FDA *Relevant* Guidance on Decentralized Clinical Trials

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Disclaimer

This talk reflects the views of the author and should not be construed to represent FDA's views or policies.

First Things First

- FDA does not have a guidance (final or draft) on the subject. Hopefully, soon.
- Guidance is not guidance until it is guidance.
  Even when there is guidance, it is developing field.
- Today's presentation
  - Whirlwind tour of current and planned relevant guidances
  - Principles that may be reflected in future guidance
  - A little emphasis in statistics principles over regulatory requirements and processes

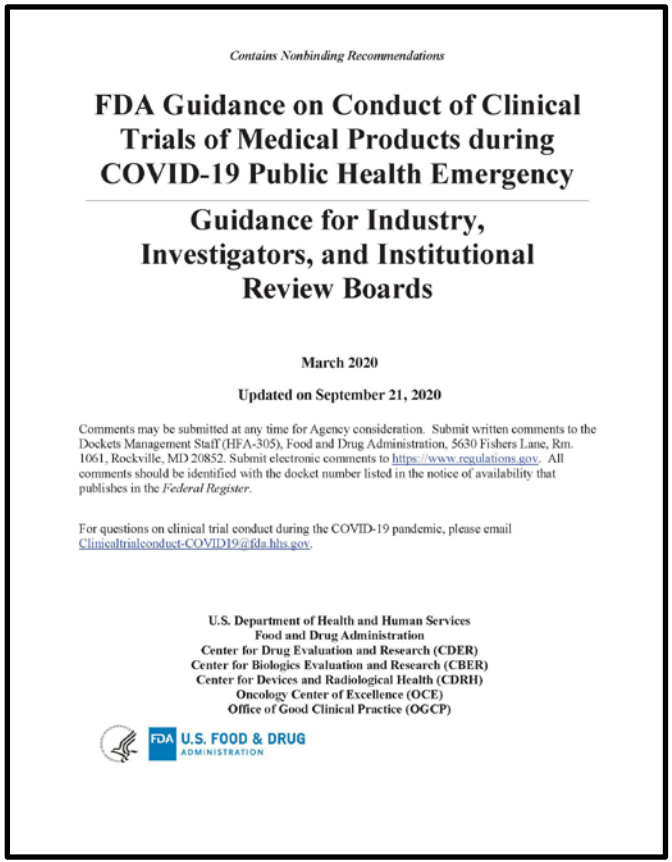
Decentralized Clinical Trials (In one slide)

- Clinical trial where some or all of the trial-related activities occur at a location separate from the investigator's location.
- Trial-related activities may take place at the homes of trial participants or in local health care environments.
- Goal to improve access to representative patient populations or trial efficiencies. May answer different questions.
- FDA's regulatory requirements are the same for DCTs and site-based clinical trials

Relevant Guidances

- Conduct and statistical issues of trial under COVID-19
- Electronic source records and informed consent
- Risk-based monitoring
- Clinical decision support software
- Digital health technology (coming)

‘Conduct’ and ‘Statistical’ Guidances on Trials During COVID-19 Public Health Emergency



Contains Nonbinding Recommendations

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 September 21, 2020

Comments may be submitted at any time for Agency consideration. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to https://www.regulations.gov. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions on clinical trial conduct during the COVID-19 pandemic, please email Clinicaltrialconduct-COVID19@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Oncology Center of Excellence (OCE)
Office of Good Clinical Practice (OGCP)

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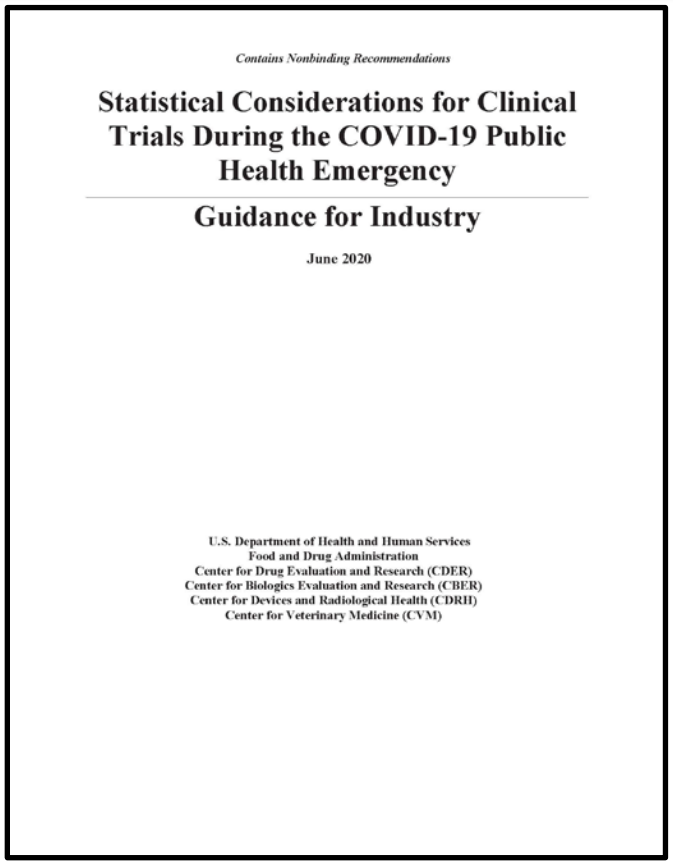


