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COVID-19 Disruptions of International Clinical Trials: Comparing Guidances Issued by Key European National Regulatory Authorities, the Australian Department of Health, Brazil's ANVISA, Health Canada and Singapore's HSA

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The COVID-19 pandemic has had a major impact on the conduct of clinical trials worldwide. Recognizing this impact, national authorities have issued guidance for sponsors, investigators and institutional review boards (IRBs)/research ethics committees (RECs) regarding the conduct of clinical trials. Following up on an earlier alert that was released on April 2, 2020, available here summarizing guidance from FDA, EMA, MHRA and PMDA, the below chart summarizes guidance related to COVID-19 and clinical trials released by additional national regulatory authorities. The chart below summarizes guidance from the European Medicines Agency ("EMA"), the French National Agency for Medicines and Health Products Safety ("ANSM"), the German Federal Ministry of Health ("BfArM"), the Italian Medicines Agency ("AIFA"), the Spanish Agency for Medicines and Health Products ("AEMPS"), Switzerland's Swissmedic and swissethics, the Australian Department of Health, the Brazilian Health Regulatory Agency ("ANVISA"), Health Canada, and Singapore Health Sciences Authority ("HSA").

Clinical Trial Considerations	Europe (including the European Medicines Agency, France, Germany, Italy, Spain, and Switzerland)	Australia: Department of Health	Brazil: ANVISA	Canada: Health Canada	Singapore: HSA
Continuing and/or Initiating a Protocol	<u>European Medicines Agency (EMA):</u> Sponsors should assess the feasibility of starting new trials or enrolling new trial participants. The protocol should address additional risks and risk mitigation measures. Sponsors should consider a temporary halt of a trial at some or all sites, a suspension or slowing of recruitment, extension of trial duration, postponement of trials or site activations, and/or closing of sites. If there is an urgent need to open a new site, the opening of the new site may be implemented as an urgent safety measure first with a substantial amendment application submitted later. <u>France:</u> In the case of a trial suspension and/or discontinuation of experimental treatments, a sponsor should inform the Ethics Committee and the French National Agency for Medicines and Health Products Safety (ANSM). <u>Germany:</u> The German Federal Ministry of Health (BfArM) will prioritize projects relating to the diagnosis and/or therapy of COVID-19. <u>Italy:</u> Ethics Committee meetings may be held by web-conferences or other teleconference technology with appropriate frequency to manage urgencies due to the current emergency. If a site is closed for COVID-19 containment measures, sponsors should assess if the clinical trial staff can guarantee the continuity of the trial itself. Where the site is unable to follow trial	Institutions, principal investigators, and sponsors should establish contingency plans to address the impact of COVID-19 on clinical trials. Plans should include assessments of the risks associated with continuing trials as designed or with necessary modifications, assessments of the ability of participants to participate in trials and alternative models for participation, and assessments of the resources available for trial continuation. Recruitment of new participants should take into account the benefits and burdens on Australia's health system and should depend on individual trial factors. A decision to close a study where an investigational product or an unregistered device, diagnostic, or biological is being provided is a substantial amendment requiring Human Research Ethics Committee (HRECs) review. COVID-19 research is prioritized and expedited review processes should be implemented. Australia's Therapeutic Goods Administration is prioritizing any trial that works towards a treatment or a vaccine for COVID-19.	The safety of the participants must be guaranteed and research must be conducted in accordance with Good Clinical Practice. For bioequivalence studies that have not yet begun, ANVISA suggests postponing the first and other periods of hospitalization of the participants. For bioequivalence studies that have begun and have not yet been carried out in one or more periods of hospitalizations, ANVISA suggests postponing these periods. The final reports of the study should describe the potential impacts of this postponement.	Halting recruitment or temporarily halting the trial may be required in some circumstances. If this happens, sponsors are to inform Health Canada using a clinical trial application notification (CTA-N).Documentation of reasons for halting recruitment or temporarily halting trial in study records is also required. Sponsors should consider suspending additional site activation and recruitment.	The implementation of any contingency measures should be done in early consultation with the sponsor, the local investigators/trial sites, Institutional Review Boards (IRBs) and HSA. It is important that trial participants are kept informed of changes to the clinical trial that could impact them. If the sponsor decides to temporarily suspend / halt screening and recruitment of trial participants in relation to COVID-19 situation, the sponsor should notify HSA of the temporary suspension of screening and recruitment by submitting a Trial Status Report to HSA within 15 calendar days of the temporary suspension.

