Bird & Bird & COVID-19 Clinical Trials Q&A

Emergency legislation / Regulatory relaxation during COVID-19 pandemic

Contents

Introduction

Background

In the current situation, planned and ongoing clinical trials are facing major challenges due to the COVID-19 situation. Against this background, guidelines have been published by many competent authorities over the globe. In Europe for instance, such guidelines have been published on a European level (e.g. the "Guidance on the Management of Clinical Trials during the COVID-19 (Coronavirus) pandemic" by EMA) as well as in several Member States.

In Asia Pacific (APAC), there have been variable responses to new, planned and ongoing clinical trials during the COVID-19 situation. As every country has its own regulatory system, each country is responsible for the management of these trials. Across the region, there has been either no response, or clear government directions on how to manage clinical trials during this time.

This overview is intended to summarise these efforts in order to support our clients in their efforts to cope with the situation. This document does not constitute legal advice, if you require more information please feel free to reach out to the country contacts in this document.

Australia

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	The **Commonwealth Department of Health** along with the **Clinical Trials Project Reference Group (CTPRG)** have published a guideline to provide general information and advice to institutions conducting or overseeing research, Human Research Ethics Committees (**HRECs**), researchers and sponsors in the context of the COVID-19 pandemic (**National Guidance**). The guideline was produced with input from all state and territory Departments of Health, the National Health and Medical Research Council (**NHMRC**) and the Therapeutic Goods Administration (**TGA**). Some states have issued an additional guidance to address requirements specific to their respective state. The **New South Wales Office for Health and Medical Research (OHMR)** released its own guidance document on COVID-19 and clinical trials that is modelled on similar advice from the HRA in the UK. The OHMR recommends that where there are inconsistencies between the NHMRC's principles and the OHMR's guidelines, Public Health Organisations and researchers should contact clinicalNSW to obtain advice on how to respond locally. The **Queensland Health Queensland Clinical Trials Coordination Unit (QCTCU)** has also issued the Queensland Health guidance for sponsors, researchers, HRECs and Research Governance Officers to enable continued conduct of clinical trials during the COVID-19 pandemic. This document was modelled off the UK NHS' guidance document as well as the OHMR's guidance document. The **Australian Capital Territory Research Ethics and Governance Office (REGO)** has published a draft guidance for HRECs and Research Governance officers in response to the COVID-19 pandemic. On 8 April 2020 the **Parliament of Western Australia (WA)** passed the Guardianship and Administration Amendment (Medical Research) Bill 2020, effective on the same day. It now provides an avenue for the inclusion of incapacitated adults in research. The Government of WA deems this to be particularly relevant at this point in time when clinical trials related to COVID-19 are of critical importance. A joint position statement from the **Research and Development Taskforce (RDTF)** titled '**S**upporting Clinical Trials During the COVID-19 Pandemic' has also been released. The RDTF comprises industry bodies such as Medicines Australia, Medical Technology Association of Australia (**MTAA**) and AusBiotech. Please note that the below explanations are a summary of the guidance given by the authorities and may be subject to revision as the situation surrounding the COVID-19 pandemic unfolds.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to**	The National Guidance prioritizes and aims to expedite the review process for research relating to COVID-19 or where there are public health grounds for rapid review. The OHMR does not prohibit new trials however, any planned clinical trial portfolio for 2020 should be reassessed to take into consideration the health system capacity and risk assessment.

	COVID-19	The QCTCU stipulates that at the date of publication of the guidance (7 April 2020), clinical trial activities are continuing across health facilities.
2b	**On suspension of ongoing CT's or recruitment stop?**	The National Guidance **does not** mandate a recruitment stop. However, decisions to recruit new participants to ongoing trials should take into account the potential benefits and burdens on Australia's health system and should depend on individual trial factors. Any new recruitment should also reflect the most current public health advice on social distancing. The QCTCU and the OHMR both provide that a study should only be suspended if there is no practical way of allowing it to achieve its primary outcomes during the COVID-19 pandemic. A study should only be stopped and closed if there is no practical way of allowing it to achieve its primary outcomes during the COVID-19 pandemic, and/or if it will not be possible to complete the study within an appropriate timeframe after the COVID-19 pandemic. Additionally, the QCTCU recommends that all research involving Aboriginal and Torres Strait Islander participants requiring face-to-face contact should be suspended for the foreseeable future. Otherwise, researchers should amend the trial protocols to allow participants to participate through telehealth/teletrials and send the investigational product directly to the participant's home. Any recruitment of new participants to the clinical trials should be suspended.
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	**Risk Assessments** The National Guidance requires institutions, individual principal investigators and sponsors to undertake contingency planning to address the potential impact of COVID-19 and responses to the crisis on current, ongoing clinical trials. This planning should include: • priority: assessment of the importance of and the risks associated with continuing the trial as designed or with necessary modifications. Responses could include continuing the trial in its present form, conducting the trial in a modified form, suspending the trial or closing the trial. • participation: assessment of the ability of participants to participate in the trial in accordance with protocol requirements and consideration of alternative models for participation that would not compromise the integrity of the trial. • capacity: assessment of the resources available for continuing the trial, including research staff, clinical support staff, pharmacy support, other support staff, space, equipment, supplies, etc. A component of a capacity assessment will be consideration of the need to re-allocate research staff to clinical care and other areas of patient support. Contingency planning will need to be an ongoing process. Amendments to existing protocols that are designed to limit exposure of participants, researchers or staff to infectious agents or to change methodology, procedures or project activity to ease the burden on participants, researchers or staff do not need to be approved by HRECs before being implemented, if timing does not enable this. In addition, necessary amendments that suspend recruitment or testing of participants, or that modify research locations or staffing and other administrative matters can be implemented as necessary. If planned modifications to a protocol is likely to negatively impact on participants' safety or increase risk to participants, then review by an HREC, or an approved delegated process, may be required. The National Guidance encourages the use of strategies to pre-approve certain categories of amendments. Such preapproved categories are at the discretion of the HREC and/or the institution but the National Guidance suggests that they may include:

		• employing virtual visits, telehealth, electronic consent or otherwise implement teletrials; • changing the 'site' to a location outside of a hospital or clinic or permit referral to another hospital or clinic; • extending protocol timeframes for visits, procedures, trial medication delivery or follow-up to accommodate isolation periods or other disruptions; • ensuring that all returned investigational medical product is destroyed in accordance with standard protocols for the destruction of biohazards, and • any other changes that do not implicate participants' safety or well-being and are intended for the purpose of safeguarding the health of participants, researchers and staff or the community via infection control or reducing the burden of participation in a trial for the participants or researchers. **Safety Reporting** Researchers should continue to follow the safety monitoring and reporting requirements under existing guidance published by the NHMRC and the TGA. In addition, any incidents associated with attendance at a clinic of a participant known, or later discovered, to be symptomatic of COVID-19 should be promptly reported as an adverse event or safety issue in accordance with existing guidance. Both the QCTCU and the OHMR require that any urgent safety measures and serious breaches impacting on patient safety and rights should be reported to HREC, Sponsor and the TGA as relevant according to current guidelines. For non-serious breaches, a post COVID-19 bulk deviation report can be submitted to the relevant bodies after the situation has resolved. The bulk report must include: • the number of patents impacted, • changes to medication dispensing, • dose interruptions, • changes to visit schedules and visit activities, • use of externals services (e.g. pathology, imaging, visit sites, pharmacy), and • Missing data.
2d	**On informed consent (including re-consent, signature and dates etc.)**	There is no specific guidance on informed consent in the National Guidance. However, as noted above, researchers may change their protocols to adopt the use of electronic consents. The QCTCU and the OHMR require researchers to obtain verbal consent from participants to provide their contact details for shipping purposes and where they require a nominated person to collect the product.
2e	**On distribution of IMP's (home delivery and storage), stock management**	The National Guidance stipulates that plans should be developed to manage the continuation of clinically essential trial medication delivery to participants affected by self-isolation quarantine periods or as a result of testing positive for COVID-19. It is important to note that while there are no specific requirements under TGA legislation or the Clinical Trials Notification (CTN) scheme regarding the movement of clinical trial medications across state and territory borders, sponsors should ensure compliance with all relevant state and territory legislation. Any such arrangements should include a process for obtaining the agreement of the participant to the delivery changes. This is similarly echoed by the QCTCU and the OHMR.

2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	The National Guidance, OHMR and QCTCU encourages alternative models for conducting clinical trials such as decentralised trials (i.e. teletrials) and hybrid models in which participants can be recruited and participate remotely and data can be captured remotely via available technology.
2g	**Are there other relevant aspects considered by the national guidance?**	The National Guidance provides that where a current trial is proceeding without modification, researchers must give participants the option to: • continue to participate in the trial; or • suspend their participation, if this is viable; or • withdraw from the trial. In trials that have been modified, participants should explicitly be given the following options to: • participate in the trial, as modified, inclusive of alternative mechanisms for engagement such as remote visits, data collection, monitoring, etc., as appropriate; or • suspend their participation, if this is viable; or • withdraw from the trial. Researchers should also remind participants of the importance of notifying the research team in advance of attending any trial visits if: • they are experiencing one or more symptoms suggestive of COVID-19 infection; • they have recently (within 14 days) returned from overseas or have been in close contact with someone who is known to have contracted COVID-19 or has symptoms suggestive of COVID-19 infection; or • they are experiencing one or more symptoms not suggestive of COVID-19 infection, but suggestive of influenza or other infectious disease or condition that includes respiratory symptoms. If a participant notifies the research team of any of the above, the primary investigator must arrange a follow up with the participant. Both the QCTCU and the OHMR require, where possible, the electronic transfer of documents and the use of digital/electronic signatures over paper documents and "wet-ink" signing processes.
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	The TGA have indicated that they are giving activities relating to the COVID-19 pandemic the highest priority. The have also published some accepted variations to the CTN Scheme in light of the COVID-19 pandemic.

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Belgium

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	Yes. The Federal Agency for Medicines and Health Products (FAMHP) has issued a guideline concerning the management of clinical trials during the coronavirus pandemic. This guideline is available here on the FAMHP's website. These new guidelines have been prepared as an addendum to the European guidance (available here). It is intended to assist clinical trial sponsors in the management of clinical trials, namely as regards clinical trials for the prevention or treatment of COVID-19 and ongoing clinical trials in Belgium (unrelated to the prevention or treatment of COVID-19). Please note that the below explanations are a summary of the national guidance given by the authorities: some are subject to notifications, authorizations, record keeping etc. which cannot all be detailed in this table.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	Yes. Even though initiation of new CTs not related to COVID-19 is not excluded, the guideline clearly indicates that priority is given to any (new) clinical trial applications for the treatment or prevention of COVID-19 infection, and/or substantial amendment applications and notifications to existing clinical trials necessary as a result of COVID-19.
2b	**On suspension of ongoing CT's or recruitment stop?**	Yes. A temporary stop (e.g. recruitment halt, halt of the trial on a site) of the trial has to be submitted to the FAMHP and the EC within 15 days of the decision. If several CTs are discontinued for the same reason, it is needed and sufficient that the applicant sends only one temporary halt notification that lists all the concerned CTs. In order to restart the trial after temporary halt, a substantial amendment will have to be submitted. The trial will only be allowed to restart upon approval by the EC and if no motivated objections have been raised by the FAMHP. If the temporary halt of recruitment is only due to the COVID-19 crisis, it will be acceptable to restart the recruitment when it becomes possible again, after a simple notification to the FAMHP and to the EC.
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	Yes. Urgent safety measures taken in the context of coronavirus may be taken without prior notification to FAMHP and the EC. However, the sponsor must inform as soon as possible the FAMHP and the EC of the measures taken and the plan for further action. For the rest, the guidance does not provide for any particular derogation/deviation from standard practice and CT management rules.
2d	**On informed consent (including re-consent, signature and dates etc.)**	N/A
2e	**On distribution of IMP's (home delivery and storage), stock management**	Yes. The guideline recalls that direct shipment from sponsor to patient is not allowed in Belgium, but it allows under the exceptional COVID-19 times, under exceptional conditions, that in cases where, for the protection of the rights (confidentiality) and the safety of the participants, a continued supply of trial medication needs to be maintained at home, trial medication is

		shipped directly, under responsibility of the principal investigator, from the trial site to the trial participants via courier. The guideline specifies that this is only possible provided that the product is suitable for transport, storage at home and administration at home use. In a nutshell, the guidance indicates that direct shipment and home administration is possible in the extraordinary COVID-19 related circumstances, but 1) this happens under the responsibility of the principal investigator 2) the shipment must take place without sponsor involvement (for personal data protection purposes) 3) the shipment must take place under correct shipping conditions 4) there must be correct and traceable documentation 5) the patient must be trained for storage, administration at home *or* the administration must be conducted by a trained (i.e. trained in terms of the protocol) care giver, nurse or physician. From an administrative point of view, if any training is provided to the participant, care giver, nurse or physician that is not mentioned in the protocol, a substantial amendment is required. Furthermore, if temporary changes to the informed consent are implemented, these changes should preferably be described in an addendum to the ICF which is temporarily valid. Non-substantial and substantial amendments on the ICF have to be submitted to the EC as soon as possible.
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	Yes. The guidance of the FAMHP notes that several investigators have cancelled on-site monitoring at their study site. 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 Belgium because it breaches the trial participants' rights – furthermore, it would involve an extra burden on site staff. Special attention to on-site monitoring will be required once it is allowed again.
2g	**Are there other relevant aspects considered by the national guidance?**	The guidance specifies electronic ways of working and accepting possible electronic signatures, and indicates in particular: • That the EU guidance has to be followed as regards the ICF or as regards (re)obtaining consent ; • That for other documents (cover letter, application form, protocol), a scan or photograph of the signed paper will be accepted, and that unsigned Word or PDF files are currently accepted (provided they indicate that a signed version will follow later) • Where qualified electronic signatures are available, they are accepted, however the guidance makes it clear that they are not mandatory and the other relaxed methods mentioned above are available.
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	Yes. As indicated above, priority is given in particular to any (new) clinical trial applications for the treatment or prevention of COVID-19 infection. In terms of timeframes, the FAMHP commits to validate and review applications in four working days, as will do the evaluating EC. When considering submitting a multi-country COVID-19 related trial, the guidance invites applicants to consider the accelerated Voluntary Harmonisation Procedure. For national COVID-19 related trials, the accelerated CTR Pilot is strongly

recommended. This pilot entails:

- a single submission to the national contact point
- a single review by the selected evaluating EC (without possible local ECs).

The structure of the submitted dossier can follow the usual requirements of the Act of 7 May 2004 or the structure of the CTR.

In cases where the requirements of the Act of 7 May 2004 are followed, a document annexed to the guidance has to be provided for each site.

