EMA Guidance on the Management of Clinical Trials during the COVID-19 (Coronavirus) pandemic
EMA 关于在 COVID-19（冠状病毒）大流行期间临床试验管理指南

中国医药创新促进会国际部翻译整理

Version 1 (20/03/2020)
第一版（2020 年 3 月 20 日）

The European Medicines Agency (EMA), Good Clinical Practice (GCP) Inspectors Working Group, the Clinical Trials Facilitation and Coordination Group (CTFG, a working group of the Heads of Medicines Agency (HMA)), the Clinical Trials Expert Group (CTEG, a working group of the European Commission representing Ethics Committees and National Competent Authorities) and the European Commission (EC) acknowledge the impact of COVID-19 on the health system and broader society, and the impact it may have on clinical trials and trial participants[1]. Extraordinary measures may need to be implemented and trials adjusted due to e.g. trial participants being in self-isolation/quarantine, limited access to public places (including hospitals) due to the risk of spreading infections, and health care professionals being committed to critical tasks. Therefore, EMA, EC and HMA strongly support the efforts of the GCP Inspectors' Working Group for developing harmonised EU/EAA-level guidance to mitigate the negative effects of the COVID-19 pandemic on the conduct of clinical trials.

欧洲药品管理局（EMA）、欧盟药品临床质量管理规范（GCP）检查员工作组、临床试验促进和协调工作组（CTFG，隶属于药品监管机构负责人组织（HMA））、临床试验专家工作组（CTEG，隶属于欧盟委员会（EC），代表伦理委员会和国家主管当局）和 EC 认识到 COVID-19 对卫生系统及广大社会的影响，以及可能对临床试验和受试者造成影响。在诸如受试者处于自我隔离或隔离状态、因存在传播感染风险而无法进入公共场所（包括医院），以及医护人员执行严峻工作时，需要实施特殊手段并调整临床试验。因此，EMA、EC 和 HMA 坚决支持 GCP 检查员工作组为制定统一的 EU / EAA 级指导方针以减轻 COVID-19 大流行对临床试验的负面影响而做出的努力。

The situation is evolving, and pragmatic actions may be required to deal with the challenges of conducting research, and in ensuring the rights, safety and wellbeing of participants. The points mentioned below are intended to provide guidance for all parties involved in clinical trials during this time.

面对不断升级的疫情，需要采取务实的行动来应对临床试验过程中的挑战，并确保受试者的权利、安全和健康。以下要点旨在为疫情流行期间参与临床试验的各方提供指导。

Due to the urgency, this guidance is issued without prior public consultation. The sponsors should note that due to the rapidly evolving situation further updates to this guidance are possible and likely.

鉴于紧急情况，本指南的发布未事先征询公众意见。申办者应注意，由于疫情的迅速蔓延，本指南有可能会做出相应修订。

Sponsors and investigators need to take into account that there might be specific national legislation and guidance in place, which they should consult and which can be used to complement this guidance, or, with respect to particular matters may take priority over these recommendations. This document is however seeking to include most of the current guidance across Member States with the aim to serve as an EU-level harmonised set of recommendations. Hence, this guidance is agreed by the Clinical Trials Expert Group (CTEG) of the European Commission supported by the EMA, the Clinical Trials Facilitation and Coordination Group (CTFG) of the Heads of Medicines Agencies (HMA) and the GCP Inspectors' Working Group coordinated by the EMA.

申办者和研究者应考虑到，可能有一些国家法律和指南已在实施，这些立法和指南应作为参考，并可用作对本指南的补充，或者就某些特定事项而言，优先遵循这些立法和指南。但是，该文件旨在囊括各成员国当前的大多数指南，以期在欧盟级别达成一致。因此，本指南经 EC CTEG 同意，并由 EMA、HMA CTFG 和 EMA 协调的 GCP 检查员工作组共同支持。

1The word « participant » is used in this text as a synonym for the term “subject”, defined in Directive 2001/20/EC as an individual who participates in a clinical trial as either a recipient of the investigational medicinal product or a control”.

