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Europe Update – Life Sciences Products and COVID-19: From Clinical Trials to Regulatory Flexibility

In March, most European Union ('EU') countries ordered some form of lockdown and adopted many national measures to address or prevent issues raised by COVID-19. The health crisis pushed national authorities to focus on their respective populations and needs, but measures were also adopted at the European level. The European health regulators, *i.e.*, the European Commission ('EU Commission'), European Medicines Agency ('EMA') and Heads of Medicines Agencies ('HMA') (collectively 'European Regulators'), worked together and tried to coordinate national actions.

This alert is threefold. After having identified the main measures adopted by the European Regulators with regard to medicinal products and medical devices (A), it discusses the Guidance on the Management of Clinical Trials During the COVID-19 Pandemic and, in particular, the direct supply of investigational medicinal products to trial subjects, an issue that is approached differently by the Member States (B). The alert then explains the Q&A on regulatory flexibility for medicinal products, insisting on the aspects that concern all medicinal products (C).

While those guidelines help companies adapting to the new environment, their implementation may prove challenging, especially in cases of divergent national measures. King & Spalding's European regulatory lawyers assist sponsors in addressing conflicting issues (patient safety, trial integrity, ethics), drafting standard operating procedures and structuring appropriate documentation for their changes to ongoing clinical trials. They advise holders of marketing authorizations on regulatory issues arising out the pandemic and, more generally, companies on the manufacture and distribution of essential health products and help them navigating national divergences.

EUROPEAN MEASURES

The European Regulators are working together in the fight against COVID-19 and the resolution of the health problems they create. Exhibit 1 below contains a list of the main EU guidelines adopted for medicinal products and medical devices since the beginning of the health crisis.

With regard to **medicinal products**, the EMA participates in the EU Executive Steering Group on shortages of medicines caused by the COVID-19 infection ('EU Executive Steering Group'), and has set up a COVID-19 EMA Pandemic Task Force ('COVID-ETF') to assist Member States and the EU Commission in dealing with development, authorization and safety monitoring of therapeutics and vaccines intended for treatment or prevention of COVID-19. The EMA also participates in the International Coalition of Medicines Regulatory Authorities ('ICMRA'), an international collaboration for the development of treatments against COVID-19.

Several guidelines have been adopted so far, including those discussed below on the management of clinical trials and regulatory flexibility and the ***Guidelines on the optimal and rational supply of medicines to avoid shortages during the COVID-19 outbreak*** (EU Commission, 8 April 2020). These last guidelines recommend measures to Member States and thus only indirectly impact companies. With regard to supply, the recommended actions are: increasing and reorganizing production; ensuring manufacturing continues at full capacity; implementing regulatory flexibility; monitoring available stocks at national level; ensuring necessary support to the wholesale sector; fully enforcing the green lanes; facilitating air freight and other forms of transport; and ensuring fair distribution.

The EU Commission also took measures in relation to **medical devices**, the most important of which probably is to propose postponing the application of the new Medical Devices Regulation by one year, from May 2020 to May 2021. No such postponement is proposed for the new In Vitro Devices Regulation. The EU Commission also adopted a general ***Guidance on medical devices, active implantable medical devices and in vitro diagnostic medical devices in the COVID-19 context*** (EU Commission, 4 April 2020) that indicates the applicable rules that have been or may be adapted due to the COVID-19.

The **European Data Protection Board** ("EDPB") is active as well. Recently, it announced a guideline on the processing of health data for research purposes in the context of the COVID-19 outbreak. Mid-March, it already published a ***Statement on the processing of personal data in the context of the COVID-19 outbreak***, stressing that data controllers and processors must ensure the protection of personal data, even in these exceptional times. Emergency is a legal condition that may legitimize restrictions of freedoms but only if these restrictions are proportionate and limited to the emergency period.

ONGOING CLINICAL TRIALS

Ongoing clinical trials are significantly affected by the coronavirus that prevents trial subjects from going to investigating sites or meeting investigators, and forces healthcare professionals, health institutions and, more generally, the entire medical community to focus on treatments against COVID-19. In mid-March several national regulators provided guidance to help sponsors deciding on and handling the changes to be made to ongoing clinical trials due to COVID-19. The European Regulators then stepped in and adopted a guideline - Guidance on the Management of Clinical Trials during the COVID-19 (Coronavirus) pandemic - on 20 March 2020 ('EU CT Guidance').

The EU CT Guidance was updated on 27 March (***Update of Guidance on the management of clinical trials during the COVID-19 pandemic***) and a new update is expected by the end of April. Moreover, on 25 March, the CHMP published a draft "Points to consider on implications of Coronavirus disease (COVID-19) on methodological aspects of ongoing clinical trials" for public consultation.

The EU CT Guidance, which primarily addresses sponsors, covers ongoing clinical trials and clinical trials for treatments of COVID-19. It is very similar to the FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic.

With regard to ongoing clinical trials, the EU CT Guidance requires sponsors to conduct a risk assessment of each trial and, on that basis, to decide the changes to be brought to the trial in order to secure, first and foremost, trial subjects' safety and then trial integrity. Any change has to be thoroughly documented in view of future GCP inspections. The EU CT Guidance discusses specific changes such as remote monitoring and auditing and related issues such as informed re-consent and financial compensation. It also explains the formalities to be carried out – or not – to implement those changes.

While the EU CT Guidance tries to harmonize the national positions, it stresses that national measures may have been adopted that complement it or prevail over it. In doing so, the EU CT Guidance expressly references national law concerns such as remote source data verification and the supply of investigational medicinal products (IMP) to trial subjects.

COVID-19 impedes trial subjects' visits to sites and investigators, and therefore the supply of IMPs to trial subjects. The EU CT Guidance indicates changes that can be made to provide trial subjects with the IMP and non-IMP as needed according to the trial protocol. Those changes have to be reflected in the protocol and communicated to the competent regulatory authorities.

- The following measures can be considered as long as that they do not create shortages of marketed medicinal products:
  - Larger amounts of trial medications than normally foreseen can be provided to the trial subject in order to sustain him for a longer period and thereby avoid non-critical visits to the investigator site. This option however requires that the continuation of treatment is under adequate supervision of the responsible investigator.
  - An appropriate stock of trial medications should be maintained to ensure treatment in case of distribution failure.
- In case of urgent shortage of IMP at some sites and a direct distribution of the IMP to a site by the usual distributor is not possible, the IMP may be re-distributed between sites in accordance with GMP Annex 13 (section 47). The same applies in case of transfer of trial subjects from one site to another site.
- Following the reduction of physical site visits, a delivery of the IMP directly to trial subjects is generally accepted but from investigating sites. Direct IMP delivery from sponsor to trial subjects is only accepted in a few Member States and strictly during this emergency situation; hence, the EU CT Guidance advises sponsors to check national guidelines. Exhibit 2 below reproduces national guidelines on the management of IMPs.

