en.pdf>.



**FDA guidelines:**



**Argentina:**

The government indicated that elderly people (60 years old and older) and with cardiovascular risk, need to be in quarantine at least until the end of the month, this means that CLEAR patient are included in that population.

**Belgium:**

* [COVID-19 impact on clinical trials, please find hereby communication from the agency (13 maart 2020)](http://link.bontrop.com/2ao)

**Brazil:**

No actions taken yet

**Colombia:**

On Wednesday (18 March 2020) and yesterday (19 March 2020) INVIMA performed a TC with Sponsor and sites and I would like to share you some topics discussed with them related to COVID-19:

- Sending of documents of sites is allowed to do electronically and the submissions to ECs can be sent by email and will be accepted.

- Sites and Sponsors/CROs should implement remote monitoring strategies (whether from home ) for very urgent matters or if they are low-risk studies, postpone visits.

- If the study hasn’t been approved by INVIMA and EC to take of samples at home, the sites can implement it without approval issued by EC and INVIMA. For studies of few patients, as in CLEAR, the site bacteriologists approved, trained and delegated should be who to take the samples.

- Shipment of medication to homes: INVIMA requests that the site document how it will be done during the contingency period. The vendor or Depot of Sponsor can do it, but it depends on each site which must guarantee that the patients receive the medication and the instruction related to management of study medication should do the pharmacist of each site according the local regulations. This strategy should be notified to ECs and INVIMA, no approval is needed to implement this strategy but if it should be notify before on 27Mar2020.

- Patients outside Bogotá: if it is an oral medication, IP could be sent and samples should be taken at home. If they are in another city, the same management should be done with IP.

- All actions done out of the stablished by protocol are considered as minor deviations when this does not involve or affect the safety of subjects.

- For Scheduled face-to-face visits with subjects:

* Implement Home medication, or organize with the sites a work plan so that according to visits patients the medication can be received by a family member with low risk (regarding COVID-19)
* Provision should be delivered for 1 month or by the time necessary.

-Each strategy and procedure should be documented by each site in a SOP , where sites describe all the actions implemented for the contingency. the deadline to submit the action plan to INVIMA in Friday 27Mar2020.

- Remote monitoring is allowed by INVIMA.

- Patient at home plan:  Remote FU would be done by telephone and the patients only should be treated at the sites if it is very necessary.

-Document signature: INVIMA receives a digital signature.

-Plans by site should be done by site.

In addition INVIMA issued a document related to this  and I send you the summary of the attachment of this email.

1. Subject presential visit already scheduled:

Sponsor/CRO with site should evaluate the possibility of implement telephone visits or extend window for those studies which do not need IP treatment at site. Should be guarantee that all critic visit are done. In case or rescheduling these deviations will not be major unless it could put in any risk to the subject.

For subjects who receive oral or subcutaneous medication, this medication should be delivered from site to subject´s home or the collect of the medication by a person authorized by the patient.

Every procedure decided should be document at the site and study.

1. Safety measures for subjects who visit sites:

For any other subject with who any of above measures can’t be implemented and the presential visit should be done, Sponsor/CRO should  supply subject with any necessary personal protection element to minimize any infection risk and guarantee transportation where subject has the minimum contact with other people.

Periodic monitoring should be done with sites, to evaluate which studies should be closed in case risks are more than benefits.

1. Recruitment

Colombia will continue with recruitment of new subjects taking into account above measures and taking into account any governmental measure specific for each city regarding assistance to health care institutions.

This measures will be only applicable for the period of contingency for COVID -19 in Colombia.

**Czech Republic:**





**Denmark:**

<https://laegemiddelstyrelsen.dk/da/nyheder/2020/ekstraordinaere-tiltag-i-kliniske-forsoeg-under-covid-19/~/media/6E5558FBC7574C50B5E79FFB1F0A37F7.ashx>

**France:**

<https://www.ansm.sante.fr/Activites/Essais-cliniques/Covid-19-Ongoing-clinical-trials/(offset)/1>

**Germany:**

No actions taken yet

**Hungary:**

* If Sponsor interrupts the study RA/EC should be notified about interruption and about new start.
* Minor Deviations, missed visits should not be reported for them (as usual).
* The Sponsor / CRO should ensure the continuity of the clinical trials, if possible, especially in indications where the regular treatment of the patients is crucial (i.e. oncology).
* If the trial site has to be moved to another facility/location due to the coronavirus situation, the Sponsor/CRO is not obliged to seek the authority's prior approval and the site can be moved upon written notification to the authority.
* If urgent safety measures are required to ensure the subjects' continuous study participation due to the virus outbreak, these measures may be implemented immediately upon written notice to the authority and the substantial amendment application may be submitted later on.
* Clinical monitors, auditors and sales reps are strongly recommended to postpone their site visits as much as possible until further notice.