1在本文中，“参与者”一词是“受试者”一词的同义词，在指令 2001/20 / EC 中定义为“参加临床试验的人是接受研究药物或对照的人”。

Introduction
I. 前言

Various challenges exist which result in restrictions of visits to healthcare facilities, increased demands on the health service and changes to trial staff availability. Participants may also be required to self-isolate, which introduces difficulties for Investigators to maintain their medical oversight. These challenges could have an impact on the conduct of trials, such as the completion of trial assessments, completion of trial visits and the provision of Investigational Medicinal Products (IMPs).

当前临床试验中存在各种挑战，这些挑战导致了医疗机构的访视限制、医疗服务的需求增加以及执行试验人员的不稳定性。受试者还可能被要求进行自我隔离，给研究者进行医疗监督带来了困难。这些挑战可能会影响试验的进行，例如完成试验评估，完成访视和提供试验用药品（Investigational Medicinal Products，以下简称 IMPs）。

The impact of COVID-19 on ongoing trials, on opening a new trial site in an existing trial, ongoing recruitment and continued involvement of participants in the trial, or on starting of new trials needs to be considered. This evaluation should take into account national recommendations including travel restrictions and confinements of trial participants and trial staff and the availability of trial staff to perform visits, enter data in the Case Report Form (CRF), notify serious adverse events and, more generally, follow the protocol. The ability to confirm eligibility and to conduct key safety assessments and trial evaluation is of particular importance. Actions should be proportionate and based on benefit-risk considerations, on contingency provisions taken nationally and locally by the authorities with priority given to the impact on the health and safety of the trial participant. Where a trial participant is unable to attend the site, other measures, such as home nursing, if possible given social distancing needs, or contact via phone or telemedicine means, may be required to identify adverse events and ensure continuous medical care and oversight. However, the limitations and risks of such methods and the requirements for data protection should be taken into account and such alternative arrangements need to be adequately documented.

对正在进行的临床试验、在现有试验和招募过程中开设新的试验机构、继续招募受试者，或者开始新试验，都需要考虑 COVID-19 的影响。该评估应考虑国家建议，包括旅行限制、受试者和试验人员的限制以及试验人员是否能够进行访视、在病例报告表（Case Report Form，CRF）中输入数据、通报严重不良事件、以及更通俗地说，遵循方案。具备确认进行关键安全性评估和试验评估的资格和能力尤其重要。采取的行动应适当，并基于利益风险的考虑，当局在全国和地方采取的应急规定，应优先考虑对受试者的健康和安全的影响。如果受试者无法进入试验机构，则可能需要采取其他措施，例如考虑到社区隔离的需求，如有可能，可进行家庭护理，或通过电话或远程医疗手段进行联系，以识别不良事件并确保持续的医疗护理和监督。但是，应考虑到这种方法的局限性和风险以及对数据保护的要求，并且这些替代性安排也必须得到充分的记录。

Initiating new trials
开展新临床试验

The feasibility of starting a new clinical trial or including new trial participants in an ongoing trial should be critically assessed by sponsors.

申办者应严格评估开始新临床试验或在正在进行的试验中招募新的受试者的可行性。

Changes in ongoing trials
进行中的临床试验的变更

The sponsors should consider in their risk assessment whether the following measures could be the most appropriate during COVID-19. Measures should generally be agreed with investigators and could be:

申办者应在其风险评估中考虑在 COVID-19 期间以下措施是否最合适。通常应与研究者达成共识，可以是：

- Conversion of physical visits into phone or video visits, postponement or complete cancellation of visits to ensure that only strictly necessary visits are performed at sites;
  将实际访视转换为电话访视或视频访视，推迟或取消访视，以确保仅严格且必要的访视在机构内执行；

- A temporary halt of the trial at some or all trial sites;
  在某些或所有试验机构暂停试验；

- Suspension or slowing down of recruitment of new trial participants;
  暂停或延缓新受试者的招募；

- Extension of the duration of the trial;
  延长试验期限；

- Postponement of trials or activation of sites that have not yet been initiated;
  推迟试验或激活尚未启动的机构；

- Closing of sites. In case it is not feasible for a site to continue participation at all, the sponsor should consider if the trial site should be closed and how this can be done without compromising safety and well-being of patients already participating and data validity;
  关闭试验机构。如果某个机构无法继续参与，则申办者应考虑将其关闭，以及如何在不损害受试者安全和健康以及数据有效性的前提下进行；

