

# **Regulatory Concerns and Challenges During and After the Covid-19 Pandemic: FDA Office of Cardiovascular Devices Perspective**

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# Disclosure Statement

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Bram Zuckerman, MD has no relevant disclosures

# Cardiovascular Device Trials pre- COVID-19

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Twenty-first century has brought significant changes to the healthcare environment

Need for clinical trials ecosystem to adapt to these new realities

Many concerns and roadblocks about doing things differently

***Pace of adaptation and change has not been optimal***

# Major Impact of Covid-19 on Device Clinical Trials

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- Most ongoing trials have been paused at least once
  - Highest priority has been on patient and research staff safety
- Many restarts in progress
- Delays in enrollment and trial completion
- More missing or out-of-window assessments
- Protocols and Statistical Analysis Plans being altered
- Risk-based approaches to clinical trial data monitoring and audits being considered
- Best practices are being considered in real time

# FDA Perspective on Cardiovascular Device Trials during and after COVID-19

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- Landscape has definitely changed
- It is even more critical to adapt to new realities in an efficient manner
- Multiple stakeholders *including patients* need to be involved in this process to achieve success
- No fundamental FDA constraints on such an effort
- Rather knowledge of FDA expectations is required
- ***FDA strongly encourages modernization and optimization of the clinical trials ecosystem during this emergency and beyond***

# FDA Device Approval Basics in the Covid-19 Era

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- Device approval standards have not changed
- Rigorous design and execution of clinical trials, analytical integrity, and complete and prompt reporting of prespecified analyses are bedrocks of the process
- A robust post-approval system is needed to maintain timely access to safe and effective devices in the US
- Coordination with CMS remains critical for reimbursement decisions
- **Within this context many options can be considered for improving and/or modifying the system**



# FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency

## Guidance for Industry, Investigators, and Institutional Review Boards

March 2020

Updated on June 3, 2020

<https://www.fda.gov/media/136238/download>

### Appendix: Questions and Answers

- Q1. Deciding whether to suspend, continue, or initiate trials.....
- Q2. Deciding whether to continue administering product appearing to provide benefit.....
- Q3. Managing protocol deviations and amendments.....
- Q4. Submitting changes to IND and IDE protocol.....
- Q5. Conducting remote (virtual) clinic visits.....
- Q6. Capturing data on protocol and process deviations.....
- Q7. Delivering low-risk investigational products to home.....
- Q8. Changing site for delivering high-risk investigational product.....
- Q9. Alternative monitoring approaches.....
- Q10. Obtaining informed consent for patients in isolation.....
- Q11. Obtaining informed consent from legally authorized representatives.....
- Q12. Remote performance and clinician-reported outcomes.....
- Q13. Remote site monitoring visits.....
- Q14. Challenges and temporary waivers for eCTDs.....
- Q15. Shipping investigational product to local provider – Form 1572 and accountability.....
- Q16. Use of commercial vs. investigational products.....
- Q17. Scheduling of meetings with review divisions.....
- Q18. Use of alternative laboratory or imaging centers.....
- Q19. Use of video conferencing for trial visits.....
- Q20. Postmarketing requirements for drugs, biologics, and devices.....
- Q21. Reporting serious adverse events for approved drugs used to treat COVID-19.....
- Q22. Reporting serious adverse events associated with COVID-19 in a non-COVID trial.....
- Q23. Collecting electronic signatures and Part 11 compliance.....

# Statistical Considerations for Clinical Trials During the COVID-19 Public Health Emergency

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## Guidance for Industry

June 2020

<https://www.fda.gov/media/139145/download>

- Trial integrity
  - Data collection for endpoint ascertainment changes
  - Approaches to minimize bias
- Trial mitigation and analysis strategies
  - Events related to COVID-19
  - Considerations for trial termination
  - Interim analyses
  - Missing data analyses
  - Trial endpoint modification

# A Note on Covid-19 FDA Guidance Documents

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- Key general principles outlined
- Provide starting points for consideration
- Dynamic environment requires efficient and regular communication among sponsors, investigators, statisticians, and FDA
- **For specific scenarios be practical, logical, reasonable and flexible**

# More Specific Discussion Needed in Heart Valve Disease Space to Develop Best Practices



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Screening and enrollment

Covid and Disease Specific CRFs

Maintenance of F/U visits

Laboratory testing and diagnostic imaging

Risk Based Trial Monitoring

Use of Tele-Health

Statistical methods for sample size reestimation, handling missing data, dealing with confounding effect of Covid-19 on key endpoints

Covid-19 CEC and DMC SOPs

# Additional Thoughts

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- Multiple reasons why there has been significant resistance, disincentives and barriers to changing the clinical trial ecosystem
- Need to consider how to remove these legal, financial and cultural barriers
- Validating new ideas and practices through stakeholder collaboration may be one method for removing barriers
- *Enabling patients to directly take an active part in development of a more patient-centric system is another key component*

# What Success Looks Like

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- Develop an improved Heart Valve Disease Learning Health Care Ecosystem for all Americans
- Discuss and develop proposals for high-quality clinical trials and research without overburdening research and hospital staff and study participants
- Commitment to continue this process – we will need to continue to reevaluate to optimally reshape the system
- Integrate new Tele-Health capabilities into this Ecosystem



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