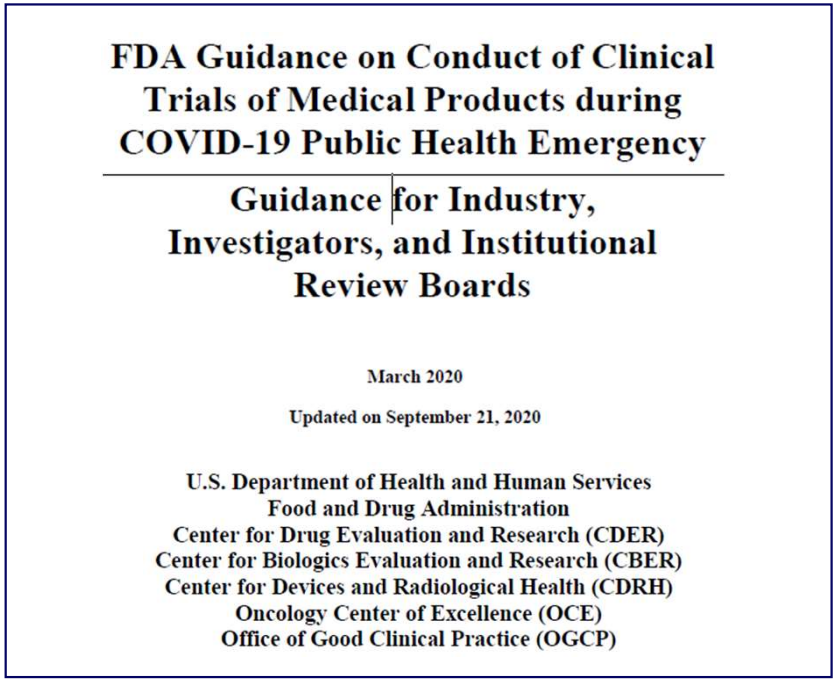
Imaging in Clinical Trials despite COVID-19

PINTaD

30-Oct-2020

On behalf of the PINTaD SC

FDA Guidance Documents



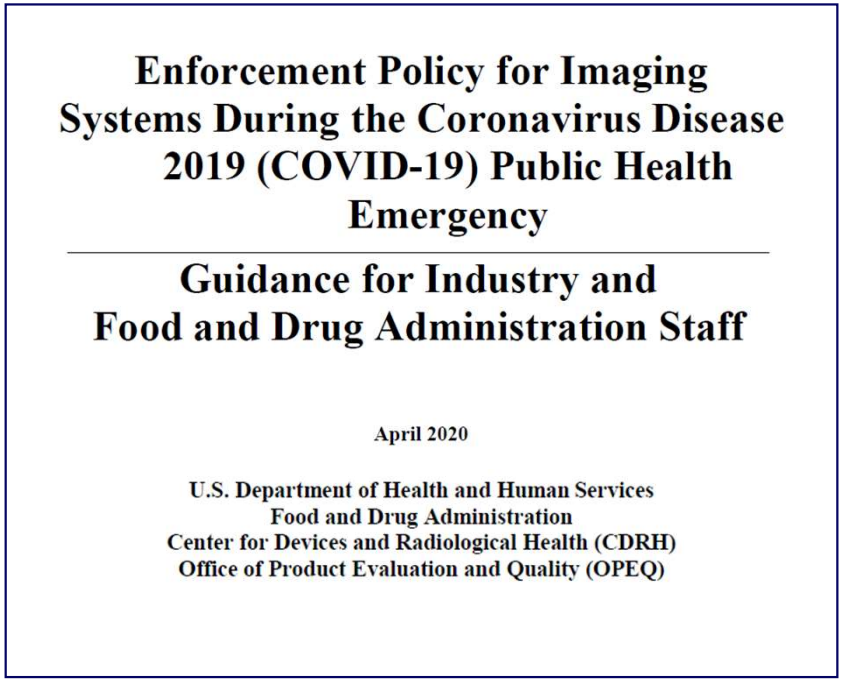
FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency

Guidance for Industry, Investigators, and Institutional Review Boards

March 2020

Updated on September 21, 2020

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)



Enforcement Policy for Imaging Systems During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency

