

Guidance on how to manage clinical trials during the COVID-19 pandemic (v3, 28 April 2020)

Disclaimer: this presentation is only complementary to the guidance which remains the primary document

Joint EMA, EC, CTFG/HMA webex conference with stakeholders

15 May, 2020

Welcome



Andrzej Rys
Director responsible for Health systems, medical products and
innovation, DG SANTE, European Commission

Technical announcements

- Only the panelists will be able to speak during the meeting and only the slides will be displayed.
- Questions were collected before the meeting from select EU organisations representing industry, academia and patients' organisations and responses to several of them will be included in the presentation.
- Requests for further clarification can be written down in the chat and will be monitored - but it is not guaranteed that all requests will be addressed during or after the meeting.
- Requests should be addressed to “all panelists »and not to one panelist in specifically. Please indicate the relevant chapter in the guidance at the beginning of your question. Questions will be addressed at the end of this webinar.
- The webinar is recorded to be published on EUtube.
- Thank you for your understanding.

Agenda

- Process, introduction of the speakers (Agnès Mathieu-Mendes)
- Introduction to the guidance
- Initiation of new trials, changes to ongoing trials
- Communication with authorities
- Changes to the informed consent
- Changes to the distribution of IMP
- Changes to monitoring
- GCP inspections

Process for drafting, review and publication

- General process:
 - Drafting team with EMA GCP-IWG, EMA, Clinical trials Facilitation and Coordination group/ Head of medicines Agencies (CTFG-HMA) and Eur. Commission DG SANTE members
 - Technical review: by CTFG (HMA), GCP-Inspector Working group (EMA) and Clinical trials Expert group (EC)
 - Publication on Eudra Lex-10 (EC website)
- Version 3: review of v2 by stakeholders, patients organisations (key points: distribution of IMP, remote source data verification)
- Endorsement by Commissioner Kyriakides, Health Ministers 27 April 2020
- Publication: 28 April

Speakers



Lisbeth Bregnhøj
(DKMA, EMA GCP-IWG)



Jane Moseley
(EMA)



Elke Stahl (BfArM,
CTFG (HMA))



Ann Marie Janson Lang
(Swedish MPA, CTFG (HMA))



Fergus Sweeney
(EMA)



Olivier Le Blaye
(ANSM, EMA GCP-IWG)

Speakers



Agnès Mathieu-Mendes
(DG SANTE)



Kristof Bonnarens
(DG SANTE)



Edit Szepessy
(DG SANTE)

Additional members of the drafting team:

Ana Rodriguez, EMA

Maria Antonietta Antonelli, EMA

Agenda

- Process, background
- Introduction of the guidance (Edit Szepessy)
- Initiation of new trials, changes to ongoing trials, risk assessment
- Communication with authorities
- Changes to the informed consent
- Changes to the distribution of IMP
- Changes to monitoring
- GCP inspections

Introduction

- Need for pragmatic and harmonised actions to ensure flexibility and procedural simplifications to maintain the integrity of the trials, to ensure the rights, safety and well-being of trial participants and the safety of clinical trial staff during the COVID-19 health crisis.
- The guidance is applicable **only until its revocation (when there is a consensus that the period of the COVID-19 outbreak in the EU/EEA, has passed)**.
- **Member States are encouraged to implement the harmonised guidance to the maximum possible extent.**
- Authorisation and oversight of clinical trials is **member state competence**. Sponsors and investigators need to take into account that **national legislation and derogations cannot be superseded**. Member States shall complement this guidance to create additional clarity on specific national legal requirements and derogations to them.

Introduction: general questions

Questions about **exit strategy, timing of the revocation of the guidance, transition back to “normal”, reverting measures:**

- The Guidance **will be revoked** when there is a consensus that the period of the COVID-19 outbreak in the EU/EEA, has passed.
- The regulatory flexibilities are **not intended to be kept** once the COVID-19 crisis is over
- It is too soon to predict the timing of the revocation or provide specifics about a transition period and reverting measures. These will rely on sustained reduction in the number of hospitalisations and/or new cases for a sustained period of time.
- It should be possible to include concrete recommendations about the transition and timelines in the communication about the revocation closer to the date.

