Breakout session Education & Training

Chairs: Begonya Nafria Escalera & Mireille Muller

Education & Training

EFPIA European Federation of Pharmaceutical Industries and Associations

Norwegian Medicines Agency

Day 2
6 October 2021

Breakout session 6
Education & Training

Multi-stakeholder workshop
5 - 6 October 2021

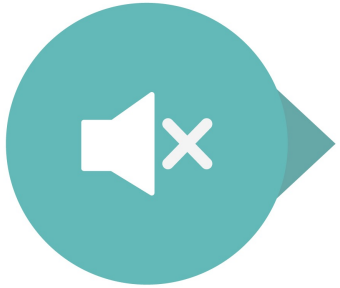
Chairs:

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.

House-keeping rules

(For active participants in the Zoom call)



- Mute your sound and video when not speaking

- Flag your intention to take the floor by raising your hand or by inputting your name into the Zoom-chat

- Introduce yourself (name, company, role) when taking the floor

Join our Q&A and online polls at

Slido.com
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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

Agenda

- Setting the scene
- Brief “tour de table”:
  - Patients
  - Regulators
  - Ethic Committees
  - Health Technology Assessment (HTA) Bodies
  - Investigators
  - Sponsors
- Workshop questions
- Final thoughts/wrap up

Education and Training

Accelerating Adoption of Complex Clinical Trials in Europe and beyond

Ethics Committee workshops

- Complex adaptive design trials increasingly
- Platform trials allow new research questions to be incorporated into an ongoing clinical trial protocol in structured way
- More efficient than opening new, separate trial
- UK Health Research Authority = ally to implementation of new and efficient designs.
- Few UK Research Ethics Committees exposed to platform protocols
- Therefore, HRA invited us to run 60--90 minutes workshops on adding a comparison to an ongoing platform trial protocol at 5 regional training meetings

Leicester (Sep-2019)

York (Oct-2019)

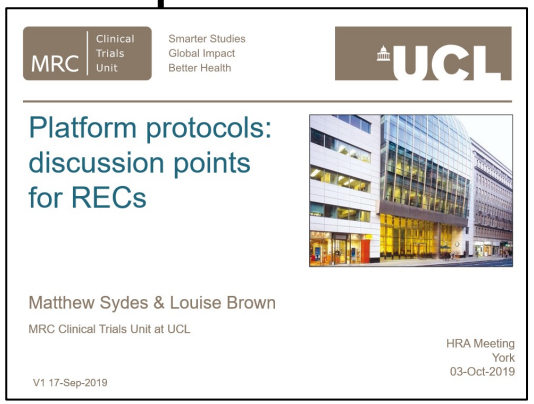
Oxford (Oct-2020)

London (Feb-2020)

Manchester (Mar-2020)

Ethics Committee workshops

- Workshops involved:
  - presentations on benefits & challenges of adding comparisons into ongoing protocols
  - Guided group discussions on issues specific to ethics review
- Training session attendees included some members of RECs who had reviewed a number of these platform protocols on previous occasions


MRC Clinical Trials Unit
Smarter Studies
Global Impact
Better Health
UCL

Platform protocols: discussion points for RECs

Matthew Sydes & Louise Brown

MRC Clinical Trials Unit at UCL

HRA Meeting
York
03-Oct-2019

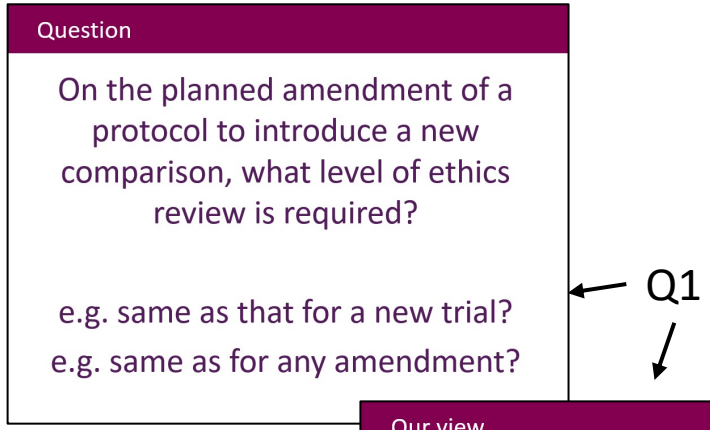
V1 17-Sep-2019


Question

What important aspects about these trials that you would like to have discussed?

