2-Day Virtual Public Meeting:
Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies
October 18 – 19, 2023 / 10 a.m. – 1:30 p.m. EDT
Keynote address

Jacqueline Corrigan-Curay, Principal Deputy Center Director, Center for Drug Evaluation and Research, FDA

Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies: A 2-Day Virtual Public Meeting
October 18, 2023
Opening remarks

Janet Woodcock, Principal Deputy Commissioner, U.S. Food and Drug Administration, FDA

Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies:
A 2-Day Virtual Public Meeting
October 18, 2023
Mitigating Clinical Study Disruptions during Disasters and Public Health Emergencies (PHEs)

Jacqueline Corrigan-Curay, MD, JD
Principal Deputy Center Director
Center for Drug Evaluation and Research
US Food and Drug Administration

October 18, 2023
Disclosures

• No relevant disclosures
• The views expressed in this presentation are mine and may not represent the views of the FDA
Outline

• Background and public meeting objectives

• Provide overview of FDA activities related to COVID-19

• Explain purpose and content of FDA Guidance on Conduct of Clinical Trials

• Discuss how clinical study conduct has changed during the COVID-19 PHE

• Facilitate discussion regarding advanced planning to mitigate disruption of clinical studies during future disasters and PHEs
In December 2022, President Biden signed into law the Food and Drug Omnibus Reform Act (FDORA) as part of the 2023 Consolidated Appropriations Act.

In accordance with FDORA, FDA is convening this public meeting to discuss the recommendations provided by FDA during the COVID-19 PHE to mitigate disruption of clinical studies.

After the public meeting, a report will be made available about the topics discussed.

In addition, FDA is facilitating discussions and soliciting input on advanced planning to mitigate disruption of clinical studies during future disasters and PHEs.
Coronavirus Disease 2019 (COVID-19)

On this page:

- Latest COVID-19 News from FDA
- Popular Topics
- COVID-19 and FDA-regulated Products
- Emergency Use Authorizations and Guidances
- Personal Protective Equipment
- Contact FDA or Report a Problem
- Information from the Federal Government

COVID-19 Vaccines and Bivalent COVID-19 Vaccines

- Pfizer-BioNTech COVID-19 Vaccine, Bivalent
- Moderna COVID-19 Vaccine, Bivalent
- Novavax COVID-19 Vaccine, Adjuvanted

EUAs and Public Health Emergency Ending

Frequently asked questions on how the May 11, 2023, expiration of the PHE affects EUAs and more.
FDA COVID-19 Key Activities During PHE

• Reviewed numerous pre-market submissions for investigational drugs/biologics/devices including applications for diagnosis, treatment, and mitigation of COVID-19

• Expanded access for investigational products

• Issued guidance for industry, investigators, and institutional review boards related to COVID-19

• Emergency Use Authorizations (EUAs) issued for medical products for the diagnosis, treatment, and mitigation of Covid-19 including drugs, vaccines, ventilators, personal protective equipment, and in vitro diagnostics

• Soliciting feedback from and conveyed up-to-date information to the public
FDA COVID-19 Guidance Activities During PHE

• More than 80 guidances issued for industry, investigators, and institutional review boards related to COVID-19

Time Period: March 2020 to December 2021

FDA colleagues have also regularly updated many guidances over the last few months to include additions and amendments.
Coronavirus Treatment Acceleration Program (CTAP)

- Designed to help facilitate the development of drugs and biologics (other than vaccines) for COVID-19 therapeutics leveraging CDER and CBER cross-agency scientific resources and expertise

- Over 600 development programs planned; >450 trials reviewed

- Examples of approved COVID-19 therapeutics:
  - Antiviral Drugs: Paxlovid (nirmatrelvir and ritonavir), Lagevrio (molnupiravir)*
  - Immune Modulators: Actemra (tocilizumab)

*Molnupiravir is not approved, only authorized by the EUA

Center for Biologics Evaluation and Research (CBER)

Granted Emergency Use Authorizations (EUA) for Multiple SARS-COV-2 Vaccines

• BNT162b2 (mRNA, Pfizer-BioNTech) – EUA granted Dec 11, 2020
  - Initial Licensure for individuals 16 years of age and up granted to COMIRNATY on August 23, 2021

• mRNA-1273 (mRNA, Moderna) – EUA granted Dec 18, 2020
  - Initial Licensure for individuals 18 years of age and up granted to SPIKEVAX on January 31, 2022

• Non-Replicating Viral Vector Vaccine

• Protein Subunit Vaccine
  - NVX-CoV2373 (Novavax) – EUA granted July 13, 2022

Developed New Guidance Documents

• Development and Licensure of Vaccines to Prevent COVID-19 Guidance (June 2020)

Center for Devices and Radiological Health (CDRH)

• CDRH authorized over 900 EUAs, including >500 tests, and granted emergency or full authorization to over 3000 devices to help combat the pandemic.

• **Partnered with NIH RADx program to improve evaluation of tests**
  – Study performance of antigen tests
  – Established Independent Test Assessment Program (ITAP)
  – Collaborated on Test Us at Home (TUAH)

• **Engaged with stakeholders**
  – Performed >120 public webinars
  – Published >30 guidance documents and >350 FAQs

• **Established Resilient Supply Chain Program** to help monitor for and mitigate device shortage supply chain issues

• **Working with manufacturers** to bring EUA devices to full authorization through traditional pathways
  – Published transition guidance documents for EUAs devices and for devices under enforcement policies issued during the pandemic
  – held public webinar.
Ongoing FDA Activities Related to COVID-19 Guidances

• Most of the COVID-19-related guidances are intended to remain in effect only for the duration of the COVID-19 PHE declaration

• Since the PHE expired on 11 May 2023, FDA has reviewed these COVID-19-related guidances and has examined whether any of the guidances should be continued past expiration of the PHE declaration

Federal Register :: Guidance Documents Related to Coronavirus Disease 2019 (COVID-19)
Post-PHE Status of COVID-19-Related Guidances
Clinical Trial Conduct Examples

• Guidance documents that will no longer be in effect:
  o e.g., *Statistical Considerations for Clinical Trials During the COVID-19 Public Health Emergency*

• Guidance documents FDA revised to continue in effect after the PHE declaration expired
  o e.g., *Conduct of Clinical Trials of Medical Products During COVID-19 Public Health Emergency*
    has been revised as:

  *Considerations for the Conduct of Clinical Trials of Medical Products During Major Disruptions Due to Disasters and Public Health Emergencies* (Sept 2023)
FDA Guidance on the Conduct of Clinical Trials During COVID-19

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

Guidance for Industry, Investigators, and Institutional Review Boards

Initial release 18 March 2020; multiple updates to 30 August 2021

https://www.fda.gov/media/136238/download
FDA Guidance ‘Conduct of Clinical Trials’
Example Topics

• Key considerations for continuing or initiating clinical trials
• Informed consent and eConsent considerations
• Remote outcome assessments
• Data management and statistical analysis plan (SAP)
• Continuing investigational product
• Investigational product administered at home or locally
• Communications with FDA
FDA Guidance ‘Conduct of Clinical Trials’
Core Principles

• Safety of trial participants is core focus of all recommendations
  o “Ensuring the safety of trial participants is paramount” is first consideration mentioned in Conduct of Clinical Trials Guidance
  o Focus also on protecting trial integrity and helping to maintain compliance with Good Clinical Practice

• Trial modifications should address safety and seek to maintain trial integrity; FDA is being flexible where appropriate

• Consider options for remote assessments and alternative delivery of investigational product, when appropriate

• Important to document COVID-19 related protocol deviations and missing data

• For specific questions that depend on factors such as study population, type of investigational product, or trial endpoint, contact the appropriate FDA review division
FDA Guidance ‘Clinical Trials Conduct’ Mailbox Inquiries

• Guidance solicited inquiries on clinical trial conduct during the pandemic to a dedicated mailbox at Clinicaltrialconduct-COVID19@fda.hhs.gov

• ‘Conduct of Clinical Trial COVID-19’ mailbox received and replied to 661 inquiries during the PHE

• Question & Answer appendix developed and expanded over time based on major issues identified and inquiries received in mailbox

• Multiple updates to the ‘Conduct of Clinical Trials COVID-19’ guidance (latest update in August 2021)
## FDA Guidance ‘Conduct of Clinical Trials’ 
### Mailbox Inquiries: *Sent by Whom?*

<table>
<thead>
<tr>
<th>INQUIRIES – ORGANIZATIONAL TYPES (N=414; data as of June 2020)</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Industry/trade association</td>
<td>126</td>
<td>30</td>
</tr>
<tr>
<td>Academic institution/hospital/clinic/research site</td>
<td>120</td>
<td>29</td>
</tr>
<tr>
<td>Trial participant/patient/private citizen</td>
<td>60</td>
<td>14</td>
</tr>
<tr>
<td>Contract Research Organization (CRO)/CRO association</td>
<td>55</td>
<td>13</td>
</tr>
<tr>
<td>Institutional Review Board/Independent Ethics Committee</td>
<td>25</td>
<td>6</td>
</tr>
<tr>
<td>Government</td>
<td>23</td>
<td>6</td>
</tr>
<tr>
<td>Patient advocate</td>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