Agenda

- Process, background
- Introduction of the guidance
- Initiation of new trials, changes to ongoing trials, risk assessment (Ann Marie Janson Lang)
- Communication with authorities
- Changes to the informed consent
- Changes to the distribution of IMP
- Changes to monitoring
- GCP inspections

Initiation of new trials

- Sponsor – in collaboration with investigators - should assess
 - Feasibility and immediate necessity of starting a new clinical
 - Specify additional risks to trial participants in benefit-risk section of the protocol

No questions or comments received

Changes to ongoing trials 1(4)

Overall well-being and best interests of the trial participants prevail

Changes should be well balanced, proportionate and fully documented

No waivers for eligibility assessment

Informed consent according to national laws and regulations

Special considerations:

Trial participants with life-threatening or severely debilitating conditions - maintaining trial treatment of key importance

Changes to ongoing trials 2(4)

- Sponsor – in collaboration with investigators - should assess risks.
- Actions below should not compromise the rights, safety and well-being of trial participants or data validity:
 - Only strictly necessary visits performed at sites
 - Temporary halt of trial at some or all trial sites
 - Recruitment slow-down
 - Extension of trial duration
 - Postponement of trials/sites not yet activated
 - Closure of sites

Changes to ongoing trials 3(4)

- Exceptional steps when nothing else possible:
 - Transfer of trial participants to investigational sites away from risk zones, or closer to home, initiation of new trial sites generally not expected (also addressed later linked to Chapter 6 urgent safety measures and substantial amendments)
 - Critical laboratory tests, imaging or other diagnostic tests could be performed at local laboratory or relevant clinical facility authorised/certified (as legally required nationally) to perform such tests routinely

Changes to ongoing trials 4(4)

- Principal Investigator (PI) of a site – if indisposed delegate duties temporarily to sub-Investigator
 - Any permanent changes in PI should be submitted to the NCA and/or Ethics Committees
- *Question: Does this mean that a PI who is indisposed for a period of time may not delegate all of his/her duties during that time – even if it is for a short period of time? Or can the decision regarding the acceptability of full delegation for a short period of time be risk-based?*
- *Answer: Delegation possible. However, permanent change of PI requires substantial amendment.*

Risk assessment 1(3)

- Potential impact of COVID-19 on trial participants who are
 - Part of a-risk group for COVID-19 or
 - Receiving treatments that could increase the risk
- Sponsor role: risk assessment of each individual ongoing trial
- Investigator role: risk assessment for each individual trial participant

Comment: Regarding Investigator risk assessment: Could the Agency provide further elaboration on the level of documentation that is expected in order to demonstrate this?

Answer: Risk assessment per trial participant is always the obligation of the investigator based on medical knowledge and experience as well as on the protocol. Individual risk assessment should be documented and included in the medical records of the trial participant.

Risk assessment 2(3)

- Measures should prioritise trial participant safety and data validity
- In case these two conflict, trial participant safety always prevails
- Reassess risks as situation develops, note local pandemic change may require investigator-driven risk assessment
- Data interpretability – EMA Biostatistics Working Party Guidance March 25 2020:
<https://www.ema.europa.eu/en/implications-coronavirus-disease-covid-19-methodological-aspects-ongoing-clinical-trials>
- *Comment: The (EMA BWP) guideline refers to phases of the pandemic (pre-, during-, post-) which will differ across regions, and across countries/states within region requiring a more flexible pathway to EMA Scientific Advice (note, question shortened)*
- *Answer: Normal procedures apply for EMA scientific advice. Clinical trials are approved and supervised by National Competent Authorities and Ethics Committees in each Member State.*

Risk assessment 3(3)

