Multi-stakeholder workshop

Accelerating Adoption of Complex Clinical Trials in Europe and beyond

5 - 6 October 2021

Multi-stakeholder workshop

5 - 6 October 2021

14:00

Introduction Day 2

Sini Eskola (EFPIA)
Peter Arlett (EMA)

Day 2
6 October 2021

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Introduction to day 2:

Evolution in clinical evidence

Accelerating Adoption of Complex Clinical Trials in Europe and beyond
5-6 October 2021

Peter Arlett, Head of Data Analytics and Methods Task Force, EMA

There is a lot going on…….

EUROPEAN MEDICINES AGENCY

COVID-19

COVID-19: latest updates Share

The latest updates on the COVID-19 pandemic from the European Medicines Agency (EMA) are available below.

HMA-EMA Joint Big Data Taskforce Phase II report:

'Evolving Data-Driven Regulation'

AT A GLANCE

Plenary – July 2021

European Parliament

European Medicines Agency mandate extension

Joint Action Towards the European Health Data Space – TEHDAS

The TEHDAS Joint Action project develops European principles for the secondary use of health data.

European Commission > Expert Groups > Details

Expert group on clinical trials (E01464)

ACTIVE

We have a plan on Big Data (HMA-EMA Big Data Steering

Jan. 2020

'Ten recommendations to unlock the potential of big data for public health in the EU'

Sep. 2020

Making best use of big data for public health: publication of the Big Data Steering Group workplan for 2020-21

July 2021

EMA MB and HMA informed of BDGS workplan 2021/2023


HMA-EMA Joint Big Data Taskforce
Phase II report:
'Evolving Data-Driven Regulation'

1st Big data steering group meeting in May 2020

May 2020

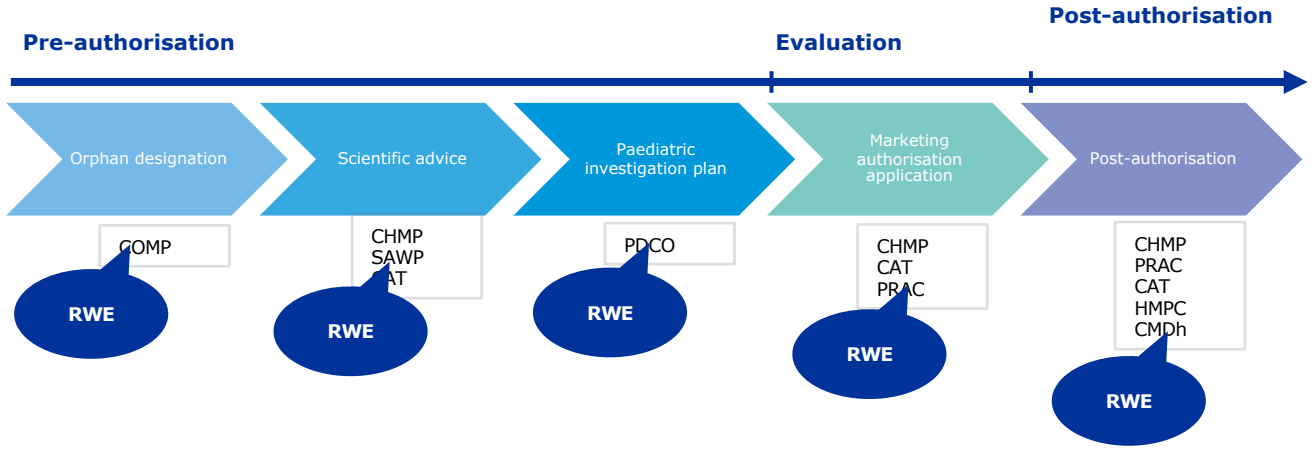
BDSG workplan 2022/2023

May and June 2021

Publication of BDSG workplan 2021/2023

Aug. 2021

Regulatory use cases of RWE supporting better decisions



- RWE has an established role to support safety evaluation of medicinal products
- Use of RWE for efficacy/effectiveness is more debated but is increasing to supplement, contextualise and, if needed, validate clinical trial results
- We need to collaborate to establish evidentiary value – use case by use case
  - Collaboration with DG Research, published call for the Horizon Europe Cluster 1 Health