[Link to FDA website](www.fda.gov)
### FDA Guidance ‘Conduct of Clinical Trials’ Mailbox Inquiries: *What was the Focus?*

<table>
<thead>
<tr>
<th>‘TOP TEN’ PRIMARY CATEGORIES OF QUESTIONS (N=414; data as of June 2020)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covid-19-related study questions</td>
<td>85</td>
</tr>
<tr>
<td>Informing/interacting with FDA</td>
<td>41</td>
</tr>
<tr>
<td>Access to/issuance of COVID-19-related regulatory guidelines or resources</td>
<td>29</td>
</tr>
<tr>
<td>Investigational product distribution/supply/suspension</td>
<td>28</td>
</tr>
<tr>
<td>Informed consent process/content/documentation</td>
<td>26</td>
</tr>
<tr>
<td>Electronic signature/record/system compliance</td>
<td>23</td>
</tr>
<tr>
<td>Remote data monitoring/wearables &amp; mobile technologies</td>
<td>23</td>
</tr>
<tr>
<td>Study/protocol amendment, change, deviation handling</td>
<td>18</td>
</tr>
<tr>
<td>Study delay/suspension/premature termination or resumption after pause</td>
<td>17</td>
</tr>
<tr>
<td>Study eligibility/screening procedures for Covid-19 and study participation</td>
<td>16</td>
</tr>
</tbody>
</table>
Considerations for the Conduct of Clinical Trials of Medical Products During Major Disruptions Due to Disasters and Public Health Emergencies

Guidance for Industry, Investigators, and Institutional Review Boards

This guidance is for immediate implementation.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(C). Submit one set of either electronic or written comments on this guidance at any time. 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. You should identify all comments with the docket number listed in the notice of availability that published in the Federal Register. For questions regarding this document, contact (CDER) Office of Medical Policy. CDEROMP@fda.hhs.gov, 301-796-2500.

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 New Drugs (OND)
Office of New Drugs (OND)
Office of Clinical Policy (OCP)

September 2023

Emergencies

- Recommendations on approaches for consideration at the time of major disruptions to clinical trial conduct and operations (e.g., hurricanes, earthquake, military conflicts, infectious disease outbreaks, bioterrorist attacks)

- Appendix further explains these approaches by providing answers to questions received by the Agency on the topics

https://www.fda.gov/media/172258/download
In Summary

• FDA worked closely with many partners to provide guidance on clinical trial conduct during the COVID-19 PHE to protect patient safety and promote clinical trial integrity.

• Lessons learned from disruptions to the conduct of clinical trials during COVID-19 will strengthen our mission to protect and promote public health.

• FDA is already incorporating lessons from the pandemic into guidance and policies relevant to the design and conduct of clinical trials.

• We look forward to discussing and applying this shared knowledge towards advanced planning strategies to mitigate disruption of clinical studies during future disasters and PHEs.
FDA Online Resources

- Coronavirus Disease 2019
- Federal Register: Guidance Documents Related to Coronavirus Disease 2019 (COVID-19)
- Considerations for the Conduct of Clinical Trials of Medical Products During Major Disruptions Due to Disasters and Public Health Emergencies; Guidance for Industry, Investigators, and Institutional Review Boards
Acknowledgements

- FDA and CTTI Planning Committee Members
Session I: Cross-cutting Industry Perspectives

Moderator: John Farley, Center for Drug Evaluation and Research, FDA

Anina Adelfio, Chief Operating Officer, Association of Clinical Research Organizations (ACRO)

David Borasky, Vice President, Compliance Review Solutions, WCG

Janice Chang, Chief Executive Officer, TransCelerate

Karla Childers, Head, Bioethics-based Science & Technology Policy, Office of the Chief Medical Officer, Johnson & Johnson

Janet Vessotskie, Deputy Vice President of Science and Regulatory Advocacy, Pharmaceutical Research and Manufacturers of America (PhRMA)

Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies:
A 2-Day Virtual Public Meeting
October 18, 2023
Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies: Cross-Cutting Industry Perspectives

Anina Adelfio, Chief Operating Officer, ACRO

email: aadelfio@acrohealth.org

October 18, 2023

www.acrohealth.org
About ACRO

• The Association of Clinical Research Organizations (ACRO) is a trade organization that brings together the industry’s leading CROs and technology companies

• ACRO hosts several committees including:
  o Risk-Based Quality Management (RBQM) Working Group
  o Decentralized Clinical Trials (DCT) Working Party
  o Ukraine Clinical Trial Response Team
  o Artificial Intelligence & Machine Learning (AI/ML) Committee
  o And others…

• Currently, 18 member companies participating in various committees

• ACRO frequently collaborates with other trade associations and industry groups, especially when the industry is facing disruptions or other shared challenges
Bringing Us Back to March 2020

• When the first wave of COVID-19 hit the US in early 2020, ACRO’s team assembled and pulled together some early data to share with the FDA on what our companies were seeing at the site-level

• Note: this was anecdotal data shared by three ACRO member companies

<table>
<thead>
<tr>
<th>Institutions Impacted</th>
<th>14 March</th>
<th>21 March</th>
<th>28 March</th>
<th>6 Apr (week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global</td>
<td>10 %</td>
<td>34 %</td>
<td>45 %</td>
<td>49 %</td>
</tr>
<tr>
<td>US</td>
<td>4 %</td>
<td>28 %</td>
<td>44 %</td>
<td>47 %</td>
</tr>
<tr>
<td>China</td>
<td>45 %</td>
<td>45 %</td>
<td>53 %</td>
<td>57 %</td>
</tr>
<tr>
<td>So Korea</td>
<td>86 %</td>
<td>82 %</td>
<td>82 %</td>
<td>69 %</td>
</tr>
<tr>
<td>Italy</td>
<td>66 %</td>
<td>79 %</td>
<td>80 %</td>
<td>82 %</td>
</tr>
<tr>
<td>Spain</td>
<td>38 %</td>
<td>78 %</td>
<td>80 %</td>
<td>80 %</td>
</tr>
</tbody>
</table>

Visits Cancelled or Delayed vs. Planned

<table>
<thead>
<tr>
<th></th>
<th>January</th>
<th>February</th>
<th>March</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global</td>
<td>7 %</td>
<td>8 %</td>
<td>33 %</td>
</tr>
<tr>
<td>US</td>
<td>14 %</td>
<td>11 %</td>
<td>35 %  (12 % - 57 %)</td>
</tr>
<tr>
<td>China</td>
<td>28 %</td>
<td>69 %</td>
<td>49 %  (35 % - 71 %)</td>
</tr>
<tr>
<td>So Korea</td>
<td>1 %</td>
<td>14 %</td>
<td>34 %  (29 % - 38 %)</td>
</tr>
<tr>
<td>Italy</td>
<td>6 %</td>
<td>12 %</td>
<td>49 %  (34 % - 57 %)</td>
</tr>
<tr>
<td>Spain</td>
<td>10 %</td>
<td>5 %</td>
<td>38 %  (8 % - 62 %)</td>
</tr>
</tbody>
</table>

Broadly defined as any site or institution where patient visits or site monitoring visits have been restricted, rescheduled, postponed, or cancelled due to COVID-19.
Bringing Us Back to March 2020

- ACRO member companies met internally, with other stakeholder groups, and with Regulators during the first few weeks of the pandemic
- Information sharing and collection of experiences were essential at this time

<table>
<thead>
<tr>
<th>Site Inaccessibility &amp; Site Closures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Global</strong></td>
</tr>
<tr>
<td>March average: ~35% sites closed</td>
</tr>
<tr>
<td>EOM March: ~70% sites inaccessible</td>
</tr>
<tr>
<td><strong>China</strong></td>
</tr>
<tr>
<td>Peak crisis: ~80% sites inaccessible</td>
</tr>
<tr>
<td>EOM March: ~40% sites inaccessible</td>
</tr>
</tbody>
</table>

| New Subject Study Enrollment: Year over Year (YoY) Difference between March 2020 and March 2019 |
| By Country | YoY Difference |
| All Countries, All TAs | -65.1% ▼ |
| India | -83.9% |
| United Kingdom | -80.1% |
| France | -68.2% |
| Spain | -68.1% |
| China | -67.5% |
| US | -66.7% |
| So Korea | -61.1% |
| Italy | -52.3% |
| Japan | -43.5% |
| Germany | -32.5% |

| By TA | YoY Difference |
| Endocrine | -80.5% |
| Cardiovascular | -69.7% |
| CNS | -68.5% |
| Dermatology | -64.0% |
| Oncology | -48.4% |
| Infectious Disease | -46.8% |
| Respiratory | -33.7% |

New Subject Study Enrollment – February vs. March 2020

Two countries did increase the % of new patients added between February and March: China and Argentina
- In China, March was 240% higher than February. This may demonstrate a potential return to normal.
• As a result of the global pandemic, CROs had made the pivot to remote monitoring and it has been successful and has enabled continued assurance of data quality and patient safety.
In March, the FDA released the first iteration of their guidance: *Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency*

On March 13, 2020, ACRO made a statement: **Considerations to support clinical trial monitoring and oversight during the pandemic.**

- Recommendations to be considered when sites had suspended visitors, when local quarantines were implemented, or when CRAs were unable to travel to sites
- Can be found using the QR code below or on acrohealth.org under the COVID-19 initiative section
In early 2020, ACRO’s RBQM Working Group was in the second year of a four-year survey project, looking at how various risk-based and remote monitoring strategies were being implemented in clinical trials.

