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

FDA U.S. FOOD & DRUG ADMINISTRATION

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

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

Background

- 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)

Coronavirus Disease 2019 (COVID-19)

COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders

COVID-19 Vaccines

COVID-19 Bivalent Vaccines

Multilingual COVID-19 Resources

Español

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.

Coronavirus Disease 2019 (COVID-19) | FDA

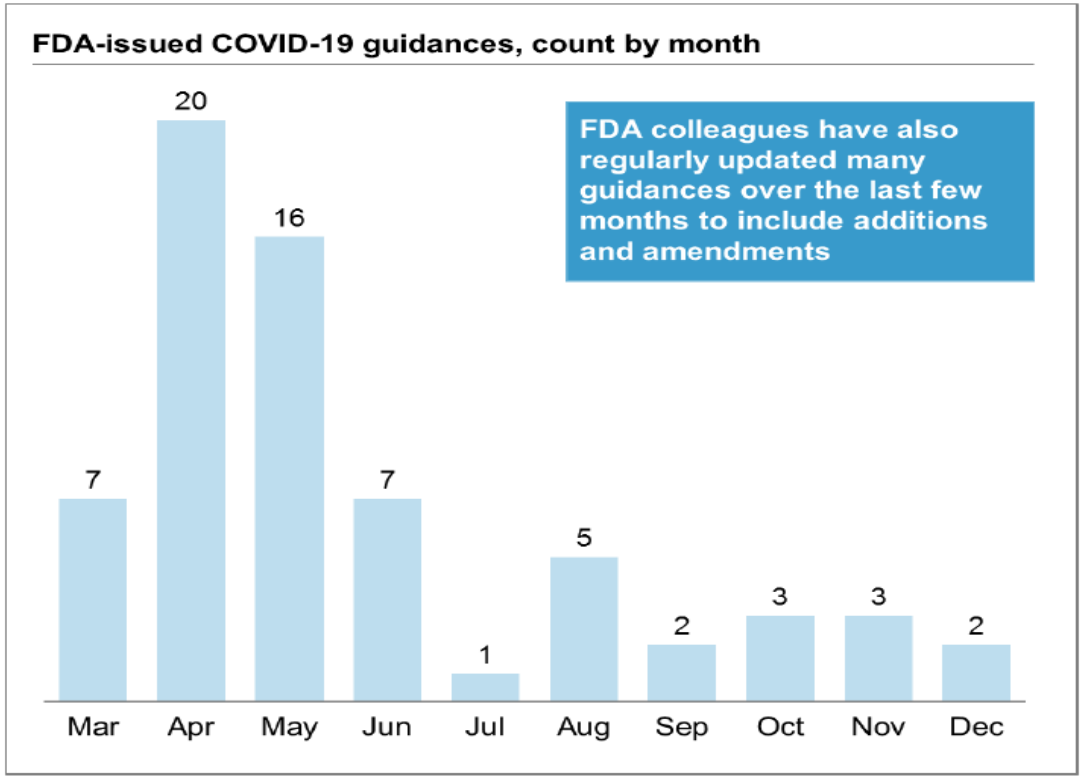
FDA COVID-19 Key Activities During PHE

- 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 COVID-19 Pandemic Recovery and Preparedness Plan (PREPP) Initiative | FDA

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

https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap

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

  - Ad26.COV2.S (Janssen) – EUA granted Feb 27, 2021

- 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)
- Emergency Use Authorization for Vaccines to Prevent COVID-19 Guidance (Originally Oct. 2020, last updated May 2021)

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

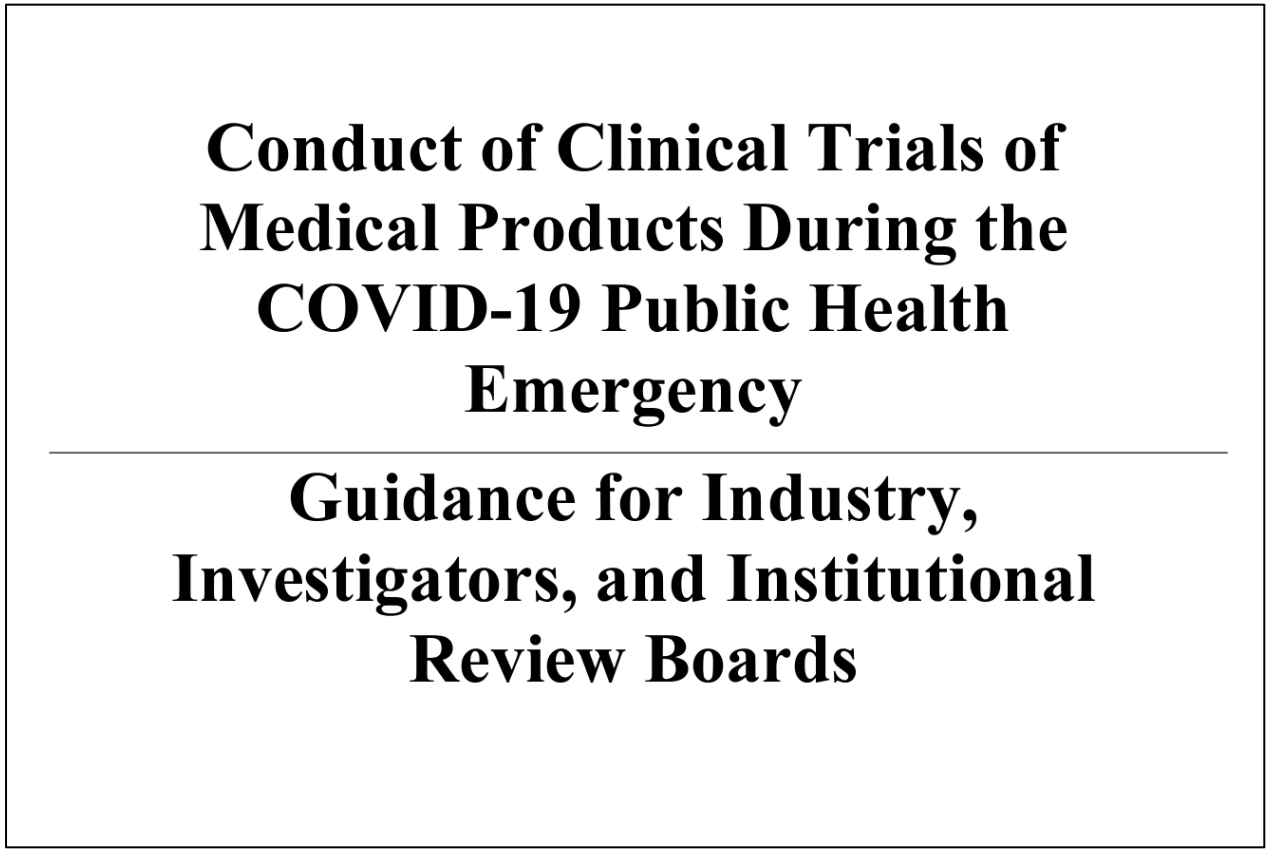
- Guidance documents that will no longer be in effect:
  - *e.g., Statistical Considerations for Clinical Trials During the COVID-19 Public Health Emergency*
- Guidance documents FDA revised to continue in effect after the PHE declaration expired
  - *e.g., Conduct of Clinical Trials of Medical Products 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)

Federal Register :: Guidance Documents Related to Coronavirus Disease 2019 (COVID-19)

FDA Guidance on the Conduct of Clinical Trials During COVID-19



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
  - "*Ensuring the safety of trial participants is paramount*" is first *consideration mentioned in Conduct of Clinical Trials Guidance*
  - 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)

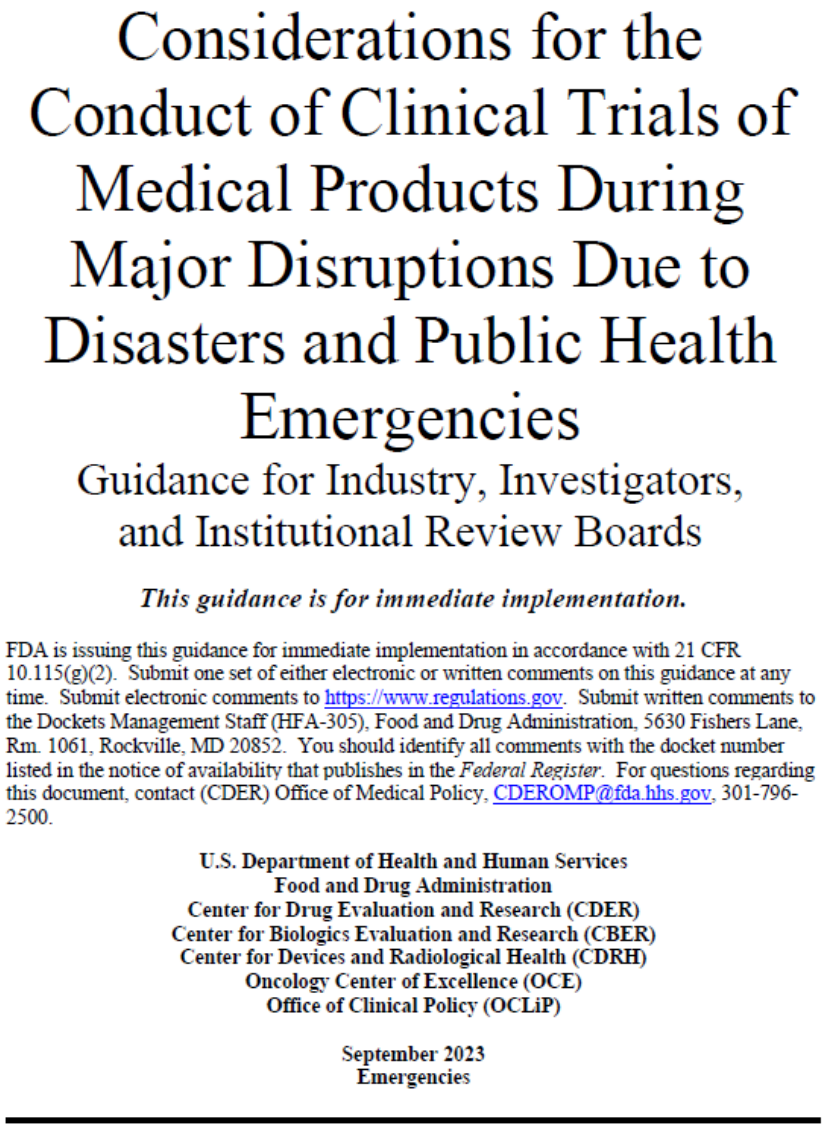
FDA Guidance 'Conduct of Clinical Trials' Mailbox Inquiries: *Sent by Whom?*