What is DARWIN EU®

DARWIN EU - federated network of data, expertise and services – formal start January 2022

EU Medicines Regulatory Network

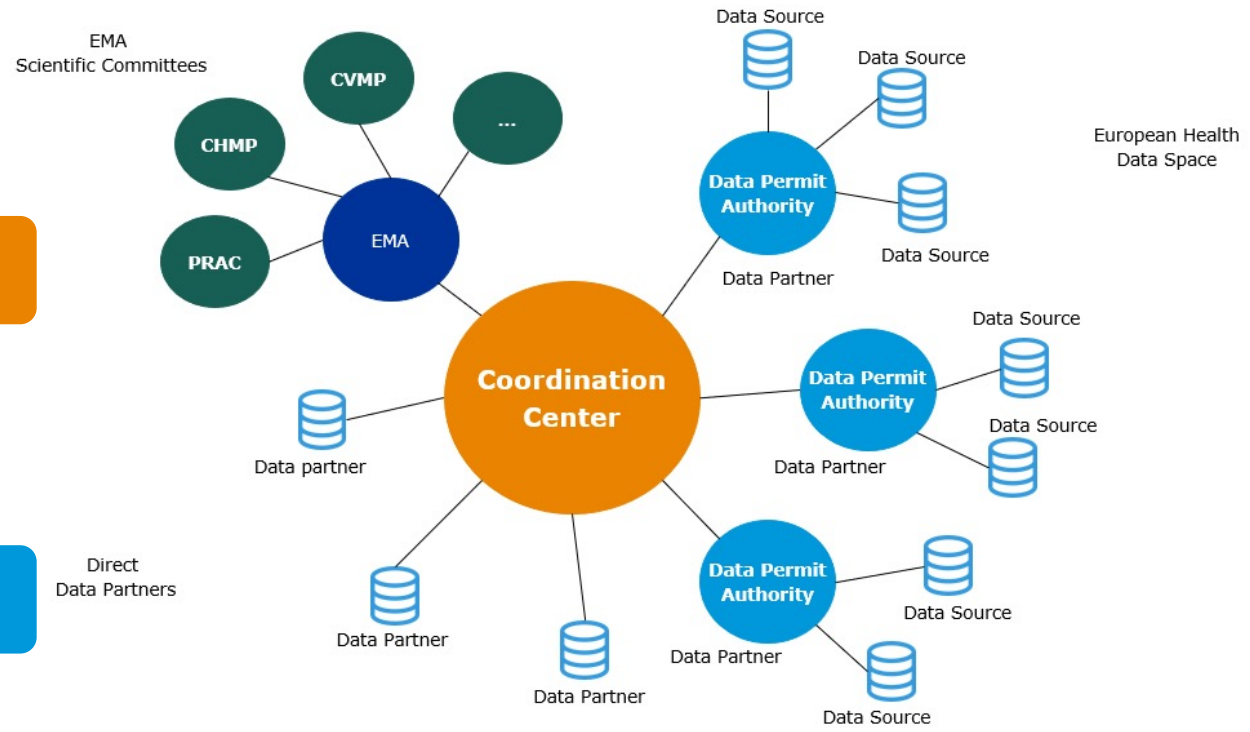
- **EMA** - provides leadership, setting standards, contracting studies,
- **EMRN -** including EMA scientific committees and working parties, national competent authorities (NCAs) and the European Commission: **request studies** via EMA

The Coordination Centre

- **Establishes** and **maintains the network** (including onboard/maintain data sources), manage the **execution of scientific studies**