<table>
<thead>
<tr>
<th>Landscape Survey Year</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
<th>2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing studies</td>
<td>6,513</td>
<td>5,987</td>
<td>4,889</td>
<td>4,958</td>
</tr>
<tr>
<td>New studies started</td>
<td>Not collected</td>
<td>908</td>
<td>1,270</td>
<td>1,004</td>
</tr>
<tr>
<td>New study starts %</td>
<td>Not collected</td>
<td>15%</td>
<td>26%</td>
<td>20%</td>
</tr>
<tr>
<td># of CROs participating</td>
<td>7</td>
<td>6</td>
<td>7</td>
<td>7</td>
</tr>
</tbody>
</table>
The impact of COVID-19:
Significant increases in off-site/remote monitoring & central monitoring
Bringing us to February 2022

• When the war in Ukraine broke out in late February 2022, many of the lessons learned through the COVID-19 pandemic were being solidified.

• Similar themes: Continuation of monitoring visits, movement of patients, supply disruptions, unprecedented situations, a lot of unknowns….

• CROs and technology vendors rallied, ACRO launched our Ukraine Clinical Trials Response Team in early March 2022.

• COVID-19 guidance documents in place from Regulators, FDA, EMA, MHRA – extremely valuable for the industry to have these guidance documents already in place.
Thank you!

Anina Adelfio, Chief Operating Officer, ACRO
email: aadelfio@acrohealth.org

October 18, 2023
www.acrohealth.org
Managing Clinical Trial Continuity During Disruptions and Public Health Emergencies

Cross Cutting Industry Perspectives

Janice Chang, CEO, TransCelerate BioPharma Inc.

October 18, 2023
TransCelerate was conceived to improve the health of people around the world by accelerating and simplifying the research and development of innovative new therapies.

In 2012, R&D Leaders formed a non-profit to collaborate to tackle common operational challenges. Combining the words “Transform” and “Accelerate”, TransCelerate was launched.

Member driven mission to collaborate across the global biopharmaceutical research and development community to identify, prioritize, design, and facilitate the implementation of solutions designed to drive the efficient, effective and high-quality delivery of new medicines.

TransCelerate has grown from 10 pioneering companies to 22 Member Companies, fostering interactions across ecosystem stakeholders, towards improvement in key value drivers in clinical research.
Rapid Response: Activation of COVID-19 Collaborative Sharing Network to Address Real-Time Trial Continuity Challenges

COVID-19 Collaborative Sharing Network

- Designed as a trusted and collaborative forum to discuss ongoing disruption to drug development caused by COVID-19
- Launched as bi-weekly meeting March 6th, running throughout 2020
- Average attendance of 50-100 clinical operations leaders

Discussion Topics Evolved Over Time

**Collaborative Focus:**
- Trial Continuity

**Representative Challenges:**
- Ensuring access to medications
- Visiting/home nursing
- Safety reporting
- Operationalizing regulatory guidance

**Early Pandemic**

**Later Months**

- Modernizing Trial Operations
  - Data collection
  - Database lock
  - Restart criteria
  - Recording COVID-19 impacts

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Leveraging Existing Workstreams, Capabilities to Support Trial Disruptions Resulting From Pandemic

Clinical Study Reporting

Best practices and “what does good look like” for final CSRs in studies that were disrupted by the COVID-19 pandemic.

Project run as an extension of existing TransCelerate workstream focused on Clinical Content and Reuse

Three deliverables: Guiding Principles, Key Considerations and Sample Text

Protocol Deviation

Suite of resources to support management of protocol deviations

Release of workstream deliverables accelerated given urgent need

Deliverables: Protocol deviation Process Guide, Map, Assessment Plan and Decision Tree
Launch Pad for TransCelerate’s Modernizing Clinical Trial Conduct Initiative

Inspired by the collective learnings from the response to the COVID-19 pandemic

The Modernizing Clinical Trial Conduct (MCTC) initiative focuses on the evolution of clinical trials to include broad adoption of technologies and solutions, as appropriate, that enable greater patient choice and flexibility while maintaining patient safety and data reliability.

Process Modernization
- Maturity Landscape Survey
- Operational Complexity Assessment Tool
- Process Frameworks and barriers to adoption for:
  - Direct-to-patient shipping
  - Electronic informed consent
  - Home health visits
  - Telemedicine
  - Digital data collection tools
  - Remote site monitoring
  - Local community-based laboratory utilization

Transformational Ideation
Clinical Trials 2031 and Beyond Report – an exercise to reimagine potential environments for the future of clinical trials. Four key observations from this work:
- Partnership and collaboration across ecosystem is essential
- High adoption of technology is key
- Reliable data is essential
- Innovation requires openness to change
<table>
<thead>
<tr>
<th>1</th>
<th>Changing How Trials Operate to Bring Clinical Research Closer to the Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Enabling Use of Pragmatic Trial and Real-World Elements to Improve Patient Experience</td>
</tr>
<tr>
<td>3</td>
<td>Enabling Data Exchange, Interoperability and Data Flow between Clinical Research and Clinical Care</td>
</tr>
<tr>
<td>4</td>
<td>Data Re-use and Optimization of Data Collection to Improve Trial Design and Reduce Patient and Site Burden</td>
</tr>
<tr>
<td>5</td>
<td>Next Generation Pharmacovigilance Capabilities to Enhance Patient Safety</td>
</tr>
<tr>
<td>6</td>
<td>Operationalizing Platform Trials for Evidence Generation and Burden Reduction</td>
</tr>
</tbody>
</table>

TransCelerate’s 3-Year Roadmap Focusing on Six Key Opportunities
FDORA Virtual Public Meeting: October 18-19, 2023

Recommendations and Considerations for Mitigating Trial Disruptions

Karla Childers
Head, Bioethics-based Science & Technology Policy
Office of the Chief Medical Officer

Johnson&Johnson
Introduction

Karla Childers
Head, Bioethics-based Science & Technology Policy
Office of the Chief Medical Officer
Johnson & Johnson

Continuing to build bioethics capabilities is a priority for Johnson & Johnson

Recent Thought Leadership
Topic: Conducting research during times of disruption
We can and should be learning from current and past disruptions and times of crisis to minimize the impact to participant safety and maintain the integrity of clinical research.
1. Future proof documents and structural elements of clinical trials

- Simplify language on Informed Consent Forms
  - Complex and difficult for potential study participants to understand

- Adopt remote monitoring and/or approval of telehealth visits

- Provide flexibility in protocols to avoid excessive number of protocol deviations
2. Access to investigational medicines and products that may have restrictions

- **Recognize ethical considerations**
  - Risk of harm from treatment disruption
  - Change in patient vulnerability

- **Increase flexibility in REMS programs** to help preserve treatment access

- **Review existing guidance** for disaster preparedness for medicines requiring healthcare provider support or oversight
3. Reduce medical device and technology-related disruptions

Medical device and technology disruption present different and potentially extensive challenges

- Potential need for physical examination post-op
- Disruption felt acutely due to closure of health care sites/facilities

Opportunities to reduce disruption

- Broaden acceptable qualifying sites for follow up or routine care needs
- Broaden network of sites or qualified doctors to perform care
Thank you.
Session II: Patient Experiences and Perspectives

Moderator: Captain Julienne Vaillancourt, Center for Biologics Evaluation and Research, FDA

Karin Hoelzer, Director of Policy and Regulatory Affairs, National Organization for Rare Disorders (NORD)

Valen Keefer, Patient Advocate, Educator, Consultant, Thermo Fisher Scientific and Otsuka America Pharmaceutical

Neena Nizar, Executive Director, Founder, Jansen's Foundation
Session III: Drugs, Biologics, and Device Sponsors’ and Investigators’ Perspectives

Moderator: Harpreet Singh, Center for Drug Evaluation and Research, FDA

Lisa Bennett, Principal Quality Lead, Roche
Kenneth Getz, Executive Director, Tufts Center for the Study of Drug Development; Professor, Tufts University School of Medicine
Chris Labaki, Research Fellow, Dana-Farber Cancer Institute (DFCI), Broad Institute of MIT, Harvard
Vinod (Vinny) Parthasarathy, Senior Clinical Monitoring Director, Medtronic
Joanne (Jo) Spallone, Clinical Quality Consultant (JS GCP Clinical Consulting Services, LLC)

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A 2-Day Virtual Public Meeting
October 18, 2023
Mitigating Clinical Study Disruptions during Disasters and Public Health Emergencies

Session III: Drugs, Biologics, and Device Sponsors’, and Investigators’ Perspectives

Lisa Bennett PhD, Principal Quality Lead, Product Development Quality, Roche
Roche committed to continuing clinical studies during COVID-19

- Primary objective was to minimise patient exposure to the SARS-CoV-2 virus whilst enabling them to continue or initiate participation in a study.