- *Comment: Several Member States request a summary of the impact in their country and description of measures put in place. This is a challenging requirement as, in many cases, where trials are being run in more than one country, the measures are taken globally to maintain the integrity of the trial; in addition, the impact will also be described in the individual CSR. If there is a substantial impact on the safety or rights of participants or the integrity of the trial (e.g. augmenting the recruitment to compensate for patients lost to follow-up) this will be preceded by a substantial amendment application.*
- *Answer: The Guidance is broadly supported in EU/EEA but the pandemic situation is not the same in different Member States. Additional national requirements are provided at the CTFG/HMA web page https://www.hma.eu/fileadmin/dateien/Human_Medicines/01-About_HMA/Working_Groups/CTFG/2020_03_CTFG_Link_to_National_guidance_on_CT_m anagmant_during_the_COVID-19_pandemia.pdf.*

Agenda

- Process, background
- Introduction of the guidance
- Initiation of new trials, changes to ongoing trials, risk assessment
- **Communication with authorities (Elke Stahl, Kristof Bonnarens)**
- Changes to the informed consent
- Changes to the distribution of IMP
- Changes to monitoring
- GCP inspections


Communication with authorities

- Communication with authorities
 - as of Dir 2001/20/EC and national law to NCA and Ethic Committees (EC)
- Communication between sponsor ↔ trial site ↔ trial participants !
- Priority is given for CT application to treat or prevent Covid-19 infection and substantial amendments to ongoing CTs as result of Covid-19 → clear MARK
- Same sponsor submit changes for multiple CTs at once to the authorities
e.g. list with changes (and information required) per CT

Legal basis – Urgent safety measures

- Current legal basis for clinical trial application and supervision is still Directive 2001/20 (and its national implementation)
- Article 10 describes how to make amendments to a trial – paragraph (b) describes the conditions for urgent safety measures :

(b) without prejudice to point (a), in the light of the circumstances, notably the occurrence of any new event relating to the conduct of the trial or the development of the investigational medicinal product where that new event is likely to affect the safety of the subjects, the sponsor and the investigator shall take appropriate urgent safety measures to protect the subjects against any immediate hazard. The sponsor shall forthwith inform the competent authorities of those new events and the measures taken and shall ensure that the Ethics Committee is notified at the same time;

 forthwith
/fɔːθˈwið, fɔːθˈwið/

adverb

(especially in official use) immediately; without delay.
"we undertake to pay forthwith the money required"

Legal basis – Substantial amendments

- Detailed guidance CT-1 (Competent Authorities) and CT-2 (Ethics Committees) apply – however, national legislation prevails
- Changes to the trial are only substantial amendments when they have an impact on :
 - the safety or physical or mental integrity of the clinical trial participants OR
 - the scientific value of the trial
- Case-by-case assessment by the sponsor
- No submission of « non-substantial » amendments to authorities required

Communication – Immediate Action

Urgent action to protect participants against *immediate* hazard !

- **Urgent Safety Measure** → USM notification
 - ex post : ASAP within national – local circumstances to NCA and EC
 - **Contain information** on cause, measure taken and plan further activities
 - Document justification for *longer than forthwith* (CT1 3.9) in Trial Master File (TMF)
 - Temporary halt due to trial medication shortage
 - Direct IMP shipping to participants /carer home/residence
 - Testing in local lab instead at trial site
 - Transfer participants to another trial site, treatment continues
 - Temporary deactivation of trial site and discontinuation of treatment
 - Open new trial site or relocation to existing trial site to accomodate for transfer of existing participants

Communication – Changes are Substantial

Changes affect *safety* of participants OR *scientific value* of CT - but not require immediate action :

- ***Substantial amendment (SA)***
 - Complete application only necessary changes
 - Avoid overreporting
 - Direct distribution to trial participants/carer home/residence
 - Introducing remote SDV !
 - Changes to as per protocol informed consent procedure
 - *National SAs also in 'VHPs' due to Covid-19 like restart after temporary halt of trial is national (can be different due to the situation in each of the Member States): SA not VHP if due to Covid 19 situation*
 - *Changes on frequency of collection of safety or efficacy (endpoints), changes of content of visits, collection at different location, change to local lab*

Communication – ,Other Changes‘

Procedural or other changes due to Covid 19 pandemic situation AND Not affecting safety of participants, **serious benefit risk** balance **or scientific value** of then CT - Cumulative changes not affect either!