- If unavoidable (it should be justified that this is a truly exceptional situation based on the personal risk-benefit ratio for the individual trial participant), transfer of participants to investigational sites away from risk zones, or closer to their home, to sites already participating in the trial, or new ones could occur. Initiation of new trial sites is generally not expected in the current situation unless no other solution exists for the trial participant. If there is an urgent need to open a new trial site for critical trial visits for example outside the hospital, this may be implemented as an urgent safety measure (USM) first, with a substantial amendment (SA) application submitted later as for the approval and initiation of an additional site later. The exceptional situation could involve e.g. a trial participant who urgently needs to stay in the trial and for whom no other sites are available. In such cases, it is important that trial participants as well as investigators (both receiving and sending) are in agreement about the transfer and that the receiving site has the possibility to access previously collected information/collected data for the trial participant and that any eCRF can be adjusted accordingly to allow the receiving site to enter new data. The impact on trial participants should be considered and arrangements made to e.g. appropriate transportation; transport;
  如果必须关闭试验机构（此为基于受试者个人风险收益比而判断的极其特殊的情况），则应将受试者转移到远离风险区或离家较近的研究机构，或者转移到已经开展试验的机构中，亦或是可能出现的新试验机构中。在当前情况下，通常不希望启动新的试验机构，除非没有其他解决方案。如果需要紧急启动新的试验机构进行关键性试验访视，例如在院外访视，则可以先作为

紧急安全措施（urgent safety measure，USM）实施，然后提交重大修改（substantial amendment，SA）申请。特殊情况可能涉及迫切需要继续参加试验且没有其他机构可用的受试者。在这种情况下重要的是，受试者和（接收和派遣）研究者都应就转移达成一致，并且接收机构可以访视之前收集的受试者信息/数据，允许接收机构对任何电子病历报告表进行相应地调整和输入新数据。应考虑转移过程对于受试者的影响并作出安排，例如合适的运输、交通等。

- There may be a need for critical laboratory tests, imaging or other diagnostic test to be performed for patient safety. In case the trial participant cannot reach the site to have these performed, it is acceptable that laboratory, imaging or other diagnostic tests are done at a local laboratory (or relevant clinical facility for other tests) authorised/certified (as legally required nationally) to perform such tests routinely (e.g. blood cell count, liver function test, X-ray, ECG etc.), if this can be done within local restrictions on social distancing. The sites should inform the sponsor about such cases. Local analysis can be used for safety decisions. If this is a trial endpoint and the samples cannot be shipped to the central lab, analysis should be performed locally and then explained, assessed and reported in the clinical study report following ICH E3.
  为了患者的安全，可能需要进行关键的实验室检查，影像检查或其他诊断检查。如果受试者无法到达现场进行检查，则可以在授权/有资质（符合国家法律要求）的地方实验室（或可进行其他检查的相关临床设施）中进行实验室、影像学或其他诊断检查。如果在当地社区隔离限制条件下可以操作，则应例行此类检查（例如血细胞计数，肝功能检查，X 射线，ECG 等）。机构应将此类情况通知申办者。地方分析可用于安全决策。如果这是试验终点，并且样品无法分发到中央实验室，则应在当地进行分析，然后在遵循 ICH E3 指导原则的情况下在临床研究报告中进行解释、评估。

The changes above may also be initiated by the investigator sites contacting the sponsor. There might also be cases where the current principal investigator (PI) of a site is indisposed for a period and may need to delegate parts of his/her duties temporarily to e.g. a sub-investigator. Any permanent changes in PI should be submitted to the National Competent Authority (NCA) and Ethics Committees as appropriate.

上述更改也可以由研究者所在机构联系申办者发起。在某些情况下，某一地区的主要研究者（PI）可能会在一段时间内无法进行试验，并且可能需要副研究者暂时代理其部分职责。如需永久变更 PI，应酌情提交给国家主管当局（National Competent Authority，NCA）和道德委员会。

When changes in ongoing trials are considered, the overall well-being and best interests of the participant should be also considered, for example in trials for patients with life-threatening or severely debilitating conditions, when participants require to stay on trial treatment. In cases, when trial halt, even if temporary only, can potentially compromise the overall well-being and best interest of trial participants, all measures need to be considered and taken to avoid this.

