Reimagining Clinical Trials: Learning from COVID-19

June 24, 2021
The MRCT Center is a research and policy center focused on addressing the conduct, oversight, ethics and regulatory environment for clinical trials.
Our Vision

Improve the integrity, safety, and rigor of global clinical trials.

Our Mission

Engage diverse stakeholders to define emerging issues in global clinical trials and to create and implement ethical, actionable, and practical solutions.
Reimaging Clinical Trials: Learnings from COVID-19

2 Meeting Dates

**June 16, 2021, 10AM-1PM EDT**
Permissible flexibilities to study conduct and coordination and the implications for the clinical trial workforce in this new environment.

**June 24, 2021, 10AM-1PM EDT**
Regulatory flexibilities, international cooperativity, and governance.
Our Goal

• What is the vision for new ways of conducting clinical trials?
• What worked, what did not work, and what we need to analyze further?
• How do we build upon experiences of clinical trials during the COVID-19 pandemic
<table>
<thead>
<tr>
<th>TIME</th>
<th>TOPIC</th>
<th>SPEAKERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:00 AM –</td>
<td><strong>Introduction &amp; Keynote speaker:</strong> The Future of Clinical Trials</td>
<td>• Barbara Bierer, Faculty Director, MRCT Center</td>
</tr>
<tr>
<td>10:30 AM</td>
<td><strong>First Panel:</strong> Useful and permissible flexibilities: A discussion</td>
<td>• Sarah White, Executive Director, MRCT Center</td>
</tr>
<tr>
<td>11:30 AM</td>
<td>of regulatory, protocol, and study conduct flexibilities that can</td>
<td>• Esther Krofah, Executive Director, FasterCures</td>
</tr>
<tr>
<td>11:40 AM</td>
<td>and should be sustained in the future, that should be eliminated, and</td>
<td></td>
</tr>
<tr>
<td>12:40 PM</td>
<td>for which further experience is necessary</td>
<td></td>
</tr>
<tr>
<td>1:00 PM</td>
<td><strong>Discussion and wrap-up</strong></td>
<td>• Moderators Paul Kluetz and Craig Lipset</td>
</tr>
</tbody>
</table>

©MRCT Center
<table>
<thead>
<tr>
<th>TIME</th>
<th>TOPIC</th>
<th>SPEAKERS</th>
</tr>
</thead>
</table>
| 10:00 AM - 10:45 AM EDT | **Introduction & Keynote speakers**  
*Reimagining Clinical Trials: Learning from COVID-19* – Fergus Sweeney  
*Aligning global clinical trial requirements* – Ginny Beakes-Read | *Sarah White*, Executive Director, MRCT Center  
*Fergus Sweeney*, Head, Clinical Studies and Manufacturing Taskforce, European Medicines Agency (EMA)  
*Ginny Beakes-Read*, Executive Director, Global Regulatory and R&D Policy, Amgen |
| 10:45 AM - 11:40 AM EDT | **First Panel** – Enabling regulatory flexibilities in a global context | *Taras Carpiac*, Executive Director, Innovation & Process Improvement, Amgen  
*Lauren Hartsmith*, Director of Regulatory Affairs, Advarra  
*Richard Moscicki*, Chief Medical Officer and Executive Vice President of Science and Regulatory Advocacy, PhRMA  
*Névine Zariffa*, Principal and Founder, NMD Group  
Moderator:  
*Barbara Bierer*, Faculty Director, MRCT Center |
| 11:40 AM - 11:50 AM | **BREAK** | |
| 11:50 AM - 12:45 PM EDT | **Second Panel** – Regulatory cooperation and communication and issues of governance in a global pandemic | *M. Khair ElZarrad*, Deputy Director, Office of Medical Policy at Center for Drug Evaluation and Research (CDER), U.S. FDA  
*Owen Fields*, Vice President for Regulatory Strategy, Research and Development, Pfizer  
*Steven Kern*, Deputy Director of Quantitative Sciences, Bill and Melinda Gates Foundation  
*Fergus Sweeney*, Head, Clinical Studies and Manufacturing Taskforce, European Medicines Agency (EMA)  
Moderator:  
*Mark Barnes*, Faculty Co-Director, MRCT Center; Partner, Ropes & Gray |
| 12:45 PM – 1:00 PM EDT | **Discussion and wrap-up** | *Barbara Bierer*, Faculty Director, MRCT Center  
*Mark Barnes*, Faculty Co-Director, MRCT Center; Partner, Ropes & Gray |
Closed Caption Settings

Closed Caption size can be increased by clicking on the Closed Captions button and viewing the “subtitle settings”.