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	participants, the trial should be temporarily halted or participants transferred to other active trial sites if possible. Contacts between the sponsor and the health structures involved must be updated according to the new agreements. <u>Spain:</u> For recruitment of new patients, prospectively anticipated deviations are not acceptable and all subjects must meet all of the selection criteria. The Spanish Agency for Medicines and Health Products (AEMPS) is prioritizing clinical trials aimed at treating or preventing COVID-19. <u>Switzerland:</u> The authorities prioritize applications for clinical trials to treat COVID-19. In general, it is expected that no new patients be recruited in trials during the COVID-19 pandemic, with exceptions for life threatening diseases with no other treatment options. A sponsor must notify the Ethics Committee and Swissmedic within 15 days of a decision to temporarily interrupt or definitely discontinue a trial. A recruitment hold does not need to be reported if enrolled participants continue to be treated.	For clinical trial proposals already submitted for review, HRECS should request modifications designed to limit physical contact between staff and participants. If a proposal has already been approved but research has not yet commenced, these changes to limit physical contact do not need to be approved by HRECs before being implemented, but the HREC should be notified at the earliest opportunity. In proposing and reviewing new research, researchers, reviewers and institutions should consider the proposed research's impact on participant well-being, institutional resources, and the health system generally. An HREC has discretion to decline to approve proposed research that may be inadvisable in the current environment.			
Continuing a Participant on Study	<u>European Medicines Agency:</u> In truly exceptional situations if unavoidable, sponsors should consider transferring participants to other sites. The potential impact of COVID-19 should be considered when deciding to start or continue trials for participants in a risk group for COVID-19 or in trials involving treatments which may increase such risk.	For trials that proceed without modification, participants should explicitly be given the options to 1) continue participation; 2) suspend their participation, if viable; or 3) withdraw from the trial. For trials that have been modified, participants should	Participants must be informed of protocol changes that may affect them. Sponsors, investigators, and Research Committees should consider whether a participant should continue to participate in clinical research, taking into account	Eligibility criteria should not be altered as a result of COVID-19. Persons should not be enrolled in a trial if they do not meet the pre-set inclusion/exclusion criteria. If missing a pre-defined study visit would put the safety of a participant at risk despite	Ensuring the safety and well-being of trial participants is paramount. Sponsors and investigators should consider the specific context and circumstance of each clinical trial, and focus on the potential impact