- **Notification**
 - **ASAP** as of national – **local** circumstances to NCA and EC (= mandatory)
 - List of all changes **contain** appropriate risk management, justification and follow up measures
 - Record all changes appropriate **in TMF**
 - Temporary halt not linked to safety of participants
 - Supply participants with larger amounts of IMP under investigator's supervision

Communication – Categories

Principle : Urgency and Impact on safety or scientific value

- Risk assessment and urgency by sponsor
- Authorities **grant flexibility** while **keep supervision**
- No fixed timelines for delay – aware of different local situations

Type depend on impact:

- Changes of visits frequency or content, of informed consent
- Change site of testing (onsite to local) critical parameter/test for participants safety or trial integrity

Communication – questions 1(3)

- Question : there is a need for additional examples

→ The guidance is an iterative effort to address frequently occurring situations for which the approach seems unclear.

Communication – questions 2(3)

- Question : there seems to be a grey area between urgent safety measures and substantial amendments, knowing that the latter are sometimes approved with delays
 - Sponsors have the responsibility to address participant safety if required. If a change cannot await the approval of a SA, the urgent safety measure route needs to be taken.
 - In case of doubt, the sponsor should consult the national competent authority (this advice should be given without delay and free of charge (CT-1)), and/or the ethics committee. Sponsors are encouraged to label exchanges on COVID-19 related questions as such

Communication – questions 3(3)

- Question : do changes in routine testing (e.g. standard blood values) need to be submitted as a SA or USM?
 - Basis reflection to do on whether the change in testing might have an impact on
 - the safety or physical or mental integrity of the clinical trial participants
 - the scientific value of the trial
 - Changes to critical parameters which have an impact (changes in protocol and participants information / IC) – might also apply for changes to certain testing infrastructure and location

Agenda

- Process, background
- Introduction of the guidance
- Initiation of new trials, changes to ongoing trials, risk assessment
- Communication with authorities
- **Changes to the informed consent (Lisbeth Bregnhøj)**
- Changes to the distribution of IMP
- Changes to monitoring
- GCP inspections

Informed consent

- Unless linked to the implementation of urgent safety measures, changes in informed consent procedures will need to be reviewed and approved by the relevant ethics committee in advance
- The informed consent procedure in all trials needs to remain compliant with the trial protocol as well as with EU and national legal framework. It is acknowledged that national provisions and approaches differ
- Sponsors should be mindful of the current pressure on the medical profession
- Trial participants should be informed by the investigator, in a timely manner, about changes in the conduct of the clinical trial relevant to them (e.g. cancellation of visits, change in laboratory testing, delivery of IMP)

New trials vs re-consent

New trials

- Possibility of alternative procedures to obtain informed consent, in case the physical consent cannot leave the isolation room
 - Temporary oral consent
 - A correctly signed and dated informed consent form should be obtained from the trial participant later, as soon as possible
- Incapacitated adults, minors, acute life-threatening situations

Re-consent in ongoing trials

- New urgent changes in trial conduct: alternative ways of obtaining such re-consent should be considered during the pandemic.

Questions and comments raised 1(7)

- The document addresses informed consent for new trials but it also needs to address the right of the patient to understand the impact of the trial discontinuation on his/her disease prognosis
- *The principal investigator is expected to thoroughly inform the trial participants about the medical consequences of trial discontinuation and to ensure a transition to post-trial treatment as is also the case in other situation where a participant ends her/his trial participation (e.g. pre-mature or planned closure of a trial)*

Questions and comments raised 2(7)

- SDV of ICF: can the site be given a checklist to perform the SDV, sign and date the checklist and return it to the central monitoring team?
- *The purpose of SDV is to verify data in source documents. Consequently, a checklist to the site cannot replace the SDV.*

Questions and comments raised 3(7)

- Are oral consent with an impartial witness and e-consent equal options?
- *Yes; however, 'Validated and secure electronic system already used in the trial in the particular member state for obtaining informed consent can be used as per usual practice and if in compliance with national legislation'. If no such systems have been in place, any obtained consent via electronic means (e.g. simple signatures in emails) are only considered temporary.*
- Further elaboration on the expectations to re-consent subjects related to implementation of changes to the trial conduct due to COVID-19 and the process when the trial participants are back at sites is requested.