Contains Nonbinding Recommendations

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

Guidance for Industry

June 2020

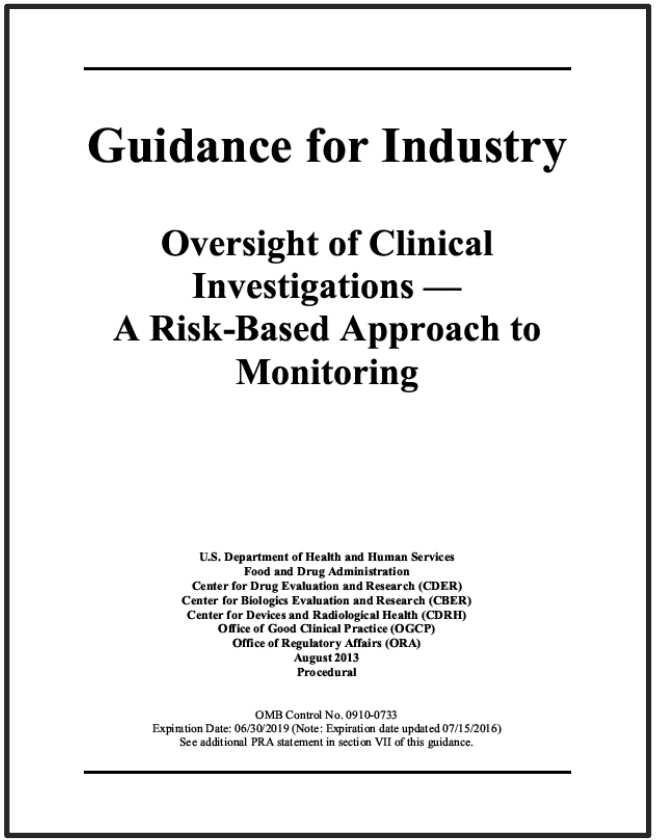
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Center for Veterinary Medicine (CVM)

Appendix: Questions and Answers

From Statistical Considerations Guidance

- **The impact of any change in endpoint definition or ascertainment, either through a change in methods or a change in timing, should be carefully evaluated in sensitivity analyses …**

Risk-Based Monitoring

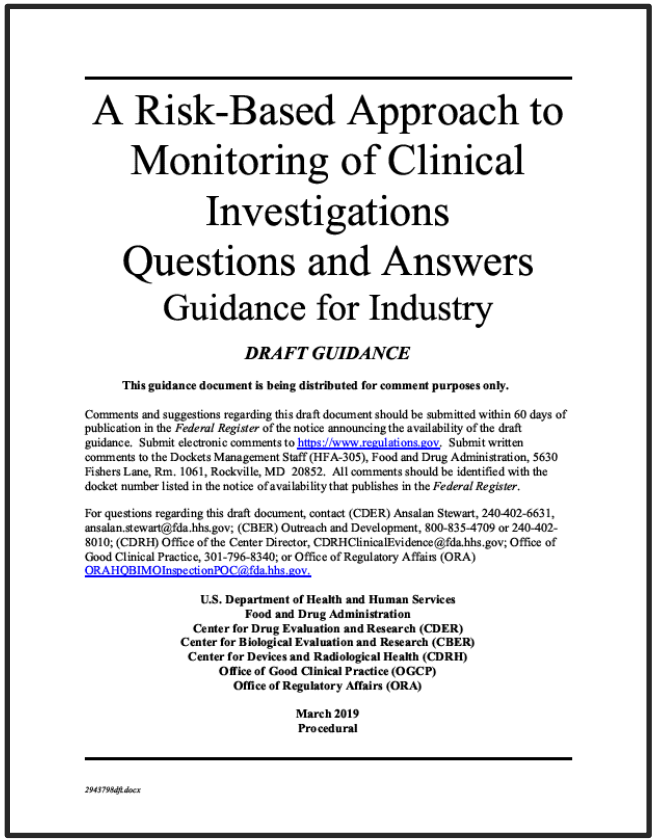


Guidance for Industry

Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Office of Good Clinical Practice (OGCP)
Office of Regulatory Affairs (ORA)
August 2013
Procedural

OMB Control No. 0910-0733
Expiration Date: 06/30/2019 (Note: Expiration date updated 07/15/2016)
See additional PRA statement in section VII of this guidance.