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

FDA Guidance 'Conduct of Clinical Trials' Mailbox Inquiries: *What was the Focus?*

'TOP TEN' PRIMARY CATEGORIES OF QUESTIONS (N=414; data as of June 2020)	**N**
Covid-19-related study questions	85
Informing/interacting with FDA	41
Access to/issuance of COVID-19-related regulatory guidelines or resources	29
Investigational product distribution/supply/suspension	28
Informed consent process/content/documentation	26
Electronic signature/record/system compliance	23
Remote data monitoring/wearables & mobile technologies	23
Study/protocol amendment, change, deviation handling	18
Study delay/suspension/premature termination or resumption after pause	17
Study eligibility/screening procedures for Covid-19 and study participation	16

FDA Guidance Revision Post-PHE



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)(2). 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 publishes 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)
Oncology Center of Excellence (OCE)
Office of Clinical Policy (OCLiP)

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


FDA
U.S. FOOD & DRUG
ADMINISTRATION

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

ACRO
Innovate
Advocate
Collaborate

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:
  - Risk-Based Quality Management (RBQM) Working Group
  - Decentralized Clinical Trials (DCT) Working Party
  - Ukraine Clinical Trial Response Team
  - Artificial Intelligence & Machine Learning (AI/ML) Committee
  - *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

ACRO Member Companies

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*

Institutions Impacted

	14 March	21 March	28 March	6 Apr (week)
Global	10 %	34 %	45 %	49 %
US	4 %	28 %	44 %	47 %
China	45 %	45 %	53 %	57 %
So Korea	86 %	82 %	82 %	69 %
Italy	66 %	79 %	80 %	82 %
Spain	38 %	78 %	80 %	80 %

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

Visits Cancelled or Delayed vs. Planned

	January	February	March
Global	7 %	8 %	33 %
US	14 %	11 %	35 % (12 % - 57 %)
China	28 % (7 % - 100 %)	69 % (47 % - 100 %)	49 % (35 % - 71 %)
So Korea	1 %	14 %	34% (29 % -38 %)
Italy	6 %	12 %	49 % (34 % - 57 %)
Spain	10 %	5 %	38 % (8 % - 62 %)

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

Site Inaccessibility & Site Closures

Global
March average: ~35 % sites closed EOM March: ~70 % sites inaccessible
China
Peak crisis: ~80 % sites inaccessible EOM March: ~40 % sites inaccessible ▲

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 %

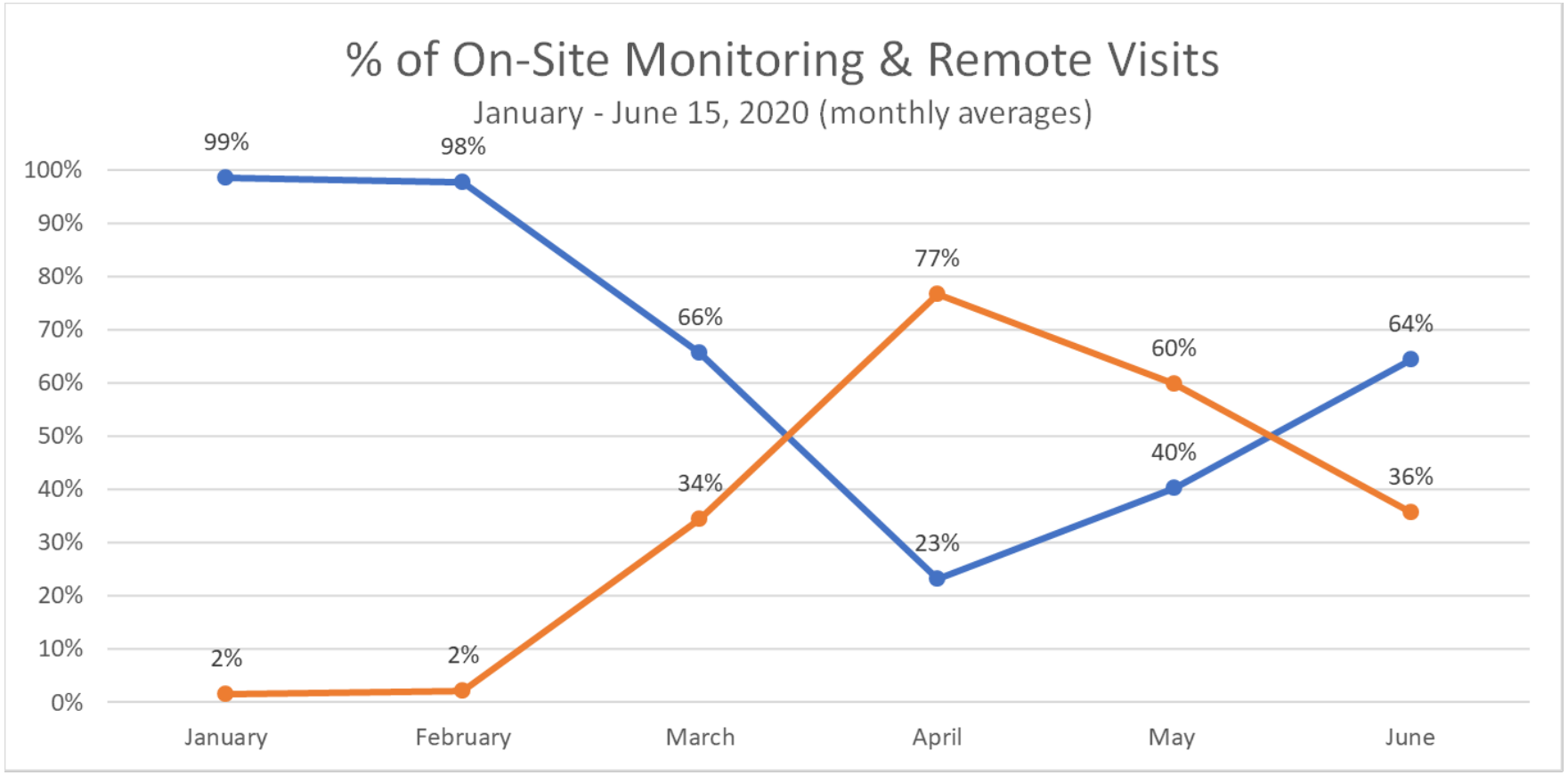
By TA	YoY Difference
Endocrine	-80.5 %
Cardiovascular	-69.7 %
CNS	-68.5 %
Dermatology	-64.0 %
Oncology	-48.4 %
Infectious Disease	-46.8 %
Respiratory	-33.7 %

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.

Progress Seen By June 2020

- 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



March 2020 - Rapid Response

- 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**

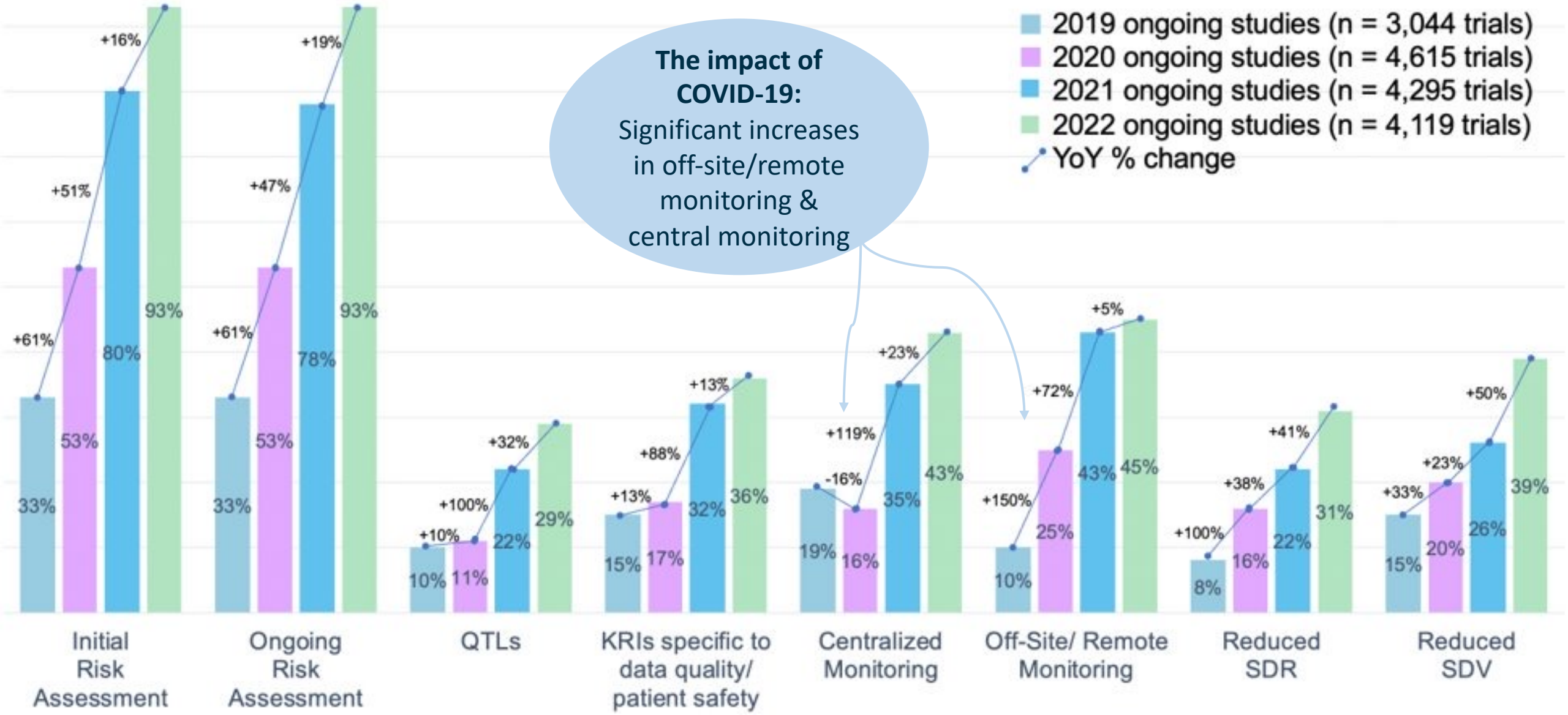
- On March 13, 2020, ACRO made a statement: **Considerations to support clinical trial monitoring and oversight during the pandemic.**
  - Recommendations to be considered when sites had suspended visitors, when local quarantines were implemented, or when CRAs were unable to travel to sites
  - Can be found using the QR code below or on acrohealth.org under the COVID-19 initiative section

RBQM Landscape Survey Project 2019-2022

- 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

Landscape Survey Year	2019	2020	2021	2022
Ongoing studies	6,513	5,987	4,889	4,958
New studies started	Not collected	908	1,270	1,004
New study starts %	Not collected	15%	26%	20%
# of CROs participating	7	6	7	7

RBQM Landscape 2019-2022



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!