Captions will look like this
Thank you to the Planning Committee

Maria Apostolaros, PhRMA
Ginny Beakes-Read, Amgen
David Peloquin, Ropes & Gray
Michele Russell-Einhorn, Advarra
Shona Sanchita Pendse, Kowa
Jessica Scott, Takeda
Moke Sharma, Alexion
Michael Steel, Novartis
Fergus Sweeney, EMA

MRCT Center team
Carmen Aldinger
Barbara Bierer
Sarah White
Keynote 1: Reimagining Clinical Trials: Learning from COVID-19

Fergus Sweeney,
Head, Clinical Studies and Manufacturing Taskforce, European Medicines Agency (EMA)
Reimagining Clinical Trials: Learning from COVID-19

Presented by Fergus Sweeney on 24 June 2021
Head, Clinical Studies and Manufacturing Task Force, European Medicines Agency
Disclaimer

These PowerPoint slides are copyright of the European Medicines Agency. Reproduction is permitted provided the source is acknowledged.

The presenter does not have any conflict of interests.
Milestones in EMA response to COVID-19 pandemic

- WHO declares pandemic
  - COVID-19 Experts’ Task Force

- Accelerated development & evaluation procedures

- Approvals:
  - Pfizer
  - Moderna
  - AstraZeneca
  - Janssen

Scientific & regulatory mobilisation
- COVID-19 Task Force
  - EU Network
  - International

Development & evaluation
- Guidance to developers
  - Early scientific advice
  - Rapid procedures

Essential medicines’ supplies
- EU coordination
- Preventing shortages

Transparency & outreach
- Public engagement
- Communication

24 June 2021
COVID-19 vaccines compared with standard vaccines

**INDICATIVE TIMELINE**

**Standard Vaccines**

1. Pharmaceutical quality
2. Non-clinical research
3. Human pharmacology studies
4. Therapeutic exploratory studies
5. Clinical efficacy and safety studies
6. Scientific evaluation and authorisation
7. Large-scale production
8. Studies after authorisation

**COVID-19 Vaccines**

1. Pharmaceutical quality
2. Non-clinical research
3. Human pharmacology studies (Phase I)
4. Therapeutic exploratory studies (Phase II)
5. Clinical efficacy and safety studies (Phase III)
6. Scientific evaluation and authorisation
7. Large-scale production
8. Studies after authorisation
Rolling review and Marketing Authorisation

- Research & development
- Standard EMA evaluation
- EMA evaluation with rolling review

STANDARD

COVID-19

Rolling review cycle

Developer applies for marketing authorisation

EMA opinion

EMA opinion

24 June 2021
Conditional Marketing Authorisation

- Approval for medicines to be used in **public health emergencies**
  - as soon as data available show that benefits outweigh the risks
  - **other data** must be provided by the company, **after approval**
    (e.g. long term protection data)

- It has **all safeguards and controls** in place to ensure high level of protection to citizens during a mass vaccination campaign
  - A robust **monitoring plan** for managing **safety**
  - Clear **legal framework** for evaluation of **emerging efficacy data**
  - **Manufacturing** controls including **batch controls** for vaccines
  - Full **prescribing information** and **package leaflet** with defined conditions for storage and use of the vaccine
  - A **plan** for **use** of the vaccine **in children**
  - **Additional studies or other data** (‘conditions’) that the company is **legally obliged** to provide with defined **timelines**
ICMRA and COVID-19 response since April 2020

- > 30 countries
- Executive level
- WHO Observer

- Forum to support strategic coordination and support public confidence in COVID-19 vaccines and therapeutics
- Bi-weekly Policy TCs ensures sharing of information and promote convergence
- Regular Working Group coordinates technical work streams
  - Vaccine Pharmacovigilance Network, including work on vaccine confidence
  - Regulatory Agility
  - Digital transformation of GCP and GMP inspections and clinical trials
- Workshops to promote convergence in regulatory approached on: responding to virus variants; inclusion of pregnant and lactating women in trials; reinforcing pharmacovigilance collaboration