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Mainland China

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	Yes, the **Center for Drug Evaluation (CDE) of National Medical Products Administration (NMPA)** is reported by a third party media here [in Chinese] to have drafted the Special Review Program for **Anti-Novel Coronavirus Drugs ("CDE Program")**, together with 4 technical guidance and 2 procedural guidance including: 1 Key Points of Application Materials for Special Review and Approval of Anti-Novel Coronavirus (2019-nCoV) Drugs (for trial implementation); 2 Key Points of Application Materials for Special Review and Approval of Clinical Trials of Novel Coronavirus (2019-nCoV) Preventive Vaccines (for trial implementation); 3 Key Points of Application Materials for Special Review and Approval of Applications of Chinese Traditional Medicine for Treatment of Novel Coronavirus (2019-nCoV) Infectious Pneumonia (for trial implementation); 4 Technical Guidelines for Application of Clinical Trial for Anti-Novel Coronavirus (2019-nCoV) Drugs (for trial implementation); 5 Evaluation Procedures for Applications of Novel Coronavirus (2019-nCoV) Drug Project (for trial implementation); and 6 Procedures for the Assessment and Review of the Novel Coronavirus (2019-nCoV) Drugs by the Drug Special Expert Panel (for trial implementation). However, the CDE Program and the above guidance have not been published and are available only to relevant applicants upon telephone enquiry to the CDE on 14 April 2020. On 21 February 2020, the **Press Conference of the Joint Prevention and Control Mechanism of the State Council** published here [in Chinese] that the NMPA has implemented emergency review and approval for drugs for prevention and control of COVID-19. On 26 February 2020, the **Scientific Research Group of the Joint Prevention and Control Mechanism of COVID-19 of the State Council** issued a notice **("Notice")** here [in Chinese] on standardizing medical institutions to carry out clinical research on drugs for treatment of COVID-19. On 28 February 2020, the State Government website reported here [in Chinese] that the NMPA has established emergency review and approval green channel for COVID-19 drugs and medical devices, and has approved clinical trials of 5 new drugs for cure of COVID-19 including remdesivir and favipiravir. On 8 April 2020, the **State Council** issued here [in Chinese] a **Letter of Implementation for the Notice.**
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new**	No, there is no specific guidance in this respect upon public information.

	CTs not related to COVID-19	
2b	**On suspension of ongoing CT's or recruitment stop?**	No, there is no specific guidance in this respect upon public information. As a general rule, the Drug Registration Regulation (2007) ("2007 DRR") provides in Article 42 that in any of the following circumstances during a clinical trial, the NMPA may order the applicant to modify the protocol, suspend or terminate the clinical trial: (1) the ethic committee fails to perform its duty; (2) safety of the subjects cannot be adequately ensured; (3) a serious adverse event is not reported within the specified timeline; (4) there is evidence to prove that the drug used for the clinical trial is not effective; (5) a quality problem of the drug used for the clinical trial occurs; (6) there is a fraud in the clinical trial; or (7) there is any other case violating the Good Clinical Practice. Meanwhile, Article 43 of the 2007 DRR stipulates that where there is any large-scale of and unexpected adverse reaction or serious adverse event, or there is evidence to prove any serious quality problem of the drug used for a clinical trial, the NMPA or the drug regulatory department of the province, autonomous region or municipality directly under the Central Government may take emergency control measures and order to suspend or terminate the clinical trial. The applicant and clinical trial institution must stop the clinical trial immediately. **It should be noted** that the 2020 DRR has been promulgated and will take effect on 1 July 2020. The above Articles 42 and 43 of the 2007 DRR are incorporated in Article 30 of the 2020 DRR.
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	Yes. The **Notice** provides the following requirements to control the risk of clinical study on drugs for treatment of COVID-19: Location - clinical research shall be carried out in designated hospitals for cure of COVID-19. Drug - the drugs shall already be listed in China for other indications (not applicable to a new drug application with COVID-19 as stated indication) Pre-clinical study - The in vitro experiment shall show clear inhibiting effect of the drug against COVID-19 or the animal trial result supports clinical research of COVID-19. Clinical study - The method of administration in clinical research should not exceed the usage and dosage of the current drug insert. The drug concentration in the human body is expected to reach the amount of effective concentration converted from the in vitro experiment. Qualification - The clinical trial shall be carried out by medical practitioners with deputy senior professional titles or above, and a comprehensive clinical research plan shall be formulated for patients with mild, moderate and severe illnesses. Risk management - Plans and management measures shall be formulated for possible risks. Safety reporting - The hospitals can hire an independent data safety monitoring committee. The committee can regularly evaluate the progress of the clinical study before the study ends. If the test group is found to have obvious side effects, or uncertain treatment effect, the committee can immediately report to the medical institution, and the medical institution can terminate the study in advance. For those with certain efficacy, the drug shall be promoted and used as soon as possible for the benefit of the patients. If

		there is no independent data safety monitoring committee, the medical institution shall always pay attention to the possible toxic and side effects of the drug. If there are obvious toxic, side effects or no certain treatment effect, the clinical study shall be terminated immediately to protect the rights and interests of the subjects. The **Letter of Implementation for the Notice** provides that for clinical research that violates the Notice and the relevant laws as well as clinical research with obvious toxic or side effects or no certain treatment effect, the scientific research group of the State Council shall promptly request medical institutions to terminate the research.
2d	**On informed consent (including re-consent, signature and dates etc.)**	No, there is no specific guidance in this respect.
2e	**On distribution of IMP's (home delivery and storage), stock management**	No, there is no specific guidance in this respect.
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	No, there is no specific guidance in this respect.
2g	**Are there other relevant aspects considered by the national guidance?**	The **Letter of Implementation for the Notice** provides the procedures to carry out clinical research of drugs for treatment of COVID-19 by different departments to increase the efficiency of study.
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	Yes The NMPA may decide to implement special review and approval regime for the drugs in response to the public health emergencies according to the **Procedures for Special Examination and Approval of Drugs (2005)** issued by the previous State Food and Drug Administration (now known as NMPA), the NMPA shall make the review decision to approve/deny the application of CT within 3 days after completion of technical review. The clinical trial approval of favipiravir was granted following this special approval regime according to the applicant's publication. Also, the 2020 DRR provides 3 other methods (2 of them are provided in the 2007 DRR) for acceleration of drug registration which can be applicable to the COVID-19 situation, including acceleration for ground-breaking therapeutic drugs, approval with condition and priority review and approval procedure. In addition, the **Press Conference of the Joint Prevention and Control Mechanism of the State Council** published here [in Chinese] on 25 February 2020 that the registration fee is waived for drugs entering the special review and approval regime and are for treatment and prevention of COVID-19, as well as COVID-19 related medical devices entering emergency review and approval procedure.

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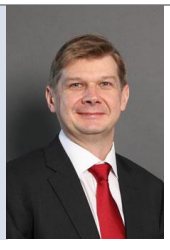

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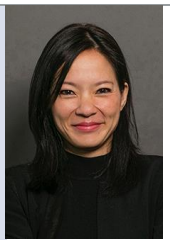

Czech Republic

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	Yes, the **State Institute for Drug Control (SUKL)** has issued a guideline on clinical trials with respect to COVID-19. The guideline is available in Czech here and in English here.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	Yes, the SUKL strongly recommends not to commence new CTs not related to COVID-19.
2b	**On suspension of ongoing CT's or recruitment stop?**	Yes, the SUKL strongly recommends not to enrol new patients in ongoing CTs not related to COVID-19. The SUKL recommends not to conduct clinical trials involving healthy volunteers, i.e. clinical trials that do not provide therapeutic benefit to the enrolled trial subjects, such as bioequivalence or pharmacokinetic studies. The SUKL recommends not to commence clinical trials involving, in particular, therapies that affect/influence the immune system.
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	The sponsors are asked to notify the SUKL and ECs of all emergency measures concerning ongoing and approved but non-initiated clinical trials in the Czech Republic. The SUKL will not consider notification of emergency measures as substantial amendment and will not require the reimbursement of costs.
2d	**On informed consent (including re-consent, signature and dates etc.)**	Yes, the SUKL does not recommend delivering the information through "personal contact", but the information should be communicated by phone or email (an acknowledgment of an email is necessary), and recorded in source documentation and CRF.

2e	**On distribution of IMP's (home delivery and storage), stock management**	Yes. 1 IMPs - stored at room temperature, any pharmaceutical forms except for parenterally administered IMPs (e.g. tablets, capsules, etc.): Possibility to provide the supply of study medication to patients during the upcoming visit for a longer period of time than originally planned. In case it is not practicable to supply the study medication directly to the patient during the upcoming visit, it is possible, as an emergency situation, to send the study medication by courier service. The courier service would collect the medicinal products at the trial site, from the investigator who is responsible for the investigational medicinal products and this fact would be recorded by the investigator in the trial subject's documentation. The courier service would deliver the study medication to the patient's home. After that, the investigator would make sure by phone that the patient has received the study medication and would record this fact to the trial subject's documentation. In case the courier service is to carry several medicinal products at one time, the investigator must also make sure that the trial subject received the correct medicinal product (by the IMP code or trial subject code), as in blinded CTs there are several medicinal products; the major purpose of the telephone check is to avoid confusion of medicinal products. The patient should start taking the therapy only after the investigator endorses the correctness of the shipment. Further option is delivering IMP to the trial subject by his/her family member, who has been previously determined by the trial subject to investigator over the phone. The investigator records it all in source data and CRF. 2 IMPs - sterile pharmaceutical forms (except for intravenously administered IMPs) such as parenteral administration, subcutaneous administration, eye drops, etc. self-applied by trial subjects at home: Procedures above under 1) shall apply. In this case, it is necessary to respect also the requirements for the storage of the study medication; mostly, this concerns products to be stored at temperatures between 2–8° C. In such a case, it is essential to arrange for transportation of the products in cooler boxes meeting this requirement. For the duration of transport, continuous temperature monitoring has to be ensured and documented in the clinical trial documentation. The courier service should be organised – and paid for – by the sponsor who is responsible for the quality of the IMP. It is, however, necessary that the investigator who is fully responsible for the trial subjects from the respective trial site, agrees to this course of action. 3 IMPs – parenteral administration – i.v. – in the form of bolus or infusion, applied by the doctor at the trial site: If permissible based on the protocol, SUKL recommends to postpone the visit as well as the application of the IMP. Protocols typically offer the possibility to postpone the administration of products by 14 days. If the product administration cannot be postponed or it has already been postponed by the maximum period permissible, the following may be arranged for: Administration at the trial site while observing safety hygienic rules. In emergencies, if necessary, administration of the IMP at the patient's home; such administration shall be carried out by adequately qualified

		healthcare staff trained for this purpose. Should the sponsor consider using the services of a specialised company licensed for the conduct of medical home care within the territory of the Czech Republic via qualified and properly trained paramedical staff, it is necessary to obtain the approval of the investigator from the respective trial site for this course of action, as the investigator is fully responsible for the trial subject and organisation of his/her treatment. This course of action should be approved by the provider of healthcare services of the respective trial site. The question is how the clinical trial insurance covers this service, how compensation for injury to health caused by a procedure conducted by "medical home care" staff would be handled. In such a case, the IMP has to be dispensed by the study staff at the trial site. Where infusions requiring preparation by pharmacy are concerned, they would be dispensed to an employee of the trial site based on a request form and after that dispensed by the investigator or appointed trial site employee to the medical home care employee. Injections that may be reconstituted prior to administration: proceed as per manufacturer's instructions and, if permissible, reconstitute immediately prior to administration at the patient's, observing all of the procedures prescribed by the pharmaceutical manual. Infusions that were prepared by the pharmacy have to be transported under strictly observed storage conditions for the reconstituted product – i.e. under continuous temperature monitoring during transport and in compliance with other conditions prescribed by the Protocol or Pharmaceutical Manual, as applicable. In case of administration of IMPs presenting the risk of anaphylactic reaction, these IMPs should be administered exclusively at the trial site where intensive and resuscitation care may be arranged for. 4 Sending of study medication directly from the sponsor, albeit via third party, is not acceptable (the sponsor cannot know trial subject's identification, his/her address etc.). 5 As for the return of study medication by the patient to the investigator at the trial site by courier service: in this case, SÚKL considers sending of unused study medication by courier service inappropriate and requires that the patient keep the unused study medication and return all medication, i.e. for control purposes, used and unused medication, only after safety measures are lifted; the medication is to be returned directly to the investigator during the trial subject's next personal visit to the trial site, when the investigator shall record everything in the trial subject's documentation. The administration of study medication that influences the immune system is not possible/is contraindicated for trial subjects with confirmed coronavirus infection.
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	Yes. Changes to the monitoring plan involving a change of a site visit to remote monitoring or change of dates of monitoring do not have to be reported to SUKL or to the ethics committee by the sponsor, yet everything has to be documented and justified in the clinical trial dossier. SÚKL does not provide its opinion on the organisation of monitoring when authorising clinical trials, either, and it does not have to be included in the annual progress report for the clinical trial. Centralised monitoring is permitted. Remote monitoring – source data are currently in paper form. Remote monitoring in the form of copying or scanning of reports or medical documentation, making and use of de-identified certified copies or certified

		copies of de-identified source documents is not acceptable. SUKL would consider monitoring organized as described above a breach of GCP and legal regulations. In case the reduced frequency of monitoring posed a hazard in respect of a particular CT, SUKL would accept an alternative approach, such as central monitoring + teleconference monitoring, if feasible with regard to the workload of healthcare staff at the trial site, i.e. an appointed study team member would read the source data and the monitor would check them against the CRFs within the scope of the TC. Nevertheless, after the emergency situation passes, data obtained in this manner would have to be verified by standard process, and for this reason, this alternative approach should only be employed in justified cases identified by risk analysis. A combination of centralised + teleconference monitoring is permissible. In case of videoconference monitoring, the representatives of the sponsor/CRO must not make any photocopies of the documents. (pictures, printscreens etc.). Videoconference monitoring must be secured by a secured transmission. It must be ensured that only the monitor (authorized person) can consult the documentation, and that no unauthorized person could have attended the videoconference. Sponsor has to establish standard procedure for such type of monitoring. It is necessary to follow requirements of GDPR as well as of Act No. 110/2019 Coll. on personal data processing.
2g	**Are there other relevant aspects considered by the national guidance?**	**Investigators - changes of investigators** In the case of investigator´s /principal investigator´s illness his duties may be temporarily taken over by his representative (co-investigator). If the investigator does not have any representative, his duties and activities may be delegated to an investigator from another trial site. Another option could be the approval of a new investigator by the local Ethics Committee (EC). **Closure of the trial site / opening of a new substitute trial site** In the case of the closure of the trial site in relation to the current emergency (all staff in quarantine etc..), the following is possible: • stay activities of this trial site for the required time. Temporarily transfer of the trial subjects to another trial site is possible with the agreement of both – the sponsor and the investigator. The trial subject has to agree with this change • or if the design of the clinical trial allows it, to stay temporarily the clinical trial • or if there is no other option, to end the clinical trial in the trial site and transfer the trial subjects from this trial site to another trial site or to stop their participation in this clinical trial. In this case, the investigator should inform trial subjects about their further treatment, if the treatment is necessary. If necessary, a new substitute trial site may be opened; all GCP requirements and requirements stipulated by effective legislation must be met (such as approval by the local ethics committee, agreement concluded by and between the sponsor and the healthcare service provider, etc.). For SUKL and MEC (multicentric ethics committee) the only notification is required (CTA form update); it is not classified as substantial amendment and reimbursement of costs for SUKL is not required. **Control visits** SUKL strongly recommends, if it is possible, a change of a physical follow-up visit of a trial subject in order to ensure the subject's safety or due to closed healthcare facilities or the Government's recommendation to restrict the movement of persons, to a telephone visit. The phone visit has to be documented with a rationale referring to the current situation. In case a

		follow-up visit is completely omitted, it has to be documented and thereafter evaluated in terms of its impact upon the validity and quality of data from the clinical trial. In case of a trial subject's visit to the trial site it is necessary to: Arrange for the visit beforehand by phone, so as to prevent any patient accumulation; dedicate specific time for healthcare staff to conduct follow-up visits – this should apply only to visits that are necessary and cannot be handled "online". Provide personal protective equipment for healthcare staff as well as for trial subjects; this is essential for immunosuppressed patients (such as patients on long-term corticosteroid therapy or on any immunosuppressive therapy, i.e. especially cancer patients and any post-transplantation patients).
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	The recommendations not to commence newly authorised CTs and not to enrol new trial subject (patients) in ongoing clinical trials does not apply to CTs in connection to COVID-19.