ACRO
Innovate
Advocate
Collaborate

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

TransCelerate BIOPHARMA INC.
Accelerating Answers.

In 2012, R&D Leaders formed a non-profit to collaborate to tackle common operational challenges. Combining the words **"Transform"** and **"Accelerate"**, TransCeler ate 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 v alue drivers in clinical research.

TransCelerate BIOPHARMA INC.

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 clin 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

Modernizing Trial Operations

- Data collection
- Database lock
- Restart criteria
- Recording COVID-19 impacts

TransCelerate BIOPHARMA INC.

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

TransCelerate BIOPHARMA INC.

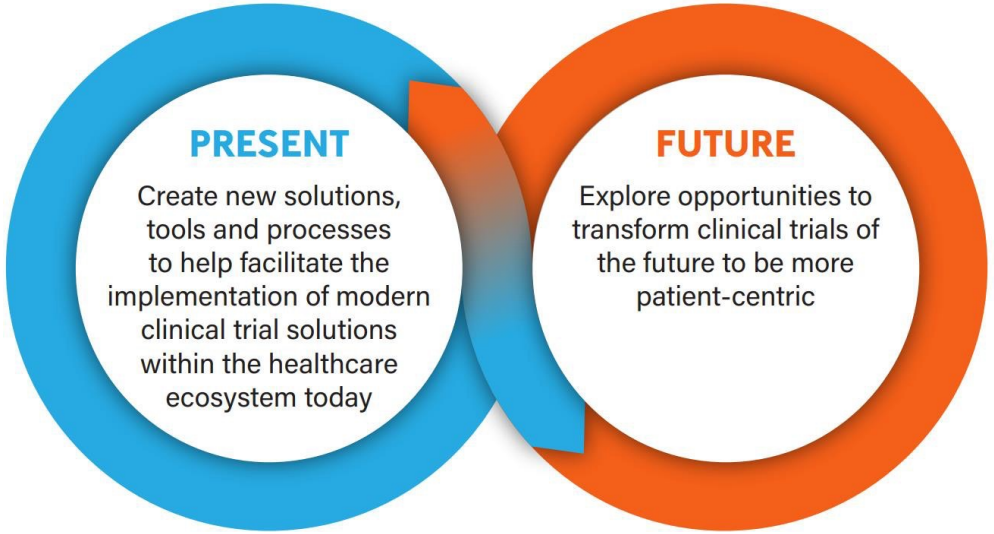
Launch Pad for TransCelerate's Modernizing Clinical Trial Conduct Initiative

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

TransCelerate's 3-Year Roadmap Focusing on Six Key Opportunities

1. Changing How Trials Operate to Bring Clinical Research Closer to the Patient
2. Enabling Use of Pragmatic Trial and Real-World Elements to Improve Patient Experience
3. Enabling Data Exchange, Interoperability and Data Flow between Clinical Research and Clinical Care
4. Data Re-use and Optimization of Data Collection to Improve Trial Design and Reduce Patient and Site Burden
5. Next Generation Pharmacovigilance Capabilities to Enhance Patient Safety
6. Operationalizing Platform Trials for Evidence Generation and Burden Reduction

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

Johnson & Johnson
Office of the Chief Medical Officer

- J&J Bioethics Committee
- Bioethics Colloquium
- Bioethics Education Programs
- Ethics-Based R&D Policies

Sector Specific	Cross Enterprise	Leadership Positions

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

Recent Thought Leadership

Topic: Conducting research during times of disruption

wcg MAGI 2023 Clinical Research Conference
May 21-24, 2023 | Loews Philadelphia Hotel | Philadelphia, PA

DIA 2023 GLOBAL ANNUAL MEETING BOSTON, MA | JUNE 25-29

PRIM&R PUBLIC RESPONSIBILITY IN MEDICINE AND RESEARCH

J&J

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

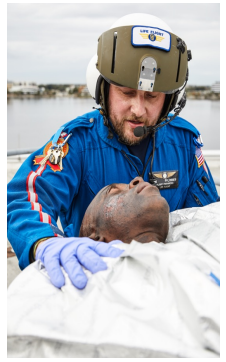
2. Access to investigational medicines and products that may have restrictions

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.

Johnson&Johnson

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)

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

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.

Mobile Nursing

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

Remote laboratories

Local labs implemented for patients living far from sites.

IMP: Investigational Medicinal Product
AE: Adverse Events
ICF: informed consent forms

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.

Home infusion of IMPs

Experience with products with sub-cutaneous formulations.

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?

Context of use

A. Related to the approach
How will the approach be used to address stakeholders needs and improve patient experience

B. Related to study results
How will the study results be used? e.g. to generate proof of concept data or for registration purposes

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?

Fit-for-purpose innovative solutions

Source: *The COVID-19 Pandemic as a Catalyst for Innovation; a Regulatory Framework to Assess Fit-for-Purpose Innovative Approaches in Clinical Research*. L Leyens, T. Simkins and N. Kronidou, Trials 23; 833 (2022)

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

Medtronic

Engineering the extraordinary

Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies

Vinny Parthasarathy

Oct 18, 2023

Enrollment and Engaged Site Trends

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

Pre-Covid

Region	Enrollments	Sites
Americas	8000	2200
EMEA	3500	900
China	600	140
APAC	2400	550

During Covid

Region	Enrollments	Sites
Americas	7200 (-10%)	2100 (-5%)
EMEA	2900 (-20%)	700 (-24%)
China	350 (-40%)	110 (-23%)
APAC	1800 (-25%)	450 (-20%)

Post Covid

Region	Enrollments	Sites
Americas	7950 (~)	2000 (-10%)
EMEA	2900 (-20%)	600 (-33%)
China	400 (-33%)	95 (-33%)
APAC	1300 (-50%)	415 (-25%)

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

Medtronic

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, attrition, 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

Medtronic

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

Medtronic

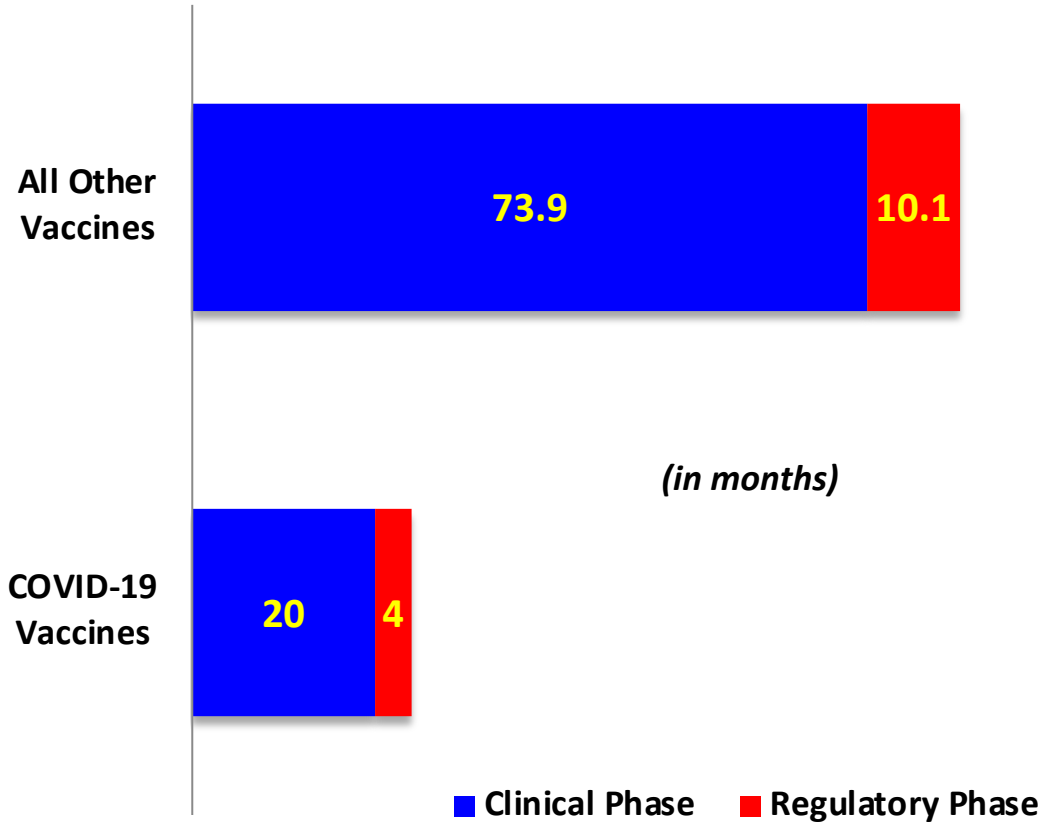
Mitigating Clinical Study Disruptions During Disasters and Public Health Emergencies

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

October 2023

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

‘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

Source: Tufts CSDD

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Unplanned Disruptions: A Common Occurrence

	2013-2015 *(N=836 protocols)*		2018-2021 *(N=952 protocols)*	
	Percentage of protocols with at least 1 substantial amendment	Mean number of substantial amendments	Percentage of protocols with at least 1 substantial amendment	Mean number of substantial amendments
Phase I	52%	1.8	67%	3.1
Phase II	77%	2.2	89%	3.3
Phase III	66%	2.3	82%	3.5

Source: Tufts CSDD 2015 and 2022 Studies

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Quantifying COVID-19 Disruptions