Data Partners, incl. Data Permit Authorities

- **Partners** who have access to data, or who may request analyses in a data source and provide results to the Coordination Centre
- This includes **Data Permit Authorities** (DPAs), already existing or to be created as part for the EHDS

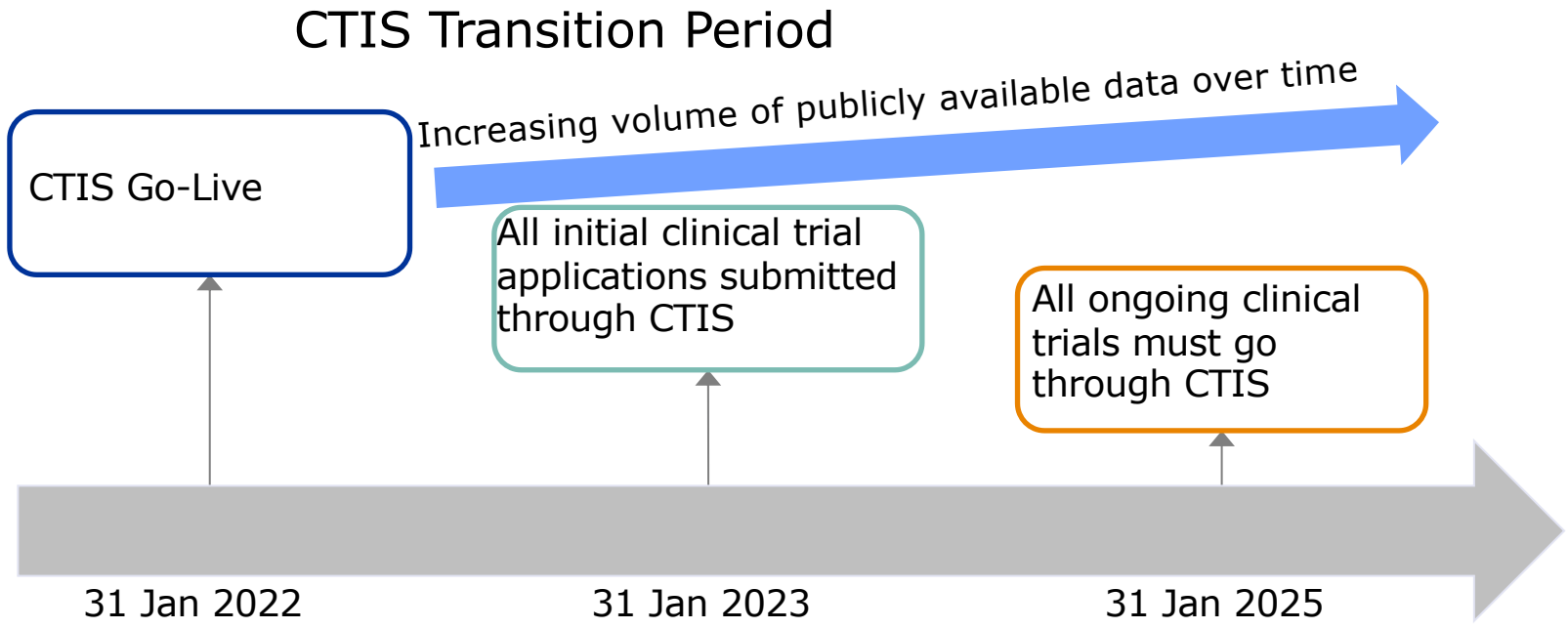


Clinical Trial Information System Go Live 31/1/21CTIS

The Clinical Trials Regulation will: **harmonise** Clinical trials and Research in the Union and will support large, multinational CTs.

CTIS will become the **single entry point** for clinical trial submission, authorisation and supervision in the EU and the EEA.

CTIS is the business tool of the **Clinical Trials Regulation**. It includes **Authority and Sponsor workspaces** and **public search functionality**.