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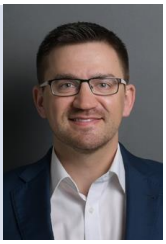

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Denmark

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	Yes, the **Danish Medicines Agency (LMS)** has updated its guidance as of 24 April 2020 concerning on-going clinical trials – available on the LMS website (in English and Danish). The guidance is subject to ongoing updates. The LMS expects that normal practices will be restored by 1 September 2020 (this date is subject to change with a 2 weeks prior notice). The guidance is based on the European guidelines, with little specific national derogation. Accelerated procedures for clinical trials related to COVID-19 (medicines) treatments have been set up by the **LMS** together with the **National Committee on Health Research Ethics (NVK)** and the underlying regional committees. **The Danish Data Protection Authority (Datatilsynet)** has not issued any updated guidance on this particular matter.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	There is no general prohibition of new trials in Denmark. However, the specific circumstances related to COVID-19 have to be taken into account, before starting the trial, i.e. consideration should be given as to how the current COVID-19 situation might affect the study's performance, including whether postponing the initiation of the trial is more appropriate. The LMS aims, as far as possible, to process all new non COVID-19 related CT applications within normal deadlines, so that the approval is in place and the CT can be initiated as soon as the situation has stabilised.
2b	**On suspension of ongoing CT's or recruitment stop?**	Yes. • There is no general recruitment stop for CTs due to COVID-19. However, the LMS Generally urge sponsors to assess whether the CT should be put on temporary halt – in which case authorities must be notified. • In regards to **First in Human (FiH) trials**, it is a requirement that there is an agreement in place with the intensive care unit, in the event that serious side effects should occur. The LMS foresees that such agreements cannot be ensured during the COVID-19 pandemic with proper contingency – it is therefore the LMS's general expectation that all FiH trials will be put on hold, i.e. recruitment for FiH trials should be haltered and new trials should not be initiated and, for ongoing trials, higher dose levels than already initiated should not be started. However, FiH trials involving critically ill patients without other treatment options may continue recruitment and dose escalation – on the condition that acceptance is obtained from the intensive care unit. The intensive care unit must be given a 1 day notice about changes in dosages and new trial subject should be informed of the risk that they will not receive IMP administration, due to lack of resources at the intensive care unit.
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	Yes. Generally the LMS refer to the European guidelines, however, there are certain Danish derogations. 6 The LMS recommend handling the following 2 types of changes due to COVID-19 as **"Urgent Safety Measures"** i.e. such changes can be

		implemented without (prior) approval from the LMS: 7 **Implementations made during COVID-19** (COVID-19 changes covered by the Danish Guidance) must be continuously logged in the Trial Master file, but notification hereof should only be submitted when the situation has stabilised (1 September 2020, this date might be delayed further by the LMS) a E.g. changes such as stopping inclusion at one or several sites (study halt), changes to the visit schedule and delivering medicine directly to participants is subject to the temporary (delayed) notification requirements. (This is a derogation, as the LMS should not be notified to the same extend as presented in the EU guidance) 8 **In case of other substantial changes**, which significantly impact the benefit-risk or the specific Danish guidance and its terms are not followed, **notification must be submitted within 7 days.** • If **substantial changes to patient safety or data integrity** occur without requiring immediate changes in the trial, these should be submitted in accordance with normal substantial amendment procedures (i.e. approval prior to implementation) – e.g. Remote SDV. The LMS does not consider addition of COVID-19 testing substantial and the LMS does not wish to be notified, if trial subjects are diagnosed with COVID-19. • **Acute shortage of IMP** without any substitution possibilities also trigger notification. Such notification must explain how safety is monitored for trial participants who are deprived of treatment. • **Premature termination of the trial** also trigger a notification requirement (in accordance with normal practice).
2d	**On informed consent (including re-consent, signature and dates etc.)**	No, there is no specific guidance in this respect. Participants will be informed about changes, however, the initial consent is considered to also cover the new COVID-19 initiatives. The LMS stress that communication to the trial subjects generally should be strengthened during the COVID-19 pandemic, as a means to accommodate for the uncertainty, increased levels of anxiety and concerns that follow the situation.
2e	**On distribution of IMP's (home delivery and storage), stock management**	Yes. In case of urgent shortage of IMP at some sites, the LMS acknowledge the need for re-distribution of IMP between sites in accordance with the GMP annex 13 (section 47). Sponsors should assess whether sites can handle and control redistribution and redistribution should follow a written procedure established in cooperation with the qualified person/person responsible for distribution. **Hand-out of IMP at on-site visits:** If on-site visits are required, but the frequency of visits is limited, it should be considered whether the trial participant can be given IMP for a longer period than normal. It should be considered for all trials whether the trial participants should have IMP handed out for a longer period than usual in the event of a deterioration of the current situation. However, it should be taken into account that certain marketed drugs are used in the treatment of COVID-19 and other critical illnesses. The primary concern is that no deficiencies arise, so that COVID-19 treatment is prevented.

		Hand-out of IMP at pharmacies: In open trials (it is not appropriate if IMP is blinded), the LMS is of the opinion that it may be an advantage to supply IMP through the Danish pharmacies, on the following terms: a This only applies to clinical trials on Danish sites during the COVID-19 pandemic and a risk assessment must be carried out with priority to patient safety. b The trial drug must be marketed and used within the approved indication (according to the SmPC). c A simple process for reimbursement of the expense should be implemented. d It must be ensured that the name of the sponsor or investor is printed on the label together with a reference code, that ensure identification of the site, investigator and trial subject. e There must be procedures in place at the investigator site to ensure that the IMP is accounted for (for compliance monitoring) **Temporary option to distribute directly to clinical trial subjects (temporary exemption from § 23 (2) of the GDP executive order due to COVID-19):** The LMS acknowledge that CTs may experience acute IMP shortages caused by COVID-19 related quarantines and cancellations of on-site visits. Considering the highly unusual circumstances, the LMS has temporarily opened up for sponsors to distribute trial medicine directly to the trial subjects without involving the investigator or hospital pharmacies. Sponsors choosing this option must adhere to 9 specific requirements listed on page 7-8 in the Danish Guidance. The temporary option is valid until 1 September 2020. The LMS will assess whether an extension is needed two weeks before expiry. **Trial subjects assigned to a Danish site but living abroad:** The LMS accepts delivery of IMPs to trial subjects, who are assigned to a Danish site, but staying abroad. However, the sponsor must consult the authorities of the country concerned, to clarify if they impose requirements or restrictions. **Stock of trial related medicinal products and medical devices** The LMS recommends that stocks of IMP and other necessary medicinal products (NIMP) are kept appropriately high to ensure continuity in the event of shortage. It is important, that it is taken into account that certain marketed drugs are used in the treatment of COVID-19 and other critical illnesses. The same applies for medical devices, including IVDs, which are used for safety/efficacy monitoring and other data collection.
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	Yes. The LMS acknowledge the need to adjust the monitoring and/or audit of CTs. The overall risk assessment should address any need for such changes and agreement with investigator sites on any changes should be obtained. Decisions should be driven based on patient safety considerations. Generally, the LMS urge the sponsor to assess whether the CT should be put on temporary halt – in which case authorities must be notified.

		On-site monitoring can be performed to the extent possible and agreed with investigator sites. If this is not possible to follow the on-site monitoring plan, monitoring should be supplemented with centralized monitoring and central review of data, if possible. Under certain conditions, **Remote SDV** is allowed in Denmark. The LMS and the Danish Data Protection Authority, Datatilsynet, have, in collaboration, set a number of conditions that must be met in order to establish Remote SDV, please refer to p. 4 of the Danish Guidelines for in depth explanation. The Sponsor has the overall responsibility to ensure GDPR compliance. The guidance list general conditions that must be met in conjunction with the conditions in one of the 3 different procedures outlining specific requirements, depending on the type remote SDV that is being established. The LMS only expect Remote SDV to be relevant for a limited number of CT. For non-commercial sponsors in Denmark, which are monitored by the Danish GCP-unites, other conditions apply, please refer to p. 5 of the Danish Guidelines for an in depth explanation. **On-site audits** should currently be avoided/postponed in order to not visit investigator sites unnecessarily. It should be considered in the sponsors risk assessment, whether remote audits and/or postponing audits is the preferred option. Onsite/remote audit should only be conducted after agreement with the investigator.
2g	**Are there other relevant aspects considered by the national guidance?**	The guidance is subject to ongoing assessment and potential changes. Therefore, it is recommended to observe the development on a very regular basis. Blood sampling and other diagnostics tests can be transferred to a local laboratory: There might be a need for blood sampling and other diagnostics tests to be performed locally due to changes to the visit schedule. The LMS accepts that blood sampling and other diagnostic tests are carried out at a local laboratory if it authorised/certified to perform such tests routinely and the facility has also implemented necessary COVID-19 precautions (to ensure COVID-19 containment). If the protocol uses a central lab for analysis,but it is not feasible for the sample to be shipped, then this should be clearly stated in the clinical study report in accordance with ICH E3 (Structure and content of clinical study reports). **Changes in visits or trial participants' affiliation to an investigator site:** The sponsor should consider whether there could be a need (in certain cases) **to transfer trial subjects from one site to another e.g. to new sites or existing sites in less affected areas**. In such cases, it is important that both trial subjects and both investigators (receiving and providing) agree on the transfer and that the receiving site has the possibility to access previously collected data/information from the trial subject and that any eCRF can be adjusted accordingly to allow the receiving site to enter new data. The sponsor (in cooperation with the principal investigator) should also consider **whether physical visits can be converted to phone visits, postponed or cancelled completely** to ensure that only strictly necessary

		visits take place. It may be considered to use electronic systems (video/telecommunications or electronic diaries) if it reliefs a burden from the trial staff – provided that the IT systems used are secure and valid. This consideration should also be part of the sponsor's risk assessment in relation to the COVID-19 pandemic. The LMS also urge to consider whether inclusion should be halted or even termination of the studies if, for example, the primary effect parameters of the study cannot be monitored on site or by using a local laboratory. Furthermore, in case it is not feasible for a site to continue participation at all, the sponsor should consider if the trial site should be terminated and how this can be done to best ensure patient safety and data validity. **Use of qualified and trained personnel to administer trial medications and conducting other diagnostic tests at the trial subject's residence:** The LMS recognise the increased need to collect blood tests, side effects, etc. at the trial subject's residence. Furthermore, it might be appropriate to administer IMP at the trial subject's residence with assistance from qualified and trained personnel. This is acceptable if carried out under the terms set in the EMA GCP Q&A (question 10), with certain additional changes under COVID-19. If an external supplier of the above mentioned service is used, the contractual conditions must comply with questions 11 and 12 in the same Q&A. Sponsor should facilitate this to the greatest extent possible during the COVID-19 pandemic. Please refer to p. 9 of the Danish Guidelines for in-depth explanation.
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	Yes. Accelerated procedures have been set up for CTs on COVID-19 treatments, which are given priority too. The modalities of submissions are specified on the LMS website here. The LMS recommend to make use of their check-list (to ensure all required documentation is provided for as a means to fast track the process). So far, the Danish Medicines Agency has approved CTs with camostat, remdesivir and tocilizumab.

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Finland

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	Yes, the **Finnish Medicines Agency (Fimea)** has issued a guideline concerning ongoing clinical trials in Finland during the COVID-19 pandemic. The guidance deals mainly with monitoring, deliveries of investigational products and payments for protocol amendments. It is available in English on Fimea's website.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	There are no specific measures or derogations on initiation of new clinical trials not related to COVID-19.
2b	**On suspension of ongoing CT's or recruitment stop?**	No
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	Yes, the **Finnish Medicines Agency** recommends avoiding such activities related to clinical trials which may potentially contribute to the spread of the virus.
2d	**On informed consent (including re-consent, signature and dates etc.)**	No, there is no specific guidance in this respect.
2e	**On distribution of IMP's (home delivery and storage), stock management**	Yes, in principle, home delivery directly from the sponsor is not permitted in Finland. During COVID-19, exceptional arrangements for the delivery of investigational products to the patient may be made. Such exceptional arrangements are required to be essential for ensuring: • the continuation of the clinical trial; • the safety of the subjects; and • the reliability of the research results. All exceptional arrangements require that the sponsor notify the Finnish Medicines Agency and submit a protocol amendment. The amendment must be accepted before deliveries can be made.
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	Yes, the **Finnish Medicines Agency** recommends to limit on-site monitoring to what is necessary and to utilise other monitoring methods. The sponsor must document these adjustments and submit a protocol amendment.
2g	**Are there other relevant aspects considered by the national guidance?**	The **Finnish Medicines Agency** refers to the website of the European Medicines Agency for more information.
3	**If the answer to Q1 is yes, are there specific procedures /**	No

recommendations concerning clinical trials in connection with COVID-19?