Feedback for future meetings

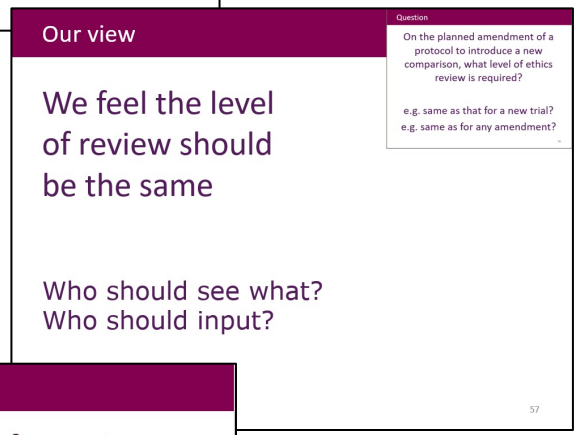
Q3


Question

On the planned amendment of a protocol to introduce a new comparison, what level of ethics review is required?

e.g. same as that for a new trial?
e.g. same as for any amendment?

Q1


Our view

We feel the level of review should be the same

Who should see what?
Who should input?

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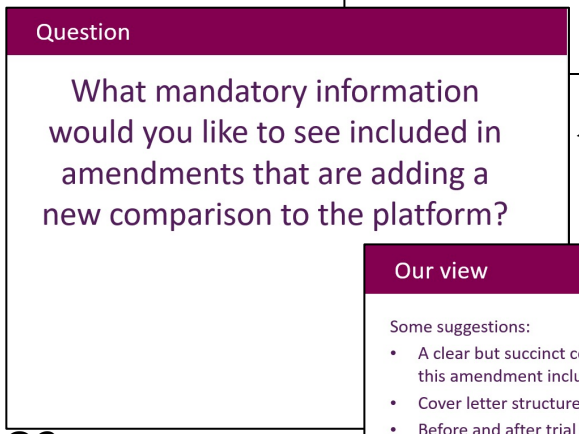
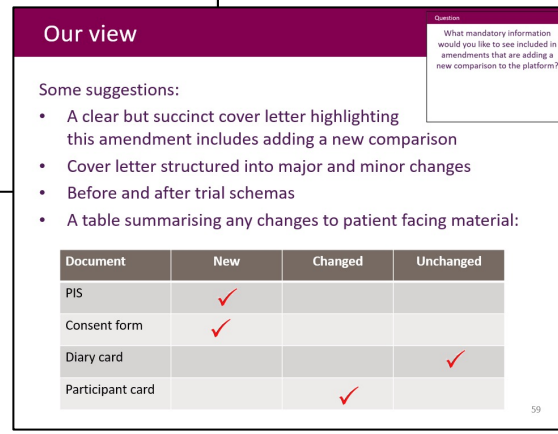
57


Question

What mandatory information would you like to see included in amendments that are adding a new comparison to the platform?

Q2


Our view

Some suggestions:

- A clear but succinct cover letter highlighting this amendment includes adding a new comparison
- Cover letter structured into major and minor changes
- Before and after trial schemas
- A table summarising any changes to patient facing material:

Document	New	Changed	Unchanged
PIS	✓		
Consent form	✓		
Diary card			✓
Participant card		✓	

Question
What mandatory information would you like to see included in amendments that are adding a new comparison to the platform?

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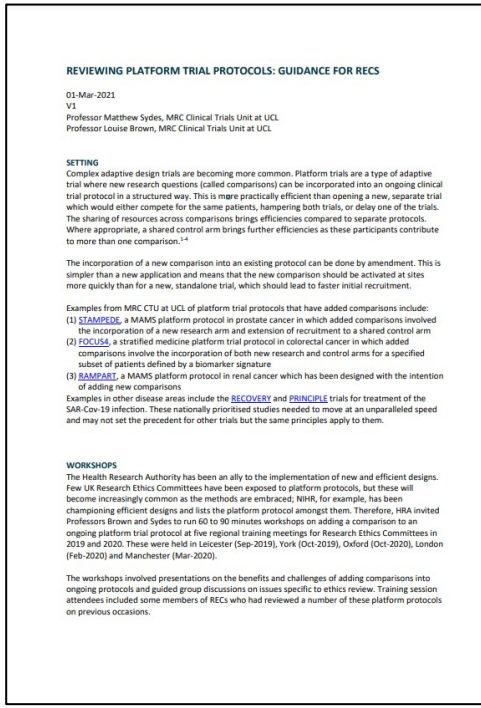
Ethics Committee workshops