- Second objective was to maintain the study integrity.

- Roche guidance took into consideration the regulatory flexibilities afforded by health authorities.

- It focused on risk assessment and mitigations for critical safety and efficacy processes, and was re-purposed for subsequent major disruptions.

- Expert clinical study teams assessed potential solutions that could be deployed to support our clinical study participants.

- Roche shared its experience with various industry representative bodies and non-profit organisations from the outset
  - BIO, EFPIA, TransCelerate, PhRMA, Lungevity

- We provided real-time feedback to regulators on both the challenges and successes associated with the practical implementation of the permitted flexibilities.
COVID-19 disruption accelerated the use of decentralized solutions

- **Telemedicine**
  - Telemedicine (where allowed) was used to mitigate the impact of missing visits.
  - Telemedicine only allowed for taking AEs/specific endpoint measures and discuss safety memo or ICF updates.

- **IMP shipments to Patients**
  - Oral IMPs shipped from site to patients' home for self-administration. In limited cases, IMP shipment to a local site for administration.

- **Mobile Nursing**
  - Mobile nursing used for lab draws, non-IMP study assessments and AE assessments.

- **Home infusion of IMPs**
  - Experience with products with sub-cutaneous formulations.

- **Remote laboratories**
  - Local labs implemented for patients living far from sites.

- **Digital health tools**
  - Beyond telemedicine, the application of digital health tools was limited. Remote collection for efficacy / safety measures was mostly done via video calls or home nursing. The pandemic has increased visibility of Digital Health Tools and more teams are considering implementation in the future.

Looking to the future, aligned global guidelines on novel operational solutions are needed for international clinical trials.

- During COVID, study teams had to manage protocol amendments to accommodate national requirements at a country level.

Roche is working to widen clinical trial access and inclusivity, reduce burden and focus on participant well-being through use of decentralised solutions within a proposed regulatory framework.
Proposed regulatory framework for fit-for-purpose approaches in clinical studies

Context - Evidence - Feasibility

Clinical Context
What are the major needs faced by stakeholders e.g. patients, caregivers, healthcare providers, and sponsors in a specific disease setting?

Evidence to support its use
**Technical validation**
What are the available data supporting the reliability of the tool?
What are the gaps and required data?

**Clinical validation**
What are the available data to show that it can be used safely and effectively in patients?

**Data relevance and integrity**
Will the generated data be acceptable for the intended use?
Can the data be reliably and consistently collected and lead to robust conclusions?

Feasibility
**Regulatory and compliance**
To what extent will the measures adhere to (global) regulatory guidances and internal Standard Operating Procedures?

**Data privacy**
Will the approach in any way compromise patient privacy?

**Operational**
What is the availability/access of vendors, devices etc?

Future Priorities

- Global collaboration across stakeholders to increase the development of harmonised guidelines related to innovative approaches.
- Addressing operational execution challenges and introducing sustainability through optimal trial design. Trial protocols and operational plans need to be simplified and allow for flexibility in implementing decentralised solutions.
- More emphasis on patient inclusivity and evaluating effective solutions through a regulatory framework.
- Understanding the global impact of COVID-19 and other disruptions on clinical development from a health authority perspective.
Doing now what patients need next
Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies
Enrollment and Engaged Site Trends

Better mitigation and recovery seen in US vs ROW within portfolio of Medtronic Clinical Research

### Pre-Covid

<table>
<thead>
<tr>
<th>Region</th>
<th>Enrollments</th>
<th>Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Americas</td>
<td>8000</td>
<td>2200</td>
</tr>
<tr>
<td>EMEA</td>
<td>3500</td>
<td>900</td>
</tr>
<tr>
<td>China</td>
<td>600</td>
<td>140</td>
</tr>
<tr>
<td>APAC</td>
<td>2400</td>
<td>550</td>
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</tbody>
</table>

### During Covid

<table>
<thead>
<tr>
<th>Region</th>
<th>Enrollments</th>
<th>Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Americas</td>
<td>7200 (-10%)</td>
<td>2100 (-5%)</td>
</tr>
<tr>
<td>EMEA</td>
<td>2900 (-20%)</td>
<td>700 (-24%)</td>
</tr>
<tr>
<td>China</td>
<td>350 (-40%)</td>
<td>110 (-23%)</td>
</tr>
<tr>
<td>APAC</td>
<td>1800 (-25%)</td>
<td>450 (-20%)</td>
</tr>
</tbody>
</table>

### Post Covid

<table>
<thead>
<tr>
<th>Region</th>
<th>Enrollments</th>
<th>Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Americas</td>
<td>7950 (~)</td>
<td>2000 (-10%)</td>
</tr>
<tr>
<td>EMEA</td>
<td>2900 (-20%)</td>
<td>600 (-33%)</td>
</tr>
<tr>
<td>China</td>
<td>400 (-33%)</td>
<td>95 (-33%)</td>
</tr>
<tr>
<td>APAC</td>
<td>1300 (-50%)</td>
<td>415 (-25%)</td>
</tr>
</tbody>
</table>

Elective Vs Non-Elective procedures had impact on subject enrollments, follow-up, and overall execution of research

Use of technology for proctoring and hands-on procedure training (e.g. Vuzix Smart Glasses) allowed for continuation of research in many cases

Use of remote patient follow-up (patient visits) in lieu of in-person office visits where possible- pilot efforts pre-COVID enabled fast deployment

Prioritization of visits (Visits outside of visit window or even incomplete visits preferred to missed visits)

Overall FDA flexibility and strong guidance in the areas of DCT, Remote Site Monitoring, Remote Patient visits were critical in mitigating and enabling recovery in US research vs Rest of the world
### Key Experiences, Benefits and Challenges - Summary

**Study Characteristics**
- STUDY CONDUCT CONSIDERATIONS (RISK-ASSESSMENT AND MITIGATIONS DOCUMENTED AT STUDY/SITE)
- STATISTICAL ANALYSIS PLAN REVIEW AND UPDATE PER COVID IMPACT
- ENHANCED FOCUS ON AE TRENDING
- SUMMARIZE COVID IMPACT ON STUDY (DEVIATIONS, VISIT COMPLIANCE, TYPE OF VISITS, ATTRICTION, AEs)
- EVALUATE EFFECT ON STUDY OUTCOMES
- ENHANCED FOCUS ON MISSING DATA (FOCUS ON PRIMARY ENDPOINTS, OUT-OF-WINDOW VISITS)
- TRIAL DESIGN ALLOWING REMOTE PARTICIPATION WAS AN ADDITIONAL ENABLER
- STUDIES WITH RIGID, HIGHLY STRUCTURED, AND DEMANDING SCHEDULES WERE MORE IMPACTED

**FDA and other guidance enablers**
- Expansion of remote monitoring and remote visits through clarity of FDA guidance.
- Documented and summarized study deviations specifically related to COVID (i.e. missed visits or missed study procedures)
- Guidance provided from the Global Principal Investigator and the physicians on the Study Steering Committee was key enabler also.

**Remote Monitoring & Patient Follow-up**

- **Guidance**
  - Clear guidance on methods, acceptable vs not-acceptable, and constant engagement with sponsor from FDA was highly positive

- **Technology**
  - Flexibility in use of technology based on site and product needs (Zoom, Teams, Telephone, Product specific technologies)

- **Site**
  - Study design, selection of sites, and contractual modifications along with effective ethics committee engagements

- **Continuous Improvement**
  - Investment in regular lessons learned, continual improvement of processes, engagement practices, and training- “perfect is enemy of good” approach

- **Outcomes**
  - Ability to continue all critical research without pause/stoppage; Over 90% of US monitoring activities switched to remote during pandemic, successful audits

- **Sustainability**
  - Sustaining at 40-50% remote activities post-COVID, continuing to leverage better technologies, selection of site practices, and study designs

**Unexpected Challenges**
- Site personnel furloughs and turnover impacted study compliance (data entry, query and action resolution)
- Wet signature requirements for site coordinators and PIs in some cases could not be overcome
- Site technology and contractual limitations in some cases prevented effective remote engagements
- Outside of US, regulatory guidance related to remote practices were slow to evolve and in many cases limiting
- Remote proctoring and training was effective only for some devices/implants

**Unexpected Benefits**
- Remote consent and remote patient visits enabled a more diverse population to participate
- Better follow-up compliance when follow-up could be executed by phone vs in-person
- Superior trial designs that allow more remote visits, leveraging technology to support procedures and visits
- Better selection and utilization of sites
KEY FOCUS AREAS FOR FUTURE EMERGENCIES

- Use of Artificial Intelligence for mitigating disruptions
- Further lessons learned on outcomes impact due to COVID
- Evolution to Patient reported evidence – impact assessment and mitigation from emergencies in this area
Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies

Ken Getz
Tufts Center for the Study of Drug Development
Tufts University School of Medicine

October 2023
‘Many Things Done Right’

- **Trusted collaborations**
- **Public-private partnerships**
- **Shared data and development risk**
- **Community and clinical care engagement**
- **Rapid deployment of virtual and remote technology**
- **Proactive, accommodating oversight**
- **Parallel clinical phase activity**