Questions and comments raised 4(7)

- *A new revision of the document is not currently planned. If re-consent is necessary for the implementation of new urgent changes in trial conduct (mainly expected for reasons related to COVID-19 or important safety issues for other trials),*
 - *alternative ways of obtaining such re-consent should be considered (e.g. contacting the trial participants via phone or video-calls and obtaining oral consents) and documented in the trial participants' medical records, supplemented with e-mail confirmation.*
 - *Approved updated patient information sheet and consent form should be provided to trial participants by the investigator by e-mail, mail or courier before re-consent is obtained.*
 - *Any consent obtained this way should be documented and confirmed by way of normal consent procedures at the earliest opportunity when the trial participants are back at the regular sites*

Questions and comments raised 5(7)

- The mention of an impartial witness during the consenting process is only referenced for initial consenting in studies involving COVID-19 patients. If a participant needs to be re-consented during the trial: is an impartial witness also a requirement when using alternative consenting methods (i.e. verbal consent)
- *If the same conditions are valid for the re-consent (If written consent by the trial participant is not possible e.g. due to physical isolation due to COVID-19 infection), the same procedures should be followed. In such cases, the witness is required to sign and date the informed consent form and the investigator is expected to record how the impartial witness was selected.*

Questions and comments raised 6(7)

- Expectations to communication/consent processes regarding IMP delivery directly to trial participants are unclear...Could the Agency clarify if this is referring to a need for the subject to confirm their consent back to the investigator in this way or is a requirement for the investigator to confirm to the depot that subject has given consent to sharing their information?
- *The investigator should confirm with the participant that they consent. The investigator then provides the participant contact details and address to the distributor. The main focus is on ensuring proper (and documented) communication with the participant to make sure that all is clear and understood by the patient. The level of communication should depend on the complexity of the trial/IMP procedures and the participant*

Questions and comments raised 7(7)

- “Site staff should inform each trial participant or designated legal representative and ensure that they do not object to the remote review of their records for trial purposes and document this process in the trial participant’s medical records.” From the fact that this paragraph speaks about objection, can it be concluded that the legal basis for the processing of personal data in this case is not consent.
- *Sponsor’s (monitor’s) right to direct access is already established/usual practice due to the originally planned on-site monitoring. Consequently, the added action is the shift from on-site to remote monitoring, which is mainly a matter relating to IT security. Therefore, informed consent as per usual procedure (ICH 4.8) is not foreseen. If in doubt, seek national advice.*

Agenda

- Process, background
- Introduction of the guidance
- Initiation of new trials, changes to ongoing trials, risk assessment
- Communication with authorities
- Changes to the informed consent
- **Changes to the distribution of IMP (Fergus Sweeney)**
- Changes to monitoring
- GCP inspections

Section 9 Distribution of IMP

- Applies to IMP, NIMPs and other products or devices supplied to participants during site visits
- Treatment should be under adequate supervision of the responsible investigator.
- Aim is to ensure:
 - Continuity of supply to trial participants with the IMP ... avoid treatment interruptions, but also avoidable visits to investigator site
 - Maintain a positive benefit-risk balance for participants
 - Protect the rights, safety and well-being of trial participants and integrity of the data collected

Section 9 IMP

- Delivery of the IMP directly to trial participants' homes:
 - Information on the dose regimen needs to be provided to trial participants along with contact information of the investigator site
 - If trial site can manage the shipment, it should be from trial sites/hospital pharmacies to trial participants. The sponsor should bear the cost.
 - If trial site is unable to manage shipment participants: the IMP may be shipped to participants by a distributor independent from and acting on behalf of the sponsor - in line with national law or temporary national emergency measures