What about medical devices? No EU guidance on management of clinical investigations during COVID-19 has been adopted. However, certain national guidelines on clinical trials specify that they cover both medicinal products and medical devices (for example, Portugal), and in practice, national competent authorities and ethics committees apply the same principles as for clinical trials.

REGULATORY FLEXIBILITY

On 10 April, the European Regulators published a ***Q&A on Regulatory Expectations for Medicinal Products for Human Use during COVID-19 Pandemic*** (EU Regulatory Q&A) that provides guidance to holders of marketing

authorizations ('MAH') on regulatory expectations and flexibility during the COVID-19 pandemic. The Q&A is divided in four sections - MA, manufacturing, quality and product information. It only includes six questions but will be regularly updated; additional questions on Good Manufacturing Practice are expected very soon.

Some questions concern products that are crucial for treating patients with COVID-19:

- Can medicinal products intended for use in COVID-19 patients be marketed without MA?
- How can changes in the manufacturing/supply chain be implemented swiftly to ensure continuity of supplies to the EU of crucial medicines for treatment of COVID-19 patients?
- Can quality requirements be waived/adapted for medicines intended to be used for the treatment of COVID-19 patients?

The EU Regulatory Q&A however neither defines nor lists those crucial products. We note that companies should identify any regulatory action relating to COVID-19 by "CONCERNS COVID-19" in order to secure a quicker treatment of their applications/requests.

Other questions apply to all medicinal products:

- *Can a renewal application be postponed?* Yes. MAHs facing difficulties in submitting renewal applications, including for conditional MA, within the regulatory deadline (at least 9 months before expiration) due to exceptional circumstances arising from the COVID pandemic, should contact the competent health regulator and file a justified request to postpone the submission.
- *Does the 'sunset clause' apply?* Yes. MAHs are reminded of the possibility of requesting an exemption in view of exceptional circumstances and on public health grounds. During the pandemic, the EU Commission may accept sunset clause requests that are based on the pandemic, without the need for any further justification.
- *Is there any flexibility in the labelling and packaging requirements to facilitate the movement of medicinal products within the EU?* Yes. It is necessary to facilitate the movement of medicinal products within the EU so that they can be made available in the Member States where they are needed the most. During the COVID-19 pandemic, Member States may accept that: the product information is not translated into the relevant official language; national specific information does not appear in the packaging/labelling; and the presentation differs from the authorized presentations. The CMDh has agreed to apply the labelling and packaging flexibilities to crucial medicines for use in COVID-19 patients, and further guidance on specific national requirements/procedures will be developed by CMDh.

What about medical devices? Like for medicinal products, the EU guidelines permit derogations from the applicable rules but primarily for the devices that are essential in relation to COVID-19. The EU Commission's ***Guidance on medical devices, active implantable medical devices and in vitro diagnostic medical devices in the COVID-19 context***, for example, indicates that Member States may authorize the marketing of individual medical devices for which the required conformity assessment procedure has not been conducted. The Guidance lists the factors to be taken into consideration by the Member States when deciding on requests for derogation, which should be temporary (the device becomes compliant, suitable substitutes become available, the health crisis disappears).

CONCLUSION

The European Regulators have adopted guidelines to help companies adapting to the new environment created by COVID-19. The implementation of those guidelines however may be challenging. On the one hand, the guidelines set out general principles to be applied on a case by case basis. On another hand, the EU guidelines are based on national measures, which they try to coordinate, and national divergences remain.

More generally, the steps taken in the EU illustrate future legal and regulatory needs. There is a pressing need to permit, encourage and organize more 'remote' activities, in particular for clinical trials, and the following months will show whether remote activities are valid alternatives for clinical research. There also is a pressing need to regulate supplies at the European level rather than at the national level to avoid shortages in and ensure equitable supplies to all EU countries.

King & Spalding's experienced European regulatory lawyers assist sponsors in addressing conflicting issues (patient safety, trial integrity, ethics), drafting standard operating procedures and structuring appropriate documentation for their changes to ongoing clinical. Risk-assessments should be conducted in the framework of a written policy and procedure, with documentation of the decision-making, and decision-making may require rapid revision of study documentation, review/revision of existing contractual arrangements, personnel training, and thoughtful recordkeeping. Furthermore, our lawyers advise MAH on regulatory issues arising out the pandemic and help companies distributing essential health products and navigating national recommendations.

If you have questions regarding the implications of COVID-19 or require support for compliance, contractual analysis, or re-negotiation, please contact:

For Europe: Geneviève Michaux, Ulf Grundmann or Elisabeth Kohoutek.

For the U.S.: Chris Markus, Nikki Reeves.

Visit the Firm's Coronavirus Task Force page here for all of the latest guidance on responding to this new legal environment.

Exhibit 1 – List of Main EU Measures for Medicinal Products and Medical Devices

Main Measures for Medicinal Products

- ***Q&A on Regulatory Expectations for Medicinal Products for Human Use during COVID-19 Pandemic*** (EU Commission/EMA/HMA, 10 April 2020).
- ***Guidelines on the optimal and rational supply of medicines to avoid shortages during the COVID-19 outbreak*** (EU Commission, 8 April 2020). The EU Supply Guidelines are addressed to the Member States and explain the measures that they are expected to adopt for avoiding shortages. The EU Commission's factsheet summarizes the EU Supply Guidelines as follows:

Showing solidarity	*Optimal use of medicines in hospitals*
• Lifting export bans and restrictions • Avoiding national stockpiling • Avoiding that misinformation leads to improper use and unnecessary stockpiling	• Equitable distribution of available medicines • Exchanging hospital protocols to treat patients • Considering alternative medicines on the basis of hospital protocols and national guidelines • Extending the expiry dates of medicines • Considering the use of magistral preparations or veterinary medicines • Encouraging clinical trials for medicines used off label

Ensuring supply • Increasing and reorganizing production • Ensuring manufacturing continues at full capacity • Implementing regulatory flexibility • Monitoring available stocks at national level • Ensuring necessary support to the wholesale sector • Fully enforcing the green lanes • Facilitating air freight and other forms of transport • Ensuring fair distribution	***Optimization of sales in community pharmacies to avoid hoarding*** • Introducing measures to reassure persons reliant on medication • Introducing restrictions on sales in community pharmacies • Limiting online sales of products at risk

- ***Antitrust guidance to companies cooperating in response to urgent situations related to the current coronavirus outbreak*** (EU Commission, 8 April 2020).
- ***Paper on the Industry Single Point of Contact (I-SPOC)*** (EU Executive Steering Group, 3 April). The system enables pharmaceutical companies to report directly to the EMA (for centralised and decentralised authorised products) with respect to COVID-19 related shortages.
- ***Update of Guidance on the management of clinical trials during the COVID-19 pandemic*** (EMA/HMA, 27 March 2020).
- Draft "Points to consider on implications of Coronavirus disease (COVID-19) on methodological aspects of ongoing clinical trials" (CHMP, 25 March 2020).