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

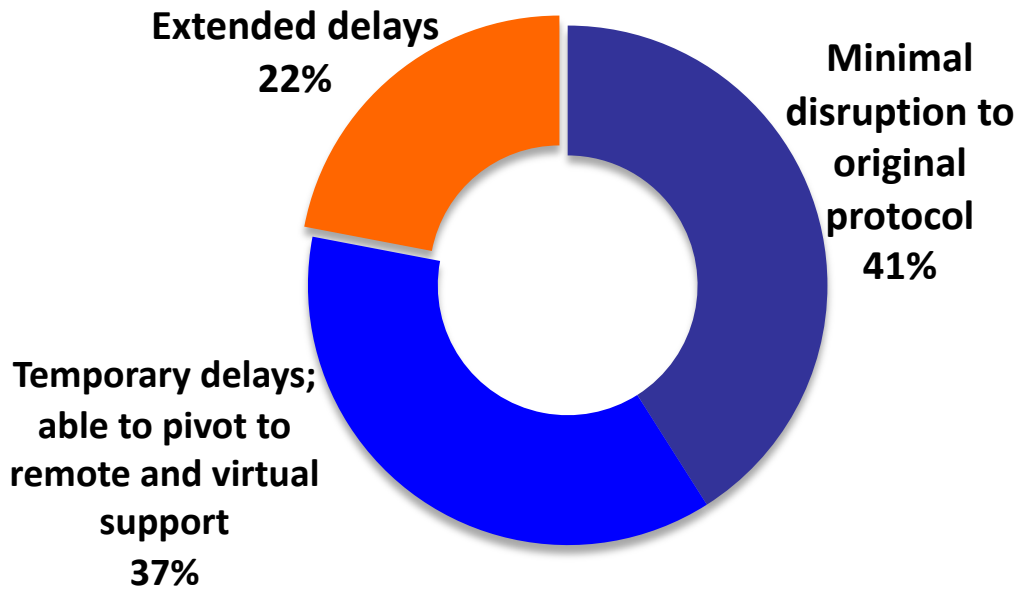
Source: Tufts CSDD 2022; n = 383 phase II/III pre-pandemic protocols and n=323 phase II/III pandemic protocols – multiple TAs

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Long-Term Impact on Investigative Sites

Clinical Trial Continuations

(As of October '20)



Site Landscape Consolidation

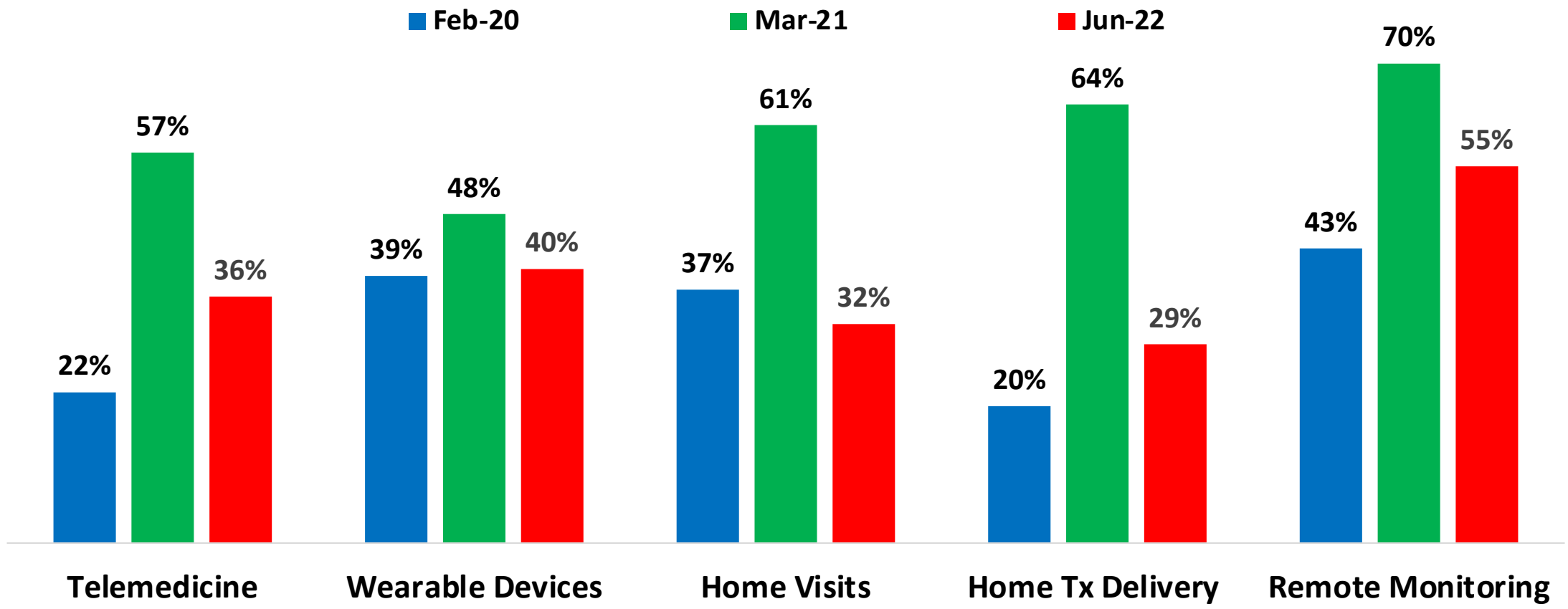
	2011	2022
Annual Volume		
1 Filing	**68%**	**43%**
2-5 Filings	**23%**	**37%**
6+ Filings	**9%**	**20%**
Setting		
AMC/Hospitals	**40%**	**43%**
P-T Community	**52%**	**45%**
Dedicated	**8%**	**12%**

Source: Tufts CSDD

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Remote and Virtual Solutions Adoption 2/20 – 6/22

Percent of Companies Report Deploying



Source: Tufts CSDD; N=54 individual companies

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

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

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

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

NIAID

NIH 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.

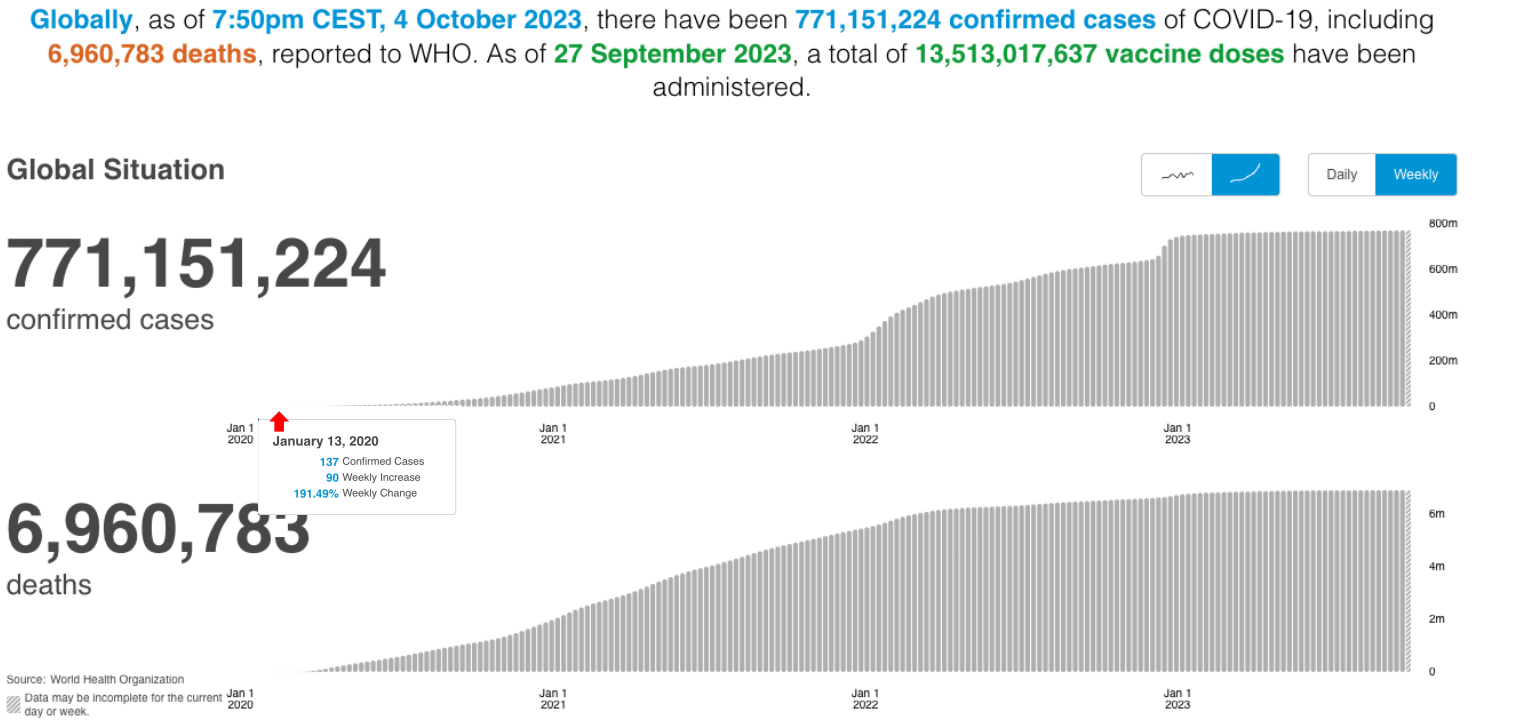
ACTT

- **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



WHO COVID-19 Dashboard

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)

