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COVID-19 Regulatory Recommendations Summary for Clinical Trials

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TRIUM Live Online Session – 24 March 2020

Learning Objectives

- At the end of these 15’ you should be able to:
  - List the official recommendation documents shared by EU, US and Japan regulatory bodies
  - Describe the key considerations and take-aways to ensure patient safety, data quality and overall compliance
  - Start adjusting your research strategies and related actions accordingly

COVID-19 Regulatory Recommendations

- EU/EEA (EC, EMA, HMA) Guidance on the Management of Clinical Trials during the COVID-19 (Coronavirus) pandemic – Version 1 (20/03/2020)
- EUROPE: COVID-19 – Overview of European Regulatory Authority Guidance – Edition 1.0, 17 March 2020
- European countries local regulatory guidance (e.g. MHRA-Managing Clinical Trials during Coronavirus (COVID-19)-GOV.UK)
- FDA Guidance on Conduct of Clinical Trials of Medical products during COVID-19 Pandemic – Guidance for Industry, Investigators, and Institutional Review Boards – March 2020
- FDA Post marketing Adverse Event Reporting for Medical products and Dietary Supplements During a Pandemic
- PMDA Basic policies for Novel Coronavirus Disease Control (Tentative translation) – February 25, 2020

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COVID-19 Challenges & Risks

- Challenges:
  - Travel restrictions
  - Quarantine (healthy volunteers, subjects, monitors, site staff)
  - Site closure; site staff not available for trial conduct; infected site staff; changes in site staff
  - Supply chain of investigational drug or device disruption

- **Risk for protocol deviations and safety issues related to**:
  - Investigational drug or device delivery & use
  - Out of window visits
  - Delays or cancellation of required lab- and/or diagnostic testing related to trial assessments
  - Delays in eCRF completion & safety reporting
  - Cancellation or delays in monitoring to confirm eligibility and ICF process
  - …

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- **Risks for clinical trials measures in general:**
  - A temporary halt of a clinical trial
  - Suspension or slowing down of subject recruitment
  - Extension of clinical trial duration
  - Site closure
  - Need for opening new sites (exceptional - USM/SA)
  - Postponement of site activation
  - Postponement of new clinical trials

KEY MESSAGE

- Guidance across global nations – key message:

  + Patient Safety, rights and well-being FIRST!
  + GCP/local regulatory compliance
  + Minimizing *risks* to ensure trial integrity (data quality)

COVID-19 Guidance Across Global Nations

- Need for new or altered policies or procedures dependent on protocol, location and disease (e.g. is delaying an assessment appropriate? Recruitment stop or withdrawal of subjects because protocol cannot be complied to?)
  - Ensure compliance with local or regional COVID-19 policies!
- All actions should be proportionate and based on *benefit-risk* considerations and on contingency provisions (aligned with local regulations) with subject health and safety as 'the' priority
- Feasibility of starting a new trial or including new subjects/sites in an ongoing way should be based on a critical *risk* assessment – COVID-19 trials have priority!

COVID-19 Guidance Across Global Nations

- Alternative means of contact (between subject and site and monitor and site) should be assessed (e.g. virtual, phone, move of subject to another site) considering the limitations and *risks* & the requirements for data protection
  - Remote SDV NOT allowed in most EU member states: NCA are looking into solutions (necessity/proportionality); also IEC/IRB and DPA agreement
  - Consider site and subject burden!
- Alternative ways of getting the investigational drug to the subject should be assessed considering the *risks* related to the product, need for qualified staff to administer the drug, shipping and storage requirements - sponsor to subject is not common, and in most countries not allowed – respect treatment blinding!
- Need for tests (lab, imaging or diagnostics) for subject safety – use of local labs(certified) are allowed if not possible at the central lab; used for safety decisions and endpoints (documented in CSR)

TAKE - AWAYS

- Guidance across global nations:
  - Risk assessment by sponsor and PI of each ongoing trial and subject; Liaise with IRB/IEC
  - Avoid site & subject burden as much as possible – ensure balanced decision making
  - No prospective protocol waivers allowed
  - No data protection breaches allowed
  - Report all protocol deviations (keep it high level!)
  - Report permanent changes in PI to NCA and IRB/IEC
  - Only enroll eligible subjects (perform planned tests, written ICF) – limit new subjects
  - Alternative ways of working always within boundaries of mandatory local restrictions and social distancing
  - Document your risk assessment, actions and deviations and report!

TAKE - AWAYS

- Guidance across global nations:
  - Subjects need to stay informed of any trial changes that could impact them
    - Validated and secure electronic systems already used for ICF can continue to be used
  - Re-consent alternatives (e.g. phone or video calls, oral consents with e-mail confirmation) only for existing subjects due to *urgent* needed changes related to COVID-19 or for COVID-19 trials as needed; 'normal' consent afterwards
  - No prior IRB/IEC and NCA approval and prior ICF needed when avoiding or handling immediate hazards or to protect subject well-being or life – report/conduct ICF afterwards, ensure justification in writing
  - Not urgent actions reported as substantial amendments – report as per SOPs and avoid overreporting!

TAKE - AWAYS

- Guidance across global nations:
  - IP accountability and documentation still required
  - COVID-19 trial priority over other trials for NCA and IRB/IEC approvals
  - PI and sponsor agreement is required for all changes proposed – e-mail exchange is accepted
  - Sponsor pays for additional costs by the subject due to the pandemic
  - Document in the eCRF why information is missing
  - CSR includes information on contingency measures and their impact, and a listing of participants affected

COVID-19 Guidance Across Global Nations

- Practice:
  - Sponsor should asap liaise with IRB/IEC and PI
  - Sponsor and PI should conduct a COVID-19 impact risk assessment asap and review ongoingly
  - Avoid, defer or mitigate highest risks in line with COVID-19 restrictions and local regulatory guidance (differences between EU member states) – liaise with NCA as applicable (e.g. EU - impact of protocol changes on data interpretation; FDA - review divisions on plans for alternative administration of IP or protocol modifications on collection of efficacy endpoints)
  - Document rationale, actions and outcomes and file in TMF
  - Report alternative actions to IRB/IEC and NCA
  - Plan for robust follow-up measures for when the situation normalizes

Need Help with your Risk-Assessment?

- Join our 1.5 hr. live online workshop called ***COVID-19 Impact Risk Assessment for Clinical Trials: Example Questions and Plans to Cover the Highest Risks***
- Includes a **template risk assessment log with prefilled risks** related to the COVID-19 pandemic to get you started fast and aligned with regulatory needs
- When? Tuesday 31 March 2020
- Time: 3.00 – 4.30pm CET
- Cost? Reduced rate of 50 euros pp excl. VAT
- Trainers: Esther Daemen and Chris de Vos, TRIUM QA and Compliance
- Registration: https://www.triumclinicalconsulting.com/calendar/4246/

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Thank you & Take Care!

References

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