A Risk-Based Approach to Monitoring of Clinical Investigations Questions and Answers
Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Ansalan Stewart, 240-402-6631, ansalan.stewart@fda.hhs.gov; (CBER) Outreach and Development, 800-835-4709 or 240-402-8010; (CDRH) Office of the Center Director, CDRHClinicalEvidence@fda.hhs.gov; Office of Good Clinical Practice, 301-796-8340; or Office of Regulatory Affairs (ORA) ORAHQBIMOInspectionPOC@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
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Office of Good Clinical Practice (OGCP)
Office of Regulatory Affairs (ORA)

March 2019
Procedural

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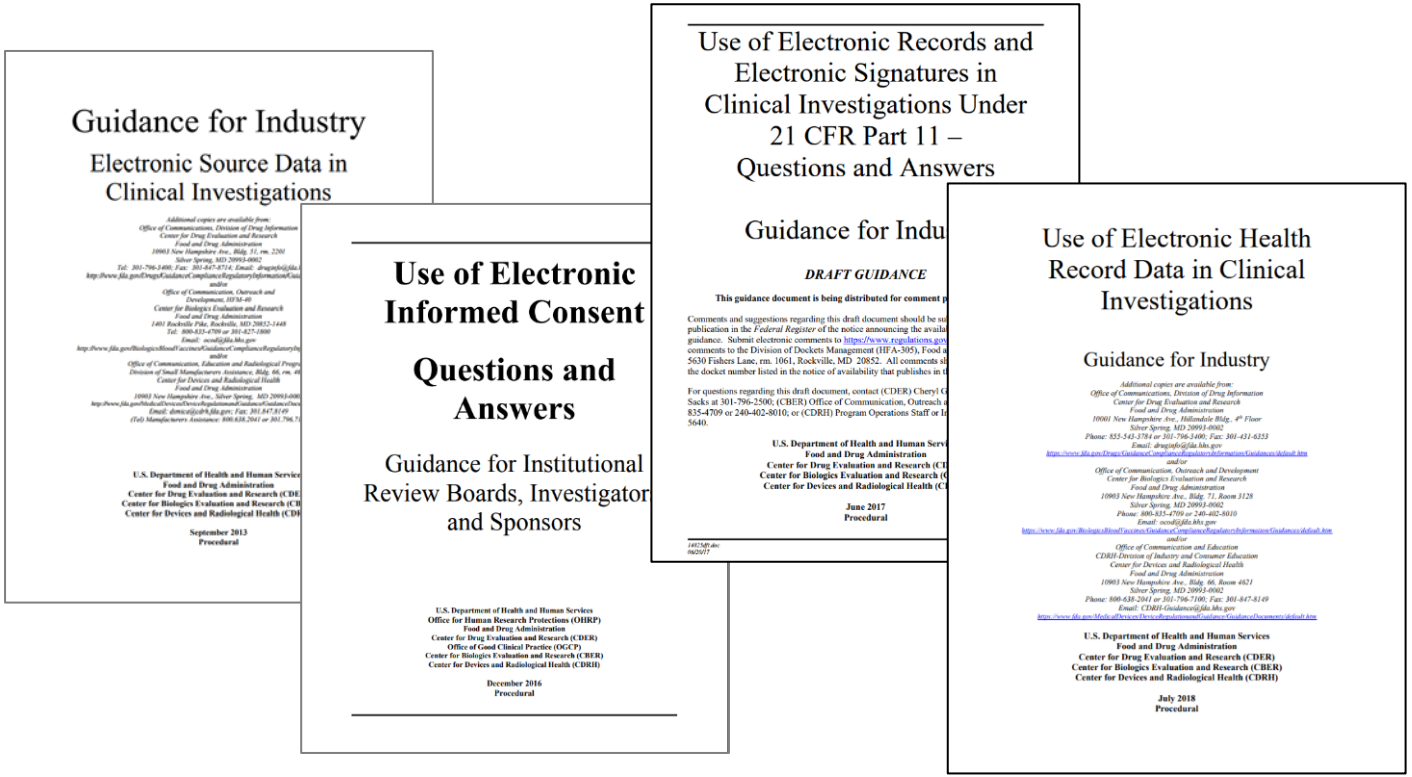
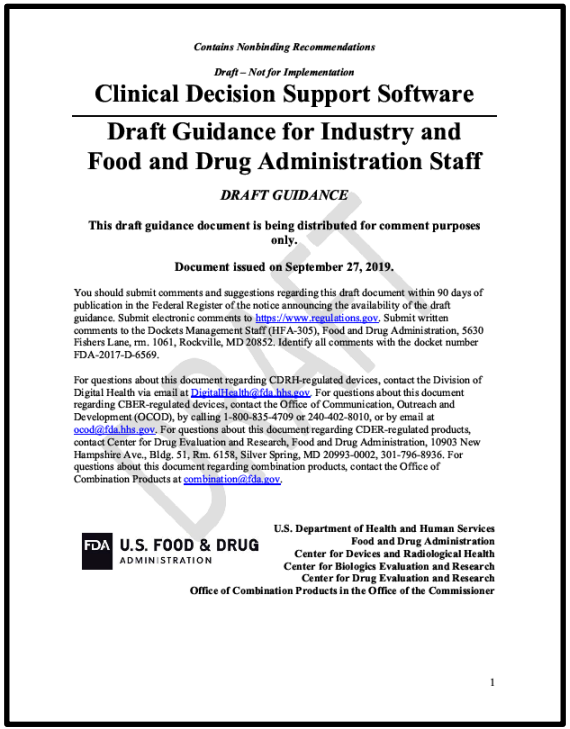
Electronic Source Records and Informed Consent