Section 9 IMP

- There should be a contract between the sponsor and the distributor. This along with the procedures involved should be documented in the sponsor trial master file.
- Shipment can take place:
 - After agreement with the investigator and with investigator's prescription. Agreement and the procedure recorded in the investigator site file;
 - After investigator obtains participant's oral consent, including for the investigator to provide the trial participant's name, address and contact details to the distributor.
 - When possible, consent should be confirmed in writing by e-mail, mail or letter sent via a courier. The oral or written consent should be documented in the trial participant's medical records;

Section 9 IMP

- Distributor should not store the personal data of the trial participant for a longer period than is required, and should not provide them to the sponsor
- Process involved should:
 - Protect blinding and ensure compliance with the randomisation
 - Safeguard the integrity of the IMP, whether physically or with regards to temperature.
 - Maintain accountability of the IMP.
- Dedicated couriers should be contracted for IMP shipment with procedures in place.

Section 9 IMP Questions 1(5)

- Could you clarify whether the mentioned ‘agreement’ should be between Sponsor and investigator or investigator and depot?
 - *There is a contract between the sponsor and the distributor, and an agreement between the sponsor and the investigator.*
- Could you clarify what ‘procedure’ is being referred to? Is it anticipated that an agreement and procedure are required for each individual dispatch via a depot?
 - *The procedure is a written document describing the process to be followed by the sponsor, distributor and investigator. Both the procedure and the contract/agreement can cover the trial overall for that site or multiple sites being served by that distributor. They are not individual to each dispatch.*

Section 9 IMP Questions 2(5)

- One aspect that is missing is making a change to administration so that there is home IV administration by qualified nurses/treating physician. This is now considered as SA in some Member States although this does not have a substantial impact on patient rights, safety or the integrity of the trial.
 - *It is not evident that this would not have an impact on patient safety. This has not been specifically considered in this guideline but can be submitted as a SA. The general rules on SA apply (ask NCA when in doubt). Immediate measures taken by an investigator to treat an individual participant should be addressed as a USM.*

Section 9 IMP Questions 3(5)

- (..) it is important to ensure the involvement of hospital pharmacists in this stage, as the qualified person/ person responsible for distribution of the IMP. Additional clarification on this would be needed since hospital pharmacists contribute to the control of IMPs (e.g. by making sure that everything is being carried out correctly and in a safe manner) while at the same time they ensure that patients are informed about the IMPs so that the clinical trial process will be performed securely.
- *The agreement of the sponsor with the investigator covers all actors at the trial site. Where the pharmacist needs to be involved this can be done by the investigator.*

Section 9 IMP Questions 4(5)

- Request for guidance to state that there is EU-wide agreement on a full exemption that the labelling on IMPs must be in an official language(s) of the Member State participating in the clinical trial. This will minimize the (re-) labelling activities, especially for urgent clinical trials to investigate COVID-19 treatments or vaccines. This should be given due consideration because drug administration is likely to be performed at a hospital by medically trained professional and no self-administration is envisaged.
- *This was not raised during the consultation and thus was not considered in the preparation of the current guidance - therefore there is no EU wide position established on this point. Request for such approach should be addressed to the concerned NCA.*

Section 9 IMP Questions 5(5)

- Could you please clarify, how these changes shall be reported, given that the change of IMP distribution (and any other change that would be caused by it) are decided on and managed on a patient by patient and case by case basis?
 - *This can be done overall as USM or SA for the clinical trial in a Member State. It is not intended to be done per participant or per site.*
- Could you please clarify how this aspect shall be handled and which updated documents are expected for a substantial amendment submission?
 - *The documents should indicate the clinical trial involved, and the process being followed.*

Agenda

- Process, background
- Introduction of the guidance
- Initiation of new trials, changes to ongoing trials, risk assessment
- Communication with authorities
- Changes to the informed consent
- Changes to the distribution of IMP
- **Changes to monitoring (Olivier Le Blaye)**
- GCP inspections

Monitoring

- The guidance provides information on
 - On-site monitoring
 - Centralised monitoring, central data review
 - Off-site monitoring
 - Remote source data verification (remote SDV)
- Questions and requests for clarification only received for remote SDV