Main Measures for Medical Devices

- ***Guidelines on COVID-19 in vitro diagnostic tests and their performance*** to support Member States in their national containment strategies (EU Commission, 15 April 2020). This document provides guidance on what information different tests can deliver (i.e. what is the intended purpose of a given test) and the level of a test's performance (i.e. how well it is able to achieve that purpose). It outlines the regulatory context of COVID-19-related in vitro diagnostic testing devices in the EU and gives an overview of different types of tests and their purposes.
- ***Guidance on temporary extraordinary measures related to medical device Notified Body audits during COVID-19 quarantine orders and travel restrictions*** (EU Commission, 8 April 2020). It outlines temporary extraordinary measures for Notified Bodies in order to allow continued availability of safe medical devices and assist in the prevention of medical device shortages.
- ***Guidance on medical devices, active implantable medical devices and in vitro diagnostic medical devices in the COVID-19 context*** (EU Commission, 4 April 2020). The document recalls the applicable rules and indicates the special measures adapted due to the COVID-19, including:
  - Free access to certain harmonized European standards
  - Possibility for the Member States to authorize the marketing of individual medical devices for which the required conformity assessment procedure has not been conducted. The Guidance lists the factors to be taken into

consideration by the Member States when deciding on requests for derogation. The derogation should be temporary and its duration strictly limited to the time required by the health crisis (the device becomes compliant, suitable substitutes become available, the health crisis disappears).

- Possibility to use medical devices off-label, i.e. for a purpose or in a way different from that intended by the manufacturer and described in the instructions for use. The Guidance stresses the need for conducting a risk-benefit assessment for each patient and indicates the factors to be taken into consideration therefor.

- ***Legislative proposal to postpone by one year the date of application of the Medical Devices Regulation*** (EU Commission, 3 April 2020).
- On 30 March 2020, the EU Commission published ***three documents to help increase production of essential medical equipment and material*** in the context of the coronavirus outbreak:
  - **Q&A on conformity assessment procedures for *protective equipment***
  - **Guidance on the applicable legislation for *leave-on hand cleaners and hand disinfectants*** (gel, solution, etc.)
  - **Q&A on conformity assessment procedures for *3D printing and 3D printed products* to be used in a medical context for COVID-19**

Exhibit 2 – EU and National Guidelines on Direct Supply of IMP to Trial Subjects

The chart below contains excerpts from guidelines

Jurisdiction	Date	
Europe (excerpt)	27.03	**9. Changes in the distribution of the IMP** Changes in the distribution of the IMP may be necessary to remove avoidable visits to sites and to provide the trial participants with needed treatments. Sponsors must assess the risks relating to the product and consider any alternative shipping and storage arrangements. Such measures raise various practical considerations, including whether the IMP is appropriate for administration and general storage at the trial participant's home, how the stability of the product will be maintained during transit (especially for cold chain product), how safe custody of product will be ensured and how IMP accountability and the evaluation of compliance to treatment (if appropriate) will be managed. The overriding objective of all changes in distribution is to provide trial participants with the IMP and other medications categorized as non-IMPs as needed according to the trial protocol to ensure the right, safety and well-being of trial participants as well as the integrity of the CT. The overriding objective of all changes in distribution is to provide trial participants with the IMP and other medications categorized as non-IMPs as needed according to the trial protocol to ensure the right, safety and well-being of trial participants as well as the integrity of the clinical trial.

		Changes in distribution of IMP may include: • The following measures could be considered, provided that they do not create shortages of marketed medicinal products: - Larger amounts of trial medications than normally foreseen can be provided to the participant (in particular IMP, when prepared specifically for the purposes of the trial). This is to sustain the trial participant for a longer period and thereby avoid non-critical visits by the participant to the investigator site. This may be done providing that the continuation of treatment is under adequate supervision of the responsible investigator. - It is recommended for all IMPs and non-IMPs in clinical trials that appropriate stock is maintained to ensure treatment in case of distribution failure; • In case of urgent shortage of IMP at some sites or transfer of trial participants from one site to another CT site, there might be a need to potentially re-distribute the IMP between sites in accordance with GMP annex 13 (section 47). This should only be considered in cases where a direct distribution of the IMP to a trial site by the usual distributor is not possible or in the exceptional circumstance where a trial participant is transferred from one site to another. Sponsors should assess whether sites can handle and control such a re-distribution process, especially in case of restricted conditions for storage such as the need for specific conditions other than room temperature (e.g. +2-8° C). Re-distribution should follow a written procedure established in cooperation with the Qualified Person or the person responsible for distribution of the IMP, and sites should be provided with sufficient information to ensure that the process can be performed securely. Associated records should be included in the transfer; • In line with the reduction of physical site visits, we foresee that there will be a need for delivery of the IMP directly to trial participants during the COVID-19 pandemic to avoid that the trial participant has to reach the site with the consequent risk of spreading/acquiring infection. The delivery is generally expected to happen from investigator sites to trial participants. • Direct from sponsor to trial participant IMP delivery is accepted only in a few MS and strictly during this emergency situation. The sponsor should check the NCA guidance regarding the possibility of direct sponsor to trial participant shipment, as it is likely that such measures can only be implemented under specified conditions (e.g. agreement with sites, dedicated couriers with procedures to only allow delivery directly to a trial participant or his/her career, solid shipment and receipt procedures,