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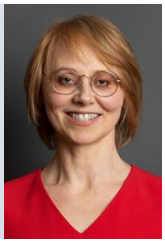

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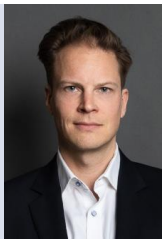

France

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	Yes, the **French Medicines Agency (ANSM)** has issued, together with the **Health Ministry**, **guidance concerning on-going clinical trials** - available here on the ANSM website in French and in English, first published on 20 March and last updated on 8 April. The ANSM guidance stresses that the measures mentioned in the guidance are exceptional and temporary. Accelerated procedures for **trials related to COVID-19 treatments** have been set up by the **ANSM together with the Ethics Committees and the Health Ministry**. The **French Data Protection Authority** (CNIL) also issued guidance in this respect – available here, in French only – (under French law, research on health data including in the context of clinical trials may be subject to an authorization from the DP Authority, in case the clinical trial does not meet the requirements of a so-called "*reference methodology*"). The CNIL gives priority to the review of authorization requests relating to research on COVID-19. Please note that the below explanations are a summary of the national guidance given by the authorities: some are subject to notifications, authorizations, and record keeping obligations etc. which are not all detailed in this table. There is also specific guidance on the ANSM website with respect to submissions to the ANSM for adaptations made to ongoing trials related to COVID-19.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	Yes. The ANSM guidance indicates that initiation of new CTs not related to COVID-19 remains possible, but stresses that the relevance of initiating new trials in the COVID-19 context must be assessed and that priority is given to trials related to the management of patients infected with COVID-19.
2b	**On suspension of ongoing CT's or recruitment stop?**	Yes. The ANSM stresses that the sponsor, in coordination with the investigators, should assess the risks of any changes considered to be made to the trial with regard to the safety of subjects and the integrity of the trial data, with priority being given to the safety of subjects. A risk assessment should be performed by the sponsor and should be made available upon request to the authorities. **Suspension of on-going CTs is possible but must be justified**. Priority must be given to patients with progressive, life-threatening pathologies. **Continuation of recruitments** may be considered in situations of unmet medical needs. Risks associated with the risk of concomitant COVID-19 infection need to be taken into account. **Suspension of recruitments** may be justified by the context of the study and/or the unavailability of teams (sponsor or investigators). *=> The ANSM and the Ethics Committee must be notified of recruitment suspensions (SM-I: Substantial modification for information, i.e. notification).* **Discontinuation of ongoing treatments** must be justified and assessed with regard to the clinical situation of each patient and associated risks. The risk assessment should consider the risks associated with interrupting

		treatment and those associated with continuing treatment in an epidemic context, as well as the strain on the research teams. *=> The ANSM and the Ethics Committee must be informed of recruitment suspensions (USM: Urgent Safety Measure followed by an SM-A: Substantial modification for authorisation).*
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	Yes. **Safety reporting – possible derogations to the normally applicable rules:** • The ANSM guidance indicates that i**t is possible to send annual safety reports** (DSUR for medicinal products) **without a handwritten signature,** notably a scanned signature or a simple mention in the email specifying the name of the person who validated the document. • The usual **deadline for submitting annual safety report (ASR) may be extended by a maximum period of 2 months** (the usual deadline for the submission is 2 months after the end of the period covered by the ASR). • **The meetings of the monitoring committees may be postponed** if it proves impossible to set up the planned meetings, after assessing the consequences for the safety of participants. **No derogation:** • To the contrary, there is no possible derogation to the **reporting of serious adverse events by the investigator to the sponsor** (they have to be reported immediately, except those mentioned in the protocol or in the brochure for the investigator as not requiring immediate notification). • **There is no possible derogation either for the declaration by the sponsor of SUSARs and for the immediate vigilance notifications**, which have to be done in compliance with the applicable regulations. **Scenario of a patient included in a trial and under treatment becoming infected with COVID-19:** The continuation or suspension of the investigational treatment should be decided by the investigator in coordination with the sponsor. The modalities for testing patients have to be in line with national recommendations. The 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 SUSA (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 in compliance with the applicable regulations.
2d	**On informed consent (including re-consent, signature and dates etc.)**	No, there is no specific guidance in this respect (only with respect of home delivery, see below).
2e	**On distribution of IMP's (home delivery and storage), stock management**	Yes. **The supply to patients of investigational products for longer durations is allowed – except for narcotics.** It has to be done in compliance with safety instructions, patient information and traceability. If visits during which the investigational medicinal products or devices should have been supplied 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.

		=> The ANSM must be notified (SM-I: Substantial modification for information, i.e. notification). **Delivery of investigational products to the patient's home is allowed,** in compliance with safety instructions, patient information and traceability requirements. *=> The ANSM must be informed (USM: Urgent Safety Measure followed by an SM-A: Substantial modification for authorisation).* This does not apply to non-self-administered investigational drugs (which would require a specific authorization). There is detailed guidance on home delivery (in French only – here). In summary: • The delivery of investigational products to the patient remains under the responsibility of the investigator and of the site's pharmacy. • The sponsor should provide support and notably pay for a specialised delivery service solution. • The sponsor should provide packaging and labelling material if requested by the site. • The sponsor should determine the delivery conditions ensuring the good storage of the product. • The data protection requirements of the GDPR, the French Data Protection Act and the French reference methodology MR-001 must be complied with – notably the subcontractor (processor) in charge of the delivery who has access to the identification data of the patient necessary for the purpose of the delivery should not get access to any health data of the patient. The patient must be informed by an information note (if the information has not been provided in the original ICF) of the processing of his personal data by the processor, in compliance with the requirements of the reference methodology MR-001.
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	Yes. Monitoring visits to trial sites are 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 subject to the availability of the research teams. The remote transmission of copies of medical records, even pseudonymised, is not authorised.
2g	**Are there other relevant aspects considered by the national guidance?**	Yes. **Change of trial site:** The trial site of a patient may be changed in order to unburden a site under strain or in order to reduce journeys, with the agreement of the patient and the investigators at both trial sites. Case report forms and all patient information must be transferred. The new trial site must be supplied accordingly. **Opening of new trial sites:** New trial sites may be opened in order to relieve others or to limit journeys for patients, following a simplified procedure. **Patient follow-up visits:** Patient follow-up visits may be adapted. 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, provided the necessary documentation is done, will not be considered as a major deviation that must be notified to the ANSM. Deviations will nevertheless have to be notified and evaluated in the final study report.
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	Yes. Accelerated procedures have been set up for trials on COVID-19 treatments, which are given priority to. The modalities of submissions are specified on the ANSM website here. The ANSM recalls that sponsors should contact the EMA as soon as possible with information about their proposed development and that the EMA provides a full fee waiver and a fast-track procedure for scientific advice.

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Germany

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	**The Association of Medical Ethics Committees** in Germany has published a guideline on potential effects of COVID-19 on Clinical Trials in Germany. The recommendations are based on the EMA Guideline and should be seen as a supplement. In addition, the **Federal Agency for Drugs and Medical Devices (BfArM)** has published information on potential Clinical Trials for medicinal products in connection with COVID-19 as well as information on ongoing Clinical Trials. *Please note that the below explanations are a summary of the national guidance given by the authorities: some are subject to notifications, authorizations, record keeping etc. which cannot all be detailed in this table.*
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	There is no general prohibition of new trials in Germany. However, the specific circumstances related to COVID-19 have to be taken into account.
2b	**On suspension of ongoing CT's or recruitment stop?**	Yes. • There is no general **recruitment stop** for Clinical Trials due to COVID-19. If a recruitment stop is imposed (for example due to the situation at the test site), this stop is generally non-required to be reported to the competent public authority, except where such a stop may have an impact on the safety of the participants (Sec. 13 par. 4 no. 4 German GCP-Ordinance (GCP-V)). • An **abortion or interruption of the clinical trial** must be reported within 15 days in accordance with § 13 Section 8 GCP-V, stating the reasons for the abortion or interruption. If an abort or interruption is made to avert immediate danger to the persons concerned, the sponsor can and must carry this out on his own responsibility in accordance with § 11 GCP-V. • A **final termination** of a clinical trial that is not due to safety reasons or lack of efficacy of one of the trial therapies requires careful ethical consideration
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	Yes • As a general rule, the BfArM emphasizes that all obligations in connection with safety reporting also apply during the pandemic. • However, if a trial subject reports a serious adverse event, the initial communication with the investigator may be by telephone. The Investigator then decides whether the subject must appear in person for security reasons e.g. to obtain further results. • If investigations within the framework of the trial protocol are to be conducted by telephone or video conference, this must be reported to the BfArM and the competent ethics committee.
2d	**On informed consent (including re-consent, signature and dates etc.)**	Yes. If there are changes to the protocol or if the IMP is delivered directly to the study subject, the relevant information must become part of an amended informed consent form.
2e	**On distribution of IMP's (home delivery and storage), stock management**	Yes. If it is required by the particular circumstances of the pandemic, it might permitted to deliver investigational products directly to the patient, if certain requirements are met:

		• Medical surveillance must be ensured in accordance with the provisions of the protocol. • It must be possible to electronically trace transport and delivery to the recipient. • The recipient must confirm reception (e.g. by returning an acknowledgement of receipt with signature and date). • In exceptional cases, the sponsor is allowed to deliver the IMP. In this event, the sponsor must appoint an external service provide and ensure that pseudonymisation and blinding are guaranteed. • If the IMP is delivered by an external service provider, a data processing agreement must be concluded. All data protection requirements of the GDPR, the Bundesdatenschutzgesetz (data protection law on the federal level) and the relevant local provisions on data protection must be observed. • The study subject must obtain all necessary information regarding use and safety of the IMP.
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	No.
2g	**Are there other relevant aspects considered by the national guidance?**	• GCP Courses for investigators in clinical trials will now be held as online courses. • The national guidance strongly recommends observing possible changes in the guidance on a daily basis.
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	Yes. • The BfArM is currently giving high priority to projects relating to the diagnosis and/or therapy of COVID-19. This concerns applications for scientific advisory procedures on drugs and medical devices as well as applications for the authorisation of clinical trials of drugs such as medical devices in the context of COVID-19. • On March 25, 2020, the BfArM granted an authorization to conduct a phase III clinical trial with hydroxychloroquine as investigational drug in the indication COVID-19. The study will include patients with mild to moderate COVID-19 disease in Germany. • On March 10, 2020, the BfArM granted approvals for the conduct of two phase III clinical trials with Remdesivir as investigational drug and the indication COVID-19. • In both studies, patients with severe or moderate COVID-19 disease in Germany are to be recruited and treated with Remdesivir.

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Hong Kong

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	No. Under Regulation 36B of the Pharmacy and Poisons Regulations, a Certificate for Clinical Trial/Medicinal Test (the certificate) is required for the purpose of conducting a clinical trial on human beings or a medicinal test on animals. This only applies to pharmaceutical products. Detailed application information can be found here: Department of Health: Drug Office - Drug Evaluation and Import/Export Control Division "Guidance Notes on the Application for Certificate for Clinical Trial/Medicinal Test"
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	N/A
2b	**On suspension of ongoing CT's or recruitment stop?**	N/A
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	N/A
2d	**On informed consent (including re-consent, signature and dates etc.)**	N/A
2e	**On distribution of IMP's (home delivery and storage), stock management**	N/A
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	N/A
2g	**Are there other relevant aspects considered by the national guidance?**	N/A
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	No No written guidance provided but the Drug Office will review any COVID related CTA urgently, although they had only received a few applications. The Drug Office said that there was no specific timeframe for review of COVID-19 related trials and that it would depend on whether the drug is a new or old drug, the phase of the trial, etc.

CTs also require an ethics committee approval.

We are aware of at least two trials involving remdesivir for COVID-19 being conducted at the University of Hong Kong Clinical Trials Centre and 3 Hong Kong hospitals. This was approved on an expedited basis by the Drug Office and the responsible ethics committees for the relevant Hospitals.

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Hungary

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	Yes, the **Hungarian National Institute of Pharmacy and Nutrition (OGYÉI)** has issued an information material on the continuity of clinical trials under COVID-19 (Coronavirus) - available on the OGYÉI website in Hungarian and English. The recommendations are based on the EMA Guideline and it can only be interpreted together with the European guidance document. The OGYÉI stresses that continuity of clinical trials must be provided especially for those patients for whom the continuation of the treatment is especially important (e.g. oncology patients). The **Hungarian Data Protection Authority** (NAIH) also issued a general guidance regarding COVID-19 data processing – available in Hungarian and English. The NAIH specifies the legal ground and other circumstances of the COVID-19 related data processing activities for health care providers (including those engaged in performing clinical trials). The **Hungarian Government** issued Governmental Decree no. 63/2020. (III. 24.) on measures related to clinical trials in the times of COVID-19 pandemic (available only in Hungarian). According to this Decree, the communication with the patients can be done via telecommunication devices. Please note that the below explanations are a summary of the national guidance given by the authorities: some are subject to notifications, authorizations, record keeping etc. which cannot all be detailed in this table.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	Yes. The OGYÉI guidance indicates that initiation of new CTs not related to COVID-19 remains possible, but OGYÉI is ready to make accelerated assessment in case of submissions of COVID-19 clinical trial applications. The new clinical trial applications and substantial amendment requests should be sent to the OGYÉI online client portal. In the current crisis situation, the Medical Research Council - Ethics Committee for Clinical Pharmacology (MRC – ECCP) cannot ensure the proper issuance of official position statements, but they bear full responsibility for their content.
2b	**On suspension of ongoing CT's or recruitment stop?**	Yes. **Suspension of on-going CT's:** The OGYÉI stresses that a thorough risk assessment of ongoing investigations should be carried out considering restrictions already applied and expected (quarantine, visitation ban in healthcare institutions, etc.) and measures should prioritise patient safety and data validation. In the event of conflict between these two objectives, patient safety should be prioritised. The OGYÉI stresses that continuity of clinical trials must be provided especially for those patients for whom the continuation of the treatment is especially important (e.g. oncology patients). Suspensions are possible but must be specified and justified. The sponsor should make a decision to suspend the trial or terminate it if it is impossible to continue the study at the test site or at a new location. This decision shall be documented. The OGYÉI should be

		informed about this decision subsequently indicating the reasons and the exact date of suspension / termination. **Recruitment continuation / recruitment stops:** Though it is not prohibited, but in general, it is considered prudent by the OGYÉI to stop the enrolment of patients during this period. In case of temporary stop of recruitment due to COVID-19, reporting this fact to the OGYÉI is sufficient and the restart of recruitment is not considered as a substantial amendment either (therefore reporting this fact is also sufficient). Reports can be sent in one letter to the OGYÉI even in case of more clinical trials.
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	Yes. A thorough risk assessment should be carried out of all ongoing investigations considering the special circumstances (quarantine, visitation ban etc.), and measures should be put in place to prioritise patient safety and data validation. In the event of conflict between these two objectives, patient safety should be prioritised. All decisions must follow ICH GCP and EU and Hungarian legislation. Patient safety is the top priority, thus, any and all changes in trials should be based on a thorough risk assessment. The risk assessment shall be repeated and properly documented if there is any evolution in the situation. Any deviation from current practice should be proportionate, verifiable and clearly documented. Changes to trial conduct should be agreed with and communicated clearly to investigational sites. To support implementation by sites, it is important that changes and local implications are made clear, including marking of changed documents with track changes. In cases when obtaining wet ink signature is difficult, agreements may be documented with alternative methods e.g. e-mail exchange. During the transition period, the number of protocol deviations may increase. All protocol deviations must be clearly documented. The authorities will take a fair approach when reviewing deviations if they are in the interests of participants and do not expose them to undue risk. In case of ongoing studies with populations particularly at risk of coronavirus (immunosuppressant treatment, over 60 years of age, chronic diseases), special considerations should be made regarding the continuation of the study. However, in general, it is considered prudent to stop the enrolment of patients during this period.
2d	**On informed consent (including re-consent, signature and dates etc.)**	Yes. In case of ongoing clinical trials, a new informed consent form may be necessary, and patients may have to be re-informed. According to Government Decree no. 63/2020. (III. 24.), the patients may be informed and may give their informed consent by telecommunications services as well, in a way that is traceable and recordable. The OGYEI's position is that alternative methods for this re-information should be considered, e.g. contacting enrolled patients via telephone or video call, and obtaining oral consent followed by email confirmation. However, each consent obtained this way has to be documented properly later on: they must be confirmed by patients with wet-ink signatures as soon as possible (i.e., when attending the site again). However, please note that in line with the standing practice and legal provisions, the patient information sheets and informed consent forms cannot be obtained electronically.