变更正在进行的试验，还应考虑受试者的整体健康和最大利益，例如存在有生命危险或严重衰弱的患者的试验，受试者需要继续接受试验治疗。在某些情况下，即使只是暂时停止试验，也有可能损害受试者的整体生命健康和最大利益时，则应考虑并采取一切措施来避免这种情况。

Changes should be well balanced, taking into account in particular the legitimate interest of trial sites in avoiding further burden in terms of time and staffing during the COVID-19 pandemic.

应当充分平衡考虑各种变化，尤其是试验机构的合法利益，以避免在 COVID-19 大流行期间造成

时间和人员的进一步负担。

Please note that prospective protocol waivers remain unacceptable and that patients should not be included in trials without proper eligibility assessment, including performance of planned tests, and written informed consent according to national laws and regulations.

请注意，预期的方案豁免仍不适用，并且在没有进行适当的资格评估（包括进行计划的测试，以及符合国家法律和法规的书面知情同意）情况下，不应将患者纳入试验。

Compliance with the trial protocol should be ensured to such an extent that an ongoing benefit-risk assessment for the clinical trial and its participants is still possible. The impact of protocol changes on clinical data interpretability needs to be properly assessed by the sponsor and the overall evidence generation package could be subsequently discussed within scientific advice with regulatory authorities. Guidance on methodological considerations is being prepared by the CHMP Biostats working party and will be linked to this document once finalized.

应严格执行试验方案，以确保正在进行的临床试验及受试者的利益风险评估不受影响。申办者应相应评估方案变更对临床数据解读的影响，随后可与监管机构对所有证据资料进行科学的建议和讨论。欧盟人用药委员会(CHMP)的生物统计工作组正在筹备方法学的指导意见，定稿后将附在该文件链接中。

Risk assessment
风险评估

The safety of the participant is of primary importance, and risks of involvement in the trial, in particular with added challenges due to COVID-19, should be weighed against anticipated benefit for the participant and society (ref: principle 2.2 of ICH GCP).

受试者的安全是最重要的，应权衡参与试验对于受试者和社会的风险，尤其是 COVID-19 带来的挑战，以及预期的收益（参考：ICH GCP 原则 2.2）。

All decisions to adjust clinical trial conduct should be based on a risk assessment by the sponsor (ICH GCP section 5.0). It is expected that the sponsor performs a risk assessment of each individual ongoing trial and the investigator of each individual participant and implements measures which prioritise subject safety and data validity. In case these two conflict, subject safety always prevails. These risk assessments should be based on relevant parties' input and should be documented on an ongoing basis. It is important that sponsors in their risk assessment consider prioritisation of critical tasks in the clinical trial and how these are best maintained.

调整临床试验的所有决定均应基于申办者的风险评估（ICH GCP 第 5.0 节）。申办者应对每个正在进行的试验和每个受试者的研究者进行风险评估，并优先考虑实施以受试者安全和数据有效性的为前提的措施。在二者冲突的情况下，始终以受试者的安全为重。这些风险评估应基于相关方的意见，并应持续记录在案。重要的是，申办者在进行风险评估时应考虑临床试验中关键目标的优先级，以及如何最好地维护这些目标。

The sponsor should reassess risks as the situation develops. This reassessment should also be documented.

申办者应根据情况的发展重新评估风险。重新评估也应记录在案。

It is possible that with the escalation of the pandemic, local circumstances lead to a local change in risk assessment, therefore the need to implement additional measures may arise, and an investigator-driven risk assessment might be necessary (and communicated to the sponsor).

随着疫情升级，当地情况可能导致风险评估在当地发生变化，因此可能需要实施其他措施，并且

有必要进行研究者主导的风险评估（并传达给申办者）。

Regarding participants enrolled in ongoing clinical trials who may be determined as being a risk group for COVID-19 or who are in trials involving therapies which may increase such risk, the potential impact of COVID-19 on these patient groups should be carefully considered when deciding to start or continue such trials.

对于正在试验中的受试者，他们本身可能是 COVID-19 风险较大的人群，或者参与的治疗可能增加风险，在决定开始或继续进行此类试验时，申办者应仔细考虑 COVID-19 的潜在影响。

Communication with authorities
与当局沟通

Priority is given to any (new) clinical trial applications for the treatment or prevention of COVID-19 infection, and/or substantial amendment applications to existing clinical trials necessary as a result of COVID-19.