Recommendations

- Initial Level of Review for Platform Trial Protocols
  - Trials that may add comparisons in future should explicitly flag this in protocol & on application forms at initial submission
- Level of Review for Amendment to Platform Trial
  - For more common reasons for protocol amendments, usual amendment route should suffice
  - When adding new comparison, triage amendment application to determine level of review REC feels is appropriate
  - eg if design & aims have not changed demonstrably, REC may prefer more limited review; otherwise, REC may prefer fuller review
- Information Required at Amendment to Support Triage
  - Should be clear what changes in amendment arise from addition of new comparison and what changes from other reasons



REVIEWING PLATFORM TRIAL PROTOCOLS: GUIDANCE FOR RECS

01-Mar-2021
V1
Professor Matthew Sydes, MRC Clinical Trials Unit at UCL
Professor Louise Brown, MRC Clinical Trials Unit at UCL

SETTING

Complex adaptive design trials are becoming more common. Platform trials are a type of adaptive trial where new research questions (called comparisons) can be incorporated into an ongoing clinical trial protocol in a structured way. This is more practically efficient than opening a new, separate trial which would either compete for the same patients, hampering both trials, or delay one of the trials. The sharing of resources across comparisons brings efficiencies compared to separate protocols. Where appropriate, a shared control arm brings further efficiencies as these participants contribute to more than one comparison.[1-4]

The incorporation of a new comparison into an existing protocol can be done by amendment. This is simpler than a new application and means that the new comparison should be activated at sites more quickly than for a new, standalone trial, which should lead to faster initial recruitment.

Examples from MRC CTU at UCL of platform trial protocols that have added comparisons include:
(1) STAMPEDE, a MAMS platform protocol in prostate cancer in which added comparisons involved the incorporation of a new research arm and extension of recruitment to a shared control arm
(2) FOCUS4, a stratified medicine platform trial protocol in colorectal cancer in which added comparisons involve the incorporation of both new research and control arms for a specified subset of patients defined by a biomarker signature
(3) RAMPART, a MAMS platform protocol in renal cancer which has been designed with the intention of adding new comparisons
Examples in other disease areas include the RECOVERY and PRINCIPLE trials for treatment of the SAR-Cov-19 infection. These nationally prioritised studies needed to move at an unparalleled speed and may not set the precedent for other trials but the same principles apply to them.

WORKSHOPS

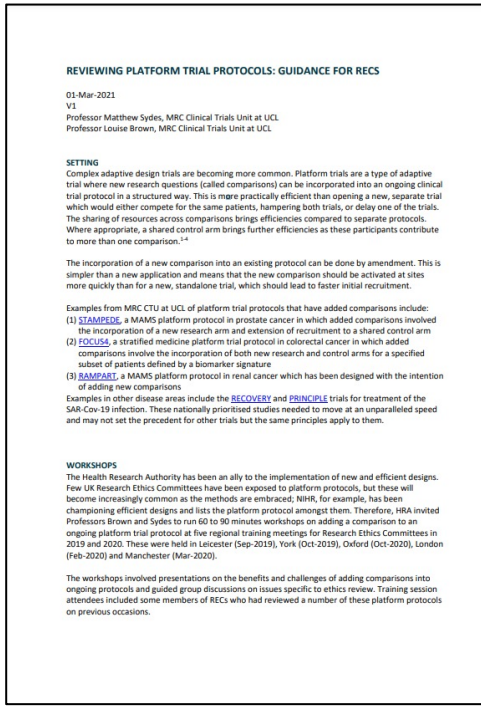
The Health Research Authority has been an ally to the implementation of new and efficient designs. Few UK Research Ethics Committees have been exposed to platform protocols, but these will become increasingly common as the methods are embraced; NIHR, for example, has been championing efficient designs and lists the platform protocol amongst them. Therefore, HRA invited Professors Brown and Sydes to run 60 to 90 minutes workshops on adding a comparison to an ongoing platform trial protocol at five regional training meetings for Research Ethics Committees in 2019 and 2020. These were held in Leicester (Sep-2019), York (Oct-2019), Oxford (Oct-2020), London (Feb-2020) and Manchester (Mar-2020).