		informed consent provisions if necessary for the sponsor's third party to handle personal information etc.), and for a limited period. • Alternative shipping and storage arrangements should not compromise the treatment blinding. Changes in IMP distribution are often associated with additional changes (e.g. in the visits schedule per protocol or replacement of physical visits with virtual ones (e.g. through telephone calls)). Such changes need to be reflected in the protocol and communicated to regulatory bodies as described in section 6.
Belgium	25.03	**4. Shipment from the site to the patient** Direct shipment from sponsor to patient is not allowed in Belgium. What is allowed under these exceptional COVID-19 times under exceptional conditions: • In cases where a continued supply of trial medication needs to be maintained at home: trial medication may be shipped directly, under responsibility of the principal investigator, from the trial site to the trial participants via courier. This is only possible provided that the product is suitable for transport, storage at home and administration at home use. • In case of home administration by the participant: a care giver, nurse or physician, training on administration at home (i.e. trained in terms of the protocol) must be provided to the participant. Any additional training must be documented. Special attention should be paid to capturing adverse events and informing the PI of the subject's health and wellbeing in this off-site setting. The GMDP and GCP requirements for transport and storage of investigational medicinal products remain in place. Concluding: - Under PI's responsibility - Shipment without sponsor involvement (personal data protection) - Under correct shipping conditions - With correct & traceable documentation - Patient is trained for storage, administration at home or administration is conducted by a trained (i.e. trained in terms of the protocol) care giver, nurse or physician To emphasize: documentation is paramount. A courier under contract of the sponsor may be implied for the shipment upon condition that documentation is present before shipment, that the PI is informed, that the patient's personal data are protected and that the

		sponsor under no circumstances can obtain the personal data (like name and address) of the patient. The responsibilities of each party in this have to be documented. It must be clear that this shipment cannot happen on the expenses of the patient. Administratively: • The shipping arrangements can be considered as a non-substantial amendment to be included with the next substantial amendment. • 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. • If it concerns temporary changes to the informed consent, these changes are preferably 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. Apart from the IMP and any other medication and material specifically used for the trial, this rule can also be applied – under the same conditions - for patient diaries, pregnancy tests. Administrations of study medication by site staff/general practitioner/ nursing staff are indeed possible outside the site (for example at home, alternative location). This should be requested by the study site. A substantial amendment should be submitted to the FAHMP and the EC in accordance with questions 10 and 11 of the Q&A: Good clinical practice (GCP): […]. All of these changes in shipment should be budgeted for by the sponsor if they are necessary to ensure the continuity of the studies.
Bulgaria	24.03	The medicinal products and medical devices in the CT should be maintained in appropriate quantities in order to ensure the continuity of treatment in case of difficulty in the delivery. In exceptional cases, in the case of shortages, redistribution of quantities between sites is permitted. The sponsor should guarantee that the storage conditions and the security of the delivery are ensured, following an established written procedure and documenting each stage of the process. A notification to BDA is required. Due to the variability of CT and possible cases, all the situations may not be covered. Trial subject safety in ensuring data validity and hence the quality of the CT conduct, is the responsibility of the sponsor. Each stage of the process of taken measures and decisions should be documented. BDA will prioritize all questions related to COVID-19.
Denmark	01.04	**4. Changes to shipment/handling/stock of IMP**

		In case of urgent shortage of IMP at some sites: need to potentially re-distribute IMP between sites in accordance with GMP annex 13 (section 47). Sponsors should assess whether sites can handle and control such a redistribution process, especially in case of restricted conditions for storage, such as the need for specific conditions out of room temperature (e.g. 2-8° C). Redistribution should follow a written procedure established in cooperation with the Qualified Person or the person responsible for distribution of IMP, and sites should be provided with sufficient information to ensure that the process can be performed securely. 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. Hand-out of IMP at pharmacies: In open trials (it is not appropriate if IMP is blinded), it may be an advantage to supply IMP through Danish pharmacies. Such procedure is subject to the following terms: - This only applies to CT on Danish sites during the COVID-19 pandemic and a risk assessment must be carried out with priority to patient safety. - The trial drug must be marketed and used within the approved indication. - A simple process for reimbursement of expense should be implemented. - The name of the sponsor or investor is printed on the label together with a reference code to identify the site, investigator and trial subject. - Procedures 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 possibility for sponsors to distribute trial medicine directly to the trial subjects without involving the investigator or hospital pharmacies. This temporary option is valid until 17 June 2020. To be assessed whether an extension is needed two weeks before expiry. Sponsors may avail themselves of this option on the following terms: - Sponsor has a MIA (manufacturing authorization) or a WDA (wholesale authorization) that covers distribution of IMPs.

		- Sponsor may only distribute IMPs for CT on Danish sites and should be on the basis of a risk assessment with patient safety as utmost priority. - Prior to the direct distribution, the viability of distribution via investigator/hospital pharmacy should have been investigated. - A courier needs to ensure that the shortest possible route of transportation is used and that the terms of storage are met in all parts of the supply chain. This must be documented. - The Danish Medicines Agency Q&A guidelines on supplying trial medicine directly to trial subjects (within the section 'virtual/telemedicine trials') must be followed to the greatest extent possible. Procedures ensure that the trial medicine is delivered to the trial subject or their relatives only, and that it is possible for the trial subject to store the medicine in a suitable way. In addition, sponsor must make sure that the trial subject has the required training to self-administrate trial medicine or otherwise assess if assistance from a nurse may be required. - Direct distribution to trial subjects is implemented as an urgent safety measure. Notification to DMA in accordance with this guidance. The trial medicine may only be dispatched to trial subjects after agreement with the investigator and on the basis of the investigator's prescription. Furthermore, procedures for the accountability of the trial medicine must be in place (among other for compliance monitoring). - Sponsor may not store the personal data of the trial subject for a longer period than is required for the purpose of dispatching the medicine to the subject. Sponsor may only authorize a limited number of employees to process the personal data in order to dispatch the medicine. - Sponsor must ensure that trial subjects is informed that the trial medicine will be delivered directly to their homes. Trial subjects assigned to a Danish site but living abroad: The sponsor in these cases must consult the authorities of the country concerned, whether they impose requirements or restrictions. Stock of trial related medicinal products and medical devices: Stocks of IMP and other necessary medicinal products (NIMP) must be kept appropriately high to ensure continuity in the event of shortage. The same applies for medical devices, including IVDs, which are used for safety/efficacy monitoring and other data collection.