**COVID-19 Vaccine Development**

Source: Tufts CSDD
# Unplanned Disruptions: A Common Occurrence

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td></td>
<td>Percentage of protocols with at least 1 substantial amendment</td>
<td>Mean number of substantial amendments</td>
</tr>
<tr>
<td>Phase I</td>
<td>52%</td>
<td>1.8</td>
</tr>
<tr>
<td>Phase II</td>
<td>77%</td>
<td>2.2</td>
</tr>
<tr>
<td>Phase III</td>
<td>66%</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Source: Tufts CSDD 2015 and 2022 Studies
Quantifying COVID-19 Disruptions

<table>
<thead>
<tr>
<th></th>
<th>Pre-Pandemic Protocols (DBL no later than February 2020)</th>
<th>Pandemic Protocols (FPFV after March 2020)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen Failure Rate</td>
<td>34.8%</td>
<td>31.3%</td>
</tr>
<tr>
<td>Completion Rate</td>
<td>71.5%</td>
<td>65.0%</td>
</tr>
<tr>
<td>Drop-Out Rate (due to patient choice)</td>
<td>18.8%</td>
<td>29.6%</td>
</tr>
<tr>
<td>Proportion of Patients with at least one Protocol Deviation</td>
<td>32.8%</td>
<td>84.7%</td>
</tr>
<tr>
<td>Mean number of Amendments</td>
<td>3.1</td>
<td>3.5</td>
</tr>
<tr>
<td>‘Actual’ Study Timelines (as a percentage of ‘Plan’)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Approval to DBL</td>
<td>+13.9%</td>
<td>+51.7%</td>
</tr>
<tr>
<td>LPLV-DBL</td>
<td>+49.1%</td>
<td>+69.4%</td>
</tr>
</tbody>
</table>

Source: Tufts CSDD 2022; n = 383 phase II/III pre-pandemic protocols and n=323 phase II/III pandemic protocols – multiple TAs
Long-Term Impact on Investigative Sites

Clinical Trial Continuations
(As of October ‘20)

- Extended delays: 22%
- Minimal disruption to original protocol: 41%
- Temporary delays; able to pivot to remote and virtual support: 37%

Site Landscape Consolidation

<table>
<thead>
<tr>
<th></th>
<th>2011</th>
<th>2022</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Annual Volume</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Filing</td>
<td>68%</td>
<td>43%</td>
</tr>
<tr>
<td>2-5 Filings</td>
<td>23%</td>
<td>37%</td>
</tr>
<tr>
<td>6+ Filings</td>
<td>9%</td>
<td>20%</td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMC/Hospitals</td>
<td>40%</td>
<td>43%</td>
</tr>
<tr>
<td>P-T Community</td>
<td>52%</td>
<td>45%</td>
</tr>
<tr>
<td>Dedicated</td>
<td>8%</td>
<td>12%</td>
</tr>
</tbody>
</table>

Source: Tufts CSDD
Remote and Virtual Solutions Adoption 2/20 – 6/22

Percent of Companies Report Deploying

### Source: Tufts CSDD; N=54 individual companies
Key Lessons and Insights

• Appoint ‘Clinical Trial’ Coach at Outset
  – High level of second guessing; inconsistent accountability and coordination

• Establish Harmonized Cross-Country Disruption Guideline(s)
  – Wide variation/inconsistent regulatory and ethical oversight between countries

• Assess, Anticipate and Shore-Up Weak Areas
  – Unanticipated ‘hardship’ in select areas of value chain

• Risk-based Approach to future Disruption Planning and Execution
  – High, and increasingly customized and fragmented clinical trial operating activity
Q&A and Thank You!

Ken Getz
Tufts Center for the Study of Drug Development
Tufts University School of Medicine

617-636-3487 Kenneth.getz@tufts.edu
Closing remarks

**Sally Okun**, Executive Director,
Clinical Trials Transformation Initiative (CTTI)

Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies:
A 2-Day Virtual Public Meeting
October 18, 2023
Opening remarks

Celia Witten, Deputy Center Director,
Center for Biologics Evaluation and Research, FDA

Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies:
A 2-Day Virtual Public Meeting
October 19, 2023
Session IV: Federal Partners’ Perspectives

Moderator: Bray Patrick-Lake, Center for Devices and Radiological Health, FDA

**John Beigel**, Associate Director for Clinical Research, Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health (NIH)

**Margaret (Meg) Mooney**, Associate Director, Chief, Clinical Investigations Branch (CIB), Cancer Therapy Evaluation Program (CTEP), Division of Cancer Treatment and Diagnosis (DCTD), National Cancer Institute (NCI)

**Salina Waddy**, Associate Director, CTSA Program Clinical Affairs, Chief, CTSA Program Clinical Affairs Branch, Division of Clinical Innovation, Clinical Affairs Branch, National Center for Advancing Translational Sciences (NCATS), National Institutes of Health (NIH)

Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies:
A 2-Day Virtual Public Meeting
October 19, 2023
Conducting COVID-19 Trials during COVID-19
Lessons from ACTT and Moderna phase 1 trial

John Beigel, M.D.
Division of Microbiology and Infectious Diseases
National Institute of Allergy and Infectious Diseases
Trials Implemented Early in COVID-19

Moderna Phase 1
- Vaccine development initiated after the SARS-CoV-2 genome was posted (Jan 10, 2020)
- Manufacture and delivery of clinical trials material was completed in 45 days
- First trial participants were vaccinated on March 16, 2020
  - 66 days after the genomic sequence of the virus was posted.

ACTT
- ACTT-1 (Remdesivir (RDV) vs placebo)
  - Started 22 days after protocol development began
  - 1062 inpatient participants at 66 sites in 10 countries in 59 days
  - Led to first treatment for Covid, and EUA/approval in 50+ countries

- ACTT-2 (Baricitinib/RDV vs RDV alone)
  - 1033 participants at 67 sites in 8 countries in 54 days
  - Led to second approved therapeutic for COVID, and EUA / approvals in 11 countries
Why it worked

• We were early.
  • Started planning both trials before there were any US cases
  • First site enrolled in ACTT when there were under 30 cases in the US

Globally, as of 7:50pm CEST, 4 October 2023, there have been 771,151,224 confirmed cases of COVID-19, including 6,960,783 deaths, reported to WHO. As of 27 September 2023, a total of 13,513,017,637 vaccine doses have been administered.
Why it worked

• For Moderna, we used existing sites (IDCRC) that we knew could implement a trial quickly

• For ACTT, we had many more sites
  • 93 sites participated in one or more stages
  • Used networks known to NIAID
  • International sites already had capacity and funding
    • Collaborators navigated in country reviews
  • Engaged many new sites
    • Went to the locations with disease

• We had highly motivated investigators
  • Could navigate and facilitate institutional approvals
Why it worked

• ACTT was designed as a platform trial
  • One protocol with common elements
  • Each stage was an appendix
    • Submitted to the same IND
    • Reviewed as amendment with the IRB
  • Didn’t need new site contracts

• Protocol balanced data /specimens and ease of implementation
Why it worked

• Moderna, Gilead (remdesivir) and Lily (baricitinib) were great partners.
  • Experienced and committed.
  • Agreements executed rapidly.
Challenges encountered / mitigation strategies

• Staff were getting sick/could not come to work
  • Vaccine trial started with 1 site
    • expanded number of sites, including the NIH Clinical Center
  • Mitigation: anticipate disruptions, and understand which centers can continue through disruptions

• Transportation disruptions /challenges in getting IP and supplies to sites.
  • Air transportation was getting delayed
    • Ended up having vaccine driven from Maryland to Atlanta
  • Mitigation: shipping/logistics team needs to anticipate shipping disruptions and re-route supplies.
Challenges encountered / mitigation strategies

• Hospitals shutting down to outside visitors
  • Monitors could not get on site for source data verification
    • Increased use of remote monitoring
  • Mitigation: Use of remote monitoring routinely, and increase as needed

• Extreme shortages of PPE
  • For ACTT – anticipated challenges seeing participants daily
  • Mitigation: design protocol to get most data from clinical records (vs data acquired just for the study.)
Challenges encountered / mitigation strategies

- Isolation - Nothing allowed to come out of the room.
  - For treatment trials, at some sites, the consent forms were considered potentially infectious and could not leave the room
    - Sites worked with IRB to get approval for alternative consent processes including consent form storage and dissemination to participant/family
  - Mitigation: with IRB, develop alternative consent and documentation processes

- Shortages of swabs/transport media.
  - Protocol was amended for flexibility in sample collection
  - Mitigation: increase storage of supplies, have alternative ways to get supplies (e.g. make transport media at a site)
Challenges encountered / mitigation strategies

• Shortages of testing supplies / delays in results
  • Protocol was amended for flexibility in inclusion criteria
  • Mitigation: anticipate shortages, and build flexibilities into protocol
Conclusions

• COVID-19 introduced many challenges that we never previously encountered

• We have changed processes to be able to meet similar challenges in the future
  • It is important to share the challenges encountered to best anticipate what we may encounter in future public health emergencies
Session IV: Perspectives of Federal Partners who Conducted or Funded Clinical Studies during COVID-19