优先审核用于治疗或预防 COVID-19 感染的任何（新）临床试验申请，和/或由于 COVID-19 而必须对现有临床试验进行的重大修订的申请。

In case the risk assessment leads to actions that affect the trial as described below in a) and b), the relevant competent authorities and Ethics Committees must be informed in accordance with the Directive 2001/20/EC and national laws:

当风险评估产生下述 a)和 b)中影响试验的行为时，则必须根据第 2001/20 / EC 号指令和国家法律告知相关主管部门和伦理委员会：

a) When a new event is likely to have a serious effect on the benefit-risk balance of the trial, it is possible that immediate actions are required by the sponsor and investigator to protect the subjects against immediate hazard. These, urgent safety measures may be taken without prior notification, but the information needs to be provided ex post to the National Competent Authority (NCA) and the Ethics Committee as soon as possible (EC 2010/C82/01; 3.9). In this communication, the sponsor is expected to provide adequate information on the measures taken and the plan for further actions;

a）如果新事件可能对试验的利益风险平衡产生严重影响，则申办者和研究者可能需要立即采取行动，以保护受试者免于急性危害。可在没有事先通知的情况下采取紧急的安全措施，但是必须尽快将信息提供给国家主管部门（NCA）和伦理委员会（EC 2010 / C82 / 01; 3.9）。在沟通中，申办者应提供有关采取的措施和进一步行动计划的充分信息；

b) If changes are likely to affect the safety or well-being of the participants and/or the scientific value of the trial, but do not require immediate action from sponsor or investigator, it should be possible to submit them as substantial amendment applications. Sponsors are encouraged to take into account the limited capacity of assessors, and submit only high quality, complete applications containing only the necessary changes. Over-reporting should be avoided (Art. 11b of Directive 2001/20/EC CT-1section3.9).

b）如果更改可能会影响受试者的安全或生命健康和/或试验的科学价值，但并不需要申办者或研究者立即采取行动，则应将其作为重大修订申请提交。申办者应考虑到评估者能力有限，并且仅提交高质量、完整的申请，其中仅包含必要的更改。应避免过度报告（条款 2001/20 / EC CT-1 章节 3.9 中的 11b 部分）。

Unless otherwise advised by relevant authorities, it is recommended to mark any contact clearly with 'COVID-19' in the subject field.

除非相关当局另有建议，否则建议在主题字段中填写“COVID-19”并清晰标记所有联系人。

Agreement with and communication to sites
与试验机构达成协议并进行沟通

Changes to trial conduct should be agreed with and communicated clearly to investigator 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. Agreements may be documented as e-mail exchange.

试验实施变更应得到同意，并明确传达给研究者所在机构。为了方便试验机构实施，应该明确更改的内容以及对当地的影响，包括使用修订痕迹修改文档。可通过电子邮件往来记录达成的共识。

Changes to informed consent
知情同意书的变更

Sponsors should be mindful of the current pressure on the medical profession and should carefully assess the pertinence of adding new subjects in ongoing clinical trials. Absolute priority should be given to clinical trials on treatments for COVID-19 and COVID19-COVID-19related illnesses, or trials on serious diseases with no satisfactory treatment option. In case a sponsor plans to initiate a trial aiming to test new treatments for COVID-19, advice should be sought on alternative procedures to obtain informed consent, as it is likely that the physical consent cannot leave the isolation room, and therefore is not appropriate as trial documentation.

申办者应警惕医学界的压力，并应仔细评估正在进行的临床试验中增加新受试者的相关性。必须优先考虑有关 COVID-19 和 COVID-19 相关疾病的临床试验，或目前无有效治疗手段的严重疾病的试验。如果申办者计划启动测试 COVID-19 新疗法的试验，则应寻求替代性手段以获得知情同意书，因为同意书可能无法离开隔离地区，因此不合适作为试验记录。

In case of emergency situations, when trial participants are incapable of giving their informed consent (for example because they are under intensive medical care), sponsors shall adhere to the provisions set out in the Directive (Art 5) and by national regulations. Informed consent of these patients or their representatives will need to be acquired later, as soon as feasible, if deferred consent in emergency situations is permitted under national law.