Estonia	01.04	**Direct supply to patient of IMP/NIMP (site to subject)** – The shipping of IMP/NIMP directly to the patient may be necessary. The shipment is usually expected to be sent only from the study site to the subject. IMP specific storage and transportation conditions must strictly be adhered to and taken into consideration when assessing the viability of direct to patient supply. Records must be kept of transfer/storage details. This option is generally considered appropriate only for self-administered treatment. The sponsor should contemplate supplying the IMP/NIMP for a longer period than would normally be considered necessary. Although a significant change in the trial conduct, under current exceptional conditions, the decision to supply IMP/NIMP from the study site directly to the patient does not require a substantial amendment (or prior approval). That change does not require a substantial amendment. A notification of the change via email is required. The email must contain justification for the changes. The notification must be sent as soon as possible. **Direct supply to patient of IMP/NIMP (sponsor to subject)** - Under exceptional conditions, having exhausted all other options, with every measure taken to ensure that the subjects' personal data are protected and that blinding procedures remain intact, under the supervision of the principal investigator and with proper documentation of the responsibilities of all parties involved (e.g. SOP, contract between the courier and the sponsor), direct shipments of IMP/NIMP from the sponsor to trial subjects may be allowed. However, this arrangement would require prior approval from the State Agency of Medicines. The sponsor must, in an email to the Agency, describe: • Shipping arrangements • Means of re-consenting the subjects • Measures of protecting the subjects' personal data from the sponsor (i.e. address, contact details) • Measures of ensuring that the blind remains intact (if applicable) • If considered acceptable, the sponsor will receive an email with permission to proceed with direct from sponsor to subject shipments. This change does not require a formal substantial amendment but prior approval is still mandatory.
Finland	19.03	Delivery of IMP to the patient As the epidemic worsens, exceptional arrangements may have to be made for the delivery of the IMP to the patient (e.g. delivery to the home address instead of handing over the medicinal products during subjects' visits to the

		research location). In such cases, these exceptional arrangements must be essential for ensuring the continuation of the study, the safety of the subjects and the reliability of the research results. The sponsor must notify Fimea of any exceptional arrangements as soon as possible and submit the protocol amendment. Fimea will prioritize the evaluation of these amendments. Delivery of IMP from the sponsor directly to the subject is not in accordance with Finnish law.
France	08.04	**Is the delivery of IMP for longer durations allowed? Yes** in compliance with safety instructions, patient information and traceability. If visits during which the IMP or devices should have been delivered to patients are skipped, arrangements must be made to assess the tolerability of the treatment and to adjust the treatment if necessary, for example by teleconsultation. ➦Notification to ANSM (SM-I) including additional measures on follow-up. ***Caution:*** narcotic products are excluded from this measure. **Is delivery of IMP to the patient's home allowed? Yes** in compliance with all safety instructions, patient information, traceability and the sponsor's instructions, established if necessary in conjunction with the manufacturer, in agreement with the research site. ➦USM then SM-A specifying the conditions for delivery, monitoring and information of participants. The delivery of the products necessary for the research to the patient remains the responsibility of the investigator and, if available at the research site, of the site's pharmacy. The sponsor provides the research site with logistical support for the transport of the products necessary for the research to the patient. If requested by the research site/pharmacy, the sponsor provides the packaging and labels. In all cases, the sponsor finances the transport. Industrial sponsors will simplify as much as possible their procedures for transporting the products needed for the research. The solutions chosen, including financial support, must limit as far as possible the additional workload for the research site and pharmacy, and must take into account the situation of each research site. For more details on the requirements to be met and the possible circuits, see the complementary document drawn up by ANSM / DGS / CNRIPH / CNIL (in French) The current version of these recommendations does not apply to the implementation of home delivery of non-self-administered IMP. If exceptionally such modalities should be considered, it is requested to

		submit a SM-A to the ANSM to ensure that all safety conditions are met for parenteral administration in the patient's home.
Germany	26.03	**2. Shipment of IMP to trial subjects** The shipment of IMP to trial subjects requires that adequate medical supervision of the subject by the investigator, in accordance with the protocol, is ensured. The following recommendations refer exclusively to IMP used autonomously by trial subjects. If it is necessary to ship IMP to trial subjects directly, shipment by the trial site itself is preferred. Shipment should be made in a manner that allows tracking of both transport and delivery. The subject should acknowledge receipt of the shipment to the trial site. In case adequate shipment by the trial site is not possible, direct transport by the sponsor may be accepted in justified exceptional cases, provided that the sponsor appoints a suitably qualified service provider as a trustee. The sponsor must contractually oblige this service provider to maintain the pseudonymization and, if necessary, blinding of the trial subjects towards the sponsor by means of appropriate measures. Both the transport and handover conditions for the IMP should be part of the contractual arrangements, so that pharmaceutical drug safety of the IMP as well as protection of the privacy and personal data of the trial subjects are adequately safeguarded. IMP must be delivered to the trial subject directly or to a person authorized by the subject and must not be given to neighbors or deposited at a storage location. Written confirmation of dose and dose regimens by the investigator should also be obtained prior to shipment. The personnel of the service provider in charge of the transport should be trained and instructed accordingly. As personal data are transferred to the service provider, this requires a contract of assignment with the sponsor or his legal representative. For direct shipment of IMP to trial subjects, written instructions on storage and return of used and unused IMP should be provided to trial subjects. When IMP is shipped by trial sites or by contracted service providers, their receipt, consumption and return must be documented in a form that allows the trial site to meet its documentation requirements (drug accountability), as defined in ICH GCP 4.6.3. Usually, the dispensing of IMP at the trial site is associated with other trial-related activities (e.g. diagnostic investigations and/or clinical evaluations). A change in the trial protocol requires in all cases approval by the higher federal authority and a favorable opinion by the ethics committee. Therefore, the intended trial protocol amendments must be submitted