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	Urgent safety measures to protect subjects against immediate hazard may be taken without prior notification to the National Competent Authority (NCA) and the Ethics Committee, but the information needs to be provided after the fact to the NCA and the Ethics Committee as soon as possible. For changes likely to affect participant safety and/or scientific value of the trial but which do not require immediate action from the sponsor or investigator, substantial amendment applications should be submitted. Where a trial is put on hold for reasons not linked to participant safety, the sponsor should notify NCAs and Ethics Committees. Participants should be informed of changes in trial conduct that affect them. <u>France:</u> A patient may change his/her trial site to unburden a center or limit his/her journey. The sponsor must get the agreement of the patient and investigators at both sites, transfer case report forms and all patient information, and supply the new site accordingly. If a trial participant becomes infected with COVID-19, the investigator and the sponsor should evaluate the continuation or suspension of investigational products. <u>Spain:</u> A sponsor may transfer a participant from one trial site to another provided that: 1) a transfer agreement is signed between the sites; 2) the new site has access to the participant's medical history and case report form; 3) the original site sends a transfer report summarizing the most	explicitly be given the options to 1) participate in the trial as modified; 2) suspend their participation, if viable; or 3) withdraw from the trial. If a participant declines or actively refuses to participate in trial activities, they should be considered to have withdrawn from the trial. Participants who choose to move off the investigational product and onto standard care and who do not wish to continue with site visits may be able to remain on trial for follow-up only. Participants should be informed of changes in trial conduct that affect them. Where public health directives or government policy prevent a participant from attending a visit or fulfilling a trial condition, sponsors and investigators are encouraged to facilitate the participant's continuation at another trial site. If a participant is symptomatic for COVID-19, the principal investigator should ensure appropriate follow-up and may advise the participant to go to another site for assessment, testing and/or further investigation.	the nature of the investigational product, the ability to monitor safety adequately, the potential impact on clinical research, the product supply chain, and the nature of the disease under study.	implementation of appropriate mitigation measures, the sponsor needs to consider having the participant discontinue taking part in the study. The ongoing safety of trial participants must be maintained. Risks and risk mitigation strategies related to use of any immunosuppressive agents should be discussed with medical professionals with expertise in immunology. Study participants must be informed of any risks/changes to the study and monitoring plan that could impact their wellbeing. Documentation of medical oversight is required to determine participants' eligibility to take part in the study. Sponsors should discuss with local research ethics boards (REBs) whether it is in the best interest of the safety, welfare and rights of the participant to continue the participant as per the study protocol or to halt the study.	on the safety and well-being of trial participants, when considering potential modifications to trial conduct in relation to the COVID-19 situation.

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	relevant participant medical data in relation to the trial and facilitates follow-up at the new site; and 4) the transfer is documented in the trial file at both sites. <u>Switzerland:</u> The transfer of participants to other trial sites is not allowed unless it is critical to ensure participant safety and the Lead Ethics Committee must be notified. A trained nurse/investigator may administer study medication at a participant's home if the medical condition requires staying on trial treatments and the participant cannot travel to the trial site anymore. Immediate actions taken to protect participants against immediate hazard must be reported to the Ethics Committee and Swissmedic within seven days.				
Implementation of Protocol	<u>European Medicines Agency:</u> The overall well-being and best interests of participants should be considered when changes in ongoing trials are considered. Prospective waivers of trial eligibility criteria remain unacceptable and patients should not be included in trials without proper eligibility assessment. Compliance with the trial protocol should be ensured to an extent that an ongoing benefit-risk assessment for the trial and participants is still possible. Decisions to adjust clinical trial conduct should be based on risk assessments by the sponsor and/or investigator. For trials to test new treatments for COVID-19, sponsors should seek advice on alternative procedures to obtain informed consent. <u>France:</u>	HRECs should consider whether to actively encourage alternative models for conducting clinical trials, such as decentralize trials (i.e. teletrials) and hybrid models in which participants can be recruited and data captured remotely. If a planned protocol modification is likely to have a negative impact on participant's safety or increase risk to participants, the review by an HREC may be required. Substantial amendments should be submitted and approved by the HREC as per processes authorized by the institution.	Adoption of protocol modifications must take into account the approved clinical protocol and the situation of the region whether the clinical research is being conducted with regard to current compliance actions. Amendments to the protocol performed exclusively due to measures to cope with COVID-19 do not require ANVISA authorization. These include changes to the protocol or in the research plan to minimize or eliminate immediate risks or to protect the lives and well-being of participants, such as reducing exposure to COVID-19. These amendments must be	Health Canada recognizes that there may be an increase in protocol deviations during the COVID-19 pandemic. The clinical trial site(s) should have a system in place to identify, document, assess and report all protocol deviations to the sponsor and REB in accordance with sponsor and REB requirements. These deviations need to be documented, to facilitate future analysis of the study findings. The sponsor should define and identify the protocol deviations to	There may be an increased incidence of non-compliances reported in relation to the COVID-19 situation. Sponsors should assess if the non-compliance fulfils the definition of a "Serious Breach" as defined in Medicines (Clinical Trial) Regulations, Part 2, Div. 2, Sec. 11. If the non-compliance is deemed to be a serious breach, the sponsor should notify HSA as soon as possible and no later than seven calendar days from the sponsor's

