TRIUM COVID-19 Live Online Session – 24 March 2020:
COVID-19 Regulatory Recommendations Summary for Clinical Trials – Q&A – 04 June 2020

1. What is the time to activate a site or conduct a submission?

I hope I understood this question correctly – if not, do resend via e-mail to ed@triumclinicalconsulting.com. Timing will depend on site or NCA priorities and backlog in workload.

2. In which EU countries is remote SDV NOT allowed?

I don't have a full list of countries where this is normally not allowed. However, in most EU countries this is not allowed when it infringes trial participant's rights. Normally, redacted/de-identified pdfs are acceptable in some countries when all other measures to ensure subject rights are ensured. **But this is now by the EU considered putting disproportionate burden on site staff and thus not acceptable in any EU country.**
The EU regulatory guidance does state that since the coronavirus emergency situation and containment measures are likely to last for a prolonged period of time, **the NCA have started looking into possible, temporary solutions related to remote access and conditions for such, providing methods used that restrict access to subject records and in line with the principle of necessity and proportionality.** This should however be clarified with other relevant authorities in the area like IRB/IEC and DPA. This is thus not allowed unless a member state has given specific guidance allowing this. I stay on the lookout for further guidance and will update this Q&A accordingly when new information becomes available.

Update! The 'Guidance of the Management of Clinical Trials during the COVID_19 (Coronavirus) Pandemic' of the European Commission/EMA and HMA dated 28/04/2020 offers guidance in general on the circumstances when remote SDV is allowed. Careful, remote SDV is only accepted during the COVID-19 pandemic and only for COVID-19 and other life-threatening trials and when local regulations allow it. Link for the detailed information: https://ec.europa.eu/commission/presscorner/detail/en/ip_20_759

In the 'Europe: COVID-19 document – Overview of European Regulatory Authority Guidance' and updated country information it states:

- The following countries do **NOT allow** remote SDV:
  - Hungary
  - Ireland
  - Spain
  - Belgium
  - France
- The following countries **DO allow** remote SDV **under strict data protection circumstances**:
  - Italy – when upfront approval of site DPO and Data Protection Authority (DPA)
  - UK – when all necessary electronic measures are in place and aligned with the COVID-19 restrictions

- Germany - when all necessary electronic measures are in place and aligned with the COVID-19 restrictions
- Denmark – under strict conditions which can be read here: https://laegemiddelstyrelsen.dk/en/news/2020/extraordinary-measures-for-clinical-trials-due-to-covid-19/~/media/259AC11DD4CB438F9966E0C06396E47A.ashx

For the other EU countries there is no guidance. We recommend contacting local experts for more information.

We continue scanning the available information and will update this document accordingly.

3. What about the investigator who sends the patient consent before screening to be signed by post so that his/ her images can be uploaded for screening?

If no additional burden to the investigator and site, the ICF may be sent by post to the potential subject, as long as the ICF process of receiving the oral trial explanation, ample time to think about participation and opportunity to ask questions is respected. After the investigator received the fully signed and dated ICF the trial related screening procedures can go ahead as per the protocol. The investigator should agree with this and it should not entail additional burden. If the case, this is not an accepted approach.

3. What do the abbreviations DPA, DPO,NCA, USM and SA stand for?

DPA: Data Protection Authority
DPO: Data Protection Officer
NCA: National Competent Authority
USM: Urgent Safety Measure
SA: Substantial Amendment

4. Are there any updates to regional regulatory guidance (e.g. EMA) provided between 24 March 2020 and 04 June 2020?

Yes, MHRA, EMA and FDA have provided updates to their guidance on handling clinical trials in light of the COVID-19 pandemic. The updated documents can be found here on the TRIUM website: https://www.triumclinicalconsulting.com/cro-services/

There are no changes to the key principles of safeguarding patient safety, rights and well-being, data quality and integrity of trial conduct. Here a few highlights per region:

EMA (update 27/03/2020):

The EMA provides further guidance to the ICF process in case of subjects that tested positive to the COVID-19 virus in that an impartial witness needs to sign in case of oral consent. The PI will have to document how the selection of the impartial witness occurred. It further describes other alternative ICF processes that could be considered in this case, like the use of a legal representative or the use of two consent forms.