The workshops involved presentations on the benefits and challenges of adding comparisons into ongoing protocols and guided group discussions on issues specific to ethics review. Training session attendees included some members of RECs who had reviewed a number of these platform protocols on previous occasions.

Short Report at www.ctu.mrc.ac.uk/media/1948/guidance_for_recs_2021-03-01_v1.pdf

Ethics Committee workshops

www.hra.nhs.uk/about-us/committees-and-services/res-and-recs/research-ethics-committee-standard-operating-procedures/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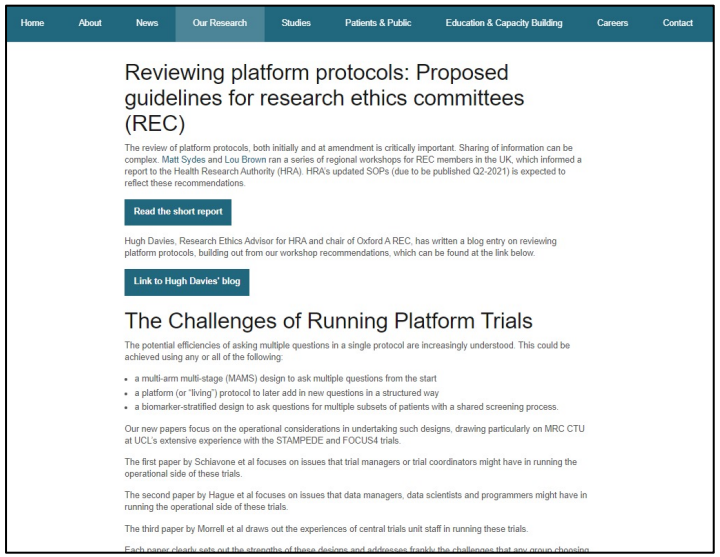
www.ctu.mrc.ac.uk/our-research/methodology/conduct/practical-implementation-of-new-trial-designs/



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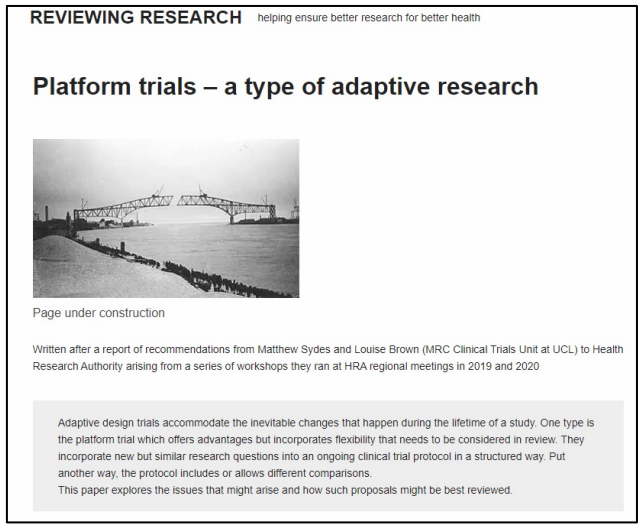
http://www.reviewingresearch.com/platform-trials/



Setting the scene

- Why is education & training important?
  - It is important to all stakeholders
  - Blagden et al. note that training is one of their key recommendations:
    - *"the necessity to adapt the trial to emerging data and the inclusion of later-phase and site-specific cohorts means that CID trials require intense involvement from investigators. This requires a high level of PI and trial committee oversight, not only to review and assess their own patients but to participate in regular conference calls/communication with other centres and trial sponsors"*
  - Informed stakeholders are better equipped to become actors in the design, implementation, organization and assessment of complex clinical trials (CCTs)

Effective delivery of Complex Innovative Design (CID) cancer trials—A consensus statement (nature.com)

What is the current status?