在紧急情况下，如果受试者无法给出知情同意书（例如，处于重症监护），申办者应依从《指令》（第 5 条）和国家法规中的规定。在根据国家法律允许在紧急情况下推迟同意时，需要在可行的情况下尽快获得这些患者或其代表的知情同意。

There may be a need to re-consent already included trial participants. However, avoid the need for trial participants to visit investigator sites for the sole purpose of obtaining re-consent. If re-consents are necessary for the implementation of new urgent changes in trial conduct (mainly expected for reasons related to COVID-19), alternative ways of obtaining such re-consents should be considered during the pandemic e.g. contacting the trial participants via phone or video-calls and obtaining oral consents supplemented with email confirmation. Any consent obtained this way should be documented and confirmed by way of normal consent procedures at the earliest opportunity when the trial participants will be back at the regular sites

已经参与试验的受试者可能需要重新签署同意书。但是，应避免受试者仅为了重新签署知情同意而特意访视研究者机构。如新的紧急变更试验行为需要重新取得同意（大部分是出于与 COVID-19 相关的原因进行变更），则应在大流行期间考虑用代替手段获得此类再次同意，例如通过电话或视频电话与受试者联系，获得口头同意并附上电子邮件确认。对于以此种方式获得的知情同意应记录在案，当受试者可以返回日常试验机构时，应该尽早通过常规程序进行确认。

Any validated and secure electronic system already used in the trial for obtaining informed consent can be used as per usual practice and if in compliance with national legislation.

在符合国家法律的规定的情况下，为获得知情同意书，任何试验中已经使用、经过验证且安全的电子系统，都可以作为常规手段使用。

Changes in the distribution of the IMP
试验用药品分发的变化

Changes in the distribution of the IMP may be necessary to remove avoidable visits to sites and to provide the patients with needed treatments. Sponsors must assess the risks relating to the product and consider any alternative shipping and storage arrangements.

可能有必要更改试验用药品的分发，以避免访视试验机构，并为患者提供所需的治疗。申办者必须评估与产品有关的风险，并考虑替代性的运输和储存方式。

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.

此类措施需要进行各种实际考虑，包括试验用药品是否适合给药和一般存放在受试者家中，在运输过程中如何保证产品的稳定性（尤其是对于冷链产品），如何确保安全保管产品，如何对清点试验用药品和评估治疗依从性（如适用）进行管理。

The overriding objective of all changes in distribution is to provide the participating patients with the IMP and other medications categorised 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.

对于所有分发变化，首要目标是为了给受试者提供试验用药品和其他非试验用药品所需药物，以确保受试者的权利、安全、生命健康，以及临床试验的完整性。

Changes in distribution of IMP may include:
试验用药品分发变化可能包括：

- In case of urgent shortage of IMP at some sites or transfer of trial participants from one site to another clinical trial site, there might be a need to potentially re-distribute the IMP between sites in accordance with GMP annex 13 (section 47). 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;
- 当某些机构试验用药品出现突发性短缺，或受试者从一个临床试验机构转移至另一个研究机构时，可能需要根据 GMP 附件 13（第 47 节）中的要求潜在地重新分发各试验机构间的试验用药品。应只在下列情况下才考虑这一操作：无法通过通常的分销商将试验用药品直接分发到试验机构，或是受试者从一试验机构转移到另一试验机构的特殊情况。申办者应评估该机构是否可

以处理和控制重新分发过程，尤其是存储条件十分苛刻的情况，如需要非室温（例如，+2-8°C）的特定条件。重新分发应遵循书面程序，建立与授权人或试验用药品分发负责人的合作，并且应向试验机构提供足够的信息以确保可以安全地执行这一过程。相关记录应保存；

- 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 (e.g. via hospital (or other) pharmacies as applicable) to trial participants;
- 为了减少实地访视，我们预测到在 COVID-19 疫情大流行期间有必要将试验用药品直接交付给受试者，避免受试者前往试验机构，增加传播/被感染病毒的几率。一般情况下，药品是在试验机构（例如，医院（或其他医疗机构）、药房）交付给受试者；
- Direct from sponsor to trial participant IMP delivery is accepted in a few member states under 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 carer, 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.