Effect on Conduct of Cancer Treatment Trials in the NCI National Clinical Trials Network (NCTN)

Mitigating Clinical Study Disruptions during Disasters & Public Health Emergencies
October 19, 2023
Meg Mooney, MD
Associate Director, CTEP, DCTD
National Cancer Institute, NIH
NCI National Clinical Trials Network Infrastructure

LEGEND:
- **Centralized Functions:**
  - NCI Central Institutional Review Board (IRB)
  - 24/7 Cancer Trials Support Unit for Administrative & Regulatory Functions
  - Radiotherapy / Imaging Core Center
  - NCI Disease Steering Review Committees
  - Electronic Common Data Mgt System w/ Central Hosting for Data Collection

- **Lead Academic Participating Sites**
- **Operations Centers**
- **Statistics & Data Management**
- **Biospecimen Banks**

5 US Group Operation Centers with Statistics & Data Management Centers & Canadian Collaborating Network Group Conducting Clinical Trials in Network Structure

Large early-phase & late-phase trials

≈ 2,200 enrolling sites across North America plus international sites
Enrolling 17,000 to 20,000 patients annually to cancer treatment trials
Operational Impediments to Clinical Cancer Research

• Decreased efficiency of physical distancing, limited patient contact, and necessary use of PPE
• Operational limitations to both outpatient clinic & inpatient resources
• Reprogramming of research staff to COVID-19-related duties
• Reduced clinical laboratory throughput
• Decreased availability of imaging and Interventional Radiology services
• Practical impediments to specimen handling
• Travel restrictions
• Decreased investigational pharmacy staffing
• Suspension of translational research laboratory activities
• Decreased Institutional Review Board (IRB) throughput
Effect of the COVID-19 Pandemic on Trial Accrual
NCTN Quarterly Intervention Accrual to Treatment Trials 2019-2022

March 2020: Onset COVID-19 pandemic in US
- Local Assessment / Tx – Telemedicine
- Appropriate study modifications
- Remote consent & auditing
- Oral agents shipped directly to patients from sites
NCI CTEP Guidances during COVID-19 Pandemic

- Initial Interim Guidance on 3/13/2020
  - Transfer of Patient’s Care to a Different Participating Study Site
  - Continuity of Care Provided by Non-Research Staff (SOC therapy, labs, imaging, physical exams, vitals, performance status, standard assessments, blood collections)
  - Mailing of CTEP IND Oral Agents from Site Dispensing Pharmacy Directly to Patients

  - Alternative Procedures Ongoing Trials - Minor Protocol Deviations (“Virtual” visits, reasonable delays in treatments/imaging/lab tests, blood collections stored locally)
  - Alternative Procedures for Ongoing Trials – Major Protocol Deviations
  - Alternative Procedures for Auditing/Monitoring of Trials (modest audit delays; remote)
  - Alternative Procedures for Informed Consent for Trials (telephone remote IC)
  - Increased flexibility in mailing CTEP IND Oral Agents (risk/benefit for shipping)
NCI CTEP Guidances during COVID-19 Pandemic

- Other Considerations
  - Clinical services, testing, and screening related to COVID-19
    - Considered usual care for patients outside research environment – No required IRB approval
    - If patient develops COVID-19 illness on study, complications related to infection reported thru trials existing AE reporting system
  - Developed harmonized way to report/collect AEs related to COVID-19 infection
  - All NCTN Groups developed methods to collect minor protocol deviations for reporting internally and to the NCI CIRB at time of continuing review; major protocol deviations still require expedited reporting per usual method
  - Some NCTN Groups developed recommendations for trial-specific minor protocol deviations, while others depended on the general guidances alone per the definition of minor protocol deviation
Throughout the pandemic, has your site ALWAYS been able to do this activity?

<table>
<thead>
<tr>
<th>Operational Clinical Trial Activity</th>
<th>% Sites that had to Stop or Pause the Activity for Cancer Treatment Trials by Trial Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Phase 1 Trials</td>
</tr>
<tr>
<td>Enroll new Patients</td>
<td>41%</td>
</tr>
<tr>
<td>Process Protocol Amendments</td>
<td>16%</td>
</tr>
<tr>
<td>Open New Trials</td>
<td>46%</td>
</tr>
<tr>
<td>Process Biospecimens</td>
<td>45%</td>
</tr>
<tr>
<td>Collect Optional Biospecimens</td>
<td>59%</td>
</tr>
</tbody>
</table>
During the COVID-19 pandemic, has your site used the following modified clinical trials processes for NCTN trials?

<table>
<thead>
<tr>
<th>Process</th>
<th>Yes</th>
<th>No</th>
<th>Average Usefulness Rating from 1 (not at all useful) to 5 (very useful)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worked with <strong>local healthcare providers</strong> to provide continuity of care for patients on NCTN trials</td>
<td>52</td>
<td>31</td>
<td>3.9 (n=63)</td>
</tr>
<tr>
<td>Used <strong>virtual study visits</strong> (telehealth / telephone)</td>
<td>85</td>
<td>5</td>
<td>4.6 (n=88)</td>
</tr>
<tr>
<td><strong>Shipped oral IND agents</strong> directly to patients enrolled</td>
<td>53</td>
<td>26</td>
<td>4.5 (n=63)</td>
</tr>
<tr>
<td>Used <strong>remote informed</strong> consent to enroll patients</td>
<td>51</td>
<td>35</td>
<td>4.2 (n=64)</td>
</tr>
<tr>
<td>Underwent a <strong>remote audit</strong> by an NCTN group</td>
<td>20</td>
<td>66</td>
<td>3.6 (n=29)</td>
</tr>
</tbody>
</table>
Many Modifications Introduced During COVID-19 Pandemic Now Integrated as Standard Practices for NCTN Trials

NCTN Quarterly Intervention Accrual to Treatment Trials from 2019-2022

- Local Assessment / Treatment by Telemedicine and Local Physicians
- Appropriate study modifications
- Remote consent & auditing
- CTEP IND Oral agents shipped directly to patients from sites

March 2020: Onset COVID-19 pandemic in US

Quarter 1
Jan-Mar

Quarter 2
Apr-Jun

Quarter 3
Jul-Sep

Quarter 4
Oct-Dec
Trial Innovation Network: During the COVID-19 Pandemic

Salina P. Waddy, MD, FAHA
Associate Director, CTSA Program Clinical Affairs and
Director, Trial Innovation Network

https://trialinnovationnetwork.org/
Goals of the TIN

• The Trial Innovation Network is a collaborative national network that focuses on operational innovation, operational excellence and collaboration and will leverage the expertise and resources of the CTSA Program.

• The Trial Innovation Network features a single IRB system, master contracting agreements, quality by design approaches, and a focus on evidence-based strategies to recruitment and patient engagement.

• The goal of the Trial Innovation Network is to not only execute trials better, faster, and more cost-efficiently but, importantly, to be a national laboratory to study, understand and innovate the process of conducting clinical trials.

https://trialinnovationnetwork.org/
Trial Innovation Network Structure

- **NCATS**
  - **CTSA** Clinical & Translational Science Awards Program
  - **TRIAL INNOVATION NETWORK**
    - **CTSA Hubs (60+)**
      - Duke University/Vanderbilt University
      - University of Utah
      - Johns Hopkins/Tufts
      - Vanderbilt University
    - **Innovation Centers**
    - **TICs**
    - **RIC**

https://trialinnovationnetwork.org/
Specific attributes of the CTSA network for emergency response

COVID required the rapid identification of study sites and PIs

**Strengths of the 60+ CTSA Hubs:**

- Over 60 academic health centers with affiliates (93 million patients, 13% African-American, 6% Asian-Americans, 2% American Indian and 13% Hispanic)
- 17% of the CTSA patient pool reside in a rural area
- Large research professional teams with ~750 research nurses employed by CTSA Centers and over 1000 research coordinators
- Able to locally prioritize studies and identify research teams to participate in COVID trials

[https://trialinnovationnetwork.org/](https://trialinnovationnetwork.org/)
Specific attributes of the CTSA network for emergency response (cont’d)

Assets Provided by the TICs and RIC:

• Robust Expression-of-Interest process: TIN can simultaneously ask 60 sites if they would want to be a study site after sharing the protocol and receive responses over a period of days

• Accelerated study start up and trial management (ex, SMART IRB, sIRB and, (REDCap) and contracting resources (Federal FDP-CTSA) and Industry sponsored studies (ACTA)

• Recruitment expertise with the RIC through use of remote approaches include decentralized methods, research registries, EMR patient portals like MyChart, and experience prioritizing inpatient COVID-19 protocols

• Partnering with N3C platform to analyze a large EMR database within a protected data enclave
TIN COVID trial submissions