		together with the intended amendments regarding IMP supply to the trial subjects as a substantial amendment according to § 10 GCP-V. When using telemedicine, the necessary standards, including the requirements for data protection, must be adhered to. If external service providers, e.g. home-care services, assume trial related tasks, it must be ensured that the source data collected by them are transmitted to the investigator and that the persons employed are subject to the investigator's instructions and reporting obligations towards the investigator. The descriptions of trial sites (which are part of the submission to the ethics committees) must be adapted accordingly. In justified individual cases, these measures can be taken to protect against immediate hazards in accordance with § 11 GCP-V. The obligation to immediately provide post-hoc information on these measures in accordance with § 13, paragraph 5 GCP-V remains unchanged. The trial subjects must be informed about the changed procedures with a supplement to the patient information and should give their consent to this.
Hungary	25.03	**IMP management** Measures to address problems with access to IMP and other medicinal products used in the clinical trial (non-IMP) shall be taken in accordance with the procedure laid down in Article 13 of The GMP. It shall be established in accordance with the procedure referred to in Article 10(2) of the processes may be carried out by a qualified and delegated person on the basis of written regulations. 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 trials where the patients self-administer the medication at home, transport of IMP and non-IMP (rescue-medication) to patients' home can be an considered. In cases like this the responsibility remains with PI. Transportation of IMPs from the site/institution pharmacy is preferred. The person who performs the transportation of IMPs must know the guidelines with regard of IMP handling. Special storage conditions must be documented all the time, but there is no need to inform National Competent Authority about this change. Any transitional measure shall be designed in such a way as to ensure that the prescribed conditions for transport/storage of the product in question during transport and storage in the patient's home, especially in special circumstances (e.g. 2-8 °C), safe custody of preparations and the relevant documentation of the accounts. To avoid IMP/non-IMP shortage an 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. Hungarian National Competent Authority agrees to make accelerated assessment in case of submissions of COVID-19 CT applications. Hungarian National Competent Authority is ready to give support to parties involved in CT. This information is updated regularly, please come back for further updates.
Ireland	02.04	Alternatives may include delivering the IMP directly from the investigator site to the subject's home. Such measures raise various practical considerations, including whether the IMP is appropriate for home administration and general storage in the home, how stability of product will be maintained during transit (especially for cold chain product), how safe custody of product will be ensured and how IMP accountability will be managed. Such measures should be coupled with infection control considerations as the situation develops. Whilst specific guidance on this topic is limited, guidance from the Pharmaceutical Society of Ireland on the home delivery of medicines may be considered during decision making (version 1, July 2014, available here) and Joint HSE and PSI guidance on home delivery of medicines (dated 30 March 2020, available here). It should be noted that the guidance applies to retail pharmacy businesses and is specific to authorized products, and does not encompass all aspects relevant to the delivery of IMP, however, the principles may be of benefit in decision making. The HPRA Guide to Control and Monitoring of Storage and Transportation Temperature Conditions for Medicinal Products and Active Substances should also be considered (IA-G0011-2, dated 17 June 2017, available here.) Changes to existing practice should be proportionate and based on benefit-risk principles, and the provision of IMP to patient directly in a healthcare facility is generally regarded as best practice, notwithstanding the potential impact of COVID-19. The direct supply of IMP from sponsor to subjects is not currently considered acceptable. The allocation of IMP is the responsibility of the investigator (ref: ICH GCP E6 4.6). As outlined under the investigator and site staff considerations section of this guidance, the supply of IMP from the investigator site to the subject's home via a delivery service may be considered, and the sponsor may provide assistance and advice to the investigator in relation to this.
Italy	16.03	**Investigational medicinal product (IMP) management**

		If possible, when the patient goes to the study site for a visit, it may be useful to provide an amount of medicinal product covering a longer period of time than is normally estimated. According to current legislation (article 7 of the Ministerial Decree 21st December 2007), the Sponsors must send investigational drugs needed for the trial to the pharmacy of the investigational site, that is in charge for their registration, appropriate storage and delivery to the investigator. Therefore, considering the COVID-19 serious emergency, direct deliveries from the hospital pharmacy to the trial subjects also through dedicated couriers can be arranged, upon indications of both the hospital pharmacy Director and the Principal Investigator (PI). It is intended that the hospital pharmacy is responsible for the process supervision; the pharmacy and the PI must be constantly informed on the delivery, according to procedures established for the correct conduction of the trial and by the above-said risk plan, that must take into account the IMP typology, administration methods, conservation and transport. Adequate remote communication ways with involved subjects must be implemented 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. All this without prejudice, if possible, to conditions set out in FAQ 10 of the EMA Document "Q&A: Good clinical practice (GCP)" – GCP Matters [...]. If the CRA of the study is not able to carry out the control on the final accounting of the IMP 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.
Latvia	17.03	4. In reasonable cases, home delivery of study drugs from CT site may be acceptable, ensuring that applicable regulations governing distribution of medicinal products are followed and that transport and storage conditions are respected. If appropriately documented, re-distribution of study drugs between study sites is also possible, if sites experience shortages in drug supplies.
Netherlands	02.04	Study medication can be sent directly to the research subject by courier from the (hospital) pharmacy for reasons of subject safety; you need not inform the review committee about this, but do record this temporary procedure in writing
Poland	30.03	**3.1.1 Delays in delivery of medicines to the center**

		1. Continuous monitoring by the Sponsor of the study / CRO of the situation related to the amount of study drug available in centers throughout the country 2. Ongoing contact with the drug supplier to ensure operational continuity by identifying potential breaks in the supplier's work 3. Determining an alternative drug supplier 4. Determining the mechanism of drug transfer between centers, if possible 5. Ensuring a greater supply of medicines in centers, increasing its availability **3.1.2 The patient cannot collect the medicine at the center** (e.g. due to quarantine, hospitalization in another center, patient's decision, a ban on leaving home, the problem of returning to the country) 1. Development of instructions for the procedure/procedure for the delivery of medicines to the patient's home by the study sponsor / CRO in cooperation with the sponsor and the center, including the transport conditions (documentation plus the conditions under which the drug may be transported). You should consider courier companies operating in Poland 2. Verification of transport conditions in terms of courier safety minimizing the risk of spreading infection (e.g. by providing procedures limiting courier-patient contacts) 3. Appropriate designation of the drug prepared for transport (drug number, patient identification number). 4. The development of a procedure by the center adapted to the capabilities of the center and the properties of the drugs used in the study (e.g. medical transport of the center, collection by a family or an authorized person together with appropriate documentation of the process). Always take into account the test drug storage and transport specification prepared by the manufacturer and approved 5. In the case of using the option of receiving the test drug by a person dedicated by the patient - confirmation of the identity of the recipient with the patient, identifying the person before dispensing the test drug, instructing the patient about telephone confirmation with the staff of the Center of the fact of receiving the drug 6. Each time confirming with patients the possibility and method of delivering the medicine to the patient's home. Before transport and confirmation of receipt of the medicine. The patient should start taking the medicine only after confirming with the Center staff the appropriate

		medicine (compliance with the assignment in the IVRS / IXRS system or other automatic system) 7. Always document how the medicine is delivered to the patient's home in medical records 8. For patients outside the country - arranging the delivery of medicines to the place of residence or redirecting the medicine from the nearest center in a given country, if possible taking into account the process of obtaining an import license, if applicable **3.1.3 Center staff cannot dispense medicine to a patient** (in connection with the closing of centers, the transformation of centers into infectious hospitals, staff caring for underage children, quarantined staff, infected staff) 1. Delegation of tasks between medical staff, within legal possibilities, to ensure substitution 2. Joining additional people to the team of the center, taking into account the necessity of training in the examination procedures and appropriate documentation of the role of the added persons and tasks delegated to them 3. Checking the possibility of using an alternative location / satellite center **3.1.4 Difficult access to the IMP in the center (restrictions on drug access at the center, short expiry date of the drug supply)** 1. Monitoring of the drug stock available at the center by dedicated staff and immediate communication of deficiencies. As far as technically possible and in cooperation with the Research Sponsor/CRO managing drug allocation, rationalization of drug use with the shortest expiry date in the first place 2. Test sponsor's examination of the possibility of extending the drug's expiry date and changing the label with the expiry date (relabeling) by trained center staff 3. Arrangement with the sponsor of the study to increase the supply of study medication **3.1.5 Access to supportive therapy (non-IMP / SoC)** (inability to provide supportive / rescue medication, limited availability of such medications in warehouses, breaks in warehouses 1. Creating a mechanism for purchasing registered supportive or rescue medications by patients at the pharmacy and ensuring reimbursement when settling patient costs