New in 2022: EMA Methodologies Working Party + guidance gaps filled

- New methodologies working party to being together different expertise (biostats, pharmacoepidemiology, modelling etc.)
- Will support:
  - EU innovation in global drug development
  - Advice and interpretation of complex clinical trials
  - Patients through better evidence

- CTEG Question & Answer on decentralised trials
- CTEG Question & Answer on complex clinical trials
- EMA Reflection Paper on single-arm trials
- Revision of EMA Guideline on Data Monitoring Committees
- EMA Guideline on registry-based studies | European Medicines Agency (europa.eu)
- (i) Metadata for Data Discoverability and Study Replicability and (ii) Data Quality Framework
- International collaboration on Real World Evidence

Key messages

- Transformation to data-driven regulation to deliver the Network Strategy to 2025
- Ambitious work programme to deliver the change
- Delivery through collaboration: role for all stakeholders
- Patient focussed – in every thing we do

"By delivering the vision of a regulatory system able to integrate data into its assessment and decision making, we can support the development of innovated medicines, deliver life-saving treatments to patients more quickly and optimise the safe and effective use of medicines on the market."

Welcome & Introduction

Moderator of the day:

Mireille Muller (Novartis, EFPIA)

Multi-stakeholder workshop 5 - 6 October 2021

Day 1: 5 october 2021

14:00

Welcome & Introduction
Sini Eskola (EFPIA)
Jan Geissler (Patvocates)

14:10

SESSION 1
Setting the scene & Sharing experience – CTA approval
Anja Schiel (EMA SAWP, NoMA)

- 5' **Introduction**
  Anja Schiel (EMA SAWP, NoMA)
- 15' **CTFG experience of CCTs**
  Elke Stahl (CTFG, BfArM)
- 15' **US pilot feedback - FDA's experience so far**
  Dionne Price (FDA)
- 15' **CTTI, European initiatives, IMI EU Pearl**
  Solange Corriol-Rohou (AstraZeneca, EFPIA)

15:00

SESSION 2
Stakeholders' priorities & expectations
Claas Röhl (NF Patients United)

- 10' **Patients**
  Dominique Hamerlijnck (EUPATI)
- 10' **Regulators - EU & beyond**
  Anthony Humphreys (EMA)
- 10' **Ethics Committees**
  Martin Brunner (Ethics Committee, AT)
- 10' **HTA bodies**
  Niklas Hedberg (TLV SE, EUnetHTA)
- 10' **Sponsors: Industry, Academia & non-profit organisations**
  Lucia D'Apote (Amgen, EFPIA)
- 10' **Investigators**
  Birgit Geoerger (Gustave Roussy Institute, FR)
- 25' **Panel discussion**

16:25 Coffee break

16:45

Breakout Sessions

1. **Design of Master Protocols**
   Christine Fletcher (GSK, EFPIA)
   Lada Leyens (Roche, EFPIA)
2. **Regulatory processes and system**
   Anja Schiel (EMA SAWP, NoMA)
   Lucia D'Apote (Amgen, EFPIA)
3. **Patient involvement**
   Claas Röhl (NF Patients United, AT)
   Solange Corriol-Rohou(AZ, EFPIA)

18:45

Concluding remarks
Christine Fletcher (GSK, EFPIA)
Mireille Muller (Novartis, EFPIA)
Anja Schiel (EMA SAWP, NoMA)

19:00 End of Day 1

Day 2: 6 october 2021

14:00

Introduction to Day 2
Sini Eskola (EFPIA)
Peter Arlett (EMA)

14:10

SESSION 1
Feedback from Day 1 Breakout Sessions
Breakout Sessions Chairs

14:40

SESSION 2 - Breakout Sessions

4. **Trials incorporating historical controls or with adaptative features**
   Christine Fletcher (GSK, EFPIA)
   Frank Bretz (Novartis, EFPIA)
5. **Operation & implementation**
   Olga Kholmanskikh (CTFG, FAMHP)
   Josse R. Thomas (Ethics Committee, BE)
6. **Education & Training**
   Begonya Nafria Escalera (eYPAGnet, ES)
   Mireille Muller (Novartis, EFPIA)