NIH NATIONAL CANCER INSTITUTE

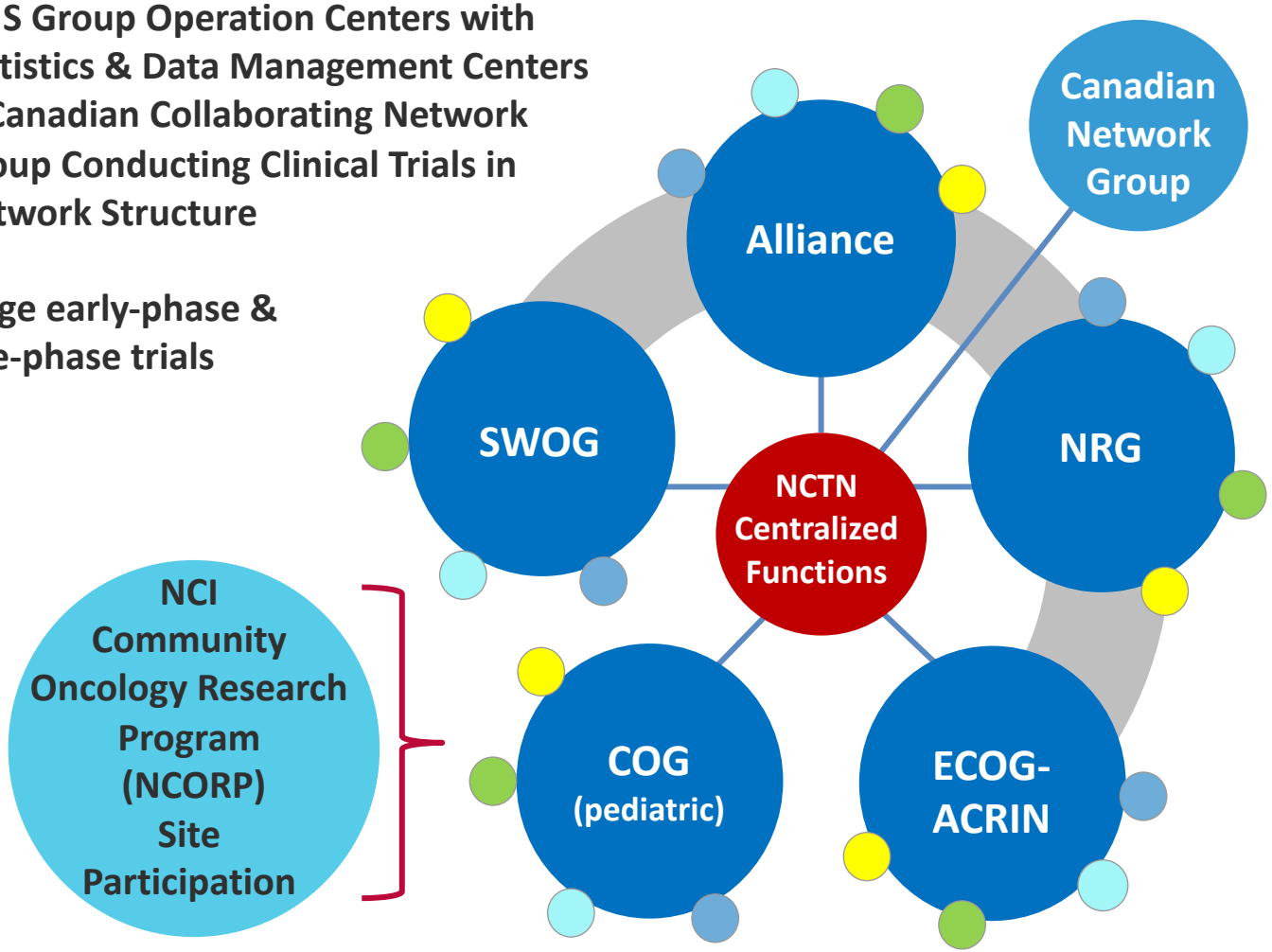
Mitigating Clinical Study Disruptions during Disasters & Public Health Emergencies
October 19, 2023

Meg Mooney, MD
Associate Director, CTEP, DCTD
National Cancer Institute, NIH

NCI National Clinical Trials Network Infrastructure

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

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

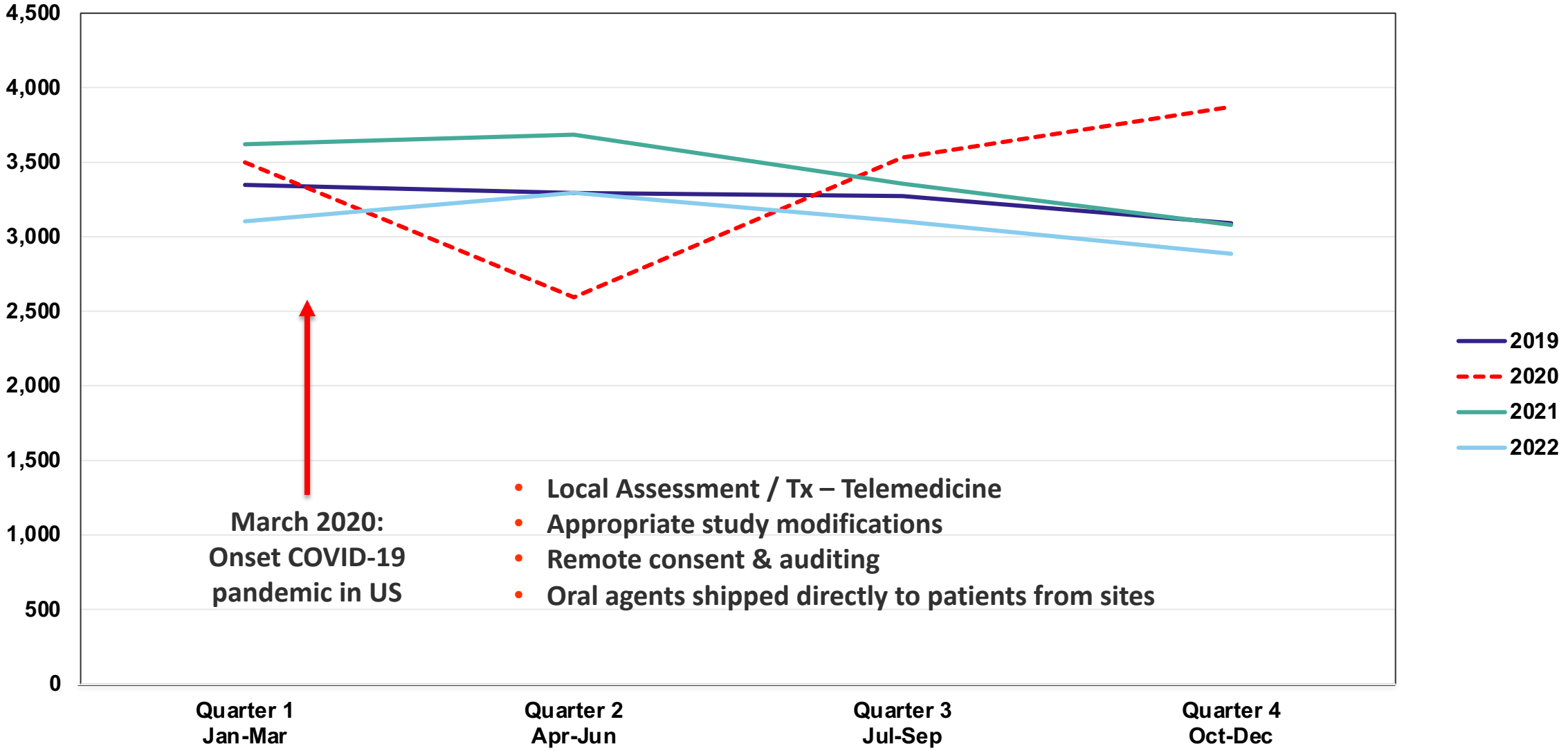
Biospecimen Banks

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



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
- **Additional Guidance on 3/23/2020 – Alternate Procedures**
  - 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

NCTN Sites Survey: High-Accruing Sites

June 29 to July 10, 2020

94 unique responses **(response rate = 42.2%)**

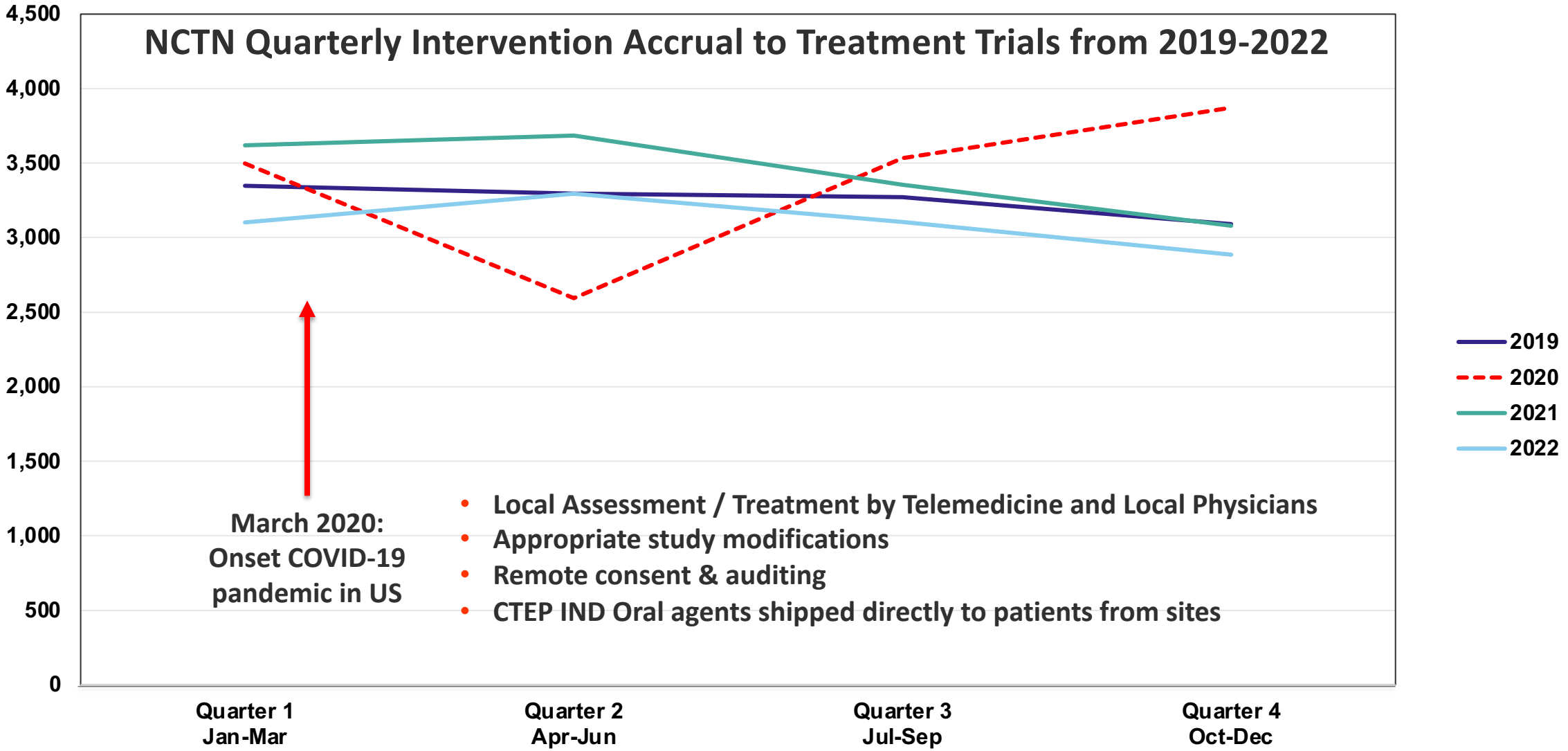
Throughout the pandemic, has your site ALWAYS been able to do this activity?