2e	**On distribution of IMP's (home delivery and storage), stock management**	Yes. During the special circumstances caused by COVID-19, the **transfer of IMPs between sites, the patient's increased supply with IMPs during on-site visits, or the dispatch of IMP from the site to the patient's home may arise.** **In case of clinical trials where the patient self-administers the medication at home, the home delivery of IMPs (and non-IMP rescue medications) is possible.** The PI is responsible for the home delivery. Home delivery of IMPs from the site or the institution pharmacy is preferred. The person who performs the home delivery must know the relevant rules for handling such IMP, and if there are any special storage conditions, they must be documented at all times. (However it is not necessary to inform the OGYEI on the special conditions/changes.) All transitional measures in connection with the distribution of an IMP must be designed in a way to ensure: • that he prescribed delivery and storage conditions of the product are met; • the safe custody of preparations; and • the relevant documentation for accounting with the IMPs. To avoid IMP/non-IMP shortage, adequate supply maintenance is recommended for those cases when transportation of IMPs to investigation sites is faced with difficulties. Direct IMP delivery from sponsor to trial participant's home is not accepted as sensitive data may be revealed.
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	Yes. In order to reduce on-site monitoring, appropriate alternative methods should be selected. The choice of alternative monitoring methods shall take into account that they do not place a disproportionate burden on the test site and staff. Remote and central monitoring through an EDC system may be an appropriate alternative, although its scope is limited. Sharing of patient data and the remote access of the Sponsor's representative to the electronic database of healthcare institutions is not acceptable. After the normalisation of the situation proper follow-up should be carried out in relation to these transitional measures.
2g	**Are there other relevant aspects considered by the national guidance?**	**Change of trial site / principal investigator:** If the epidemiological situation subsequently so requires, consideration should be given to the transfer of subjects to existing or new test sites. Such relocation may only be carried out with the agreement of the subjects and the principal investigators (transfer and host), by appropriately transferring the eCRF to ensure that the new test site has access to all information and previously collected data, and to record new data. The relocation agreement should be documented in the TMF (e.g. by e-mail). If any site moves to another settlement of the institution, or other health care institution due to the evolved crisis, and there the study is continued, the OGYÉI only needs to be informed subsequently giving the exact dates of the address change. There is also an opportunity for the investigator to move the patient care to a private clinic that has not been marked as a satellite-site before, but the OGYÉI and the MRC – ECCP needs to be informed, and subsequently this needs to be submitted as an amendment. In every case, when the principal investigators cannot complete their tasks due to protective measures or illnesses, the sub-investigator

		previously delegated to the study can take over their role. **Critical laboratory tests** The performance of critical laboratory tests, imaging procedures or other diagnostic tests may be needed for patient safety. If the participant cannot attend the site, then it is acceptable to perform the laboratory, imaging or other diagnostic procedures in accredited local laboratories, taking the epidemiological restrictions into account. The site needs to inform the sponsor about the change. The examinations carried out in the local laboratory can be used for decisions regarding patient safety. If laboratory tests serve as endpoints in the trial, and biological samples cannot be transported to the central laboratory, this fact must be documented in the Clinical Study Report at the evaluation of the results, according to ICH E3. **Patient follow-up visits:** Sponsor, in agreement with the PI, shall consider converting or deferring on-site visits to telephone visits or terminating them on the basis of the risk assessment, in order to ensure that it is strictly necessary visit to the test sites. Currently, the OGYÉI does not support visits carried out at the patient's home, because of its limited availability, its negative effect on the spread of the virus, and the disproportionate burden of the investigational staff.
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	Yes (limited). The OGYÉI guidance indicates that OGYÉI is ready to make accelerated assessment in case of submissions of COVID-19 clinical trial applications. Otherwise, there is no particular difference between the recommendations for COVID related and non-COVID related clinical trials.

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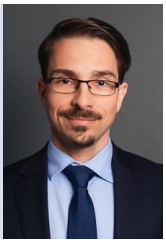

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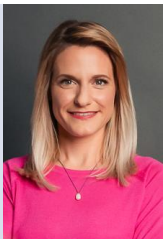

Italy

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	Yes, the **Italian Medicines Agency (AIFA)** has issued guidance concerning both conduction of ongoing trials and simplified procedures for COVID-19 clinical trials and compassionate use (available here). The mentioned measures are exceptional and temporary due to the health emergency.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	There is no general prohibition of new trials in Italy. However, the specific circumstances related to COVID-19 have to be taken into account.
2b	**On suspension of ongoing CT's or recruitment stop?**	Yes. There is not a general suspension of on-going CT's due to COVID-19. In principle, the intent is to provide some guidelines able to guarantee the continuing of trials assuring the highest protection of people involved. In this sense, to avoid any possible infections due to hospitalization is recommended, whether possible, to adopt measures able to manage the trial activities outside of the hospitals (e.g. if possible, providing the trial drugs directly to patients or patients' homes; home assistance to patients and so on). Whether the site is closed to the public for COVID-19 containment measures, and the clinical trial staff is not able to guarantee the continuity of the trial itself, the study should be temporarily halted or, where possible, enrolled patients should be transferred to the nearest active trial site. The transfer of clinical trial can be made only in favour of sites already authorized for the relevant clinical trial. In such case, shall be assured the information exchange between PIs, as well as the transmission of clinical documentation and other trial material (e.g. IMPs) between sites. Contacts between Sponsor and health structures involved shall be updated according to new agreements. Anyway, in case it is not possible to adopt the necessary measures to avoid possible infections, may be considered the suspension of the trial by the risks valuation and/or unavailability of teams (sponsor or investigators). Regarding the recruitment of new patients, the inclusion and enrolment of new patients should be avoided as much as possible except for those cases whose participation in the study is of fundamental necessity, as in the absence of a valid therapeutic alternative, or in cases of enrolment in COVID-19 clinical trial. In the event that the Sponsor temporarily suspends enrolment and / or treatment in a clinical trial, to comply with the measures in place due to COVID-19, it will be necessary to notify a substantial amendment to the Ethics Committees of the centres involved (regardless of their activation) both when the measurement is

		introduced and when the measurement is cancelled.
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	Yes. As a general rule, because there is not a specific exemption, all the provisions related to with safety reporting shall apply. Anyway, Sponsors / CRO are invited, taking into account the indications contained under the Decree issued by the Italian government (so called DPCM) concerning urgent measures to be taken for the purpose of the containment and management of the pandemic emergency from COVID-19 and the specific Ordinances of the different Regions, to draw up an evaluation plan for the risk and to implement an action plan proportionate to the risk, in the pre-eminent protection of the clinical trial participants, with the purpose to minimize the contacts between participants and investigators, staff and also in order not to overload the healthcare facilities. The Sponsors are also invited to inform the trial centres and to agree with them timely about all the alternative measures, related to the contingent situation, adopted for the management of the participants. Whether compatible, may be considered the carrying out of procedures directly at the participants' home, carried out by the staff of the trial centre or by third parties. These home health care activities can include both clinical procedures that cannot be carried out otherwise (e.g. collection of adverse events, vital signs, etc.), and the administration of non-self-administered therapies (e.g. infusions).
2d	**On informed consent (including re-consent, signature and dates etc.)**	Yes. Whether is necessary to obtain an informed consent (activation of new studies or, amendment to the informed consent for studies already started or for the implementation of emergency measures or simply to avoid exchanges of paper material possible source of infection), in case is not possible the standard method (that is preferred), shall be considered alternative procedures for obtaining it. The implementation of these alternative procedures (telephone contacts, followed by confirmation e-mails or validated electronic systems) does not exempt from obtaining written consent as soon as the situation permits, on the first occasion in which the participants will be at the site. Whether the patients are in isolation is possible to use cameras or photographs of the documentation taken through the transparent isolation barriers. In the case of temporary verbal consent, the presence of an impartial witness who certifies the successful administration of the consent and affixes the date and signature on the informed consent document is required. The investigator shall certify the method of selection of the impartial witness. In any case, the rules in relation to the processing of personal data shall remain in force, especially those related to the acquisition of consent to the processing of data carried out in the context of clinical trials. According to the principle of accountability, the data controllers are required to identify suitable measures and prove the successful acquisition of a valid consent to the processing of personal data (e.g. through the voice recording of the telephone consent or the retention of the email).
2e	**On distribution of IMP's (home delivery and storage), stock management**	Yes. The delivery of investigational products for a longer period of time is recommended. The investigational products could be delivered to participants' relatives or other person designed by the participants (e.g. caregivers).

		As well as, considering the COVID-19 serious emergency, the investigational products could be directly delivered from the hospital pharmacy to the trial participants also through dedicated delivery, upon indications of both the hospital pharmacy Director and the Principal Investigator (PI). In such case, the hospital pharmacy is responsible for the process supervision; the pharmacy and the PI shall be constantly informed on the delivery, according to procedures established for the correct conduction of the trial and by the risk plan that must take into account the IMP typology, administration methods, conservation and transport. As well as, where the Sponsor / CRO has already identified or has an authorized warehouse, where the drug is stored, may be considered the direct delivery by the warehouse to the trial participant. In such case, shall be implemented procedures able to guarantee the control and traceability of delivery (including transport conditions and specific agreements with the trial centres). Shall be implemented adequate remote communication methods with involved trial participants able to replace the information that will no longer be provided in person. Depending on the case, telephone and/or video call can be used to inform the patient, where deemed necessary. Adequate tracking of what is being implemented in this emergency situation is recommended. If the CRA of the study is not able to carry out the control on the final accounting of the investigational medicinal product for the purpose of reconciliation, and this operation is considered as impossible to be postponed, it can be carried out by a pharmacist of the hospital pharmacy or by the study coordinator/data manager, appropriately trained. The IMP can be returned to the Sponsor directly by the hospital pharmacy.
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	Yes. Sponsors are invited to draw up a risk evaluation plan and implement an action plan taking into account the need to reduce unnecessary contacts in this period of COVID-19 epidemiological emergency. First of all, it should be assessed whether in-situ monitoring visits can be replaced by an enhanced centralized monitoring or whether such local visits can be postponed. Exceptional methods such as telephone contacts or, even better, videoconferences with the trial site staff can be implemented for the purpose of source data verification. These methods must be described in a specific SOP by the Sponsor/CRO and must be evaluated and approved by the Personal Data Protection Officer of the trial site. Other unusual monitoring methods involving more risky ways of accessing sensitive data, such as video recording of source document or making available to monitors original documents in shared electronic areas, must always be agreed with the Personal Data Protection Officer of the hospital, but it is considered appropriate that a specific opinion by the Italian Data Protection Authority be obtained.
2g	**Are there other relevant aspects considered by the national guidance?**	**Clinical tests** Clinical tests shall be performed in laboratories near to the patient's home, preferably in public health structures or private structure authorized pursuant to the Ministerial Decree March. 19th 1998 or private labs auto certified pursuant to AIFA decision n. 809/2015. The use of private sites, not recognized eligible pursuant to the Ministerial Decree of 19th March 1998, shall be considered only in the case it represents the unique possibility for the participant's protection; the use of such data shall be explained in the study report.

		Possibility of exceptional expenses reimbursement Taking into account the exceptional situation, if, in order to implement urgent measures for the protection of clinical trial participants, expenses are foreseen to be charged to them, the Sponsor/CRO is allowed to reimburse such expenses to the Clinical trial participants, upon appropriate supporting documentation, the receipts issued by external structures must clearly indicate the protocol code or the EudraCT number of the study. In order to avoid direct contacts between participants and Sponsor/CRO, the preferred method would be the dispatch of receipts or the delivery (when possible) by the participants to the trial site which will, through its administration, invoice this amount to the Sponsor / CRO that will provide to reimburse expenses.
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	Yes. According with the Article 17 of Legislative Decree n. 18/2020, in derogation to the standard procedure, COVID-19 clinical trials shall be: • preliminarily evaluated by AIFA Scientific Technical Commission ("CTS") and Clinical Trial Office; • evaluated by National Ethic Committee of Spallanzani Hospital ("*Comitato etico nazionale dell'INMI Spallanzani*") located in Rome; • approved by AIFA. Accelerated procedures have been set up for trials on COVID-19 treatments, which are given priority to. The modalities of submissions are specified on AIFA website (see link provided in Q1). The submission can be done both by mail, email and by OsSC platform (that is the preferred option). The COVID-19 Clinical trials already approved are published here.