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	Any modifications the sponsor intends to be permanent must be submitted for authorization to the authorities (ANSM and/or Ethics Committee). Italy: If it is necessary to supply participants with investigational drugs and/or carry out trial activities at a participant's home or another site in order to limit the risk of COVID-19 infection or difficulties reaching a trial site, sponsors will have to submit a substantial amendment for immediate implementation to the Ethics Committees involved, indicating urgency due to the current emergency. Sponsors and CROs are encouraged to establish a risk evaluation plan and implement an action plan to ensure the maximum protection of trial participants. Spain: Any exceptional measures taken must be documented, however, they do not require prior approval on a case-by-case basis as a substantial modification by AEMPS or by the Drug Research Ethics Committee (CEIm), nor the individual notification of serious breaches of protocol, except in the event of an interruption of the trial leading to the cessation of treatment. In that instance, the sponsor must note these measures as "urgent security measures" and explain the measures adopted to guarantee the alternative treatment of the patients by sending an Ad Hoc report to AEMPS and CEIm in the 15 days following the interruption or termination.	Amendments eligible for pre-approval would be at the discretion of the institution and/or HREC and might include trial modifications to: a) employ virtual visits, telehealth, or electronic consent; b) change the 'site' to a location outside the hospital or permit referral to another hospital; c) extend protocol timeframes for visits, procedures, trial medication delivery or follow-up; d) ensure all returned investigational medical product is destroyed according to standard protocols; and e) any other changes that do not implicate participants' safety and are intended for safeguarding the health of participants, researchers and the community via infection control or reducing the burden of participation. Amendments designed to limit exposure to infectious agents or to ease the burden on participants, researchers or staff do not need to be approved by HRECs before implementation if timing does not permit this. Amendments that suspend recruitment or testing of participants, or that modify research locations or staffing can be implemented as necessary. Such protocol changes should be reported to	submitted in the annual research report, including their justification due to COVID-19, the possible impacts on the integrity of the research, and which participants were impacted.	be reported. Unless the deviations may place participants at risk, sponsors will not be required to report these deviations to Health Canada. Sponsors should consider alternate methods to prevent protocol deviations and document the reasons for any protocol deviations. Sponsors may consider submitting at regular intervals a cumulative list of deviations occurring in a particular study, rather than individual notifications.	awareness of the Serious Breach. In the event that contingency measures (e.g. remote study visits) need to be implemented urgently for the safety of trial participants in relation to the COVID19 situation, sponsors may consider implementing these contingency measures as Urgent Safety Measures. Sponsors should notify HSA of the Urgent Safety Measure as soon as possible and no later than 7 calendar days from the implementation of the Urgent Safety Measure. If contingency measures in relation to the COVID-19 situation fulfil the definition of substantial amendments, sponsors should submit the substantial amendments to HSA for review and approval.

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		the sponsor and the HREC in accordance with usual processes. Amendments that include the addition to an existing trial of new COVID-19 related elements is acceptable so long as appropriate protection is put in place for handling of any biological samples collected.			
Informed Consent Changes	European Medicines Agency: For trials involving COVID-19 patients, if written consent by the trial participant is not possible then oral consent can be given in the presence of an impartial witness who must sign and date the informed consent document. Having the trial participant and person obtaining consent sign and date separate informed consent forms can also be considered. In cases of acute life-threatening situations where it is not possible to obtain prior informed consent, informed consent will need to be later acquired. Visits to sites for the sole purpose of obtaining re-consents should be avoided. If re-consents are necessary for implementation of new urgent changes in trial conduct, alternative ways of obtaining such re-consents should be considered, including via phone or video calls and obtaining oral consents supplemented with email confirmation. Approved updated patient information and consent forms should be provided to participants by e-mail, mail, or courier before re-consent is obtained.	For amendments that include the addition to an existing trial of new COVID-19 related elements, sponsors and investigators should consider use of a separate specific information sheet and consent form to provide information about additional tests rather than modifying an existing form.	Not specifically addressed.	Sponsors should discuss with REBs alternative methods of informed consent for the study or amendments to the study protocol if in-person visits are not possible (e.g., electronic consent, recorded telephone consent). Sponsors may have to change processes, for example, an electronic alternative may have to be considered in place of a wet ink signature.	For remote study visits, sponsors may want to assess whether the informed consent form should be amended.
Study Visits	European Medicines Agency: Sponsors should consider converting physical visits to phone or video visits,	Sponsors should consider employing virtual visits, telehealth, and changing the	Sponsors should determine whether it is necessary to carry out face-to-face visits,	Investigators may need to evaluate whether alternative methods for	If trial participants are unable to return to the trial sites for study