Operational Clinical Trial Activity	% Sites that had to Stop or Pause the Activity for Cancer Treatment Trials by Trial Phase		
	Phase 1 Trials	Phase 2 Trials	Phase 3 Trials
Enroll new Patients	41%	22%	18%
Process Protocol Amendments	16%	5%	4%
Open New Trials	46%	31%	30%
Process Biospecimens	45%	31%	29%
Collect Optional Biospecimens	59%	46%	41%

During the COVID-19 pandemic, has your site used the following modified clinical trials processes for NCTN trials?

	Yes	No	Average Usefulness Rating from 1 (not at all useful) to 5 (very useful)
Worked with **local healthcare providers** to provide continuity of care for patients on NCTN trials	52	31	**3.9** (n=63)
Used **virtual study visits** (telehealth / telephone)	85	5	**4.6** (n=88)
Shipped oral IND agents directly to patients enrolled	53	26	**4.5** (n=63)
Used **remote informed** consent to enroll patients	51	35	**4.2** (n=64)
Underwent a **remote audit** by an NCTN group	20	66	**3.6** (n=29)

Many Modifications Introduced During COVID-19 Pandemic Now Integrated as Standard Practices for NCTN Trials



NIH NATIONAL CANCER INSTITUTE

www.cancer.gov

www.cancer.gov/espanol

Trial Innovation Network: During the COVID -19 Pandemic

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

TRIAL INNOVATION NETWORK

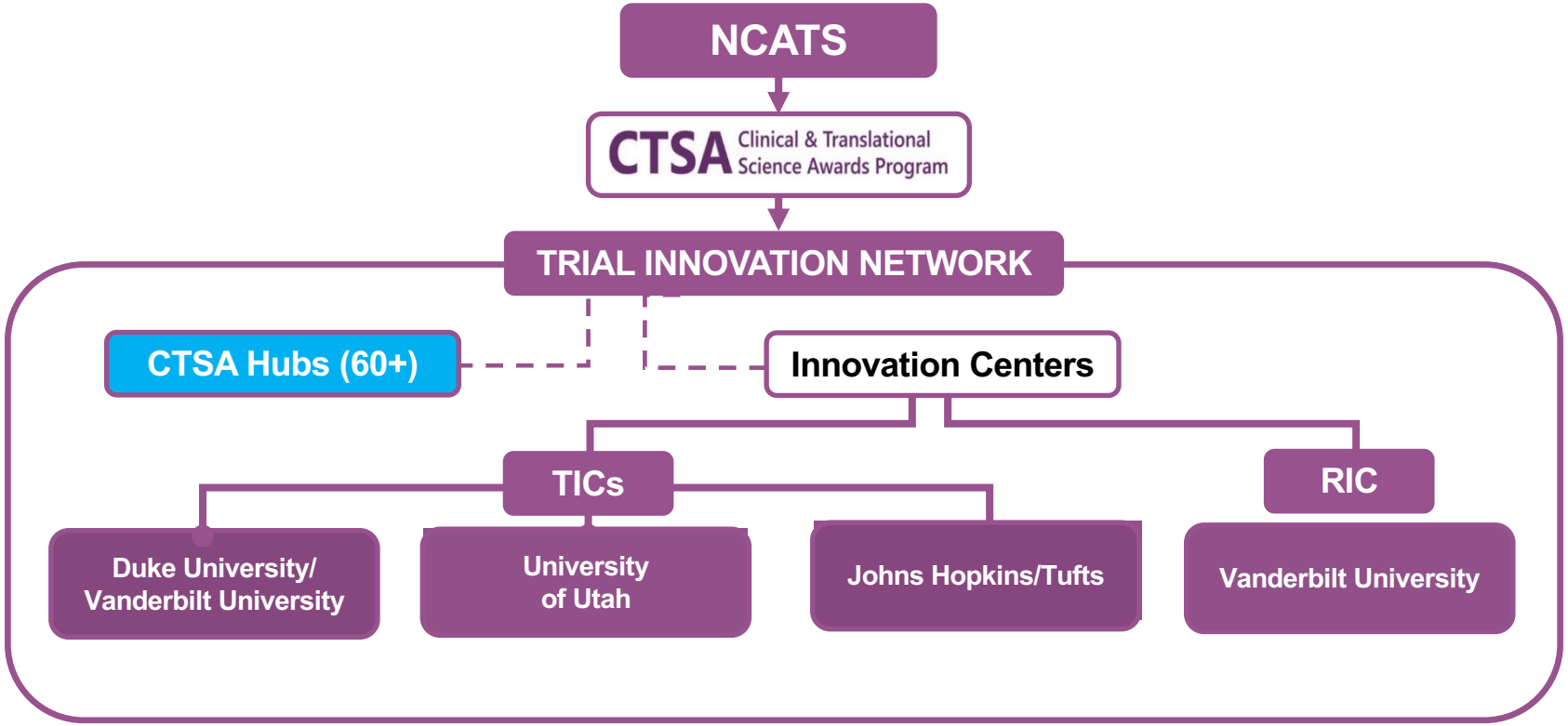
https://trialinnovationnetwork.org/

CTSA Clinical & Translational Science Awards Program

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.

Trial Innovation Network Structure



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:

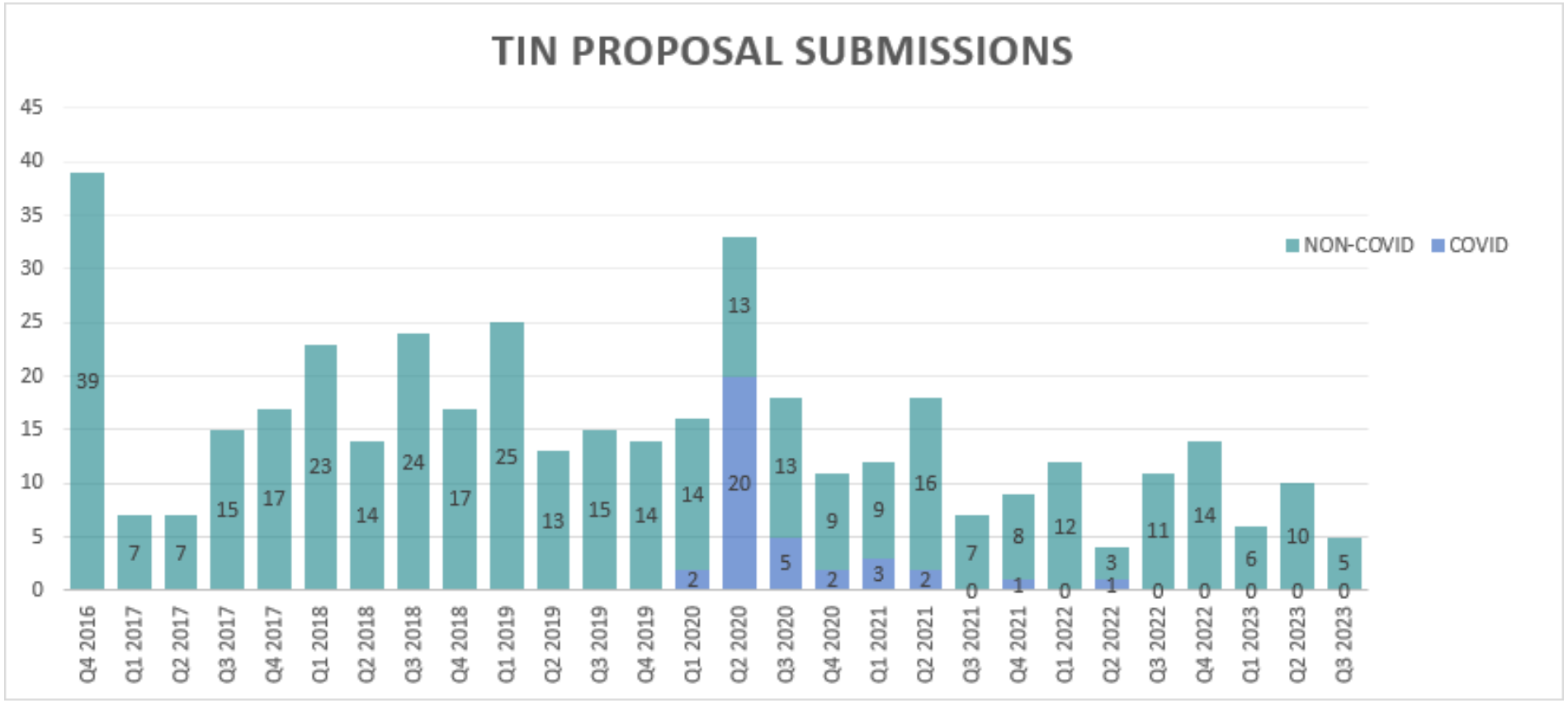
- Over 60 academic health centers with affiliates (93 million patients, 13% African-American, 6% Asian-Americans, 2% American Indian and 13% Hispanic)
- 17% of the CTSA patient pool reside in a rural area
- Large research professional teams with ~750 research nurses employed by CTSA Centers and over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

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



TRIAL INNOVATION NETWORK

https://trialinnovationnetwork.org/

CTSA Clinical & Translational Science Awards Program

TIN COVID Studies

TIN proposal date range	# of studies
March 2020	2
Apr-Jun 2020	20
Jul-Sep 2020	5
Oct-Dec 2020	2
2021	6
2022	1

Sample size	# of studies
< 100	4
100 - < 1000	13
1000 - < 5000	11
5000 +	8

Study type	# of studies (multiple possible)
Acute care	8
Outpatient	12
Platform/Tech/EHR	5
Registry	2
Predictive modeling	2
Schools	2
Treatment	18
Prevention	4
Observational	4
Surveillance	3
Prospective	5
Exploratory	1