**Ireland:**

<https://www.hpra.ie/homepage/medicines/regulatory-information/clinical-trials/covid-19-(coronavirus)-and-cts>

**Italy:**

<https://www.aifa.gov.it/web/guest/-/gestione-degli-studi-clinici-in-italia-in-corso-di-emergenza-covid-19-coronavirus-disease-19->



**Mexico:**

No information yet

**The Netherlands:**

<https://www.ccmo.nl/actueel/nieuws/2020/03/13/advies-voor-de-uitvoering-van-klinisch-onderzoek-ten-tijde-van-de-beperkende-maatregelen-door-het-coronavirus>

**Poland:**

No information yet

**Portugal:**

No information yet

**Romania:**

* To identify the potential impact of the general protection measures to the COVID-19 pandemic on the current activities conducted within each clinical study;
* To notify NAMMDR of the plan of specific measures that need to be taken; these can be considered urgent safety measures with immediate implementation, as the case may be.

**Russia:**

No actions taken yet

**Spain:**

<https://www.aemps.gob.es/informa/notasinformativas/medicamentosusohumano-3/2020-medicamentosusohumano-3/medidas-excepcionales-aplicables-a-los-ensayos-clinicos-para-gestionar-los-problemas-derivados-de-la-emergencia-por-covid-19/>

Translation (via Google translate):



The most important things:

* The patient visits can be postponed or changed for pone visits. In the case of rescheduling visits, these protocol deviations  will not be considered serious violations unless they affect patient safety.
* The Sponsor together with the investigator have to make a risk analysis and prioritize the activities that are critical and how they should be carried out.
* Within four months of the date on which the COVID-19 crisis is considered to have ended in Spain, the sponsor must communicate for each trial a report with the exceptional measures adopted, which will be sent to the Spanish Agency and the EC.
* Any exceptional measures adopted must be documented in the file.
* The sponsor, together with the investigator, based on a benefit/risk assessment that takes into account the characteristics of the trial and the circumstances of the participating sites, may interrupt the recruitment and even stop the treatment of the trial patients in order to avoid unnecessary risks and ensure the best for the patients´ health care.
* In the event of a trial interruption that leads to a halt of treatment in part of the patients, the sponsor would have to notify such measures as "urgent safety measures" explaining the steps taken to ensure alternative treatment of the patients by sending an Ad Hoc report to the AEMPS and to the Ethics Committee within 15 days of the interruption or termination.
* They recommend that the sponsor update the trial monitoring plans for the next four months by prioritising centralised monitoring and remote monitoring of participant sites that does not overburden site staff or review source data, and postpone source data verification as much as possible until medical records can be accessed in person. The Sponsor will agree with the participant sites and teams the conditions for these monitoring.

**UK:**

* NHS: [COVID-19: Guidance for sponsors, sites and researchers (v2.1 20 March 2020)](http://link.bontrop.com/2ap)
* MHRA: [Guidance on Coronavirus (20 maart 2020).](https://mhrainspectorate.blog.gov.uk/2020/03/20/mhra-guidance-on-coronavirus/)
* MHRA: [New arrangements for MHRA Good Practice (GxP) inspections due to coronavirus (COVID-19) (20 maart 2020).](https://www.gov.uk/government/news/new-arrangements-for-mhra-good-practice-gxp-inspections-due-to-coronavirus-covid-19--2)
* MHRA: [Guidance – Managing clinical trials during Coronavirus (COVID-19) (19 maart 2020)](https://www.gov.uk/guidance/managing-clinical-trials-during-coronavirus-covid-19)
* MHRA: [Guidance – Clinical trials applications for Coronavirus (COVID-19) (19 maart 2020)](https://www.gov.uk/guidance/clinical-trials-applications-for-coronavirus-covid-19)
* MHRA: [Collection – MHRA guidance on Coronavirus (COVID-19)](https://www.gov.uk/government/collections/mhra-guidance-on-coronavirus-covid-19)
* MHRA: (blogpost) [Advice for Management of Clinical trials in relation to Coronavirus (12 March 2020)](http://link.bontrop.com/2aq)
* Public Health England: [Guidance COVID-19: safe handling and processing for samples in laboratories.](https://www.gov.uk/government/publications/wuhan-novel-coronavirus-guidance-for-clinical-diagnostic-laboratories/wuhan-novel-coronavirus-handling-and-processing-of-laboratory-specimens)

**US:**

* CDC: [Information for Laboratories](https://www.cdc.gov/coronavirus/2019-ncov/lab/index.html)
* CDC: [Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with Coronavirus Disease 2019 (COVID-19)](https://www.cdc.gov/coronavirus/2019-nCoV/lab/lab-biosafety-guidelines.html)
* FDA: [FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic (Maart 2020).](https://www.fda.gov/media/136238/download)
* FDA: [Coronavirus Disease 2019 (COVID-19) Update: Foreign Inspections (10 maart 2020).](http://link.bontrop.com/2ai)
* FDA: [Coronavirus Disease 2019 (COVID-19)](https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/coronavirus-disease-2019-covid-19)