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Netherlands

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	Yes, the **Dutch Central Committee on Research Involving Human Subject** (**CCMO**) has published recommendations in English for the conduct of clinical research at the time of restrictive measures due to the coronavirus and are applicable both with the CCMO as with the MRECs. These recommendations are based on the EMA Guidelines and should be seen as a supplement. The **Ministry of Infrastructure and Water Management** (**IenW**) has implemented an emergency regulation (in Dutch) to accelerate the authorisation procedure for research into gene therapy or a medicinal product containing a genetically modified organism (GMO), that is aimed at combating COVID-19. This has been repealed as a result of Regulation 2020/1043 (press release in English). For the time being no GMO license is required for clinical research on COVID-19. Accelerated procedures (fast track) review of COVID-19 treatments has also been set up by the CCMO and the MRECs. Please note that the below explanations are a summary of the national guidance given by the authorities: some are subject to notifications, authorizations, record keeping etc. which cannot all be detailed in this table. Also everything is subject to change.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	Yes. • As a sponsor or investigator, you should consider whether the clinical research, or parts of the clinical research, can be temporarily halted or not; • Set up a risk analysis on the consequences of the coronavirus on the conduct of the clinical research, whereby the safety of the participants is paramount; • The obligation to submit a cover letter with a wet signature for initial applications and substantial amendments to the review committee and/or the competent authority has been suspended. Instead, a digital or scanned signature of the applicant is sufficient. **Restart and start clinical trials** • The restart of clinical research after it was fully or partially suspended due to COVID-19, has to be notified to the review committee and in case of a clinical trial with an investigational medicinal product to the competent authority as well. The start or restart of the clinical research is subject to conditions as stated below. • Prior approval from the review committee for restarting the trial is required when the restart of the clinical research involves substantial modifications. In the case of a substantial amendment to a clinical trial with an investigational medicinal product, a "statement of no ground for non-acceptance" must also be issued by the competent authority. The Dutch Health and Youth Care Inspectorate published amended recommendations on 25 August 2020, subject to change, relating to clinical trials that fall within the scope of the WMO (available in English). • The research location/institution in charge of the start or restart of the clinical trial should base the start or restart on institutional policy • The principal investigator revises and evaluates, with or without the collaboration of the head of the department, the study specific risk analysis and documents the process • Upon starting or restarting of the clinical trial, the burden to provide

		supportive services and the regular flow of patients should be taken into account. The basic principle is that this does not are hardly leads to any extra movement of patients. In addition, the consequences of potential downscaling due to an increase, whether or not local, of COVID-19 infections should be considered • The rights, safety and wellbeing of trial participants, other patients and staff at the research location/institution prevails • The start or restart should be approved by the management • An overall risk analysis should be performed and evaluated at the institutional level, in order to demonstrate the central oversight of the impact on ongoing and new clinical trials. A positive outcome is a prerequisite for a possible start or restart of a clinical trial or group of clinical trials. In case of consecutively starting or restarting clinical trials, the new situation should be the starting point • To ensure central oversight, the board of directors of the health care or research institution, or another body mandated to do so, should approve the start or restart of the clinical trials in writing while taking into account that continuity of regular health care by the institution is ensured and interference with the necessary care for COVID-19 patients is avoided • The start or restart of a clinical trial without substantial changes, meaning changes that might have a substantial effect on either the safety or the rights of the trial participants or the reliability and robustness of the research data, compared to a previously approved research file, should be submitted as a notification to the medical research ethics committee (MREC) and the competent authority • Also, the start or restart of a clinical trial that does not involve substantial changes to the research file should be submitted, following the procedure in force, for review and approval by the MREC and the competent authority.
2b	**On suspension of ongoing CT's or recruitment stop?**	Yes. **Suspension/termination clinical trial** • If the trial is (partially) suspended, for reasons of subject safety, this must be reported immediately to the review committee; a temporary halt for other reasons should be reported within 15 days; • If the study is terminated prematurely, this must be reported to the review committee as soon as possible, but at the latest within 15 days.
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	Yes. • As a general rule the CCMO emphasises that the procedure for notifications to the Dutch competent authority both during and after the study has not been changed. In addition, the competent authority will not send a confirmation of receipt for a temporary halt and restart of the trial. Also, in contrast to the normal situation, a 'declaration of no objection' will not be send for this type of notification during the COVID-19 pandemic; • The procedure for submitting a substantial amendment to the review committee has not been changed. If it concerns an amendment which has an impact on the safety of research subjects and requires a fast-track assessment procedure given the emergency of the situation, you are advised to contact the review committee about the procedure to be followed; • Record all deviations from the protocol and the standard procedure in writing; unless the subject's safety is at stake, these protocol deviations need not be submitted to the review committee; • A deviation from the protocol or a protocol modification due to urgent safety measures to eliminate immediate hazards to the subject can take place without prior approval by the review committee. However, this must be reported immediately to the review committee.

		• The CCMO does not consider logistical changes (e.g. telephone visits instead of physical visits, adjustments to scheduled visits), the direct delivery of investigational medicinal products to the trial participant and changes to the monitor plan (e.g. remote monitoring or remote SDV) as a substantial amendment which needs to be approved by the review committee.
2d	**On informed consent (including re-consent, signature and dates etc.)**	Yes. In case a subject is unable to provide (re)consent to (continue to) participate in a clinical trial in an emergency situation, obtaining consent can be deferred under specific conditions. The applicable conditions for such a deferred consent are described in the CCMO memorandum with flow chart Deferred Consent (in Dutch). To be able to use the possibility of deferred consent it is mandatory to obtain approval by the review committee (MREC/CCMO). The information concerning the fast-track procedure for the review of the deferred consent procedure can be found here
2e	**On distribution of IMP's (home delivery and storage), stock management**	Yes. • Study medication can be send directly to the research subject by courier from the (hospital) pharmacy for reasons of subject safety. • Study medication can be send by a hospital pharmacy to a public pharmacy under the following requirements (in Dutch here): – The requesting pharmacy must request the medicines in writing – The pharmacy must be able to prove receipt and subsequent dispensation – The supplying pharmacy must also keep comprehensive records – The pharmacies must organise transport of the medicines in such a way that the product remains of good quality • It is not required to inform the review committee about this, but do record this temporary procedure in writing. Consent by trial participants for using personal information and sharing this information with the mentioned parties is obligatory for sending IMP. Consent may be given orally and should be documented and confirmed by the trial participant via email if possible. Obtaining written consent retrospectively is not required. • It is not allowed that the investigator sends study medication to the trial participants.
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	Yes On-site monitoring will not or is barely possible **Remote source data verification** is allowed under strict conditions and for a limited group of clinical trials. The Dutch Health and Youth Care Inspectorate stresses that it does not give consent for remote source data verification for clinical trials in general. According the European guideline the clinical trials is: – COVID-19 related; – Relates to a serious illness for which there are not appropriate treatment options; or – At a stage where it might result in a delay of registration of the medicinal product. It is only permitted on the basis of the outcome of the assessment of a risk analysis per clinical trial, including the motivation of the critical data that should be verified. The health and safety of subjects should be paramount. **Direct remote access electronic health record** is temporarily, during the COVID – 19 situation, and under certain conditions allowed for data verification of critical data that is relevant for clinical trials by

		monitors/CRA's. This should preferably take place from the office and subject to the following preconditions and/or restrictions: – From a special, access-controlled room (1 person, logged etc.); – With a logged PC or laptop (who, what, when); – In advance a screenshot or short video impression (not during access to the electronic health record) of the setup (office and/or home situation); – No recordings (video, screenshot, screen-capture) are made in any way. In addition, the functionality to do this must be disabled; – Adequate documentation. The agreed method and conditions have been recorded and confirmed in writing. The Dutch Health and Youth Care Inspectorate prefers, if possible (depending on safety, technical possibilities, load on the research team etc.) the remote source data verification under the direction of the hospital or research centre. This means that the monitor or CRA is given access to the electronic health record and/or other relevant source documents by reading along with on the screen of the person in the hospital or research centre. The platform to be used must be safe and usable by both parties (guidance on privacy aspects of video calling is published by the Dutch Data Protection Authority, in Dutch). If this method is not possible due to the work load of the hospital and or research centre, direct remote access to the electronic health record by the monitor or CRA may be an alternative. Access to the electronic health record should be assigned by name and function (it is not allowed to use accounts that are already in use). In general, the following should be taken into account: – The monitor or CRA shall only have access to the electronic health records of participants and only to those parts that are necessary to verify the critical data. It should be fully and correctly reasoned and documented what data has been identified as critical data and to which data access is therefore necessary. Access to more than the critical data must be substantiated. Unauthorized access to more than the documented critical data is identified as a data breach and must be reported as such to the Dutch DPA. – For each clinical trial, it is determined which monitor or CRA has access to the electronic health record and to which ones. The number of monitors or CRA's is kept to an absolute minimum. – Participants are informed in advance about the remote access to the electronic health record by means of an updated Subject Information Sheet and can refuse or revoke consent if they wish. – Data verification is not allowed using copies from the medical records. – It is also not allowed for source data to be read out.
2g	**Are there other relevant aspects considered by the national guidance?**	Along with CCMO, a number of accredited MRECs have also set up fast track procedures for the accelerated review of research files on the occurrence and/or treatment of COVID-19 (link).
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	Yes. An accelerated review (fast-track procedure) of research files concerning studies on COVID-19 are allowed by the CCMO. The procedure can be found on the website of the CCMO (in English). In addition, MRECs and the competent authority have set up fast-track procedures for the accelerated review of research into the occurrence and/or treatment of COVID-19.

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Poland

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	Yes, Polish **Office for Registration of Medicinal Products, Medical Devices and Biocidal Products (URPL)** has issues a short guideline of 19 March 2020 on clinical trials conducted during the pandemic – available in Polish here. The industry has also issued a non-binding Good practice for CTs during the COVID-19 epidemic – available here. The document was prepared by POLCRO, GCPpl oraz INFARMA. This Good practice may be helpful, since it is much more detailed than the official URPL's guideline. However, since it is not issued by the authority nor has it been officially endorsed by the URPL, we do not describe it in this below report.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	The guideline includes a general recommendation to "consider the appropriateness of submitting, in the present situation, new applications for the commencement of a clinical trial of the medicinal product and applications for authorization to conduct a clinical trial of a medical device." Therefore, initiation of new CTs remains possible, but current extraordinary circumstances should be considered.
2b	**On suspension of ongoing CT's or recruitment stop?**	Yes. The URPL stresses that the efforts of healthcare providers are currently focused on COVID-19. Ongoing CTs should carry out a risk assessment taking into account current epidemic situation. If necessary to ensure the safety of subjects, it is possible to make modifications, suspend or abort ongoing CTs. Such decision must be immediately reported to the URPL and a relevant bioethics committee, but the procedure is less formal than in ordinary circumstances and it is possible to submit the notification by e-mail.
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	No
2d	**On informed consent (including re-consent, signature and dates etc.)**	No
2e	**On distribution of IMP's (home delivery and storage), stock management**	No
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	No
2g	**Are there other relevant aspects considered by the national guidance?**	No

3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	No

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Singapore

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	Yes, the Health Sciences Authority of Singapore ("HSA") has issued guidance concerning the conduct of ongoing clinical trials during COVID-19, available here There are no regulations issued specifically with respect to clinical trials in connection with COVID-19. Please note that the below explanations are a summary of the national guidance given by the authorities: some are subject to notifications, authorizations, record keeping etc. which cannot all be detailed in this table.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	There is no general prohibition of new trials in Singapore. However, the specific circumstances related to COVID-19 have to be taken into account.
2b	**On suspension of ongoing CT's or recruitment stop?**	Yes. While it is not mandatory to temporarily suspend screening and recruitment for CTs, the sponsor may decide to do so and must notify HSA by submitting a Trial Status Report within 15 calendar days of the temporary suspension.
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	Yes. • As a general rule, **ensuring the safety and well-being of participants in CTs is paramount**. Sponsors and investigators are advised to consider the specific context and circumstances of each clinical trial, and focus on the potential impact on the safety and well-being of trial participants, when considering potential modifications to trial conduct during the COVID-19 season. • When implementing contingency measures for CTs in relation to the COVID-19 situation, sponsors of CTs are advised to take into account:- – The availability and feasibility of alternative methods for appropriate efficacy and safety monitoring of trial participants; – Whether the alternative methods for safety monitoring and assessment would be sufficient to assure the safety of trial participants; – The ability to appropriately manage adverse events/toxicity and/or to implement dose modifications or discontinuations in accordance with the protocol in a timely manner; and – Where there are compelling reasons for certain efficacy and safety assessment not to be completed, to use the best medical judgement in weighing the benefits and risks of continuing treatment in the absence of such study assessments. • Investigators are advised to review the results of all remote study visits promptly and **contact trial participants to follow up laboratory results, adverse events and concomitant medications in order to assess trial participant safety**. • 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**. • Sponsors should **notify HSA** about the following **prior to**

		implementation:- – Remote monitoring protocols – Remote study visits – Supply of the investigational product directly to patient's homes to be self-administered • In the event that contingency measures need to be implemented urgently for the safety of trial participants in relation to the COVID-19 situation, sponsors may consider implementing these measures as **Urgent Safety Measures**. Sponsors should **notify the HSA as soon as possible, and no later than 7 calendar days** from the implementation of the Urgent Safety Measure. • If contingency measures have to be implemented that constitute a substantial amendment for the purposes of the regulatory guidance *Determining Whether an Amendment to a Clinical Trial is a Substantial Amendment*, sponsors should **submit the substantial amendments for HSA's review and approval**.
2d	**On informed consent (including re-consent, signature and dates etc.)**	Yes. Sponsors of clinical trials where remote study visits are conducted are advised to assess if the protocol and/or the informed consent form should be amended, and if so to submit a substantial amendment for HSA's review and approval.
2e	**On distribution of IMP's (home delivery and storage), stock management**	Yes. If the sponsors and investigators determine that the investigational product ("**IP**") can be safety and properly self-administered by trial participants without the supervision of the investigator and/or study team, the sponsor can arrange for a **Direct to Patient service** ("**DTP**") for the IP to be delivered directly to participant's homes. Further guidance on DTP delivery may be found here. • HSA must be notified about the DTP prior to implementation. • The investigator must maintain oversight of the IP delivery to trial participants, since the investigator is ultimately responsible for the medical treatment and care of trial participants. • The IP must be supplied directly from the trial site to the patient's homes. Use of any alternative location will require the sponsor to submit to HSA details on additional measures to safeguard trial participant privacy and data confidentiality, before implementing this plan. • For early phase clinical trials where there is limited experience with the dose level being tested and safety of the dose level is still being assessed, it is generally not recommended to send more than 1 cycle/visit of IP to trial participants. If there is an intention to do so, HSA must be informed and consulted. • Sponsors and investigators should take into account the following when deciding to implement DTP services:- – Provide written instructions to trial sites on handling and storage of the IP when using DTP services; – Inform trial participants about the DTP service. The information may be conveyed to trial participants verbally and documented in the trial participants' medical records; – Ensure the IP is delivered to trial participants' homes within the recommended storage temperature for the IP and in a secured manner; – Consider viable alternatives in the event the trial participant / trial participant's legal representative is unable to receive the IP personally at home; – Provide written instructions to trial participants on using the IP and contact

		details of the study staff for any enquiries. The investigators should ensure that trial participants use the delivered IP correctly in accordance with the protocol; – Ensure traceability throughout the IP supply chain; – Maintain documentation relating to shipment, receipt, storage, dispensing and accountability, return and destruction; – Ensure that trial participant privacy and data confidentiality are safeguarded; and – Ensure that treatment blinding is not compromised by the DTP approach.
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	Yes. **<u>Remote Monitoring Protocols</u>** **Sponsors should assess if on-site monitoring plans should be adjusted to centralised monitoring or remote monitoring** in light of the COVID-19 situation. • HSA must be notified about the implementation of remote monitoring protocols prior to implementation. • Sponsors should obtain written agreement from the trial sites prior to implementation of remote monitoring. • Sponsors and investigators should take into account the following to safeguard trial participant privacy and data confidentiality during remote monitoring:- – All trial participant identifiers should be removed from the source documents prior to transmission, and replaced with trial participant ID; – The site staff should implement a quality control process to verify that trial participant identifiers have been removed for every redacted source document being transmitted; – The redacted source documents should be transmitted in a secure manner to the monitor; – The transmission and receipt of the redacted source documents should be documented; – The sponsor should implement a quality control process to verify that trial participant privacy and data confidentiality have been safeguarded in the redacted source document; – The monitor should re-verify the data from the corresponding source documents during the subsequent on-site monitoring visits; and – The monitor should destroy the redacted source documents and document the destruction. **<u>Remote Site Visits</u>** **Sponsors may consider alternative methods should trial participants be unable to return to the trial sites for study assessment and procedures** – e.g. alternative locations for laboratory tests, remote follow-up with participants via voice/video calls. • Sponsors should consider the following when making arrangements for remote study visits for trial participants:- – Determine if remote facilities are able to perform the study procedures in accordance with the protocol. Accreditation certificates, list of normal reference ranges and laboratory director's curriculum vitae may be collected from the remote facilities, where possible; – Reimburse trial participants for additional costs incurred from remote study visits; and

		– Assess if the protocol and/or informed consent form should be amended. • Investigators should consider the following when making arrangements for remote study visits for trial participants:- – Obtain sponsor approval for use of the remote facility; – Provide trial participants with written information on the type and frequency of study procedures and protocol-specific parameters (where required) to be performed remotely; – Collect information on the name and contact details of the remote facility; – Establish timelines for transfer of source documents (e.g. laboratory test results, CT/MRI scan results etc.) from the remote facility / trial participant to the trial site; – Review the results of all study procedures performed promptly and contact trial participants to follow up on laboratory results, adverse events, and concomitant medications in order to assess trial participant safety; and – Document all contacts between trial sites and trial participants / remote facilities / sponsors and maintain them on file.
2g	**Are there other relevant aspects considered by the national guidance?**	**Non compliance:** The HSA recognises that there may be an increased incidence of non-compliances reported in relation to the COVID-19 situation. Sponsors should assess if non-compliance constitutes a Serious Breach, and in the event it should notify HSA as soon as possible no later than 7 calendar days of the sponsor becoming aware of the Serious Breach. **Clinical Study Report:** Sponsors should ensure that the following information is included in the Clinical Study Report:- • All contingency measures in relation to the COVID-19 situation; • Subject IDs of all trial participants affected by the COVID-19 situation and how their participation has been altered; and • Impact of the contingency measures on safety and efficacy data for the clinical trial.
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	No.