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	and postponement or cancellation of visits to ensure only strictly necessary site visits take place. If a participant cannot reach a site for safety assessments, laboratory, imaging, or other diagnostic tests may be done locally. Sites should inform sponsors of such cases. If it is a trial endpoint and samples cannot be shipped to a central lab, analysis should be performed locally and documented.	'site' to a location outside of a hospital or clinic or permitting referral to another hospital or clinic. Sponsors should also consider extended protocol timeframes for visits, procedures, trial medication delivery or follow-up.	whether for safety assessments or the safe use of the product under investigation. Sponsors should consider implementation of alternative methods of assessment, including telephone contacts, virtual visits, and alternative sites for evaluations, including laboratories and imaging centers.	safety assessment are feasible should participants not be able to come to the investigational sites as specified in the study protocol. Alternative methods may include phone contact, virtual visits via telemedicine or alternative care sites. Alternative locations for imaging studies and laboratory tests may need to be considered. If alternative monitoring is done, careful documentation will be required to capture the reason why it was done; the method used to collect the information; what data were collected; who provided the information; and how the source of the information was verified. Study protocol amendments will not be needed. The use of alternative sites may create issues of confidentially related to participant's medical records (Electronic Health Record). Trial participants will need to consent to any identifiers leaving the original site to be provided to the alternate site and be assured that their	assessments and procedures in relation to the COVID-19 situation, sponsors may consider alternative methods for efficacy and safety monitoring, for example, alternative locations for laboratory tests and CT/MRI scans, remote follow-up with trial participants via telephone / video calls. Sponsors should consider whether the safety of trial participants can be reasonably assured with the implementation of the alternative efficacy and safety monitoring approach. If remote study visits are to be implemented urgently for the safety of trial participants, these may be considered as Urgent Safety Measures. Sponsors should notify HSA of these Urgent Safety Measures.

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				confidentially will be protected.	
COVID-19 Screening Procedures	Not specifically addressed.	Not specifically addressed.	Subject to the discretion of health authorities, screening procedures for COVID-19 in clinical research participants do not need to be reported to ANVISA as a protocol amendment unless the sponsor intends to incorporate data collected on COVID-19 as part of a new research objective.	If a participant has COVID-19, sponsors must decide quickly whether the study should be placed on hold (i.e. not administering the investigational product until the participant has recovered) or whether the participant's involvement in the study should be discontinued. All participants affected by a COVID-19 related study disruption should be documented by a unique participant identifier, site and a description of how the individual's participation was altered.	Not specifically addressed.
Monitoring Activities	<u>European Medicines Agency:</u> Temporary, alternative proportionate mechanisms of oversight may be required. On-site monitoring, if feasible, should take into account national/local restrictions, urgency and availability of site staff, and should only be performed as agreed with sites. Temporary measures include cancellation/postponement of on-site monitoring visits, implementing phone and video visits, and centralized monitoring and review of data. Remote source data verification is not allowed in most Member States and provision of redacted/de-identified pdf files will not be acceptable. <u>Italy:</u> Telephone contacts or videoconferences with trial site staff may be implemented	Remote monitoring visits are encouraged and must adhere to patient confidentiality protocols already in place. Remote source data verification may be done electronically as long as appropriate security arrangements can be put in place. If remote monitoring is not feasible, CRAs may continue to undertake on-site monitoring visits as long as they are not symptomatic, have not returned from overseas in the last 14 days or had contact with a known case of COVID-	Sponsors should consider using central and remote monitoring if scheduled monitoring visits at the site are interrupted.	Monitoring activities may need to be re-assessed and should prioritize critical activities to ensure participant safety. It is advisable to document any changes and their impact. Central monitoring of clinical trials should also be considered and any delayed site visits must be documented.	Sponsors should assess whether the monitoring plan requires adjustment in relation to the COVID-19 situation if monitors are unable to conduct on-site monitoring visits. Sponsors may consider implementing centralized monitoring or remote monitoring (i.e. remote Source Document Verification) as alternative options for site monitoring visits. Sponsors and investigators should notify HSA about the remote monitoring for