TIN PROPOSAL SUBMISSIONS

- Q4 2016: 39
- Q1 2017: 7
- Q2 2017: 15
- Q3 2017: 17
- Q4 2017: 23
- Q1 2018: 14
- Q2 2018: 24
- Q3 2018: 17
- Q4 2018: 25
- Q1 2019: 13
- Q2 2019: 15
- Q3 2019: 14
- Q4 2019: 2
- Q1 2020: 13
- Q2 2020: 13
- Q3 2020: 14
- Q4 2020: 20
- Q1 2021: 9
- Q2 2021: 9
- Q3 2021: 16
- Q4 2021: 5
- Q1 2022: 2
- Q2 2022: 3
- Q3 2022: 2
- Q4 2022: 7
- Q1 2023: 8
- Q2 2023: 12
- Q3 2023: 11
- Q4 2023: 10

NON-COVID vs COVID submissions.
## TIN COVID Studies

<table>
<thead>
<tr>
<th>TIN proposal date range</th>
<th># of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 2020</td>
<td>2</td>
</tr>
<tr>
<td>Apr-Jun 2020</td>
<td>20</td>
</tr>
<tr>
<td>Jul-Sep 2020</td>
<td>5</td>
</tr>
<tr>
<td>Oct-Dec 2020</td>
<td>2</td>
</tr>
<tr>
<td>2021</td>
<td>6</td>
</tr>
<tr>
<td>2022</td>
<td>1</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Sample size</th>
<th># of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 100</td>
<td>4</td>
</tr>
<tr>
<td>100 - &lt; 1000</td>
<td>13</td>
</tr>
<tr>
<td>1000 - &lt; 5000</td>
<td>11</td>
</tr>
<tr>
<td>5000 +</td>
<td>8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study type</th>
<th># of studies (multiple possible)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute care</td>
<td>8</td>
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<tr>
<td>Outpatient</td>
<td>12</td>
</tr>
<tr>
<td>Platform/Tech/EHR</td>
<td>5</td>
</tr>
<tr>
<td>Registry</td>
<td>2</td>
</tr>
<tr>
<td>Predictive modeling</td>
<td>2</td>
</tr>
<tr>
<td>Schools</td>
<td>2</td>
</tr>
<tr>
<td>Treatment</td>
<td>18</td>
</tr>
<tr>
<td>Prevention</td>
<td>4</td>
</tr>
<tr>
<td>Observational</td>
<td>4</td>
</tr>
<tr>
<td>Surveillance</td>
<td>3</td>
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<tr>
<td>Prospective</td>
<td>5</td>
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<tr>
<td>Exploratory</td>
<td>1</td>
</tr>
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</table>
Decentralized elements of design for trials conducted during COVID

<table>
<thead>
<tr>
<th></th>
<th>Participant-informed study design</th>
<th>Ethics and Informed Consent</th>
<th>Screening/Enrollment</th>
<th>Recruitment</th>
<th>Confirmation of eligibility</th>
<th>Intervention</th>
<th>Data collection/Endpoints</th>
<th>Monitoring</th>
<th>Retention/Reminders</th>
<th>Return of results/Return of value</th>
</tr>
</thead>
<tbody>
<tr>
<td>REACT-AF</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
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<tr>
<td>CSSC-004</td>
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<td>✔</td>
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<td>✔</td>
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<tr>
<td>BEACH</td>
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<td></td>
<td></td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
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<td>✔</td>
</tr>
<tr>
<td>PREVENTABLE</td>
<td>✔</td>
<td></td>
<td></td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>TREAT Now</td>
<td>✔</td>
<td></td>
<td></td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>ACTIV-6</td>
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<td></td>
<td></td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
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<td>✔</td>
</tr>
<tr>
<td>OIAC19</td>
<td>✔</td>
<td></td>
<td></td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Autism Sleep</td>
<td></td>
<td></td>
<td></td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>CASH</td>
<td></td>
<td></td>
<td></td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>CARE4kids</td>
<td>✔</td>
<td></td>
<td></td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
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<td>✔</td>
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<tr>
<td>Niclosamide</td>
<td></td>
<td></td>
<td></td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>

Decentralized elements of design for trials conducted by Trial Innovation Center (TIC) or Recruitment Innovation (RIC) Center investigators or through TIC or RIC coordinating centers.

Standard Agreements to streamline COVID Study start up

![Bar chart showing the impact of standard agreements on contract execution for COVID-19 studies.](chart.png)

- **Historical Data**: 103 days for 60 US sites
- **ACTIV-1**: 40 days for 44 US sites
- **ACTIV-4HT/NECTAR**: 75 days for 60 US sites
- **PassItOn**: 16 days for 25 US sites

Visit [https://trialinnovationnetwork.org/](https://trialinnovationnetwork.org/) for more information.
eConsent and COVID-19

Contactless Consent
- Review and sign on own devices
- No direct contact with study staff required
- PDF copy displayed after signing
- Signed copy stored in secure file repository
- Audit trails track changes

Multi-Lingual Module:
- Allows Research Teams to more easily integrate different language versions of an instrument in eConsent

<table>
<thead>
<tr>
<th>METRICS</th>
<th>Pre-Pandemic (March 2020)</th>
<th>Post-pandemic (Sept 2023)</th>
</tr>
</thead>
<tbody>
<tr>
<td># of eConsent Projects</td>
<td>3,100</td>
<td>&gt;58,554</td>
</tr>
<tr>
<td>REDCap Consortium-wide</td>
<td></td>
<td></td>
</tr>
<tr>
<td># of eConsent transactions</td>
<td>50,625</td>
<td>&gt;4,719,451</td>
</tr>
<tr>
<td>REDCap Consortium-wide</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

REDCap Consortium-wide

TRIAL INNOVATION NETWORK
https://trialinnovationnetwork.org/

CTSA Clinical & Translational Science Awards Program
## COVID resources in TIN Toolbox

<table>
<thead>
<tr>
<th>Resource</th>
<th>Submitted by</th>
<th>Date Posted to TIN Toolbox</th>
<th>Number of views as of 9/18/23</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Community Engagement Alliance (CEAL) Against COVID-19 Disparities</td>
<td>National Institutes of Health (NIH)</td>
<td>10/6/2020</td>
<td>182</td>
</tr>
<tr>
<td>N3C Domain Teams and Leaders</td>
<td>University of Colorado</td>
<td>11/13/2020</td>
<td>105</td>
</tr>
<tr>
<td>RIC COVID-19 RECRUITMENT + RETENTION TOOLKIT</td>
<td>Recruitment Innovation Center</td>
<td>7/30/2021</td>
<td>381</td>
</tr>
</tbody>
</table>
Community Feedback to Develop the Covid Toolkit

Purpose: to share the community input we received, and the resources we have developed, that can help study teams conduct trials in a manner that is safe, trustworthy, and respectful of all participants.
# TIN Collaboration Webinars on COVID-19 Topics

<table>
<thead>
<tr>
<th>Webinar Date</th>
<th>TIN Collaboration Webinar Title</th>
<th>Institution(s)</th>
<th>Topic</th>
<th>Attendee Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/31/20</td>
<td>REDCap, eConsent, and Part-11 Validation</td>
<td>VUMC</td>
<td>New technical methods enabling institutions to connect REDCap to their local EHR system for automated project-level data exchange, leveraging HL7/FHIR-based technology in multisite studies</td>
<td>400</td>
</tr>
<tr>
<td>8/3/20</td>
<td>No Participants, No Trial (Don't Plan for Everything, but Recruitment)</td>
<td>University of Washington</td>
<td>Practical guidance to develop effective recruitment plans, track and measure success, and create eye-catching recruitment materials</td>
<td>82</td>
</tr>
<tr>
<td>9/16/20</td>
<td>Social Media and Participant Recruitment: What we’ve learned so far</td>
<td>University of Florida</td>
<td>Stakeholder-informed process as a case study to demonstrate establishment of social media guidelines and evaluation of Facebook effectiveness to recruit research participants</td>
<td>156</td>
</tr>
<tr>
<td>1/20/21</td>
<td>Patient Engagement in the time of COVID-19: Virtual Community Engagement Studios</td>
<td>VUMC</td>
<td>Obtaining patient-center feedback from underrepresented groups to enhance research projects even during COVID. How to transition to Zoom technology for community engagement, address issues of tech-equity and literacy, and effectively facilitate group dialogue in a virtual forum</td>
<td>49</td>
</tr>
<tr>
<td>2/1/21</td>
<td>Using National COVID Cohort Collaborative (N3C) Data to Inform your Protocol Development</td>
<td>National COVID Cohort Collaborative, OHSU</td>
<td>Researchers planning COVID-19 trials with the Trial Innovation Network (TIN) can leverage the N3C to inform their research hypotheses. N3C aligns its infrastructure for the curation of value sets and phenotype variables relevant to COVID-19, such as ventilator support, ICU use, and definitions of COVID-19 cases</td>
<td>32</td>
</tr>
<tr>
<td>4/21/21</td>
<td>The Innovative Climate of Study Teams and Their Adoption of Innovative Study Designs within Clinical Trials</td>
<td>Drexel University</td>
<td>The challenges that COVID adds to the landscape of clinical trials also brings potential for new pathways of clinical trial design and innovation</td>
<td>27</td>
</tr>
<tr>
<td>7/21/21</td>
<td>Recruitment Innovation Center COVID-19 Recruitment and Retention Toolkit</td>
<td>VUMC</td>
<td>The RIC COVID-19 Recruitment and Retention Toolkit provides practical information on integrating community feedback into the operations of recruitment and retention planning for COVID-19 research</td>
<td>40</td>
</tr>
<tr>
<td>10/4/21</td>
<td>Using REDCap to Improve Recruitment and Data Collection for Clinical Research</td>
<td>VUMC</td>
<td>Impactful uses of REDCap Clinical Data Interoperability Services for clinical research, including COVID-19 trial recruitment and multi-site critical care studies</td>
<td>116</td>
</tr>
</tbody>
</table>

[https://trialinnovationnetwork.org/](https://trialinnovationnetwork.org/)
New Faster Together Course – Visitors Before and After COVID-19
Faster Together, Enhancing the Recruitment of Minorities in Clinical Trials

Platform dedicated to improving the representation of racial and ethnic minorities in medical research.