16:40 Coffee break

16:50

Feedback from Day 2 Breakout Sessions
Breakout Sessions Chairs

17:20

Panel session to discuss main outputs & propose next steps/action plan
Anja Schiel (EMA SAWP, NoMA)
Nick Sykes (Pfizer, EFPIA)

EU Commission
Kristof Bonnarens
(EC DG SANTE)

FDA
Dionne Price (FDA)

CTFG
Elke Stahl
(CTFG Co-Chair, BfArM)

Ethics Committees
Josse R. Thomas
(Ethics Committee, BE)

Patient representatives
Rita Magenheim (GENTURIS)

HTA bodies
Niklas Hedberg
(SE TUV, EunetHTA)

Industry
Christine Fletcher
(GSK, EFPIA)

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(EORTC)

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Concluding remarks
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Mireille Muller (Novartis, EFPIA)
Anja Schiel (EMA SAWP, NoMA)

18:30 End of Day 1

Multi-stakeholder workshop

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List of speakers

- **Peter Arlett**
  Head of Data Analytics and Methods Task Force, EMA
- **Kristof Bonnarens**
  European Commission, DG SANTE
- **Frank Bretz**
  Novartis - EFPIA
- **Martine Brunner**
  Ethics Committee, AT
- **Solange Corriol-Rohou**
  AstraZeneca - EFPIA
- **Lucia D'Apote**
  Amgen - EFPIA
- **Sini Eskola**
  EFPIA secretariat
- **Christine Fletcher**
  GSK -EFPIA
- **Jan Geissler**
  Patvocates
- **Birgit Geoerger**
  Gustave Roussy Institute, France
- **Dominique Hamerlijnck**
  EUPATI
- **Niklas Hedberg**
  SE TUV, EunetHTA
- **Antony Humphreys**
  Head Regulatory Science Strategy Task Force, EMA
- **Olga Kholmanskikh**
  CTFG - FAMHP
- **Stephane Lejeune**
  EORTC
- **Lada Leyens**
  Roche - EFPIA
- **Rita Magenheim**
  ePAG- GENTURIS
- **Mireille Muller**
  Novartis - EFPIA
- **Begonya Nafria Escalera**
  eYPAGnet, SE
- **Dionne Price**
  Director, Division of Biometrics IV, CDER, FDA
- **Claas Röhl**
  NF Patients United, AT
- **Anja Schiel**
  Chair EMA SAWP, NoMA
- **Elke Stahl**
  CTFG Co-Chair - BfArM
- **Nick Sykes**
  Pfizer-EFPIA
- **Josse R. Thomas**
  Ethics Committee, BE

Join our **Q&A** at

Slido.com
#867 213

Direct link to our Q&A:
https://app.sli.do/event/htnou5aw

You can scan the QR-code with your mobile device
for direct access to the Q&A

Multi-stakeholder workshop 5 - 6 October 2021

Day 2
6 October
2021

14:00

Introduction to Day 2

Sini Eskola (EFPIA)
Peter Arlett (EMA)

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Feedback from Day 1 Breakout sessions

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Breakout Sessions

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Day 2
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Day 2
6 October
2021

SESSION 2
Breakout Sessions

4 **Trials incorporating historical controls or with adaptative features**

Chairs: Christine Fletcher (GSK, EFPIA)
Frank Bretz (Novartis, EFPIA)

5 **Operation & implementation**

Chairs: Olga Kholmanskikh (CTFG, FAMHP)
Josse R. Thomas (Ethics Committee, BE)

6 **Education & Training**

Chairs: Begonya Nafria Escalera (eYPAGnet, ES)
Mireille Muller (Novartis, EFPIA)

Day 2
6 October 2021

Breakout session 4

Trials incorporating historical controls or with adaptive features

Multi-stakeholder workshop
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Chairs:
Christine Fletcher (GSK, EFPIA)
Frank Bretz (Novartis, EFPIA)

This session highlights two case studies of complex innovative clinical trials that incorporate historical control data or have adaptive features. The first case study illustrates the borrowing of information from external data sources in a randomized pediatric trial in multiple sclerosis. The second case study uses a complex Bayesian adaptive design to explore dose ranging and generate safety and efficacy evidence. The discussion focuses on key questions allowing different stakeholder views to be shared, with the objective to foster the use of such clinical trials designs.