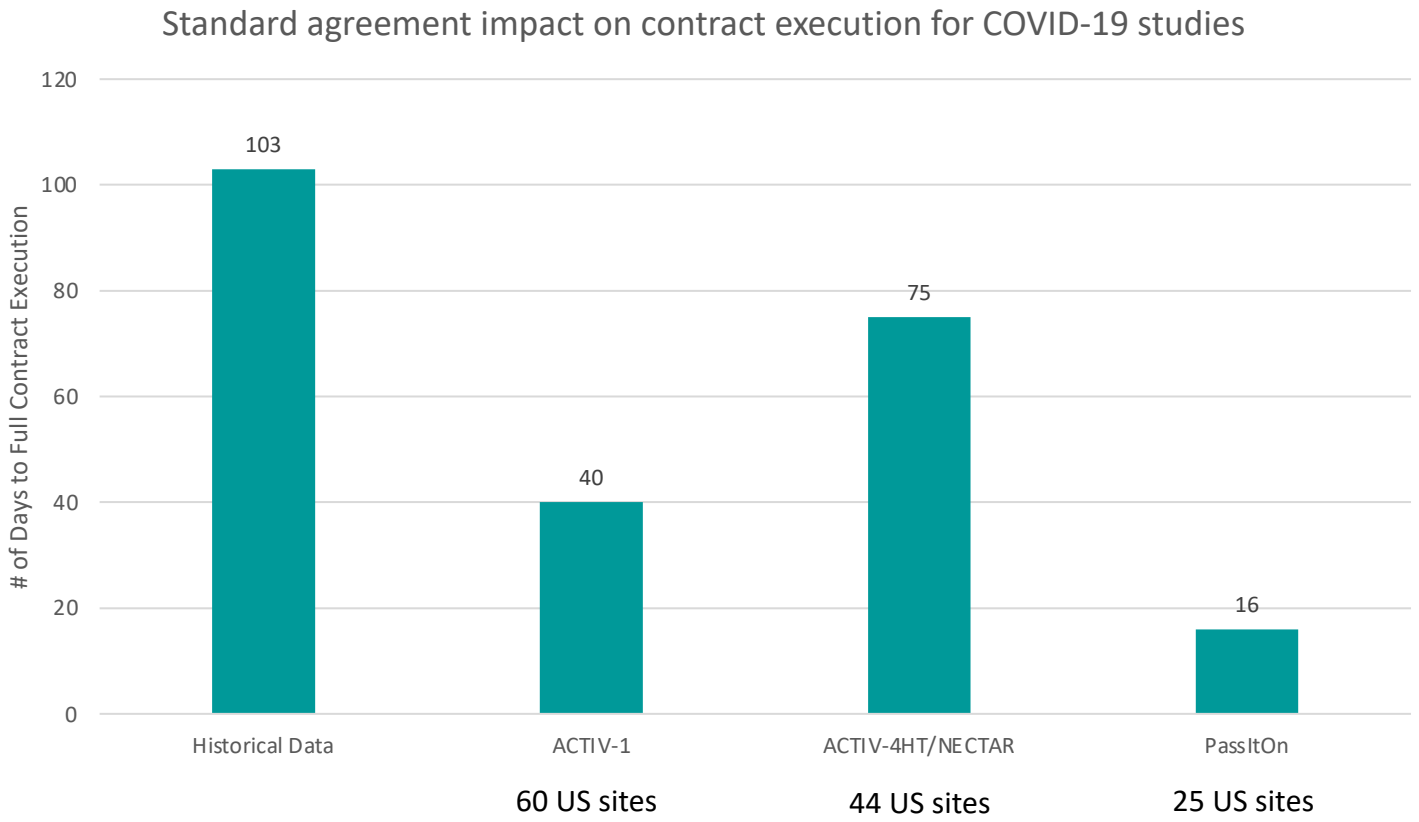
Decentralized elements of design for trials conducted during COVID

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

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.

Hanley et al. Decentralized clinical trials in the trial innovation network: Value, strategies, and lessons learned. J Clin Transl Sci. 2023

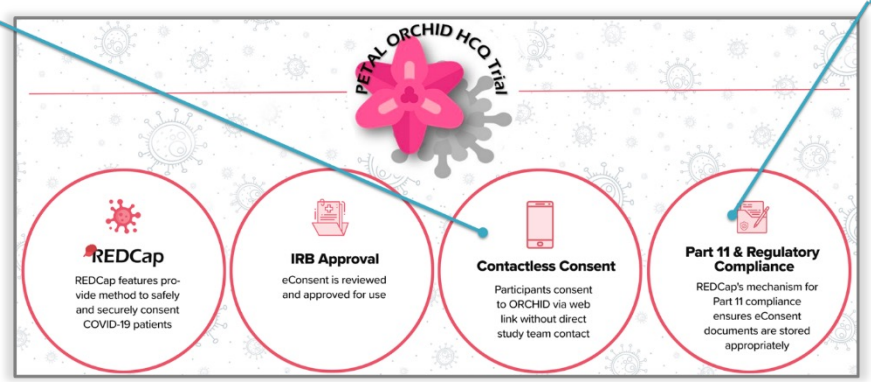
Standard Agreements to streamline COVID Study start up



eConsent and COVID-19

Contactless Consent

- Review and sign on own devices
- No direct contact with study staff required



Part-11 Compliant

- 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

METRICS

	Pre-Pandemic (March 2020)	Post-pandemic (Sept 2023)
# of eConsent Projects REDCap Consortium-wide	**3,100**	**>58,554**
# of eConsent transactions REDCap Consortium-wide	**50,625**	**>4,719,451**

COVID resources in TIN Toolbox

Resource	Submitted by	Date Posted to TIN Toolbox	Number of views as of 9/18/23
The Community Engagement Alliance (CEAL) Against COVID-19 Disparities	National Institutes of Health (NIH)	10/6/2020	182
N3C Domain Teams and Leaders	University of Colorado	11/13/2020	105
Best Practices for Conducting Trials during the COVID-19 Pandemic	Clinical Trials Transformation Initiative	12/29/2020	239
RIC COVID-19 RECRUITMENT + RETENTION TOOLKIT	Recruitment Innovation Center	7/30/2021	381

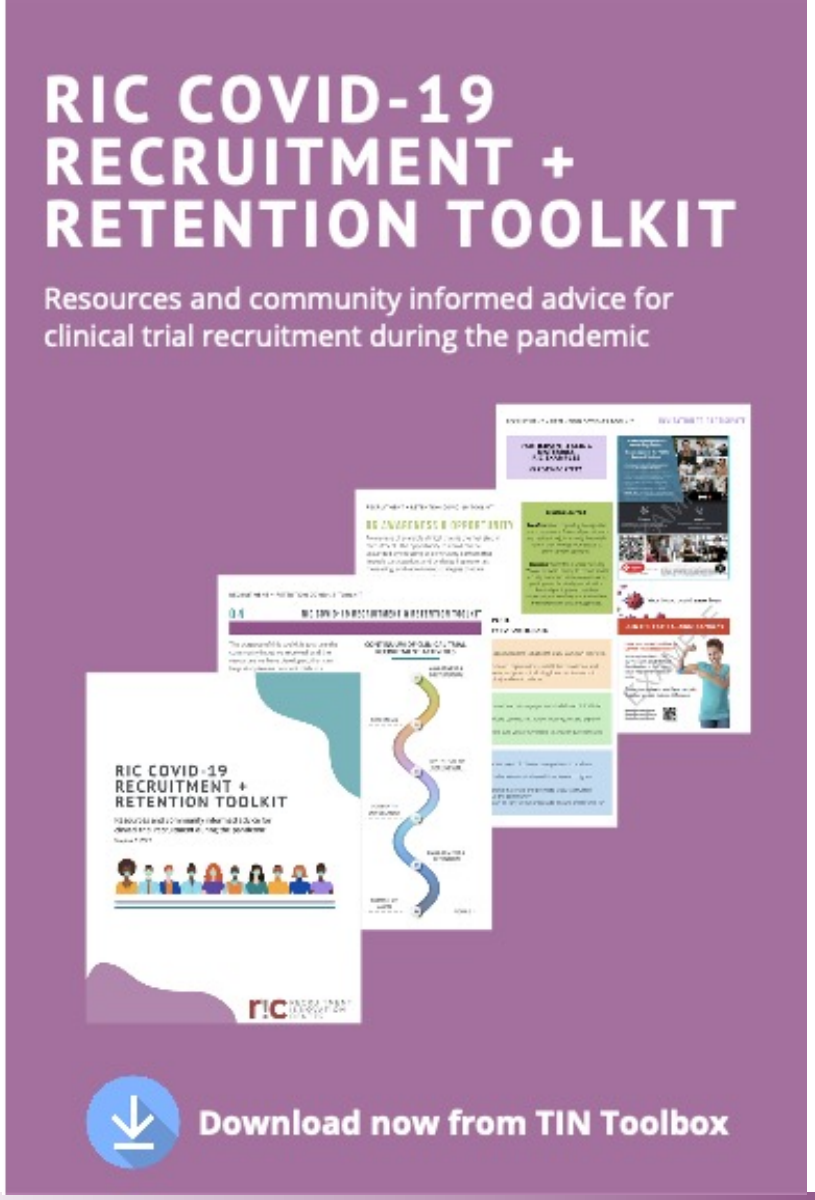
Community Feedback to Develop the Covid Toolkit

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.**

8 # of COVID Studios

58 # of experts
- Healthcare workers
- Essential workers
- African American/Black
- Hispanics/Latinx
- Older adults 65+

17 # of states represented for geographic diversity



CTSA Clinical & Translational Science Awards Program

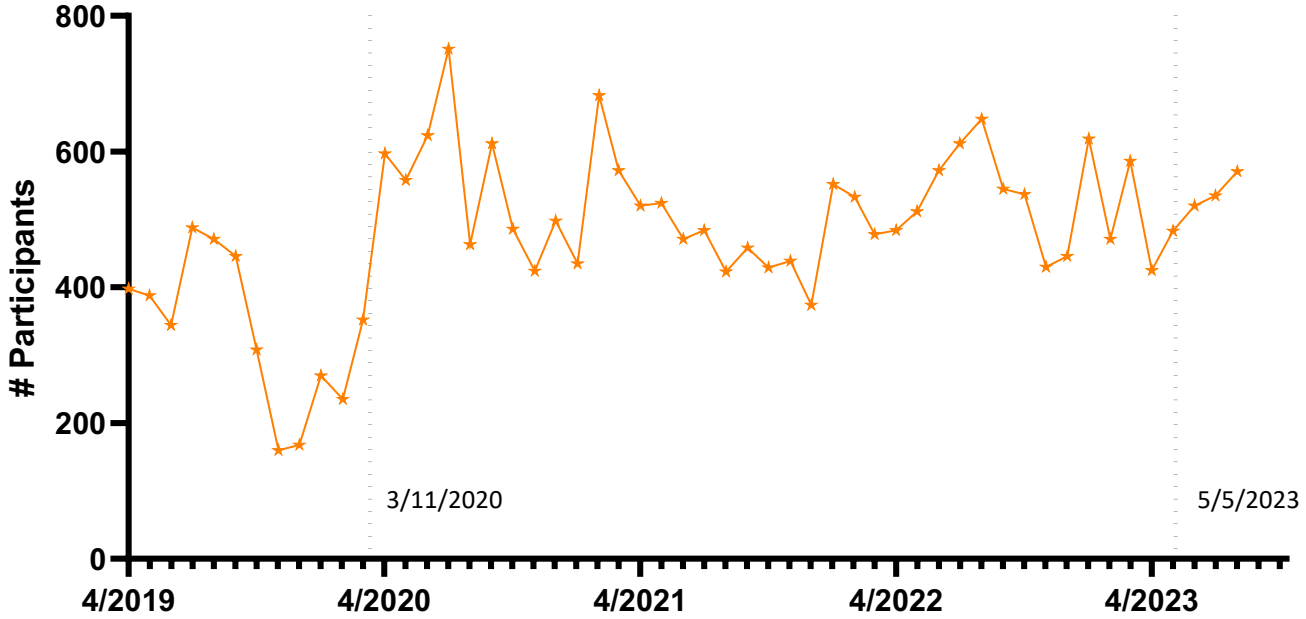
TIN Collaboration Webinars on COVID-19 Topics