- 在此类突发疫情之下，一些成员国采纳了由申办者直接将试验用药品交付受试者的方式。申办者应根据 NCA 指南确认申办者直接交付受试者方式的可行性，因为很有可能这些措施只能在特定条件下方可实施（例如，与试验机构达成协议，根据规程指定专门的快递员并负责直接送至指定的受试者及照看人，可靠的交付和收据程序，必要的知情同意条款以保证申办者的第三方机构处理个人信息，等等），且在一定期限内。

Alternative shipping and storage arrangements should not compromise the treatment blinding.

变更运输和存储安排不应违背治疗盲法设计。

Changes to monitoring
监查的变更

Certain sponsor oversight responsibilities, such as monitoring and quality assurance activities need to be reassessed and temporary, alternative proportionate mechanisms of oversight may be required. The extent of on-site monitoring, if it remains feasible, should take into account national and local restrictions, the urgency (e.g. source data verification can often be postponed) and the availability of site staff, and should only be performed as agreed with investigator sites. The burden of the introduction of any alternative measures for the site staff and facilities should also be considered in order to strike an acceptable balance between appropriate oversight and the capacity of and possibilities at the site.

需要重新评估某些申办者的具体监查职责，例如监查和质量控制，可能需要临时的、可替代的监督机制。如果现场监查仍然可以运行，其监查范围应当充分考虑国家和地方法规的限制，紧急状态（例如，源数据核查通常可以推迟）以及现场工作人员的可用性，并且仅应在研究者所在试验机构同意的情况下进行。还应考虑采取任何替代性措施给试验机构工作人员和设备带来的额外负担，以确保在适当的监督与试验机构承载能力之间取得可接受的平衡。

Possible temporary, alternative measures could include:
临时、替代性方法可能包括：

- Cancelling of on-site monitoring visits and extending of the period between monitoring visit;
- Implementing phone and video visits (without unnecessarily increased burden to the investigator site and taking into account trial participant integrity);
- Adapting the on-site monitoring plan when it is impossible to follow, supplementing it with (additional/increased) centralized monitoring and central review of data if possible and meaningful.
- 取消现场监查访视，及延长监查访视的间隔；
- 进行电话和视频访视（避免为试验机构人员增加不必要的负担，同时考虑到受试者的完整性）；
- 无法遵循原有计划时需改变现场监查访视计划，在可行且有意义的前提下，可将（附加/增加）中央监查和中央数据审评作为补充。

Results of adjusted monitoring/review measures should be reported to the sponsor in monitoring reports and in the clinical study report.

调整后的监查/审评措施结果应在上报给申办者时完整体现在监查报告和临床研究报告中。

It is essential that robust follow-up measures are planned and ready to be implemented when the situation is normalised. This should likely include increased on-site monitoring for a period that is sufficient to ensure that the impact of the reduced monitoring could be rectified and problems resolved or properly documented for reporting in the clinical study report.

在情况恢复正常后，计划并准备好强有力的后续跟进措施至关重要。措施包括增加现场监查时间，以确保纠正先前减少监查的影响，并解决问题或在临床研究报告中适当地把问题记录下来。

So-called remote source data verification (e.g. providing sponsor with copies of medical records or remote access to electronic medical records) is currently not allowed in most member states as it might infringe trial participants' rights. In addition, provision of redacted/ de-identified pdfs files will not be acceptable as it puts disproportionate burden on site staff.

目前，大多数成员国不允许采用所谓的“远程源数据验证”（例如，向申办者提供病历复印件或远程查阅电子病历），因为这可能会损害受试者的权利。此外，提供已修改的/去标识的 PDF 文件也不可接受，因为这会大量增加试验机构工作人员的负担。

Nevertheless, since the coronavirus emergency situation and containment measures are likely to last for a prolonged period, several NCAs have started to look into possible, temporary solutions related to remote access and conditions for such, providing that methods can be used that restricts access to trial participant records, in line with the principles of necessity and proportionality. This should however also be clarified with other relevant authorities in this area (such as, without limitation, Ethics Committees and data protection agencies) and is consequently not allowed unless a member state has given specific guidance allowing this.