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	for source data verification. These methods must be described in a specific SOP by the Sponsor/CRO and must be evaluated and approved by the site's Personal Data Protection Officer. Other monitoring methods involving more risky ways of accessing sensitive data must be agreed to by the site's Personal Data Protection Officer and a specific opinion by the Italian Data Protection Authority should be obtained.	19, and in accordance with public health guidance.			their protocols prior to implementation. The implementation of remote monitoring need not be submitted to HSA as a substantial amendment or Urgent Safety Measure as defined in Medicines (Clinical Trial) Regulations, Part 2, Div. 2, Sec. 11. Sponsors should obtain a written agreement from the trial sites for remote monitoring prior to implementation.
Investigational Product Delivery and Accountability	<u>European Medicines Agency:</u> Sponsors must assess risks relating to the investigation medicinal product (IMP) and consider alternative shipping and storage arrangements. Changes in distribution may include providing larger amounts of trial medications to the participant to sustain him/her for a longer period. Re-distribution of IMP between sites should only be considered in cases where direct distribution by the usual distributor is not possible of in the exceptional circumstance where a participant is transferred between sites. Re-distribution should follow a written procedure established with the person responsible for the distribution of IMP. EMA notes it foresees direct delivery of IMP from sites to participants. Sponsors should check NCA guidance regarding direct sponsor to participant shipment. EMA recommends appropriate stock of in vitro diagnostic devices and medical	Principal investigators, pharmacies, and sponsors should develop plans to manage continuation of clinically essential trial medication delivery. Sponsors should ensure compliance with all relevant state and territory legislation regarding the movement of clinical trial medications across state and territory borders. There must be a process for obtaining the agreement of participants to changes in delivery of trial medication.	There may be direct delivery of experimental medication to a participant's home if the drug is for use at home. Participants should be properly educated on the at-home use and should maintain records of medication receipt. These measures must be reported in the study's annual report.	The Food and Drug Regulations (FDR) do not prohibit the shipment of clinical trial investigational products (IP) from Canadian sites directly to patients. This approach would be acceptable for all product formulations (*e.g.*, tablets, injectables). This approach can only be considered for specific trial designs and drugs that a subject could take on their own (*e.g.*, subject already in a trial and on medication, and if the trial uses a medication that does not have to be administered in a hospital/clinic setting or have any special conditions for handling). The investigational products must be	If trial participants are unable to return to trial sites in relation to the COVID-19 situation, sponsors and investigators may consider delivering the IP to the trial participants' homes via Direct to Patient (DTP) service after the sponsor and investigator(s) have determined that the investigational product can be safely and properly self-administered by trial participants remotely without the supervision of the investigator and/or the study team. Ensuring IP security, accountability, traceability and