Clinical Decision Support Software



Contains Nonbinding Recommendations

Draft – Not for Implementation

Clinical Decision Support Software

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on September 27, 2019.

You should submit comments and suggestions regarding this draft document within 90 days of publication in the Federal Register of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Identify all comments with the docket number FDA-2017-D-6569.

For questions about this document regarding CDRH-regulated devices, contact the Division of Digital Health via email at DigitalHealth@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach and Development (OCOD), by calling 1-800-835-4709 or 240-402-8010, or by email at ocod@fda.hhs.gov. For questions about this document regarding CDER-regulated products, contact Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6158, Silver Spring, MD 20993-0002, 301-796-8936. For questions about this document regarding combination products, contact the Office of Combination Products at combination@fda.gov.

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research
Center for Drug Evaluation and Research
Office of Combination Products in the Office of the Commissioner

1

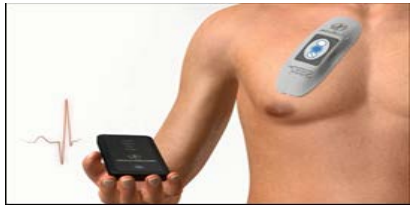
- **Software may be regulated as a device**
- **Clarifies when a software may be a device and subject to regulatory oversight**
- **Examples: feature identification in image analysis, processing accelerometer for measuring tremors**

What are digital health technologies?

Biosensors

Continuous glucose monitor

Continuous ECG monitor



Continuous blood pressure monitor

Fall detector

Smart pills

Actigraphy

Interactive mobile applications

Patient reported outcome

Cellphone camera

Coordination test in Parkinson's

Digital Health Technologies Guidance (Coming)

- **Regulatory question: Is the quality of the evidence from the DHT adequate for experts to make the right conclusions?**
- **Method of ascertainment v. clinical endpoint**
  - **Does the DHT measure what it is supposed to from a technology point of view**
  - **Does the DHT produce a measurement important to patients**

Decentralized Trials: Potential Challenges (1/2)

- Remote efficacy and safety assessments
  - Validation of digital health technology and remote assessment methods
  - Variability and missing data in remote assessment
  - Retention of participants
  - Obtaining and transmitting data
- Safety monitoring
  - Identifying and managing participant safety issues

Decentralized Trials: Potential Challenges (2/2)

- Remote monitoring
  - Identification of trial conduct issues
- Regulatory
  - Sponsor, investigator, study team, and provider responsibilities
  - Handling of investigational product
  - Documentation and record keeping

Some Principles

- **Discuss feasibility, design, implementation, and analysis of a DCT with the relevant FDA review division**
- **Employ appropriate planning, training, oversight, and up-front risk assessment and management**
- **Consider risk-based monitoring approaches and use of centralized monitoring**
- **DCT may not be suited for IPs that involve complex administration procedures, have a high-risk safety profile especially in the immediate post-administration period, or are in early stages of development**

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Thank you

mark.levenson@fda.hhs.gov