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Breakout session 5

Operation & Implementation

Multi-stakeholder workshop
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Chairs:

Olga Kholmanskikh (CTFG, FAMHP)

Josse R. Thomas (Ethics Committee, BE)

Complex innovative trial designs require much more upfront planning, anticipation, strong communication and flexible problem-solving approaches across multiple stakeholders. This session will discuss each of the steps: planning, implementation, execution and oversight of complex clinical to identify the most important challenges in the implementation of complex innovative clinical trials. Aspects such as collaboration vs. competition, use of common templates and governance will be discussed to elaborate best practices and recommendations.

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Breakout session 6
Education & Training

Multi-stakeholder workshop
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Chairs:

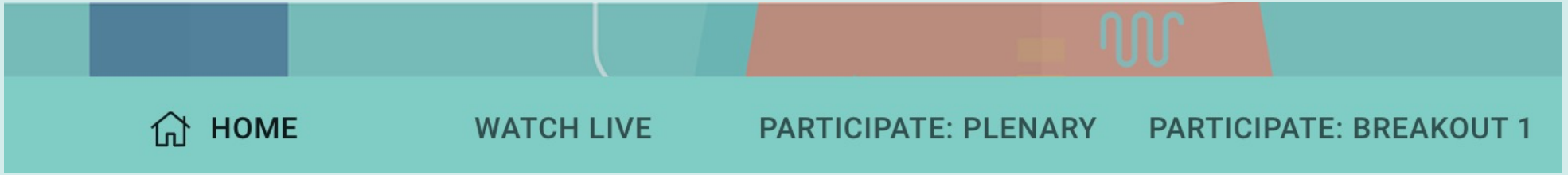
Begonya Nafria Escalera (eYPAGnet, ES)
Mireille Muller (Novartis, EFPIA)

Having patients, regulators and HTA bodies, ethic committees, investigators and sponsors sufficiently familiarized with complex innovative clinical trials is essential for a healthy clinical research environment. This breakout session will provide a status update on available education and training material and identify training gaps regarding complex clinical trials. The session will help to assess the most pressing educational needs for the various stakeholders and start brainstorming on best suited organisations to provide such training and develop the necessary material/guidance.

How to go to the breakout session?

As a viewer

Click on the “home” and “Watch Live” respectively in the navigation and find the breakout session you want to follow and click on “Live”.



As an active participant

If you have been selected as an active participant, you will see the link e.g. ”Participate: Breakout 1” in the navigation of the webinar platform. Open the link and click “Live”. This will invite you to a zoom-session.


Coffee
break

Multi-stakeholder workshop

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Feedback from Day 2 Breakout Sessions

Breakout Sessions Chairs

Chairs: Christine Fletcher (GSK, EFPIA)
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Chairs: Begonya Nafria Escalera (eYPAGnet, ES)
Mireille Muller* (Novartis, EFPIA)

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2021

Breakout session feedback

BO4 Trials incorporating historical controls or with adaptive features

EMA Patients United · efpia European Federation of Pharmaceutical Industries and Associations · BARC · PPD · Norwegian Medicines Agency

Key outcomes

1. *Agencies open for discussion for new designs, including incorporation of historical data (or RWD) BUT lot of discussion about management of Type I error, meaning of this in Bayesian context...*
2. *Sources of data need to be assessed in view of the question*
3. *Good practice: look at the question first, then look at the available sources of data and last define the global design and approach*
4. *Need to draw the line between advice, collaborative discussion between regulators and sponsors and approval activities ("there is no pre-approval")*