- ↗ CCTs scientific publications
- ↗ specialised (inter-)national congresses or symposia
- Useful material available in the closed communities?
- Only limited information in the public domain

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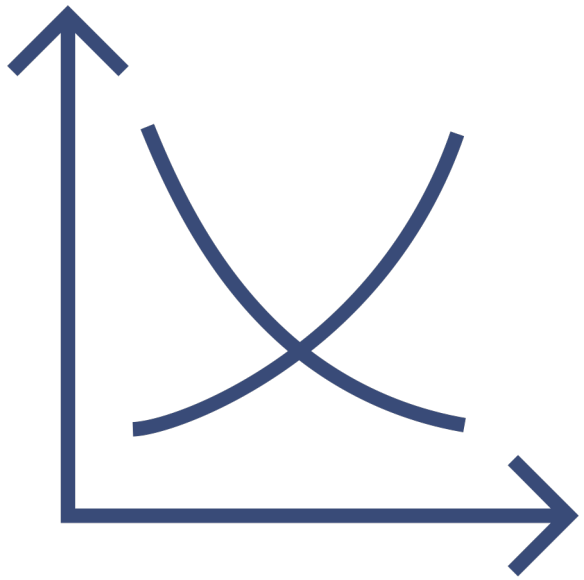
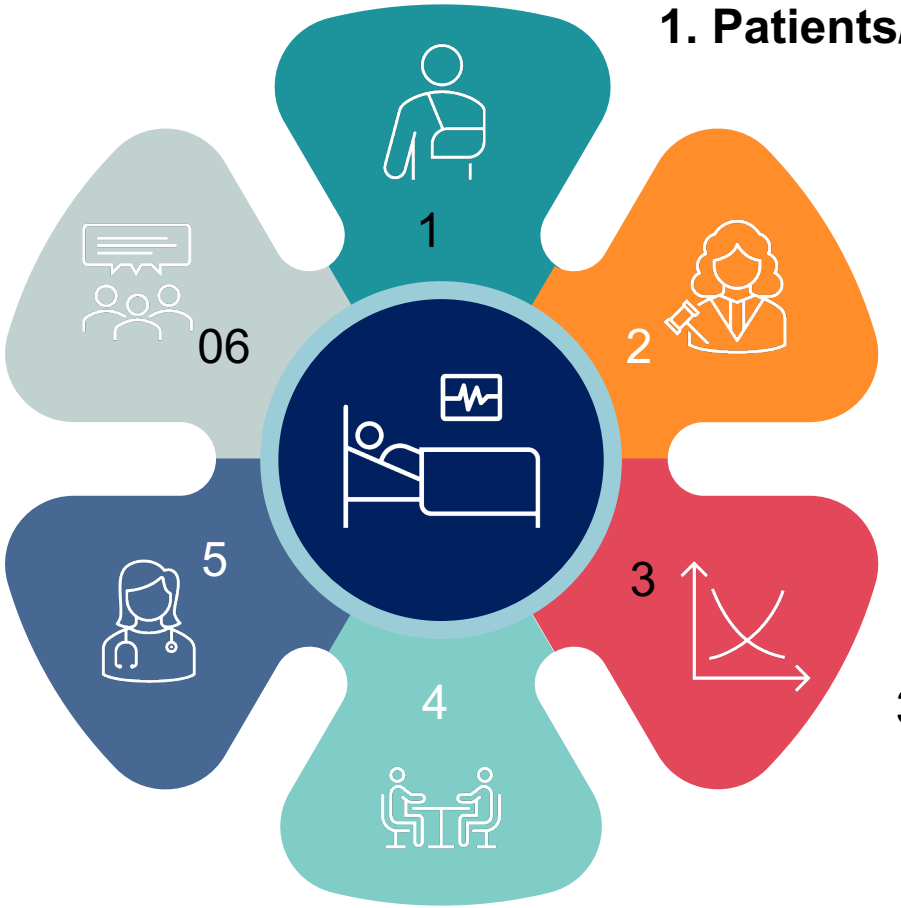
Huge gap between supply and demand



Let’s hear from the different parties



1. Patients/Caregivers

2. Regulators

3. HTA Bodies

4. Ethic Committees

5. Investigators & clinical staff

6. Sponsors

Question 1

- Where is there a need for more targeted education?
  - Is this sufficient for e.g., Patients, investigators, sponsors - what is still needed?
  - How difficult is it to find the right training?
  - How useful is the training? What metrics could be used?
  - How did the training help during the specific task? Was it fit for purpose?