Guidance for Industry and Food and Drug Administration Staff

April 2020

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health (CDRH)
Office of Product Evaluation and Quality (OPEQ)

Intended to remain in effect only for the duration of the public health emergency related to COVID-19

Decentralizing and Delaying Efficacy Assessments

Decentralization of Imaging Procedures *(FDA guidance)*

- *"…patients may be unable to travel to designated site…"* (Q16)
- *"…alternative sites may be used for … imaging assessments … when such tests and assessments are routinely performed in those settings…"* (Q19)
- *"…if the results of … imaging assessments are the basis for … primary or secondary efficacy endpoints and some safety endpoints, sponsors should consult with the relevant FDA review division…"* (Q19)
- *"with respect to efficacy assessments, FDA recommends consultation with the appropriate review division regarding protocol modifications for the collection of efficacy endpoints, such as use of virtual assessments…"* (section IIIA- ongoing trials)

may increase variability and thus affect type I and type II error rates

General Considerations for Decentralization applicable to Imaging assessments *(FDA guidance Q13)*

- prioritization of trial participant safety and privacy
- maintenance of data quality/integrity, incl. minimizing missing data
  - *documentation and audit trails*
  - *secure remote data acquisition, transmission, and storage*
- potential for increased variability
  - *consistency across sites, participants and visits*
- appropriate training for personnel and trial participants
- availability of technology and technical support for remote assessment

Delayed efficacy assessments *(FDA guidance)*

- *"…continuing study participation, albeit with potentially delayed assessments, may be an appropriate option when suitable alternative arrangements cannot be made."* (Q8)

- *"…consideration of whether it is appropriate to delay some assessments for ongoing trials…"* (section IIIA- ongoing trials)

- *"With respect to efficacy assessments, FDA recommends consultation with the appropriate review division regarding … delays in assessments…"* (section IIIA- ongoing trials)

Rethinking Clinical Trials Reform During the COVID19 Pandemic. Nabhan et al., JAMA onco, sept 2020

- Routine tests may be done locally, provided no special expertise is needed
- Telemedicine is being more widely adopted and incorporated into clinical trials
- Imaging may be performed less frequently
  - For ongoing trials, delayed imaging when appropriate
  - For new studies, design with increased time between imaging exams

Potential Benefits: *patients exposed to less radiation/contrast material and lower overall trial costs*

Challenging statement: *designate OS as the primary endpoint in more studies*

Impact of the COVID-19 Crisis on Imaging in Oncological Trials. Deroose et al., EJNMMI, Jun 2020

- Increase flexibility and re-evaluate imaging frequency within existing trial protocols
- Imaging studies can be directed to local sites with spare capacity
- Group clinical, laboratory and imaging visits
- Imaging frequency may be increased to monitor complications (of COVID19)

Opportunities: *(Re)discover the true value of imaging, and critically review the need for imaging and/or imaging frequency.*

Modifications to approved indication of Imaging

Imaging Systems during the COVID19 pandemic (FDA guidance)

- *"FDA does not intend to object to modifications to the FDA-cleared or approved indications … where the modification does not create an undue risk…" (section IV-A)*
  - expansion of indications for use (e.g. extremity-only use expanded to other body parts) where no alternatives exist at a facility
  - modifications that expand mobility, portability, or relocation of medical imaging systems
  - modifications to protect the operator or patient
  - design modifications to improve the ability to clean, disinfect, and/or sterilize the product

One Sponsor's Practical Approach

Getting Scans

- **Subject** can't get to site on schedule, or site scanners are not working

Off-site, on schedule
On-site, delayed
Off site, off schedule
Skip assessment

- Investigator

- Inform IRB of alternate imaging site
- Send imaging guidance from site manual
- Get copies of scans to evaluate (and upload to iCRO)
  - Alternate site can upload, if already trained
- Document off-site scan/other issues with searchable tag ("COVID-19")

Missing Scans

- Plan in advance, fix a date
- Close queries and read all available scans
- Classify impact of each missing scan
  - Separate impact for PD and BOR
  - Algorithm/predefined scenarios + iCRO med/sci judgment
    - Collaboration between imaging, stats, iCRO team
- Use impact to drive mitigation
  - Focus on highest impact to chase down missing data
  - Aggregate impact to support trial decisions
    - delay, change endpoint, etc.

Thank you!