Potential solutions/call for action

- Interest for learning together from both sides
- Opportunity for a platform to share experiences, maybe not only on a product basis
- Value the good practice: Have the question first, and then have a multistakeholder discussion in order to better address the question. Explain clearly why you are proposing a given approach rather than the "traditional" approach (eg RCT...)
- Ensuring data sharing to avoid unnecessary burden, to improve education, training and re-use of data.
- Need to improve Drug Development using innovation, not only in paediatrics or rare disease area

Breakout Session #5
Implementation & Operational aspects

Chairs: Olga Kholmanskikh (CTFG, FAMHP), Josse Thomas (BAREC)

EFPIA European Federation of Pharmaceutical Industries and Associations

Norwegian Medicines Agency

Three main topics discussed

- Collaborative, competitive and mixed approaches for planning, conducting and reporting of CCTs
- Practical aspects and solutions to transform challenges to opportunities
- Best practices sharing: the way forward

Examples

- **EU PEARL**
  - Build standard templates
  - Integrated Research Platforms
  - Used for multiple disease settings eg: Depression, TB, NASH , Neurofibromatosis, Multiple Sclerosis
    - A proxy for building new projects

- **STAMPEDE**

  A platform for multiple treatments in PC
  - 7 Pharmaceutical companies
  - 15 years – 5 changes of std of care, handle carefully, plan ahead
  - Work backwards – coordinate with the sites

- **RECOVERY**

Key Topics

- CI responsibilities – Huge and massive
  - Consider Dividing out responsibilities
- Simultaneous and Sequential tasks
  - Flexible staffing – Core and Flex
  - Bigger teams – need more team management
- Laying the foundation - Help mitigate the burden
  - Build standard templates ,
  - Clin Ops best practice tools and checklist
  - Structured Cover letters, Tracking amendments to MP and Intervention specifics
  - Integrated Research Platforms
  - Built for any disease – Depression, TB, NASH , Neurofibromatosis
    - A proxy for building new projects
  - Legal concepts – Liability – CT agreements
  - IP protection

Feed Back

- Planning Setup
  - Acknowledgement of increased challenges with multiple sub-studies/subprotocols
  - Design include the Why and How questions for communication
- Conduct/execution
  - Mitigate challenges through planning
  - Templates for protocols, communication between stakeholders
  - Anticipation of amendments
- Oversight
  - Consideration of the governance – particularly with multiple assets
  - Understanding between partners, multiple companies
  - Sponsor vs multiple Sponsor (Co-Sponsorship – CTR)
- Recommendations
  - Shared mindsets to all collaborators
  - Real time access to information

Breakout session feedback

BO session 6

Education and Training

EUPATI Patients United · efpia European Federation of Pharmaceutical Industries and Associations · BARC · PPD · Norwegian Medicines Agency

Key outcomes

1. *Complexity of trial is increasing and the need of training is always higher*
2. *Useful material already available but limited to closed communities. Experience sharing and common template helped to streamline and optimize the implementation and operations of complex clinical trials*

→ Whose responsability is it to organise, update and share the learnings/trainings with all key players?

3. *Take time to build 'center of excellence' and to establish the necessary connexions between all the stakeholders*
4. *Importance of the involvement of patient experts at each steps and at each level, especially at a national level*
5. *Need to raise the barriers of education, especially the funding*

Potential solutions/call for action

- Need to develop efficient knowledge sharing platforms (eg peer coaching, discussion groups) between all the key players to share the learnings
- Need to develop trainings with all key players but accessible to everyone (e.g. without languages, exposure or financial barriers)
- Need modular training for CCTs, treating general aspects, as well as targeted training towards specific subgroups of members
- Need to include trainings in the curriculum of medical staff and ensure the access to the appropriate courses

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Thank you