Patients

- EUPATI or EURORDIS ACADEMY are good sources for basic information on clinical research in general
  - Insufficient resources for complex clinical trials available
  - When specialised knowledge is required, then it is difficult for patients to cope with the cost of expert training
    - A luxury that patient advocates and patient organisations can not afford!
- Experienced patient advocates working at international level can locate the right training
  - More challenging for national patient advocates

Regulators

- Some regulators developed in-house trainings, others attend conferences or workshops
- In most HAs, structured training is not yet available
  - Awareness is there
  - Experience is gained
  - “Learning by doing”

Ethics Committees (EC) 1/2

- Training for ethic committees even more challenging due to the diversity in membership, educational and professional members' background
  - Compostion varies, clinical staff (physicians, nurses, technicians), clinical trial methodologists, biostatisticians, pharmacists, ethicists, legal advisors, patient and human volunteer representatives, etc.
  - Very diverse knowledge of clinical trials, and even more so of complex clinical trials
- Currently no specific training is available
  - Mainly self-study and learning by doing

Ethics Committee (EC) 2/2

- Would need modular training for CCTs, treating general aspects, as well as targeted training towards specific subgroups of members
  - General high-level training for all
  - Specialised training e.g., biostatistics training
  - Specific training for patients and human volunteers in lay terms
- Some national EC-organisations have started working on training
  - Willingness to participate in European initiative to create an online toolbox with training material on CCTs (“train the trainer”)

CCT: complex clinical trials
EC: ethics committe

Health Technology Bodies (HTA)

- Training mainly by attending workshops & conferences
  - Professional societies such as ISPOR a good source of information
- Might be insufficient for complex clinical trials
- Some HTAs have interactions with regulators on this topic
  - But interaction doesn’t mean alignment
  - Different assessment focus

Investigators & clinical staff

- Offers important opportunities for more junior researchers to learn about the delivery of clinical trials
- Inclusion into the curriculum of medical, nursing and pharmacology students would be desirable
- Ensuring access to appropriate continued or higher education on the topic
- Some governments have committed to programs to embed expert understanding on innovative trials

Sponsor

- Several sponsors have set up internal taskforces for the development of training on complex clinical trials and best practice sharing but it is *ad hoc* and not coordinated across different sponsors
- Although several sponsors actively participate in public private partnerships such as IMI or CTTI, these consortia do not appear to have a major focus on wide-scale education and training for CCTs. However, the set-up of these consortia do lend themselves to be in a good position to deliver an Education and Training programme that can be widely applicable
- Most commercial sponsor project teams should have sufficient access to subject matter experts in addition to general training
  - Peer coaching is also one avenue used especially for less frequently used designs
  - Training and coaching tend to be directed towards investigators and their staff who will be executing the trial
- Training and education tends to be specific for the trial to be conducted and, often, cannot be replicated across studies or between sponsors
- Experience sharing and common template helped to streamline and optimize the implementation and operations of complex clinical trials