Webinar Date	TIN Collaboration Webinar Title	Institution(s) Presenting	Topic	Attendee Number
3/31/20	REDCap, eConsent, and Part-11 Validation	VUMC	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	400
7/15/20	Recruitment in the Time of **COVID-19**: Single and Multisite Study Strategies Using ResearchMatch	VUMC	Lessons to optimize recruitment messaging, REDCap survey options, and strategies when using ResearchMatch	125
8/3/20	No Participants, No Trial (Don't Plan for Everything, but Recruitment)	University of Washington	Practical guidance to develop effective recruitment plans, track and measure success. and create eye-catching recruitment materials	82
9/16/20	Social Media and Participant Recruitment: What we've learned so far	University of Florida	Stakeholder-informed process as a case study to demonstrate establishment of social media guidelines and evaluation of Facebook effectiveness to recruit research participants	156
1/20/21	Patient Engagement in the time of **COVID**- Virtual Community Engagement Studios	VUMC	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	49
2/1/21	Using National **COVID** Cohort Collaborative (N3C) Data to Inform your Protocol Development	National COVID Cohort Collaborative, OHSU	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	32
4/21/21	The Innovative Climate of Study Teams and Their Adoption of Innovative Study Designs within Clinical Trials	Drexel University	The challenges that **COVID** adds to the landscape of clinical trials also brings potential for new pathways of clinical trial design and innovation	27
7/21/21	Recruitment Innovation Center **COVID-19** Recruitment and Retention Toolkit	VUMC	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	40
10/4/21	Using REDCap to Improve Recruitment and Data Collection for Clinical Research	VUMC	Impactful uses of REDCap Clinical Data Interoperability Services for clinical research, including **COVID-19** trial recruitment and multi-site critical care studies	116

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***.



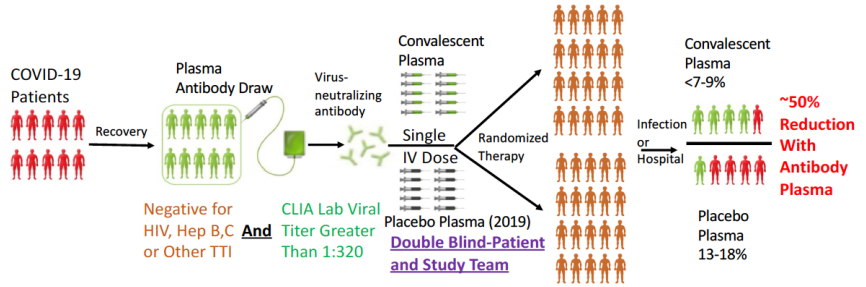
Note:
4/1/2019 – Faster Together Coursera course launches
3/11/2020 – World Health Organization (WHO) declares COVID-19 a pandemic
5/5/2023 – WHO declares end to COVID-19 emergency
Data is from 4/2019 until 8/2023.

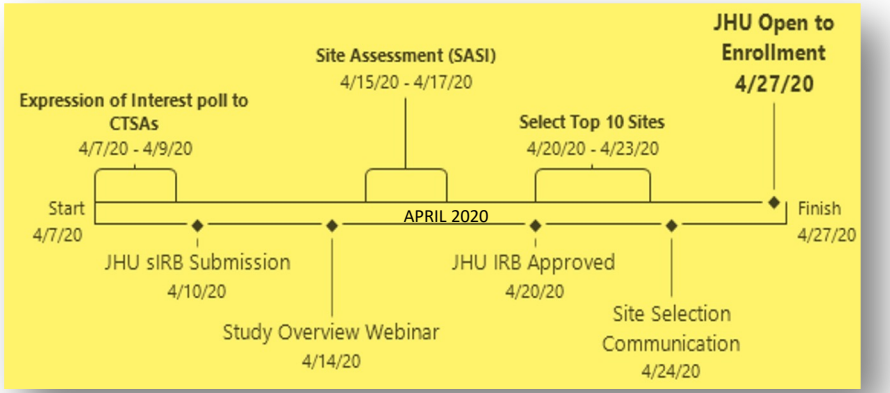
TIN Use Cases – COVID-19 Trials

COVID-19 PLASMA TRIALS

SPONSORED BY JOHNS HOPKINS UNIVERSITY

- 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)





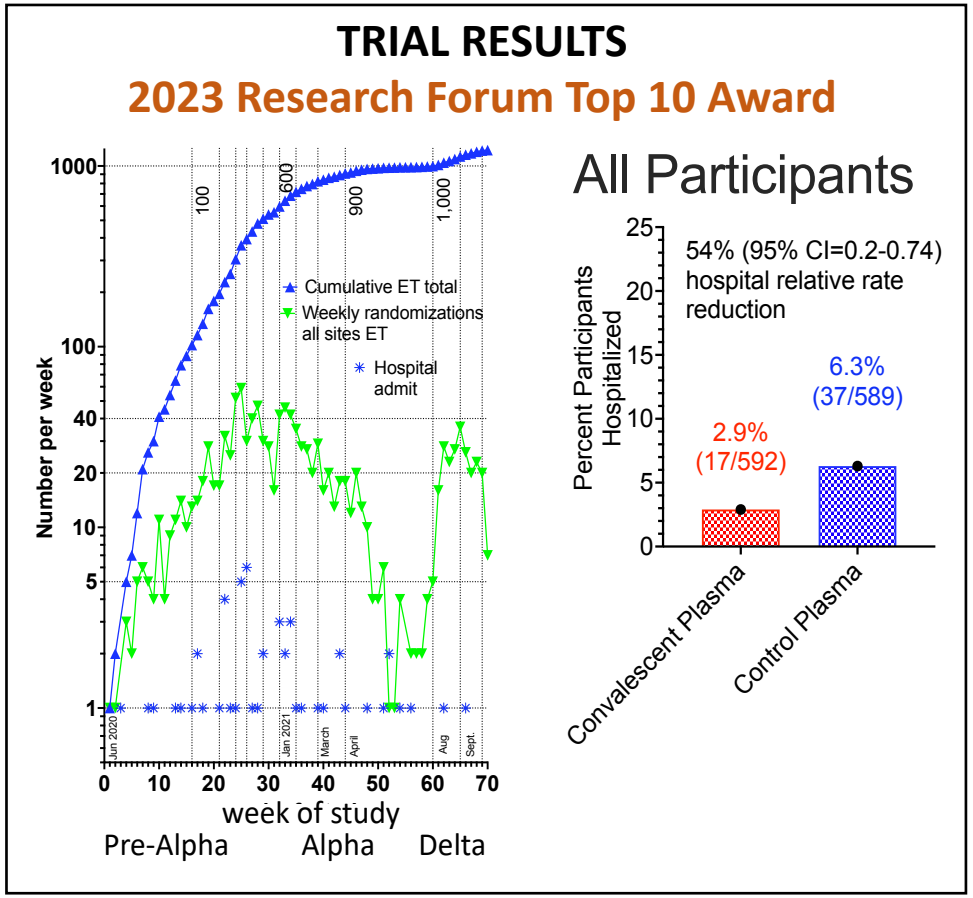
TRIAL INNOVATION NETWORK

https://trialinnovationnetwork.org/

CTSA Clinical & Translational Science Awards Program

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 INNOVATION NETWORK

https://trialinnovationnetwork.org/

COVID-19 PLASMA TRIALS

SPONSORED BY JOHNS HOPKINS UNIVERSITY

ranslational
vards Program

Pandemic Metrics & Network Performance

COVID-19 PLASMA TRIALS
SPONSORED BY JOHNS HOPKINS UNIVERSITY

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

TIN publications

Trial Innovation Network

TIN Summary paper- https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2810186
Invited commentary- https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2810198
Enhancing informativeness of clinical trials https://www.cambridge.org/core/journals/journal-of-clinical-and-translational-science/article/approaches-for-enhancing-the-informativeness-and-quality-of-clinical-trials-innovations-and-principles-for-implementing-multicenter-trials-from-the-trial-innovation-network/74D5273A19D6D9816212DDFB1F66C20D
Decentralized trials- https://pubmed.ncbi.nlm.nih.gov/37654775/

Recruitment Innovation Center

RIC marker paper- https://www.cambridge.org/core/journals/journal-of-clinical-and-translational-science/article/recruitment-innovation-center-developing-novel-personcentered-strategies-for-clinical-trial-recruitment-and-retention/D1583E46F3F5E8FFB0C1CA526FAAF9A5
Top 4 things Researchers should know about Recruitment and Retention https://www.cambridge.org/core/journals/journal-of-clinical-and-translational-science/article/what-we-wish-every-investigator-knew-top-4-recruitment-and-retention-recommendations-from-the-recruitment-innovation-center/D7D12A2D307FE5549A864D7AA6695C0A

Trial Innovation Center

Accelerated Clinical Trial Agreements paper- https://www.cambridge.org/core/journals/journal-of-clinical-and-translational-science/article/quantitative-assessment-of-the-impact-of-standard-agreement-templates-on-multisite-clinical-trial-start-up-time/5D7F4408016C708396E40C1346025D35
SIRB lessons learned https://www.cambridge.org/core/journals/journal-of-clinical-and-translational-science/article/key-lessons-and-strategies-for-implementing-single-irb-review-in-the-trial-innovation-network/2179CB3611FE0D561E1C2C5A25FBA64B

https://trialinnovationnetwork.org/

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

Post public comment by April 19, 2024

LINK

To have comments considered in discussion at public meeting, submit by January 19, 2024

Register for March 19-20, 2024 public workshop

LINK

Virtual and in-person (DC) options available

But….it will take a village…

Graphics from: https://nursing.jhu.edu/excellence/community/

Thank you!