		2. Creating the possibility of non-cash settlements between the pharmacy and the center and refunding these purchases to the Center by the survey sponsor **3.1.6 Management and the form/method of administration of the IMP (drug that must be administered by medical staff, the need to assess the patient's state of health before and after administration of the test drug)** 1. Checking the requirements for technical conditions and equipment necessary for proper preparation of the drug for administration. In addition, checking the conditions necessary for proper administration of the drug to the patient and legal requirements regarding the management of a given class of the drug (e.g. providing protection against cytostatic, even in the form of PO, which are treated as hazardous substances, requiring appropriate handling, storage and disposal - practically eliminating the possibility of sending and administering such treatment at the patient's home) 2. Checking the possibility of self-administration by the patient in parenteral (non-intravenous) form 3. Delegation of an authorized person from the research team (e.g. nurse, co-investigator), with the required precautions ensuring the safety of both the patient and the delegated person, to administer the medicine as part of the home visit, after obtaining the patient's consent for such procedure by phone and with appropriate documentation in patient's medical records 4. Appropriate preparation of the drug that would be administered at home to the patient in accordance with the instructions in the study and ensuring the transport of the drug in accordance with the manufacturer's instructions. Each step should be documented in the patient's medical records 5. Checking the possibility of performing laboratory tests in a local laboratory if necessary before administering the medicine 6. Checking the possibility of hiring external nursing staff to administer the study medication at the patient's home - Patient Concierge **3.1.7 Return of the drug (collection of unused medicines and empty packaging in patients / facilities)** 1. Organizing the collection of medicine from patients and delivering to the center using the drug supplier. If this is not possible, leave unused medicines / packages after the used medicines on the patient until visiting the center **3.1.8 Documenting deviations from the study protocol**

		1. Ongoing documentation of any activities undertaken outside the audit procedures approved by regulatory authorities and bioethics committees by the Center 2. Verification of the above by the test monitor, documenting in reports on visits / telephone contacts 3. Establishing a procedure for reporting deviations from protocols to Regulatory authorities and bioethics committees **3.1.9 Infringement of patients' personal data** (improper procedures for passing medicine to a patient through third parties Develop a procedure and ensure that the courier / drug supplier will not provide the Sponsor / CRO with patient data
Portugal		**D. Direct dispensing at home of IMP** Given the exceptional circumstances, dispensing at home can be accepted, based on the following premises: • Ensuring that the Principal Investigator and the research team (including the hospital pharmacy) maintain the supervision of this process, ensuring communication channels that allow participants to clarify doubts. • Ensure that access to personal information (name and address) is allowed by the participant. • Records are made to track transport from the point of departure (rehearsal center), to delivery to the participant. • Records on packaging methods are ensured. • Guaranteed temperature / humidity records during transport. • In cases where reconstitution is necessary, the period of stability of the medicine between the time of reconstitution and its administration must be taken into account, this possibility being only applicable in cases where the administration does not require the intervention of a health professional* that the patient receives all the information and is informed about the administration and surveillance process, as well as has the necessary contacts for the communication of adverse effects / serious adverse effects • Ensure that the test concealment is not broken, in the applicable cases. * in cases where the administration requires the intervention of a health professional, it is not possible to guarantee that this will be carried out at the participant's home (ensuring all safety conditions for the patient and the

		health professional, as well as all means technicians), transferring the patient to another alternative clinical trial center should be considered. If the transfer is not possible, the research center must be closed, with all the procedures inherent to the end of the study, ensuring the safety and well-being of the participants. The follow-up of patients after early trial completion at the research center should follow the guidelines outlined in the clinical trial protocol for these cases. The provisions of section 10 of the document "Q&A: Good clinical practice (GCP)" - GCP Matters should also be considered. **B. Disruption of supply of the ME** Ensure reserve stock for the participants, for at least 3 months. In case of impossibility to guarantee reserve stock: • evaluate the possibility of suspending the recruitment of participants • evaluate the need to suspend the CE, according to the criticality of the participants' health status, therapeutic indications, and risks of discontinuation (p (e.g. cytotoxic) **C. Disruption of supply of NIMPs / Disruption of supply of medical devices necessary for the administration or manipulation of the ME** Assess whether they belong to the Strategic Medicines Reserve, published in Diário da República, Order No. 3219/2020 […]. If not, guarantee reserve stock for the participants, for at least 3 months.
Romania		For the term specified in Order 74527 / 23.03.2020 […] (14 days starting with 24.03.2020), scheduled visits of subjects enrolled in CT will no longer be allowed, unless deemed an emergency by the doctor (main investigator) on a case-by-case basis, any delay in the respective case likely to affect the subject's/patient's safety.
Slovakia	02.04	Provision of IMP to participants in the SC • One possibility may be to provide IMP and concomitant medicines (non-IMP) for a longer period of time than originally planned; • In order to minimize visits to healthcare facilities, we recommend an authorized transporter, if it can be used (e.g. the dosage form is suitable for home administration and storage), who will ensure the transport of IMP from the CT center to the CT participant' place of residence. Delivery of IMP to CT participant directly from sponsor is not allowed in Slovakia. For the transport of IMP, the investigator is responsible for the costs but they are borne by the sponsor (contractual arrangement). The sponsor shall also ensure that the CT participant's protection of personal data is maintained (contractual terms) i.e. unauthorized