The EMA further describes the possibility for having bigger IP/ID stocks than usual, the need for the sponsor and investigator (contact the subject through alternative means like a phone call) to continue safety reporting per the (local) regulations, the requirement to add additional risks to subjects in the risk-benefit section in the protocol along with risk mitigation measures for new trials, and the need to postpone non-essential audits.

For details, see the EMA guidance document:
https://www.triumclinicalconsulting.com/wp-content/uploads/2020/03/EMA-Guidance-to-sponsors-on-how-to-manage-clinical-trials-during-the-COVID-19-pandemic-version-2_20.pdf

EMA (update 10/04/2020):

The EMA provides further guidance and explains some regulatory flexibilities that can be applied to help pharmaceutical companies cope with the consequences of the pandemic, while ensuring a high level of quality, safety and efficacy for medicinal products made available to patients in the EU. The Q&A document outlines areas where regulatory flexibility is possible to address some of the constraints marketing authorization holders may be faced with in the context of COVID-19. The measures introduced cover different areas of the regulation of medicines such as marketing authorizations and regulatory procedures, manufacturing and importation of active pharmaceutical ingredients (APIs) and finished products, quality variations, and labelling and packaging requirements with flexibility to facilitate the movement of medicinal products within the EU. Some of the measures described are reserved for crucial medicines for use in COVID-19 patients.

For details, see the EMA guidance document:
https://www.ema.europa.eu/en/news/guidance-regulatory-requirements-context-covid-19-pandemic

EMA (update 28/04/2020):

Key recommendations of the guidance cover:

- Distribution of medicines to patients in clinical trials: the purpose is to protect the safety and wellbeing of trial participants and the integrity of the clinical trials. This recommendation considers social distancing measures and possible limitations in trial site/hospital resources.
- Remote source data verification (SDV): the verification of the raw data in hospitals can become extremely difficult during the pandemic due to safety measures, such as social distancing. Remote SDV to conclude a trial could facilitate the marketing authorization of coronavirus and life-saving medicines.
- Communication to authorities: urgent actions to protect trial participants against any immediate hazard or other changes with an effect on patient safety or data robustness might become necessary to mitigate disruptions during the ongoing public health crisis. The guidance clarifies the classification and notification of these actions.

These measures will be used exclusively during the coronavirus pandemic and will be revoked once the current health crisis in the EU/EEA has been surpassed.
For details, see the EMA guidance document:
https://ec.europa.eu/commission/presscorner/detail/en/ip_20_759

FDA (update 27/03/2020):
The FDA added a Q&A section in an appendix, offering further guidance to ensure compliance.
For details, see the FDA guidance document:
https://www.triumclinicalconsulting.com/wp-content/uploads/2020/03/FDA-update-I_Guidance_on_Conduct_of_Clinical_Trials_of_Medical_Products_during_COVID-19.pdf

FDA (update 11/05/2020):
For details, see the FDA guidance document:
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-public-health-emergency

FDA (update 03/06/2020):
For details, see the FDA guidance document:
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-public-health-emergency

MHRA (update 24/03/2020) :
The MHRA provided small alternations to the original guidance.
For details, see the MHRA guidance document:
https://www.gov.uk/guidance/managing-clinical-trials-during-coronavirus-covid-19#history

MHRA (update 09/04/2020) :
Added new information in the section on Reporting of serious adverse events (SAEs), suspected unexpected serious adverse reactions (SUSARs), and submission of annual safety reports (DSURs).
For details, see the MHRA guidance document:
https://www.gov.uk/guidance/managing-clinical-trials-during-coronavirus-covid-19#history