24 June 2021
Opening our Procedures at EMA to Non-EU authorities: the OPEN Initiative

- Under OPEN WHO and medicines regulators from outside the EU take part in EMA's scientific evaluations
- Drivers: sharing scientific expertise, tackling common challenges, enhancing transparency on regulatory decisions
- Pilot launched December 2020 for COVID-19 vaccines and therapeutics with TGA Australia, Health Canada, MHLW/PMDA Japan, Swissmedic and WHO
- Participate in CHMP assessments and COVID-19 EMA pandemic Task Force
- Experts keep full scientific and regulatory independence, and participate under existing confidentiality arrangements; have no role in final CHMP B/R decision
Enable continuation of treatment

Ensure Safety reporting

Ensure reliability of trial results, enable trials to continue

Mitigate burden on clinical site staff and facilities and on participants.

Enable management of clinical trials whilst maintain social distancing.

Use Risk assessment

Changes to:

- informed consent process
- distribution of IMP, diagnostics etc
- monitoring and auditing
Learning from Experience

Rapid responses and regulatory flexibilities

Pandemic still ongoing and evolving, fast learning and adaptation

Evolving regulatory landscape:

• Use of digital tools has been accelerated
• Dialogue has been significantly increased along development pathway
• Reflect on experience, improve and select what works
• Need feasible, sustainable, tools for longer term, but it will be a new, different, landscape
• We can change now to act by design, and less by reaction to necessity
• Keep regulatory standards high along with speed and innovation
Key developments

• Complex Clinical Trials:
  • Ongoing discussions with industry and academia associations and Q&A development – CTFG, EMA, European Commission

• Decentralised Clinical Trials.
  • Ongoing discussions on frameworks and pilots CTFG, EMA, European Commission.
Redesign our approach to enable innovation in a Rapidly Evolving Ecosystem

Set the foundations to enable innovation by design and not by reaction
Clinical Trials of the Future – some of the challenges

• Digitalisation – use of more diverse tools and data sources, changing means of interaction between people and information, building trust in the data and in its use

• Ensuring, sufficiently powered (often large), well designed, randomised, clinical trials

• Platform trials and master protocols – maximising the benefit of scientific investigation on a large scale
• Establish a quality continuum throughout design and conduct. Design that involves engagement with stakeholders including patients and investigators.

• The purpose of clinical trials is to generate information to support decision making - their quality must be sufficient to protect participants and generate results that support good decision making.

• ICH E8 focus on achieving quality by good design, with a risk based, proportional approach, ICH E8 and E6 need modernising to set the foundation for:

  • future medicines, future trial designs, future technologies, future data sources

ICH GCP Renovation

Quality Continuum

E8 Design ↔ E6 Conduct

ICH E8 General Considerations on Clinical Studies, ICH E6 Good Clinical Practice
ICH GCP Draft Principles

10- Clinical trials should generate reliable results.

- 10.1 The quality and amount of the information ....sufficient to provide confidence in the trial’s results and support good decision making.

- 10.2 Systems and processes ...... implemented in a way that is proportionate to the risks to participants and the reliability of trial results.

- 10.3 Tools ......should be fit for purpose, should capture the information required by the protocol, and should conform to principles that ensure reliable results.

- 10.4 Digital systems used for clinical trial purposes should consider the factors critical to their quality in their design and be fit for purpose. To this end, validation of systems, data protection, information technology (IT) security and user management are important elements that should be addressed.
10.5 ...efficient and well-controlled processes for managing information ... data integrity, traceability, and protection of personal information, thereby allowing the accurate reporting, interpretation, and verification of the clinical trial-related information.

10.6 ......information ...retained .. by sponsors and investigators........to enable reconstruction of the trial conduct and results in order to ensure reliability of trial results.

10.7 The transparency of clinical trials ....includes registration on publicly accessible and recognized databases, and the public posting of clinical trial results.

10.8 The principles .....apply irrespective of the type of media used.
Digitalisation - Challenges

• Establishing Trust
  • Data provenance, validity (technical and scientific)
  • New data sources
  • Personal data protection – ensure protection whilst enabling clinical trial data to be used well – both are legitimate expectations of trial participants
  • Complex landscape or data generation, collection and analysis, digital communication, remote visits, use of wearables, electronic informed consent

• Need to set standards for use of digital tools and information that are universally applicable, future proof, ensure data trust and participant protection but support innovation and new approaches

• EU GCP IWG Draft Guideline on computerised systems and electronic data in clinical trials - open for comment 18 June to 17 Dec 2021

The benefits of large scale RCTs

International coordination needed to encourage conduct of large, decision-relevant COVID-19 clinical trials

Press release 15/05/2020

Regulators are highlighting the need for a comprehensive international coordination mechanism to allow the conduct of adequately powered, randomised controlled trials, which can generate sound evidence on the effects of therapeutics or vaccines against COVID-19. This follows a call made by EMA’s Human Medicines Committee (CHMP) for the research community to pool resources into large, well-designed, multi-arm clinical trials to determine which investigational or repurposed medicines would be safe and effective for the treatment or prevention of COVID-19.