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Slovakia

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	Yes, **the State Institute for Drug Control in the Slovak Republic (SIDC)** *(in Slovak: "Štátny ústav na kontrolu liečiv")* (further as "the SIDC" only) has issued a navigation on clinical trials in the Slovak Republic during the occurrence of extraordinary circumstances (COVID-19) (further as "the Guidance" only). The Guidance shall be rather recommendatory and of a temporary nature only, and shall be in effect during the extraordinary situation – *in Slovak: "mimoriadna situácia"*, state of urgency – *in Slovak: "núdzový stav"* or state of emergency – *in Slovak: "mimoriadny stav"* declared by the relevant authorities in the Slovak Republic. The Guidance is available in Slovak language here. In addition, **the SIDC** has issued the measurement on prioritised approving of clinical trials with respect to the COVID-19 patients as well as the methodical instruction regarding the procedure on submission of application for drugs' clinical trial. The above measurement is available in Slovak language here. The above methodical instruction is available in Slovak language here. Please note that the below explanations are a summary of the national guidance given by the authorities: some are subject to notifications, authorizations, record keeping etc. which cannot all be detailed in this table.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	We are not aware of any general prohibition on new clinical trials in the Slovak Republic. However, the specific circumstances related to COVID-19 as well as prioritisation of clinical trials with respect to the COVID-19 patients (as mentioned within Q1) have to be considered.
2b	**On suspension of ongoing CT's or recruitment stop?**	The Guidance does not contain any particulars in this respect.
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	The Guidance does not contain any particulars in this respect.
2d	**On informed consent (including re-consent, signature and dates etc.)**	Yes Primarily for the safety reasons, all physical visits of the clinical trials' facilities for the control purposes shall be replaced by the control performed via telephone (if possible). The control performed via telephone shall be duly evidenced in the medical documentation – in particular the reason for contacting, epidemiologic circumstances as well as the consent on further steps shall be evidenced. The consent of the clinical trial's participant on further steps shall be preferably confirmed also via e-mail. Once the situation is stable and the physical visit of the clinical trials' facilities is allowed, the new "validation" consent of the clinical trial's participant on all changes/steps made during the epidemiologic restrictions shall be made.

2e	**On distribution of IMP's (home delivery and storage), stock management**	Yes The provision of IMP and non-IMP for longer time than originally intended may be allowed. If possible (to eliminate the physical visits of the clinical trials' facilities), it is recommended to use the authorised carrier for IMP transport from the clinical trials' facilities to clinical trials participant's house. The direct transport from the clinical trials' sponsors to clinical trials participant's house is not allowed in the Slovak Republic. The clinical trials' sponsors shall bear the costs of the transport as well as they shall be liable for the personal data protection issues. The transport shall be duly evidenced and such data shall be retained at the clinical trials' facilities. Under certain circumstances, the particular medical staff of the clinical trials' facilities may be instructed to secure the IMP transport. Furthermore, the clinical trial's participants shall be trained on how to take and store the IMP. It is also possible to instruct the relatives of the clinical trial's participants on how to take over the IMP, and thus upon telephone verification between the clinical trial's participant and the clinical trial's facility. The handover of the IMP shall be confirmed via telephone and evidenced in the source documentation. If applicable, it is possible to navigate the clinical trial's participants on how to handle and store the rest of unused drugs. The detailed written instructions regarding the IMP distribution made by the clinical trial's sponsors shall be provided to the SIDC. In case the physical visit of the clinical trial's facility is unavoidable because the IMP application must be processed by the doctor or other medical worker, it is recommended to postpone the physical visit to the maximum possible extent. If this is not possible or the physical visit has already been postponed to the maximum, the IMP application shall be processed in the clinical trial's facility upon the implementation of best safety hygienic measures.
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	Yes. As already mentioned, primarily for the safety reasons, all physical visits of the clinical trials' facilities for the control purposes shall be replaced by the control performed via telephone (if possible). The control performed via telephone shall be duly evidenced in the medical documentation – in particular the reason for contacting, epidemiologic circumstances as well as the consent on further steps shall be evidenced. The consent of the clinical trial's participant on further steps shall be preferably confirmed also via e-mail. In case the physical visit of the clinical trials' facilities for the control purposes is postponed or does not occur at all (due to safety reasons), the impact on validity and quality of data of clinical trial shall be evidenced and evaluated. Is the physical visit of the clinical trials' facilities unavoidable and the clinical trials' facilities allow it, the clinical trials' facilities shall put all efforts to adopt the best safety hygienic measures aiming at prevention from cumulating of the patients in the facilities (prior telephone reservations etc.) and to be able to provide the patients as well as own medical staff with the appropriate protective tools. As per monitoring of the clinical trials, the monitors will be disabled to proceed with personal monitoring visits in the clinical trials' facilities according to the monitoring plans. Thus, the Guidance recommends (i) to cancel or postpone the personal monitoring visits in the clinical trials' facilities during the COVID-19 pandemic or to prolong the intervals between the visits of the clinical trials' facilities, (ii) (if possible) to implement the phone or video calls on condition the rights of the

		clinical trials' participants are guaranteed, (iii) to update the monitoring plans based on consideration of new risks including additional or increased centralised monitoring (if reasonable and possible), (iv) to verify remotely the source data. The remote selective visits of the clinical trials' facilities and the training activities of the clinical trials' facilities are allowed if they are unavoidable and are not burdensome for the clinical trials' facilities.
2g	**Are there other relevant aspects considered by the national guidance?**	For now, we are not aware of any other relevant aspects except for those stipulated in this table.
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	Yes. As mentioned within the response to Q1 above, the SIDC has issued the measurement on prioritised approving of clinical trials with respect to the COVID-19 patients. The application for the approving of clinical trials with respect to the COVID-19 patients may be processed electronically to SIDC when sending such application at trial-sukl@sukl.sk The application shall also contain the EUDRACT No., protocol or synopsis of clinical trials, IMP and non IMP identification. When processing the application, the methodical instruction regarding the procedure itself, issued by the SIDC shall be followed. In addition, the relevant documentation shall be equally submitted to the ethical commission for the purposes of approving the clinical trials.

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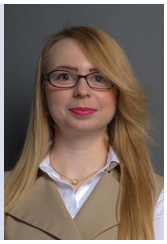

Spain

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	Yes, the Spanish Agency for Medicinal Products and Medical Devices (AEMPS) has published a guide to both ongoing clinical trials and potential clinical trials for medicinal products in connection with COVID-19. The recommendations are based on the EMA Guideline and should be seen as a supplement. The exceptional measures in ongoing clinical trials do not require (i) authorization (as a substantial trial modification), or (ii) individual notification (for serious non-compliance with the protocol). This notification is only required in the case of a trial discontinuation involving a treatment stop in part of the patients as referred to in Q2.2. In any case, any of the exceptional measures taken should be (i) documented in the trial file and (ii) documented in a special final report. This special final report should be submitted by the sponsor to AEMPS and Ethics Committee for Medicinal Products Research (CEim) within four months after the end of COVID-19 crisis in Spain. However, please note that the below explanations are a summary of the national guidance given by the authorities: some are subject to notifications, authorizations, record keeping, etc., which all cannot be detailed in this table.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	There is no general prohibition of new trials in Spain. However, the specific circumstances related to COVID-19 must be taken into account (as indicated in point Q3, potential clinical trials for medicinal products in connection with COVID-19 will be treated on a preferential basis).
2b	**On suspension of ongoing CT's or recruitment stop?**	Yes. • The sponsor together with the investigator may **interrupt** the trial to avoid unnecessary risks and to ensure the best possible health care for the patients. This decision shall be based on an assessment of the characteristics of the trial and the characteristics of the Healthcare Centers. The Guideline states that this assessment should be made especially in clinical trials with immunosuppressive treatments because there is a higher risk of infection. If the trial interruption involves stopping treatment in some patients, the sponsor should notify the AEMPS and the CEim. This notification should indicate an alternative treatment for the patients. This report must be submitted within 15 days of the interruption. • **Recruitment continuation/ recruitment stops**: The Guideline also allows the sponsor together with the principal investigator, after assessing the circumstances, to agree to discontinue patient recruitment. The adoption of this measure, as explained in Q1, does not require authorization (as a substantial trial modification) or notification (for serious non-compliance with the protocol) but should be documented in the file and, when the COVID-19 crisis is over, include it in the special final report to be submitted to the AEMPS and CEim.
2c	**On risk assessment and/or safety reporting (i.e. communication with**	No, there is no specific guidance in this respect.

	authorities)	
2d	**On informed consent (including re-consent, signature and dates etc.)**	No
2e	**On distribution of IMP's (home delivery and storage), stock management**	Yes The guideline establishes that the medicinal products should be provided under the same conditions as they were being given. However, the sponsor, the principal investigator and the Pharmacy Service are allowed to assess the circumstances of each specific case and agree: (i) either to dispense a quantity of medicinal products to patients attending scheduled visits that covers a longer period of treatment; or (ii) to dispense the medicinal products to a person authorized by the patient of the trial; or (iii) to send the medicinal products directly to the patient's home.
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	Yes **Monitoring visits**: The Guidance recommends that sponsors update trial monitoring plans for the next four months by prioritizing centralized monitoring and remote monitoring of participating centers. It also recommends that the sponsor postpone, as much as possible, verification of source data until the medical history can be accessed in person. **Healthcare centre visits**: The Guidance recommends postponing these types of visits or replacing them with telephone visits. However, the Guideline states that it should be ensured that critical face-to-face visits should continue to be conducted. Rescheduling visits should not be considered a serious breach of the protocol unless it would jeopardize patient safety.
2g	**Are there other relevant aspects considered by the national guidance?**	**Transfer of patients from one center to another:** The transfer of a patient from one trial center to another is allowed provided that (i) a transfer agreement is signed between the centers; (ii) the new center has access to the data collection notebook and patient's medical records (or a copy of these records is sent to the new center by the original center); (iii) the original center summarizes the patient's most relevant medical data related to the trial to facilitate follow-up at the new center; and (iv) the transfer of the patient is documented in the trial file of both centers.
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	Yes. • Clinical trials aimed at investigating new medical products against coronavirus: – Applications for authorization of clinical trials shall always include the word 'COVID-19' in the title. – When the AEMPS receives a request in this regard, it will respond within 48 hours. In its response, the AEMPS may propose to the sponsor to join another study that is already underway or being organized. – Where these trials are non-commercial, and in order to facilitate the start-up of non-commercial sponsor clinical trials, the clinical contract with the healthcare center may be replaced by a document of agreement from the healthcare center's management. – In accordance with the Sixth Additional Provision of Royal Decree - Law 13/2020, 7 April, no fees are required if the clinical trials (both to medical products or medical devices) are carried out for non-commercial purposes. • Prospective follow-up observational studies with coronavirus-related medicinal products: – Applications should also be indicated under the heading "URGENT COVID-

19".

- When the AEMPS receives a request in this regard, it will resolve it as soon as possible, normally on the same day as the request and within a maximum of two working days.
- In this type of study, if the promoter is a researcher from an independent organization (research groups, scientific societies) they will be considered of health interest and classified as EPA-AS.
- In these cases: (i) the AEMPS will provide methodological support ; (ii) only the protocol and the favorable opinion of the CEIM are required for the authorization of the study; and (iii) the authorization will be issued within a maximum of 7 days from the receipt of the opinion of the CEim.
- In addition, for this type of observational study, the AEMPS will facilitate collaboration between investigators from different centers proposing studies with common objectives, bringing them together to conclude collaboration agreements or multi-center studies.