Question 2

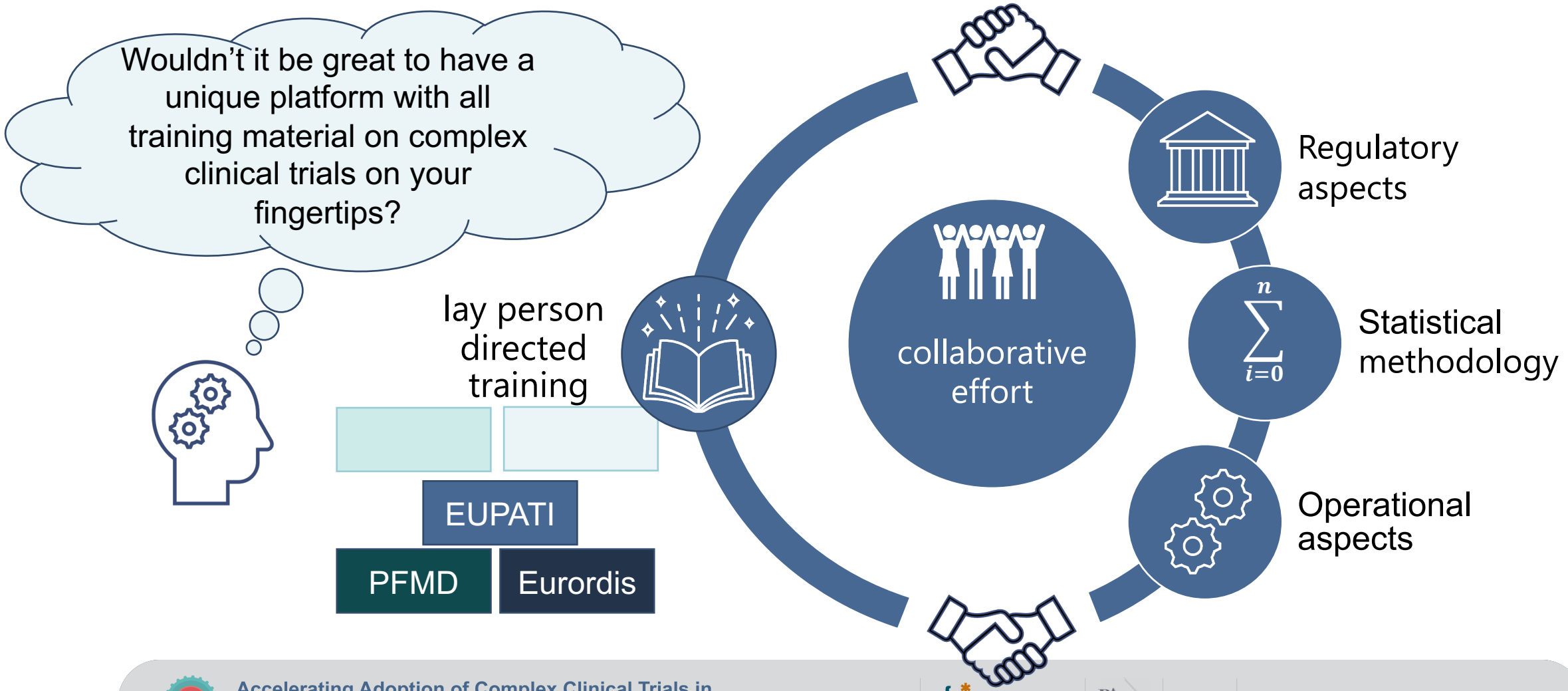
- Who has to provide education and training for each of the stakeholders? (source of guidance)
  - Maintenance, update and sustainability

- Interest and feasibility of an EU-wide or international initiative?
- If an EC-EMA-HMA initiative on CCTs would be launched, delivery of E&T material should be part of it.

Question 3

- How to achieve common messaging across all the different guidelines?

What would be the vision for the future?



Final thoughts

- ICH E20's role in training & education
  - Unclear if training material is foreseen and might at best only available end of 2024

Pre-reads

1. EUPATI: EUPATI Open Classroom: All courses
2. Conferences like DIA, EFSPI etc.:
3. Blagden et al. Effective delivery of Complex Innovative Design (CID) cancer trials—A consensus statement (nature.com)

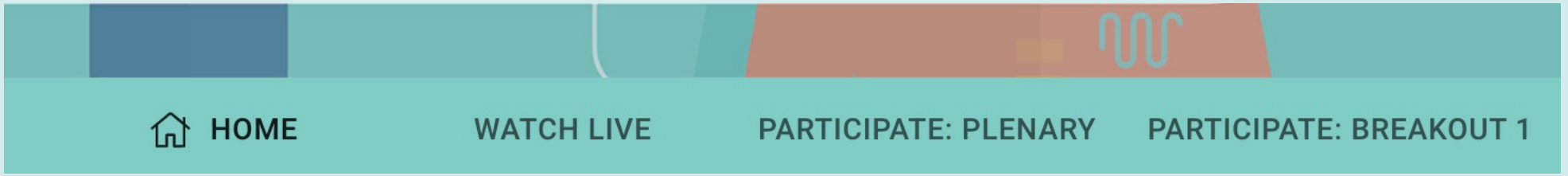
Topics for discussion

- Where is there a need for more targeted education?
  - Is currently available training sufficient for e.g., Patients, investigators, sponsors - what is still needed?
  - How difficult is it to find the right training?
  - How useful is the training? → would be metrics useful?
  - How did it help during the specific task? → Is available training fit for purpose?
- Who should provide education and training for each of the stakeholders? (source of guidance)
  - Who should ensure maintenance, updates and sustainability?
- How to achieve common messaging across the different guidelines?

How to go back to the plenary session?

As a viewer

Click on the “home” and “Watch Live” respectively in the navigation and find the continued plenary session and click on “Live”.



As an active participant

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