Although the scientific community has responded to the COVID-19 challenge in an unprecedented manner, there are concerns about the growing number of COVID-19 stand-alone clinical trials with a small number of participants and observational studies, which might not generate the data required for regulatory decision-making.

- Experience and data in clinical trial registers shows that far too many trials are small, underpowered and poorly designed.
- Fewer, well designed, large RCTs, run multinationally would deliver better information for regulatory and healthcare decision making.
- COVID experience has reinforced this message very strongly

Clinical Pharmacology & Therapeutics

Clinical trials for Covid-19: can we better use the short window of opportunity?

Hans-Georg Eichler, Marco Cavaleri, Harald Enzmann, Francesca Scotti, Bruno Sepodes, Fergus Sweeney, Spiros Varvakas, Guido Rad

First published: 14 May 2020 | https://doi.org/10.1002/cpt.1891

24 June 2021

Classified as public by the European Medicines Agency
Enabling large trials

- Build and maintain large investigator networks
- Link national and regional investigator networks, at regional and multi-regional level
- Provide infrastructure for the networks, independently of public or private trial sponsors
- Enable trials involving (multiple) public health and or private sponsors
- Build infrastructure for health bodies to sponsor international trials across different jurisdictions and to act as the lead and applicant across all jurisdictions
- Address drivers of small trials – poor funding, lack of network opportunity, need for academic recognition
- How can small trial proposals be referred to large trial groups?
Platform trials

• Some clear successes during COVID19

• Challenges:
  • Running platform trials across multiple countries and regions as a clear single protocol with a clear sponsor to apply for and manage the clinical trial
  • Managing trials with products in development and established products (registration goal and therapeutic guidance/repurposing of established medicines)
  • How much can be managed in a single platform trial
  • Scientific and methodology challenges
  • Objectives – medicine registration, repurposing....
  • Infrastructure and trial management
  • Clinical trial authorisation – thinking outside of the box – e.g. is a platform trial one or several, grouped, trials for purposes of
Change the way we all work – don’t add more to the status quo.

Change Management is the greatest challenge

– adjusting behaviors, attitudes – away from preconceived ideas and interests – and on to a new, better, way of working.

“Perfection is achieved not when there is nothing more to add but when there is nothing left to take away”  Antoine de Saint-Exupéry

“Everything should be made as simple as possible but not simpler”  Albert Einstein
Build future for clinical trials by design

Develop standards for digital tools used in clinical trials. Enable new data sources

Build trust in the validity of data and in protection of participant privacy

Ensure properly powered, large, randomised clinical trials

Enable large investigator networks, and link networks between regions. Develop infrastructure to support them.

Develop the science and regulatory models for platform trials. Enable them to work across countries and regions
And now the discussion

Further information

Fergus.Sweeney@ema.europa.eu

Official address  Domenico Scarlattilaan 6  •  1083 HS Amsterdam  •  The Netherlands
Telephone  +31 (0)88 781 6000
Send us a question  Go to www.ema.europa.eu/contact

Follow us on  @EMA_News
Keynote 2: Aligning global clinical trial requirements

Ginny Beakes-Read,
Executive Director, Global Regulatory and R&D Policy, Amgen
ALIGNING GLOBAL CLINICAL TRIAL REQUIREMENTS
• Amgen used SmartSheet tool to collect content and Amgen interpretation of global regulatory guidelines

• Colors in charts visually illustrate Amgen interpretations of regulatory guidance, such as:
  – Additional procedural steps needed
  – No guidance available
  – Guidance permits a flexible approach
### COMPARISON GRID OF SELECT HEALTH AUTHORITIES