Remote source data verification

- Constraints
 - Protect the rights of trial participants (confidentiality of personal data and medical information)
 - Limit the burden on trial site staff (remote SDV can create very high workload)
- Consequences
 - Strict limitation of the situations where remote SDV could be considered

Remote source data verification

- Implementation
 - New trials (COVID-19): can be foreseen in the initial protocol
 - Ongoing trial: substantial amendment (COVID-19 or final data cleaning steps before database lock in pivotal trials investigating serious or life-threatening conditions with no satisfactory treatment option)
- Technically: several options possible, annex on the protection of trial participants' rights

Remote source data verification 1(7)

- Question
 - Could EMA provide more guidance on which platforms definitely are (or are not) acceptable for videoconference ?
- No. We do not know each and every possible platform; it may also depend on the security settings implemented

Remote source data verification 2(7)

- Question
 - Videoconferencing: what sort of measures does the EMA consider appropriate to protect against 3rd party access ?
- Several measures are to be considered, such as (not limited to)
 - End-to-end encryption
 - Access control
 - Viewing conditions (preventing viewing over the shoulder)
 - No copy of the video / screen capture

Remote source data verification 3(7)

- Question
 - Confidentiality agreements by monitor: really needed, as access to medical records is standard practice ? Covered by existing non-disclosure agreements ? To be prepared by site or sponsor ?
- Specific agreements needed as remote SDV is not standard practice. Template can be provided by sponsor to save time and limit burden on sites.

Remote source data verification 4(7)

- Question
 - Who defines “serious or life-threatening conditions with no satisfactory treatment option”: sponsor ? Competent authority ?
- Evaluation by the sponsor, will be checked by the competent authority when reviewing the protocol / substantial amendment

Remote source data verification 5(7)

- Question
 - Annex 1: define “third countries”
- Countries that are not part of the European Union / European Economic Area (not: countries other than the one where the trial site to be monitored is located)

Remote source data verification 6(7)

- Question
 - If remote SDV is introduced via a substantial amendment, can we start immediately after submission or is prior approval needed ?
- Prior approval needed – just like any other substantial amendment

Please note that remote SDV can not be considered as an USM

Remote source data verification 7(7)

- Question
 - Can non-pseudonymised data be made available to the monitor using a cloud-based system ?
- Systems which store documents on a server to make them available remotely to other users may be used to share pseudonymised documents with the monitor if they meet the requirements detailed in Annex 1, but **not** non-pseudonymised documents.

Agenda

- Process, background
- Introduction of the guidance
- Initiation of new trials, changes to ongoing trials, risk assessment
- Communication with authorities
- Changes to the informed consent
- Changes to the distribution of IMP
- Changes to monitoring
- GCP inspections (Jane Moseley)

GCP inspection Questions/comments

- Impact on GCP inspections of clinical sites for applications under review.
- (..) unless remote access to source data is permitted, it will be difficult for GCP inspections to occur. This could delay the approval of submitted MAAs and variations and subsequently patient access to medicines
- *For CTs included in Centralised Marketing Authorisation Application, decisions are taken on case by case basis: Need for the inspection (i.e. concerns) vs impact (on the including medical need, Time Table). CHMP can seek additional reassurance from the Applicant. If concerns remain, on-site inspection postponed until the security/safety risks decrease to an acceptable level for EMA and MSs. Remote inspection considered if deemed appropriate (depending on the scope of the inspection). Guideline for remote GCP inspections developed by the GCP IWG (to be published end of May). Scope limited to Sponsor and CRO inspections.*

Other

- Reference is made to the BSWP guidance document; The consultation period for this document is now over – is EMA able to confirm when an update may be received and what may change in this?
- *CHMP Biostatistics Working Party is currently drafting an updated version of the Points to Consider on implications of Coronavirus disease (COVID-19) on methodological aspects of ongoing clinical trials taking into account the comments received from 30 stakeholders. Aim to publish an updated version addressing some most important issues as soon as possible / end of May.*

Q&A