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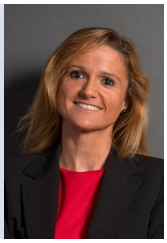

Sweden

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	The Swedish MPA ("Läkemedelsverket") cooperates with the Public Health Agency ("Folkhälsomyndigheten"), the National Board of Health ("Socialstyrelsen"), The Swedish Civil Contingencies Agency ("MSB"), The Swedish National Food Agency ("Livsmedelsverket"), The Swedish Work Environment Authority ("Arbetsmiljöverket") – competent regulator of Medical devices industry – and the regions/infection-control physicians. It is Folkhälsomyndigheten that coordinates the infection-protection in Sweden and, among other things, produces recommendations on how to fight the infection. The most important guideline however, regarding clinical trials, is issued by the Swedish MPA, on 14 February 2020, last updated on 7 April 2020. The Swedish Data Protection Agency ("Datainspektionen") has – yet – not issued any guidance regarding CTs. The answers and recapitulation below of the (current) Swedish regulatory landscape constitutes an executive summary. It cannot and should not be basis for any actions from clients, and if is so made, the firm hereby rejects future of indemnification claims that may occur. For sufficient advise, please contact our office for detailed assessment and recommendation for action/s.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	There are no obstacles for initiation of new CTs, unrelated to COVID-19. Nor are there limitations because of the priority given to COVID-19 trials. But the priority of the COVID-19 CTs may prolong the response time from the MPA and its adjunct agencies – such as EPM – to approve/validate any submission. It is also palpable that new clinical trials, exploiting the emergency-protocol privileges for COVID-19 trials, may find themselves as objects for audits of a newly (Jan. 2020) formed national *review board against dishonesty in research* ("Npof").
2b	**On suspension of ongoing CT's or recruitment stop?**	Yes, the Swedish MPA has produced the following details. **Situations that may need to be handled as *Urgent Safety Measures ("USM")*** Emergency situations in relation to COVID-19 can be treated as USG and means that suspensions can be carried out without the approval of the MPA. This provision however requires that the MPA must be informed about the suspension *without delay*. How long the delay can be is not pinpointed, but the agency emphasizes that the patient safety is of the highest priority, which is why all planned suspensions and such, should be based on a careful risk assessment. **Document deviations carefully** The MPA demonstrates, in written form, its understanding that deviations may occur as a result of test-subjects nog being able to conduct trials as planned under the current circumstances. However , the agency urges sponsors to accurately document non-conformities and decide whether these need to be reported as a serious violation to the MPA in accordance with the Swedish GCP-ordinance, LVFS 2011:19 (chapter 8 § 11). **Changes to the trial** If the sponsor deems that changes to the approved protocol must take place, it must be submitted in the form of an application for material change in accordance with the Swedish GCP-ordinance, LVFS 2011:19 (chapter 7, *Changes to trial).*

		The changes to be made must be clearly justified; the consequences for the test-subjects and the scientific value of the examination must be clearly described in the application. **Monitoring remotely** The MPA's assessment is that neither ICH, GCP or national patient-data regulation allow any possibility to verify source-data remotely. **Treatment of trial drugs, at the test-subjects homes** The MPA, in written form, expresses its understanding of the difficulties of delivering the drugs to the hospitals, and allows drugs to be delivered to test-subjects homes if the following four (4) cumulative requirements are met: • The integrity of the test-subject must be protected. • The delivery must meet the temperature requirements. • Assurance that the *right trial drug* in the *right quantity* is delivered to the *right person*. • Assurance that a delivery is not replacing a scheduled medical contact. **Recruitment stop** There is no recruitment stops, nor are there any obligation to report such a decision. Only in regards to the test-subjects health and security, are there obligations under the Swedish GCP-ordinance, LIVFS 2011:19 (chapters 7 and 8), to report such divergence from recruiting test-subjects.
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	Yes **Safety reporting - allowed derogations** The MPA do not consider protocol divergences during the pandemic, making it difficult for test-subjects to perform, as serious breaches. But it leaves to the sponsors to decide whether or not any safety incidents/breaches, that otherwise would constitute such a breach, matter for reporting according Swedish GCP-ordinance, LIVFS 2011:19 (chapter 8, § 11). **Safety reporting – derogations not allowed** According to Swedish GCP-ordinance, LVFS 2011:19 (chapter 8, 3 §) the investigator still have to report serious incidents/breaches to the sponsor, except incidents in the approved protocol or investigators brochure that do not need to be consider as such serious incidents/breaches. Furthermore, according the Swedish GCP-ordinance, LVFS 2011:19 (chapter 1, §3 and chapter 8, 6 – 9 §§) the sponsor still have to report to the MPA, but also to the Etikprövningsmyndigheten, EPM, serious adverse events or adverse reaction ("Susar"), with short deadlines. **Possible Scenarios and the MPA's possible requirements** The Swedish MPA has not released any guidance of possible scenarios regarding COVID-19 situations. The sponsor, during and USM-period, should not regard the situation as a cart blanch to getting rid of safety reporting. To the contrary, the sponsor should not take the risk of exploiting safety-reporting compliance.
2d	**On informed consent (including re-consent, signature and dates etc.)**	There are no changes to the strict requirements regarding the informed consent from the test-subject.
2e	**On distribution of IMP's (home delivery and storage), stock management**	Yes As briefly outlined above, the Swedish MPA tolerates, during the ongoing COVID-19 pandemic, that there may be a need, *in some cases,* to deliver IMP's to test-subjects homes. The considerations required from sponsors are:

		• The test-subject's privacy must be protected. Sponsor cannot know the identity of the test-subject. Shipping to a test-subject must therefore be from a hospital/clinic or from a pharmacy involved in the trial. • Product quality. Deliveries must meet the temperature requirements specified for storing the product. • Control of each product throughout the chain: It must be ensured that the right trial drug, in the right quantity is delivered to the right person. Test drugs cannot be left in a mail-box, outside the door or the like. The delivery must be documented. • Patient safety: a home delivery cannot replace a scheduled medical contract.
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	Yes, and No The MPA's assessment is that neither ICH, GCP or national patient-data legislation allow any possibility to verify source-data remotely. Nevertheless the MPA advises the sponsors to conduct and document a renewed risk analysis and update its monitoring plan during ongoing pandemic. It is, for instance, possible to postpone monitoring-visits if a sponsor documents the logical basis for their position, and/or, increase their central monitoring of data (collected electronically) and have an ongoing contact with participating clinics via tel./e-mail.
2g	**Are there other relevant aspects considered by the national guidance?**	The relevant Swedish Agencies, with the MPA spearheading the instructive guidance of clinical trials, through the ongoing pandemic, demonstrates a great deal of tolerance for deviations from standard procedures regarding clinical trials and invites sponsors to find pragmatic solutions, as long as the safety and integrity of the test-subjects is not excavated. The Swedish Innovation Agency (Vinnova), working close with the MPA, has announced funding for trials and other research against the COVID-19 pandemic.
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	Yes. The Ethics Review Authority ("Etikprövningsmyndigheten, EPM") has established a priority scheme for the handling of applications for ethical review of research related to COVID-19. An ethical authorization from EPM, for the CT, basically becomes decisive for the Data Protections Agency's ("DI") approach on whether the health data regarding research on COVID-19 meets the legal requirements for legitimate use. Also other institutions, such as the Biobanks have guaranteed priority procedures for applications. Finally, the Swedish Government appoints a national coordinator for clinical trials on drugs against COVID-19. Since there are a number drug treatments currently being used for COVID-19, with insufficient knowledge, the government now formally interferes and authorizes a central designee with staff, to connect ongoing trial data to WHO Solidarity Trial.

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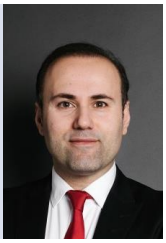

UAE

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	All clinical and research trials within the UAE require human subject consent, as well as the written approval of the Ministry of Health and Prevention ("MOHAP"), or other concerned governmental authorities, after a review of an application for such trials. There have been announcements that UAE has commenced clinical trials of plasma therapy for COVID. All clinical trials in the UAE must follow the principles laid out in the Guidance for conducting Clinical Trials Based on Drugs/ Medical Products & Good Clinical Practice of 2017 ("Guidance"). The Guidance further states that all clinical trials should follow the World Medical Association Declaration of Helsinki on ethical principles for medical research involving human subjects. As at 14 April 2020, we are not aware of any published legislation or protocol in relation to amendment of the Guidance or any processes in relation to clinical trials in the UAE in the wake of COVID-19 outbreak. That said, we have not been able to verify independently with the MOHAP whether any changes to the existing practices and procedures to be followed in relation to clinical trials have been made in practice, given the closure of the authority as a result of the COVID-19 outbreak.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	N/A
2b	**On suspension of ongoing CT's or recruitment stop?**	N/A
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	N/A
2d	**On informed consent (including re-consent, signature and dates etc.)**	The Guidance provides that no national, ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects and therefore, consent still remains important unless changes are made to the Guidance or the protocols.
2e	**On distribution of IMP's (home delivery and storage), stock management**	N/A
2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	N/A

2g	**Are there other relevant aspects considered by the national guidance?**	N/A
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	N/A

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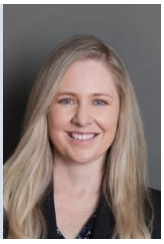

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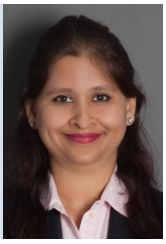

United Kingdom

1	**Did national authorities issue guidance on clinical trials in the context of COVID-19, if yes which ones?**	Yes, the **Medical and Healthcare products Regulatory Agency (MHRA)** has published guidance on both managing clinical trials during COVID-19, and applying for clinical trials for COVID-19. For the former situation, protocol deviations should be well documented but an increase in protocol deviations in relation to COVID-19 will not constitute a serious breach, therefore there is no need to report this to MHRA unless patients are being put at risk; however, protocol waivers are unacceptable. In relation to COVID-19 related trials, fast-track processes to review new studies and amendments to existing studies, often within a few days of application, are in place (see Qn. 3 below for details). In addition, the National Health Service (NHS) Health Research Authority (HRA) has published guidance on how to amend an existing study, use of patient data etc. Please note that the below explanations are a summary of the national guidance given by the authorities: some are subject to notifications, authorisations, record keeping etc. which cannot all be detailed in this table. The situation may well evolve over time.
2a	**If the answer to Q1 is yes, are there specific measures/derogations provided for by your national guidance:** **On initiation on new CTs not related to COVID-19**	The MHRA and HRA (and devolved administrations in Scotland, Wales and N Ireland) will continue to provide an approvals service for all studies, while prioritising COVID-19 related trials (other applications are likely to be delayed or potentially moved to a later Research Ethics Committee (REC) meeting than originally planned). Until further notice, the National Institute for Health Research Clinical Research Network is pausing the site set up of any new or ongoing studies at NHS and social care sites (unless nationally prioritised COVID-19 studies).
2b	**On suspension of ongoing CT's or recruitment stop?**	Yes. • There is no general recruitment stop for CTs due to COVID-19. A Sponsor or Investigator can use discretion to temporarily halt a trial or halt recruitment. • If the trial has been halted due to COVID-19, there is no general obligation to inform the MHRA unless one of two scenarios occurs: – A direct participant safety issue, especially if there is the potential to impact other trials – inform MHRA in the usual way; or – A medicines supply issue – inform MHRA who can escalate this to the Department of Health and Social Care (DHSC) – inform MHRA directly by phone or email rather than an amendment form.
2c	**On risk assessment and/or safety reporting (i.e. communication with authorities)**	Yes • MHRA acknowledges that capacity issues related to COVID-19 may prevent timely reporting of serious adverse events, and submission of annual safety reports and end of trial notifications – if this occurs, MHRA encourages reporting this as soon as possible after the capacity issue is resolved. • Deviations from protocol defined timelines in the case where there are capacity issues related to COVID-19 do not require a substantial amendment notification to MHRA. • Attention should still be paid to **timely reporting** of **suspected unexpected serious adverse reactions (SUSARs)** which put the trial participants' safety at risk or have the potential to impact participants of

		other trials. • The MHRA have stated that the first priority in any case should be the safety of trial participants and this will remain the focus.
2d	**On informed consent (including re-consent, signature and dates etc.)**	Yes. In relation to the distribution of IMPs, the participant must consent verbally to providing contact details for shipping purposes. Remote monitoring is supported by MHRA where appropriate but trial participants must consent to any identifiers leaving the site and be assured that their confidentiality will be protected. If the process requires wet-ink signatures, the MHRA suggests alternative methods of demonstrating approvals such as email confirmation. Inspectors are encouraged to take a pragmatic approach, but MHRA suggest considering a Standard Operating Procedure (SOP) deviation to cover this in the interim.
2e	**On distribution of IMP's (home delivery and storage), stock management**	Yes. If a trial volunteer cannot attend a trial site, then delivery of IMPs to a patient's home is allowed with no substantial amendment notification to the MHRA required. Sponsors should do a risk-assessment and record this internally. If the participant does not want to sign for the delivery due to self-isolation, then a follow up phone call could be used to confirm they have received the package. The sponsor should also consider if any training is required for administration of the IMP. The following factors need to be taken into consideration if providing an IMP to a participant at home: **Storage requirements:** • Whether the medicine has any specific storage requirement and how those are managed during posting; • What assurance can be given about the integrity of the product during transit, for example should a temperature monitoring device be used; • The stability of the product and margin of safety: for example a product with a very stable profile at temperature extremes would require less monitoring than one with a narrow stability range. The expiry of the product may need to be shortened if it is delivered in ambient temperature. **Medicine accountability considerations:** • The mechanism for confirming that the subjects have received the IMP and it has not been delivered to someone else; • Whether the medicine needs to be signed for and sent by courier or recorded delivery; and • Whether there needs to be a follow-up call to the subject.

2f	**On monitoring (cancellation of site monitoring, implementing remote visits, remote site selection visits etc.)**	Yes. **Remote monitoring for trials is supported by MHRA; consider the following:** • Direct access to patients Electronic Health Records (EHR) away from the site creates issues around confidentiality. Consider where this access takes place, for example, will CRAs (Clinical Research Associates) be accessing records in an open plan office, public space or other location where others who are not authorised could view sensitive information. • Trial participants will need to consent to any identifiers leaving the site and be assured that their confidentiality will be protected; • Increased pressures on clinical staff during this period is likely so it is important to make sure that extra burdens are not placed on investigators around scanning and uploading many documents; and • The use of alternative means of oversight such as teleconferences/videoconferences is encouraged. **Reducing the number of participant monitoring visits** CT-1 guidance does regard a reduction in the number of monitoring visits as a substantial amendment. However, if participant monitoring visits need to be reduced due to COVID-19, this will not require a substantial amendment notification.
2g	**Are there other relevant aspects considered by the national guidance?**	**Restarting a trial after it has been halted** If the restart of the study does not involve any substantial changes to the Clinical Trial Authorisation (CTA), then a substantial amendment notification to MHRA will not be necessary. If changes do need to be made to protect participant safety moving forward, then this should be submitted as a substantial amendment in the normal way. **Changes to trial conduct** During the COVID -19 pandemic it is acknowledged that Sponsors may need to send 'Dear Investigator' Letters to inform investigator sites of changes to trial conduct. These do not require regulatory oversight and should not be submitted to the MHRA. **Subject Safety** Subject safety is the MHRA's highest priority. Sponsors should consider the risk/benefit of conducting trials in medicines that act as immuno-suppressants, for example in early phase healthy volunteer trials, where there is no therapeutic benefit to the volunteer, but taking part in the trials does pose a risk of infection.
3	**If the answer to Q1 is yes, are there specific procedures / recommendations concerning clinical trials in connection with COVID-19?**	Yes. • COVID-19 assessments are being prioritised and the MHRA have procedures in place for rapid scientific advice, reviews and approvals. • COVID-19 applications are to be submitted directly to the Clinical Trial Helpline (an email address) as well as through the normal CESP route to allow work to begin as soon as possible. • The study should contain the official acronym for the coronavirus disease (COVID-19) in the title field of the trial registration data set. • The MHRA do **not** get involved in deciding whether someone is eligible to participate in a clinical trial, but COVID-19 trials that are open for enrolment should be registered on a public site.

The full process for fast-track reviews is set out in the Standard Operating Procedures for Research Ethics Committees

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About us

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Bird & Bird is a global law firm. Altogether, we have over 1,100 lawyers and legal practitioners working on our clients' issues and business goals worldwide. Our core objective is to select and develop people who possess a rare and invaluable grasp of strategic commercial issues.

By combining this talent with exceptional legal expertise and deep industry knowledge, our advice is always informed, up to date, focused and relevant.

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