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia (CTPRG / TGA)</td>
<td>Not Required</td>
<td>Depends on Nature of Deviation or Modification</td>
<td>Notify and/or submit in bulk</td>
<td>Yes</td>
<td>Permitted; Requires notification</td>
<td>Permitted</td>
<td>Permitted; No notification required</td>
</tr>
<tr>
<td>Belgium (FAMHP)</td>
<td>Notification Only</td>
<td>Depends on Nature of Deviation or Modification</td>
<td>Additional considerations. See comments.</td>
<td>No</td>
<td>Not addressed in guidance</td>
<td>Permitted</td>
<td>Permitted; Additional notification/submission considerations. See comments.</td>
</tr>
<tr>
<td>Canada (Health Canada)</td>
<td>Notification Only</td>
<td>Not Required</td>
<td>Notification</td>
<td>Not addressed in guidance</td>
<td>Permitted; No notification required</td>
<td>Requires notification and/or approval</td>
<td>Permitted; No notification required</td>
</tr>
<tr>
<td>European Union (EMA)</td>
<td>Notification Only</td>
<td>Not Required</td>
<td>Follow Sponsor’s standard procedures</td>
<td>Follows EMA Guidance Under special circumstances</td>
<td>Permitted; Requires notification</td>
<td>Requires notification and/or approval</td>
<td>Permitted; Additional notification/submission considerations. See comments.</td>
</tr>
<tr>
<td>Germany (BfArM / PEI)</td>
<td>Submission; Approval Required</td>
<td>Depends on Nature of Deviation or Modification</td>
<td>Not addressed in guidance</td>
<td>Under special circumstances</td>
<td>Permitted; Additional notification/submission considerations. See comments.</td>
<td>Permitted</td>
<td>Permitted; Additional notification/submission considerations. See comments.</td>
</tr>
<tr>
<td>Japan (PMDA)</td>
<td>Not Required</td>
<td>Not Required</td>
<td>Document</td>
<td>Not addressed in guidance</td>
<td>Permitted; No notification required</td>
<td>Not addressed in guidance</td>
<td>Permitted; No notification required</td>
</tr>
<tr>
<td>UK (MHRA)</td>
<td>Not Required</td>
<td>Not Required</td>
<td>Document</td>
<td>Under special circumstances</td>
<td>Permitted; No notification required</td>
<td>Additional considerations</td>
<td>Permitted; No notification required</td>
</tr>
<tr>
<td>United States (FDA)</td>
<td>Not Required</td>
<td>Depends on Nature of Deviation or Modification</td>
<td>Document</td>
<td>Yes</td>
<td>Permitted; Additional notification/submission considerations. See comments.</td>
<td>Permitted</td>
<td>Permitted; Additional notification/submission considerations. See comments.</td>
</tr>
</tbody>
</table>

**Legend:** Colors and shades vary from Dark Green (most permissive or flexible) to Dark Red (most restrictive, or most process required). Yellow indicates that no guidance is provided.
First Panel:

Enabling regulatory flexibilities in a global context

10:45 AM – 11:40 AM EDT
Panelists

Taras Carpiac
Amgen

Richard Moscicki
PhRMA

Barbara Bierer
MRCT Center

Lauren Hartsmith
Advarra

Névine Zariffa
NMD Group
BREAK
10 min
Second Panel:
Regulatory cooperation and communication and issues of governance in a global pandemic

11:50 AM – 12:45 PM EDT
Panelists

M. Khair ElZarrad
US FDA

Owen Fields
Pfizer

Mark Barnes
MRCT Center & Ropes & Gray

Steven Kern
Bill & Melinda Gates Foundation

Fergus Sweeney
European Medicines Agency
Discussion and Wrap-up
Recordings Available


The first meeting (June 16, 2021, 10AM-1PM EDT) will focus on permissible flexibilities to study conduct and coordination, including site flexibilities, decentralized trials, and other changes, and the implications for the clinical research workforce in this new environment. The second meeting (June 24, 2021, 10AM-1PM EDT) will focus on regulatory flexibilities, international cooperativity, and governance. The meeting is open to all interested stakeholders and to the public.

**REGISTER** for the first meeting, June 16, 2021, 10 AM – 1 PM EDT

**REGISTER** for the second meeting, June 24, 2021, 10 AM – 1 PM EDT

**June 16, 2021: 10:00 am - 1:00 pm EDT**

- **Agenda**

- **Speaker Information**

- **June 16, 2021 Webinar Recording, Slides and Transcript**

**June 24, 2021: 10:00 am - 1:00 pm EDT**

- **Agenda**

- **Speaker Information**

**Planning Committee**
Thank You