FDA U.S. FOOD & DRUG ADMINISTRATION

COVID-19: Lessons Learned

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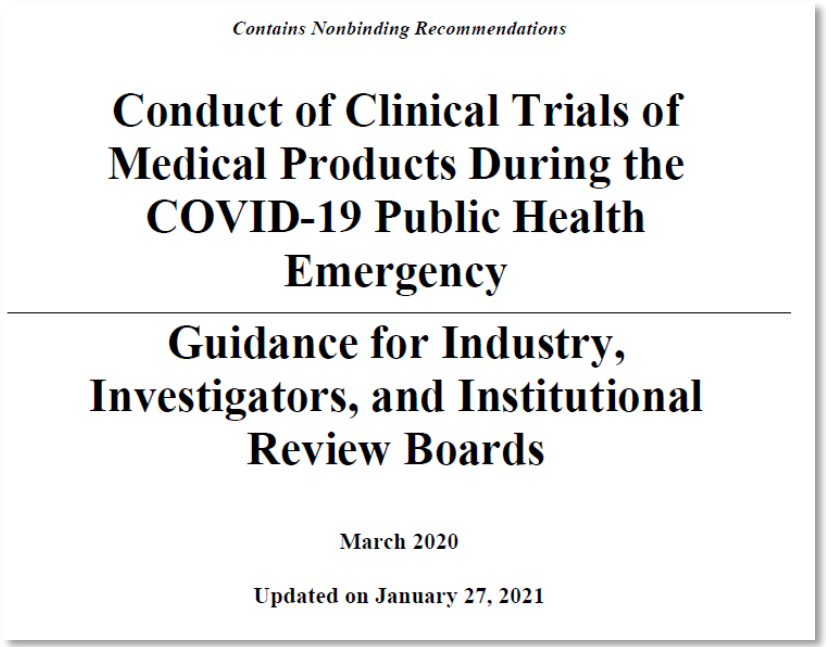
Disclaimer

Views expressed in this presentation are those of the speaker and do not necessarily represent an official FDA position

The Covid-19 Pandemic

FDA response

Q5. Conducting remote (virtual) clinic visits.
Q7. Delivering low-risk investigational products to home
Q10. Alternative monitoring approaches
Q11. Obtaining informed consent for patients in isolation
Q12. Obtaining informed consent from legally authorized representatives
Q13. Obtaining informed consent when electronic and paper forms cannot be provided
Q14. Remote clinical outcome assessments
Q15. Remote site monitoring visits
Q20. Use of alternative laboratory or imaging centers
Q21. Use of video conferencing for trial visits



Contains Nonbinding Recommendations

Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency

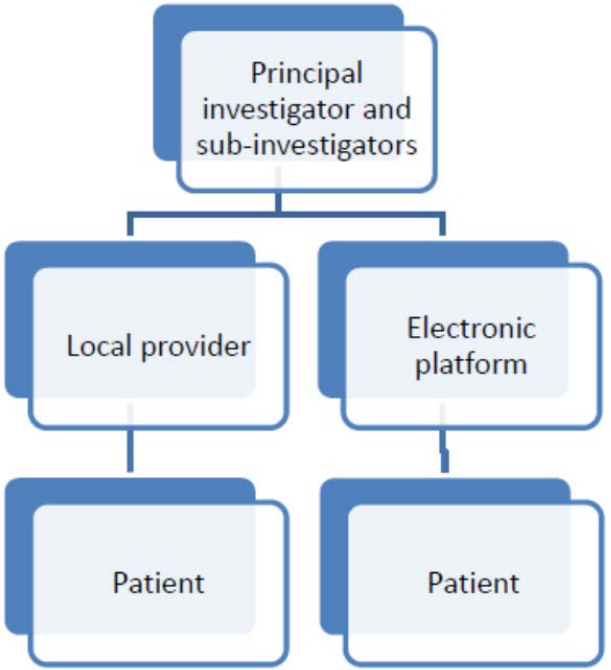
Guidance for Industry, Investigators, and Institutional Review Boards

March 2020

Updated on January 27, 2021

Definition of Decentralized Clinical Trials (DCTs)

DCT refers to a clinical investigation where some or all of the trial-related activities occur at a location separate from the investigator's location.



DCTs are subject to the same regulatory requirements as other FDA-regulated clinical trials

Whether a trial can be conducted in a decentralized manner will depend on the indication, the nature of the IP to be studied, and the design of the trial.

Division of Psychiatry experience

- According to DP reviewers, almost 100% of the INDs in their portfolios had a COVID-19-related amendment in one or more protocols
- We reviewed requests for early termination of clinical trials
- Most of the amendments were accepted with reference to the FDA COVID-19 Guidance (ref. previous slide)
- In some cases, safety changes, albeit motivated by the increased risk of exposure to COVID-19, were rejected because the safety of subjects could not be guaranteed (e.g., lack of on-site observation)
- We engaged with stakeholders to better understand the challenges and the strategies to address them

ISCTM

Regulatory viewpoints from EMA and FDA on contemporary challenges and strategies for conducting and analyzing clinical trials in the COVID-19 era

Chairs:
Michael Davis, MD, PhD
FDA Division of Psychiatry.
Richard Keefe, PhD
Duke University; VeraSci
Valentina Mantua, MD, PhD
FDA Division of Psychiatry

Division of Psychiatry experience: outcomes

- The following clinical scales were among those reviewed for remote administration during the COVID-19 public emergency:

MADRS, CMAI, NPI-NH, YMRS, PANSS, C-SSRS, CGI-SS, CGI-S, CGI-I, CDSS, AIMS, BARS, SQLS, EQ-5D-5L, DAI-10, PSP, SCID-5-CT, NPRS, ZAN-BPD, CDRS-R

- In some cases, part of a clinical outcome assessment was deemed not adequate for remote administration because some items required direct observation
- With reference to the FDA Guidance, the Division requested that sponsors document missing observations
- The Division is receiving sensitivity analyses of pre- and post-pandemic datasets.
- The Division will evaluate differences between remote and in-person administration of outcome assessments as well as strategies to handle intercurrent events related to the amendments implemented during the COVID-19 pandemic

COVID-19: lessons learned

- The Agency was able to respond promptly to the COVID-19 public health emergency, and a multi-disciplinary team of experts across FDA centers elaborated guidance for sponsors to resume clinical trial operations and ultimately support the continued development of medical products for patients
- The international network of regulators was able to exchange information and collaborate in order to support R&D at an international level
- A number of clinical trial operations can be performed remotely effectively
- The pandemic brought many clinical trial innovations to the forefront (e.g., DCTs). Even after the public health emergency is over, there will likely be permanent changes to the conduct of clinical trials based on the infrastructure established during the pandemic

COVID-19: lessons yet to be learned

- Factors with potential impact on trial outcomes:
  - Impact on mental health of COVID-19-related restrictions
  - Psychiatric short- and long-term manifestations of COVID-19 disease
  - Change in clinical trial operations/assessment modality
- Statistical methods
  - Strategies to handle missing data
  - Estimand definition
  - Strategies to handle post-randomization events
  - Interim analyses and adaptive clinical trials
  - Early study termination
  - Secondary or sensitivity analyses of pre-, during-, and post-COVID-19 datasets

Dr. Janet Woodcock
@DrWoodcockFDA

I spoke at a workshop today about lessons learned as we've been fighting #COVID19. One of the hallmarks of our prep & response to a public health crisis is the continuous evaluation & application of lessons learned from experience. Our response to the pandemic is no different.

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