Note:
4/1/2019 – Faster Together Coursera course launches
5/5/2023 – WHO declares end to COVID-19 emergency
Data is from 4/2019 until 8/2023.

https://trialinnovationnetwork.org/
TIN Use Cases – COVID-19 Trials
• Early COVID-19 outpatient treatment with high titer convalescent plasma
• TIN Expression of Interest survey of 65 CTSA sites
• TIN Led - Rapid Consortium organization, FDA IND, DoD (and other) funding, with sIRB approval
• Rapid 1-month study planning and 14-day site activation program
• Innovative, diverse recruitment: Local registries and national media marketing (The Bliss Group)
• 16 months FPFV to data analysis; 1 month to publication & change FDA indication for use (IFU)

https://trialinnovationnetwork.org/
TIN-CTSA Emergency Response Results

- FDA issues emergency allowance Dec 27, 2021
  - for high titer plasma use in immuno-suppressed individuals (one week after public release of early CCP effective outpatient treatment results)
  - continued collections remain in use with response adaptability to each virus mutation
- Direct-to-Participant RETURN OF RESULTS webinar May 2022
- 37 accepted publications
- >12 new international CCP Guidelines
- Biologic License Application for early CCP under review by American Association of Blood Banks & FDA
- Generalizable emergency process for future pandemics

TRIAL RESULTS
2023 Research Forum Top 10 Award

All Participants

- Convalescent Plasma <=5 days
- Control Plasma <=5 days
- Convalescent Plasma >5 days
- Control Plasma >5 days

Percent Participants Hospitalized

- 2.9% (17/592) Convalescent Plasma <=5 days
- 1.9% (5/258) Control Plasma <=5 days
- 3.5% (12/334) Convalescent Plasma >5 days
- 3.6% (12/330) Control Plasma >5 days

Hospital relative rate reduction

- 80% (95% CI=0.49-0.93) for Convalescent Plasma
- 54% (95% CI=0.2-0.74) for Control Plasma

Percent Participants Hospitalized

- 6.3% (37/589) for Convalescent Plasma and Control Plasma

TRIAL INNOVATION NETWORK
https://trialinnovationnetwork.org/

COVID-19 PLASMA TRIALS
Sponsored by Johns Hopkins University
## Pandemic Metrics & Network Performance

<table>
<thead>
<tr>
<th>Plan</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design, Approval, Start</td>
<td>Protocol to IND approval 6 weeks</td>
</tr>
<tr>
<td>Used TIN expression of interest (EOI) for 65 CTSA sites</td>
<td>TIN consult to 17 sIRB approved sites - 8 weeks</td>
</tr>
<tr>
<td>Commercial outreach to stakeholders; combined radio, TV, internet, internet media and mailer recruitment approach</td>
<td>Recruitment inclusion Black (14%), Hispanic (14%), Native American (1%), and pregnant women (&lt;1%)</td>
</tr>
<tr>
<td>Trial duration</td>
<td>FPFV to LPLV 15 months</td>
</tr>
<tr>
<td>Trial completion – Integration to Practice</td>
<td>19 months to publication &amp; new indication and use in routine non-pandemic practice</td>
</tr>
</tbody>
</table>
TIN publications

**Trial Innovation Network**
- TIN Summary paper: [https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2810186](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2810186)
- Invited commentary: [https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2810198](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2810198)

**Recruitment Innovation Center**

**Trial Innovation Center**
Session V: Creating Resilience in Clinical Studies Through Advanced Planning for Disruptive Emergencies

Panel Discussion #1 | Emergency Preparedness in Clinical Studies

Panel Discussion #2 | Digital Health Technologies (DHT) and Study Monitoring during Disruptive Emergencies

Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies: A 2-Day Virtual Public Meeting
October 19, 2023
Session V: Creating Resilience in Clinical Studies Through Advanced Planning for Disruptive Emergencies

Panel Discussion #1 | Emergency Preparedness in Clinical Studies
Moderator: Paul Kluetz, Deputy Director, Oncology Center of Excellence (OCE), FDA

John H. Alexander, Professor of Medicine/Cardiology, Duke Clinical Research Institute, Duke University; Co-Chair, Clinical Trials Transformation Initiative (CTTI)

Jeffrey Blank, Adult Patient with Cystic Fibrosis

Marianne Chase, Senior Director of Clinical Trial Operations, Neurological Clinical Research Institute/Healey & AMG Center for ALS at Mass General Hospital

Hassan Kadhim, Director, Head of Clinical Trial Business Capabilities, Global Development Operations, Bristol-Myers Squibb

Nina Movsesyan, Manager, Clinical Research Programs, Metabolic Disorders Division, Children’s Hospital Orange County

Veronica Suarez, Global Product Leader, Vaccines Innovation Unit, CSL
Session V: Creating Resilience in Clinical Studies Through Advanced Planning for Disruptive Emergencies

Panel Discussion #2 | Digital Health Technologies (DHT) and Study Monitoring during Disruptive Emergencies

Moderator: Kassa Ayalew, Center for Drug Evaluation and Research, FDA

Cindy Geoghegan, Patient Advocate, Advisor, and Activist
Catherine Gregor, Chief Clinical Trial Officer, Florence Healthcare
Patrick Naldony, Global Head, Clinical Data Management, Clinical Sciences & Operations, Sanofi
Pamela Tenaerts, Chief Scientific Officer, Medable
Ramya Thota, Investigator, Intermountain Health
Marion Wolfs, Head, Risk Management and Central Monitoring Oncology, Johnson & Johnson Innovative Medicine
Closing remarks

M. Khair ElZarrad, Director, Office of Medical Policy, Center for Drug Evaluation and Research, FDA

Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies: A 2-Day Virtual Public Meeting
October 19, 2023
FDA is committed to advancing and modernizing clinical trial design & conduct

- Let’s not wait for disruptions to innovate
- Responsive guidelines that are informed by the community
- Engagement and communication
- Implementation

Flexibility by design and futureproofing

- Informed consent process
- Risk aversion and other implementation barriers
- Active learning from successes AND failures

Fit for purpose and avoiding the all – or – nothing approach

- “Optionality” of decentralization and other design elements
- Technology not always designed with the heterogeneity of patients in mind, etc.
- Reducing complexity and burden
Patients first
- Diversity of the population that will likely use the intervention if approved
- Transplant community and the COVID vaccine
- Participants with disabilities

Collaboration and engagement
- Effective global harmonization
- Implementation barriers
- Mutual learning
- Communication

A focus on quality and critical areas
- Data quality vs. quantity
- Risk-based approach

Building capacity
- Innovating beyond the pandemic
- Expanding the reach of clinical trials
- Clinical trial “coach”
FDA is Committed to Modernizing Clinical Trials

FDA is already incorporating lessons from the pandemic into guidance and policies relevant to the design and conduct of clinical trials. Our policies:

- Support **proportionality** and **risk-based** approaches
  - Encourage a focus (of efforts and resources) on what matters most (areas of relevance to participants’ safety and results reliability)

- Encourage **fit-for-purpose** approaches

- Focus on the diversity of the **population** that will likely use the intervention, if approved

- Incorporate **learnings** from innovative trials and lessons from public health emergencies/pandemics

- Encourage trial **registration** and **result reporting**

- Encourage **better informed consent process**

- Promote fit-for-purpose **innovations** in design and technologies

- Facilitate the utilization of available **healthcare infrastructure**, processes, and workforce
Enhancing Adoption of Innovative Clinical Trial Approaches

To understand the state of innovation in clinical trial design and conduct, CDER is gathering information from internal and external stakeholders on the barriers and facilitators to incorporating innovative clinical trial approaches in drug development programs.

We are looking for your perspectives via comments to our public docket FDA-2023-N-4489 and/or participation in a public workshop hosted in partnership with the Duke Margolis Center for Health Policy on March 19 and 20, 2024.

We look forward to your Participation!

For more information please contact:

Food & Drug Administration
Kevin Bugin
Deputy Director of Operations
Kevin.Bugin@hhs.fda.gov

Duke Margolis
Luke Durocher
Senior Events & Marketing Manager
margolisevents@duke.edu

Register for March 19-20, 2024 public workshop
Virtual and in-person (DC) options available
But...it will take a village...
Thank you!