		persons, including the sponsor, will not access personal data (name and address). • GMDP and GCP requirements for IMP transport and storage should be maintained (e.g. transport temperature control). The carrier will be ordered by the investigator and subsequently confirms the takeover of the IMP to the participant by telephone and records it into the CT documentation source. CT sites must be trained to administer and store IMP. IMP transport should be in accordance with GCP requirements documented. Records of IMP shipments containing the participant's personal data, should be kept at the CT center for traceability. If needed, copies of records of IMP transport should be kept in TMF e.g. documentation of protocol deviation, pseudonymized copies that do not allow identification of the CT participant. Where collateral transport of IMP from the CT center directly to CT participants is a substantial burden, the CT center can entrust other medical activities staff, while the responsibility remains with the investigator (GCP 4.2.5, 4.2.6); • in the event that the CT participant has to bring unused IMP during the planned visit, it can be directed not to use the remaining packs and to bring them when he/she can meet come to the investigator, if applicable • Another possibility is to have the IMP picked up by a relative after the investigator verifies such an option with the center for a particular CT participant. Subsequent acceptance of IMP by the CT participant will be verified by telephone by the investigator and recorded in the source documentation together with information on the previous issue of IMP to a relative; • the sponsor shall provide detailed written instructions to the investigator for each study concerning the distribution of IMP to the CT participants, and will send them to SUKL for information • if the assistance of a physician or other health care provider is necessary to administer the IMP, the employee and participant must visit the CT center. We recommend to postpone the personal visit of the CT participant at the center for as long as possible. If it is not possible to postpone the administration of IMP at the CT center, or it is no longer possible to postponed more, the administration of IMP at the CT center should be carried out in compliance with safety Hygiene rules (referred to above when providing healthcare).
Spain	16.03	**Clinical trials** 3. Access to trial treatment Patient access to trial medication must be guaranteed in the same conditions in which it was occurring. It is recommended that the

		investigator assesses the possibility and convenience that, when the patient comes to a scheduled visit, he receives a quantity of medicine that allows him to cover a longer period of treatment. The Pharmacy Services of the hospitals may take the measures they consider necessary, for example, dispensing to a person authorized by the trial subject of a treatment that must be taken at home or sent the treatment at the patient's home when their circumstances make it advisable. In relation to the latter, the conservation of the treatment during the transportation and communication with the patient that allows reception and adequate administration of the same. Section 10 of the document "Q&A: Good" will be taken into account clinical practice (GCP) "- GCP Matters". The situation must be assessed in each particular case, by the sponsor, the main investigator and the Pharmacy Service.
	07.04	**Observational Trials** Idem
	Order SND/293/2020 – 27.03	**Medicines used in clinical trials** As regards products that are currently being used in CT, the hospital pharmacy will be allowed to dispense the amount of products needed to cover a treatment for a period longer than the ordinary one. Furthermore, the regional authority may also adopt measures so that patients participating in the trial may receive the product in their domiciles. For such purposes, the competent authority may give instructions to the sponsor of the trial ordering it to provide the necessary logistics under the direction of hospital pharmacy services and of the principal investigators. **Hospital used medicines** Finally, regional authorities may also approve measures so that medicines which are normally restricted for use only in hospitals may be administered to patients at their domiciles or outside the premises of the hospital if this is convenient considering the condition of the patients, their pathologies, the characteristics of the product or the epidemiological situation.
Sweden	24.03	**Handling of trial medication** The regulation presupposes that trial medication is being delivered to the trial site and then handed over to the patient. However, during the current circumstances, we understand there might be situations with a need for delivering trial medication directly to trial subjects in their private homes. Some important aspects to consider are: - The integrity of the trial subjects must be protected. The identity of the subject must be kept unrevealed to the sponsor. All delivery of trial

		medication to a trial subject's home must therefore be performed from the hospital/clinic or from a pharmacy involved in the trial. - Product quality: The deliveries must fulfill the temperature storage requirements specified for the product. - Control of each product throughout the entire chain: It must be ensured that the correct trial medication and quantity is delivered to the correct subject. The trial medication must not be delivered to a mailbox, outside the door or equivalent. The delivery handling shall be documented. - Patient safety: Home delivery must not replace a planned investigator contact. The above aspects can be handled as Urgent Safety Measures.
Switzerland	07.04	The implementation of changes in the distribution of IMPs is strictly limited to the COVID-19 pandemic period. The sponsor must assess the risk relating to the product and the appropriateness of storing and administering the IMP at the study participants' home. It lies within the responsibility of the investigator to assess, whether the administration of the study medication at the patients' home is medically justified and ensures best patient safety. Therefore, a change in the distribution may only be introduced in agreement with the investigator. The procedure is only permitted for IMPs, which are suitable for use at home. The study participants have to be informed appropriately upfront. Please use the new addendum to the study patient information made available by Swissethics on swissethics.ch / COVID-19. The sponsor should establish written procedures in order to ensure the stability of the IMPs during the transport and the storage at home. The receipt of the IMP should be confirmed by the study patient to the investigator. The requirements with respect to the drug accountability as defined in ICH GCP E6(R2) have to be fulfilled. The delivery of the study medication may only be made from the trial site to the study patient. The distribution of study medication from the manufacturer/warehouse to the study patients is not allowed. It must be assured by appropriate measures that personal data of the study participants (e.g.: name, address, phone number) are not transmitted to the sponsor for the purpose of IMP delivery. Changes in the distribution of the study medication have to be notified to Swissmedic and to the lead ethics committees for information. The authorities reserve the right to contact the sponsor for further clarifications if needed. - Swissmedic: The sponsors are requested to confirm in writing (using the form "Submission of Changes to a Clinical Trial and Answer to

		Conditions") that the only change is the shipment of the IMPs from the trial sites to the patients' home. Swissmedic will issue an acknowledgement of receipt, but the change can be implemented before this acknowledgement is issued. - Lead ethics committees: The "silent acknowledgement" procedure applies.
U.K.	09.04	**MHRA** If a trial volunteer cannot attend a trial site, then delivery of IMP to a patient's home is acceptable and no substantial amendment notification to the MHRA will be required. Sponsors should do a risk-assessment and record this internally. Participants must consent verbally (and this should be documented in their notes) to providing contact details for shipping purposes. 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 requirements, 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 is delivered in ambient temperature **Delays in posting** This will depend on the trial, but it is worth considering if there is potential to affect continuity of supply. Shortage of the medicine may be crucial for some trials but not others. **Medicine accountability** 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

		Whether there needs to be a follow-up call to the subject
	26.03	**HRA** **3.1.3. Studies where treatment or IMP need to be sent by courier direct to participants or other alternative mechanisms of provision** Sponsors must assess the risks relating to the product and consider any shipping and storage arrangements. Participants must consent verbally to providing contact details for shipping purposes. Where participants are self-isolating or in quarantine, arrangements for a nominated person to collect product may be implemented with the participant's verbal consent. Any such temporary arrangements should be handled as a **non-substantial amendment** that does not require HRA/HCRW Approval or R&D agreement. For studies involving the NHS/HSC, these should be marked **by the sponsor** as category C and not requiring assessment and sent directly to sites following the instructions above. These should be implemented at sites on the date specified by the sponsor.