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	devices be maintained in case of distribution failure. Italy: Direct deliveries of IMP from the hospital pharmacy to the trial participant may be arranged upon agreement of both the hospital pharmacy Director and the Principal Investigator. Adequate remote communication methods with the participant regarding the IMP must be implemented to replace information that will no longer be provided in person. If the CRA is unable to carry-out the final accounting of the IMP for the purpose of reconciliation, it can be carried out by the hospital pharmacist or by a trained study coordinator/data manager. Spain: A site's Pharmacy Services may take measures to deliver IMP to a participant's home. Each particular case should be assessed by the sponsor, the investigator, and the Pharmacy Service. Switzerland: The implementation of changes to the distribution of IMPS is strictly limited to the COVID-19 pandemic period. A change in distribution may only be introduced after obtaining agreement of the investigator. Distribution changes are only permitted for IMPS which are suitable for use at home and participants must be appropriately informed by phone and give their written consent later. The participant should confirm receipt of the IMP to the investigator. The delivery of the IMP may only be made from the trial site to the participant. The sponsor must notify Swissmedic and swissethics of changes in IMP distribution			transported, handled and stored in a manner that mitigates the risk of exposure to temperatures outside labelled storage conditions. Verification that the investigational drug has been received by the participant is required. Accurate documentation of the process in the participant's study record is required.	compliance to IP storage requirements will be pertinent. Sponsors and investigators should notify HSA about the DTP service via email for their protocols prior to implementation. The implementation of DTP service need not be submitted to HSA as a substantial amendment or Urgent Safety Measure. The investigator should maintain oversight of the IP delivery to trial participants since the investigator is ultimately responsible for the medical treatment and care of the trial participant. The DTP service should only involve supplying the IP from the trial site directly to the trial participants' homes. In the event the sponsor is planning to supply the IP from alternative locations (e.g. manufacturer, sponsor, central depot or distributor etc.) to trial participants' homes, the sponsor should provide details on additional measures to safeguard trial participant privacy and data confidentiality

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					to HSA before implementing this plan.
Data Capture and Study Reporting	<u>European Medicines Agency:</u> Sponsors are expected to continue safety reporting. Audits should be avoided or postponed. Sponsors should escalate and manage protocol deviations in accordance with their standard procedures. Additional financial compensation that is provided to sites/investigators for reimbursement of exceptional expenses should be documented. <u>France:</u> If a trial participant becomes infected with COVID-19, the infection should not be declared as a new event except in the case of specific measures taken by the sponsor. If this even corresponds to a SUSAR or a serious adverse event that may be linked to the act of implementing the medical device, it should be declared to ANSM according to current requirements. The deadline for submitting annual safety reports may be extended a maximum of two months after informing the ANSM by email. If planned meetings of the safety committee are impossible to arrange, the sponsor may consider postponing such meetings after assessing the consequences for participant safety. Sponsors should document the postponement decisions to members of the supervisory committee, investigators, the ANSM, and Ethics Committee. <u>Spain:</u> In the four months following the date the COVID-19 crisis has ended in Spain, the	Investigators, sponsors, institutions, and HRECs should adhere to existing guidance for safety monitoring and reporting. All protocol deviations must be reported to the sponsor. Protocol deviations can be reported to the HRECs in the usual manner or submitted in bulk form at the end of the crisis.	ANVISA acknowledges there may be inevitable protocol deviations due to COVID-19. These protocol deviations should be documented. The sponsor should consider discussing with ANVISA any protocol modifications that may result in a change in data management and/or analysis.	For IDP, record keeping must comply with regulatory requirements of section C.05.012 of the FDR. As per C.05.012(3)(e), the sponsor must maintain complete and accurate records in respect of the use of a drug in a clinical trial, including records respecting the shipment, receipt, disposition, return and destruction of the drug.	Sponsors should ensure the following are included in the Clinical Study Report: a) All contingency measures implemented in relation to the COVID-19 situation; b) Subject IDs of all trial participants affected by the COVID-19 situation and how their participation had been altered; c) Impact of the contingency measures on safety and efficacy data for the clinical trial. Sponsors and investigators should document the reasons for any contingency measures implemented and perform an impact assessment of the implemented measures on trial participant safety and on data credibility and trial integrity. Any missing trial data in the case report forms due to these measures should be explained and documented.

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	sponsor must send a report for each trial detailing the exceptional measures adopted to the AEMPS and the CEIM.				

This alert is one of a series of advisories and webinars issued by Ropes & Gray on COVID-19 topics. Please check our Coronavirus Resource Center for additional information and updates.