然而，鉴于冠状病毒突发疫情及其防控措施可能会持续很长一段时间，一些国家主管机关已开始研究与远程访问及其条件相关的一些可能的临时解决方案，如有限制地查阅受试者的记录，并符合必要性和相称性原则。此外还应当向该领域其他相关机构（例如但不限于伦理委员会和数据保护机构）

进行澄清，并最终在成员国颁布具体指南许可的前提下采取这一方式。

Protocol deviations
临床试验方案偏离

We acknowledge that the COVID-19 situation is likely to introduce more protocol deviations than normal. We expect that the sponsor escalates and manages such protocol deviations in accordance with their standard procedures. A proportionate approach will be taken by the GCP inspectors when such deviations are reviewed during inspections, in particular where the best interest of the participant is maintained, and the participant is not put at risk.

我们认为 COVID-19 疫情可能会导致更多的与原有方案偏离的情况。希望申办者能够按照其标准方案进行上报、管理。特别是在保护受试者利益，避免给受试者带来风险的情况下，如果 GCP 监察员在检查过程中发现了方案偏离，监察员应相应采取适当方法解决。

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

与 COVID-19 情况相关的方案偏离的增加，本身不会造成 GCP § 5.20 中要求的行为，但是应根据 ICH E3 要求在临床研究报告中评估和报告。

Reimbursement of exceptional expenses
特殊费用的报销

Taking into account this exceptional situation, if, in order to implement urgent measures for the protection of participants involved in a clinical trial, expenses may arise which may be borne initially by the participants, these should typically be compensated subsequently by the sponsor via the investigator. If additional financial compensation is provided to sites/investigators (e.g. to cover the cost of using couriers for IMP delivery), this needs to be documented and performed according to national legislation. Handling of reimbursement of such expenses should follow national legislation and/or guidance.

考虑到疫情特殊情况，若为保护临床试验受试者执行的紧急措施，产生的费用最初可能由受试者承担，然后应由申办者通过研究者予以报销补偿。如果需向试验机构/研究者提供额外的经济补偿（例如支付寄送试验用药品的快递费用），则需要依据国家法规执行。此类费用的报销应遵循国家法律和/或相关指南。

Initiation of new trials aiming to test new treatments for COVID-19
启动研究 COVID-19 新疗法的新临床试验

The Member States support the submission of large, multinational trial protocols for the investigation of new treatments for COVID19[2].

成员国需支持关于 COVID-19 的新疗法研究的大型的跨国试验方案 。

[2] https://www.ema.europa.eu/e n/n ews/call-pool-research-resources-large-multi-ce ntre-multi-arm-cli nical-trials- gen erate-sou nd-evide nee

In addition, sponsors are encouraged to consider the submission of such applications for an accelerated Voluntary Harmonisation Procedure3 (VHP) assessment when possible. In order to avoid or minimise delays due to the harmonised review, sponsors are recommended to prospectively contact the proposed Ref NCA to explore the feasibility of an accelerated VHP (plus) process.

此外，鼓励申办者考虑提交关于加快“自愿协调程序（VHP）”评估的申请。为避免或减少因统一审核造成的延误，建议申办者预先联系相关主管机关，探讨加速 VHP 流程的可行性。

It should be noted that the developers of medicines or vaccines are invited to contact EMA as soon as possible with information about their proposed development by emailing 2019-n cov@ema.europa.eu. EMA provides a full fee waiver and a fast-track procedure for scientific advice4.

请注意，药物或疫苗的开发人员应尽快与 EMA 联系（联系邮箱：2019-n cov@ema.europa.eu），就其拟开发药品的信息进行沟通。EMA 将提供免费的科学咨询，并予以快速审评程序。

最后，在此特别感谢张丹博士在本文翻译过程中提供的帮助与指导

张丹
方恩（天津）医药发展有限公司董事长兼 CEO
中国医药创新促进会药物研发专业委员会、创新研发服务专业委员会副主任委员

3https://www.hma.eu/fileadmi n/dateie n/Huma n Medic in es/01-About HMA/Working Groups/CTFG/2016 06 CTFG VHP guidanee for sponsor v4.pdf
4https://www.ema.europa.eu/e n/n ews/covid-19-developers-medic in es-vacc in es-be nefit-free-scie ntific-advice