Network initiatives and activities to address critical and major issues reported by stakeholders regarding CTR implementation

Clinical Trials Coordination Group

Preparation of request for information (RFI) and strengthening the role of RMS

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ACT EU Multi-stakeholder Platform Advisory Group

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Topics

- ACT EU master list of issues
- Request for further information
  - Issues identified
  - CTCG activities to date
  - CTCG future plans
- Strengthening the role of the RMS
  - Issues identified
  - CTCG activities to date
  - CTCG future plans
- Questions/comments?

ACT EU: Master List of Issues – RFI and RMS

- Issues identified from feedback through different channels including MSP AG, CTAG (stakeholder survey) and CTR Collaborate were combined.
  - To facilitate finding solutions and identifying responsible bodies

Issues (RMS and RFI)	19	Priority
Critical	6	2 high priority
Major	2	
Minor	1	
Ungraded	10	

Request for further information (RFI)

RFI issues identified in the ACT EU Master list

Volume

- **Large number** of RFIs in Part I and especially of Part II (duplications and poor clarity)
- RFIs are **compilations of individual comments** rather than a consolidated set of key issues focused on priorities.
- **No triage** of RFI is leading to inconsistent challenges for the Sponsor.
- Need to simplify assessment and reduce number of considerations for **low-intervention trials**
- Sponsors **limit the number of MSs** included to reduce the number of Part II questions in particular.

Content

- A number of considerations are raised that are not considered critical matters - high number of **"nice-to-know" considerations**.
- MSCs have **different perception** on "nice-to-know" and "need-to-know" issues.
- **Additional work burden for RMS** arises from too many 'nice to know' considerations raised at assessment phase.
- Difficulty as RMS to **identify blocking issues from MSC**

Timelines

- **Deadlines are short for Sponsor** responses to major questions in RFI, and for assessment of RFI response.
- Perception that MS may respond negatively or with questions of limited value in order **to keep timelines**
- Inconsistent timelines for approval processes i.e. **early approval of Part II in anticipation of Part I is not advantageous**

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Issues identified RFI

- Key take-away:

High RFI volume: Too many uncoordinated and non-essential RFIs create delays and extra work for sponsors.

How can CTCG help?

Activities to date

- **CTR Collaborate stakeholder meeting** (11th September 2024)
  - 270 stakeholders
  - Discussion focused on:
    - Harmonisation within the EU CT Framework
    - ***New strategies for streamlining review and approval process***
    - Fostering innovation
    - Enhancing functionality of CTIS
  - Relevant actions:
    - Enhanced collaboration within and across member states
    - Joint development of best practices
    - Use of ART

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How can CTCG help?

Activities to date

- Increased use of **CTCG ART meetings: "Case studies”**
  - New initiative introduced in September 2024:
    - Aim: *To share learnings and experiences on the assessment of clinical trials between MSs to optimise the assessment process*.
  - MSs present on real cases to share best practice on assessment and examples of considerations raised
  - Clinical, statistics, quality, non-clinical topics, validation, ethics
  - Sessions recorded and can be used by MSs for training purposes

How can CTCG help?

Activities to date

- CTCG training sub-group have volunteered to participate in the **IncreaseNet JA: Work Package Training NCA**
  - Planned module: '*how to write a draft and final assessment report for a clinical trial application*'
    - Write an understandable and well-defined consideration
    - Distinguish between minor and major issues
    - Highlight critical issues to other MSCs
    - Explain what constitutes grounds for rejection/conditional approval
    - Develop clear and logical grounds for rejection/conditional approval

How can CTCG help?

Activities to date

- CTCG **workplan 2025**:
  - Participate in the ACT EU workplan 2025-2026:
    - Operation of the CTR – implementation of CTR.
    - Maximising impact of clinical trial design and conduct of excellent clinical trials
      - clinical trials methodologies
      - consolidated advice on clinical trials

How can CTCG help?

Activities to date

- CTCG External Best Practice Sub-group:
  - Assist EMA with sponsor queries
    - Aims to improve application process and reduce RFIs
  - Developing a FAQ document

- CTCG Best Practice Sub-group:
    - Continually updating existing and developing new Best Practice documents
      - Aims to increase harmonisation among MSs
    - Collaboration with MedEthicsEU started on Best Practice considerations
    - Ongoing work to disseminate information and monitor the use in practice

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How can CTCG help?

Activities to date

- CTCG Pre-CTA Advice and SAWP-CTCG Advice pilots:
  - To assist with the development of a high quality dossier to limit the number of considerations.

- CTCG participation in CTIS Bite size talks and walk-in clinics:
  - Support and guidance for sponsors to assist with clinical trial applications

How can CTCG help?

Future plans

- Continue with initiatives outlined
- Collaborate workshop March 21st for assessors (NCA and Ethics)
    - How to foster EU Attractiveness for CTs and the role of the MS (NCA and Ethics)
    - State of play CTR Collaborate: initiatives already ongoing
    - identify areas for improvement and next steps to put into actions
    - *Plan is to include a session on RFIs and on strengthening the role of RMS*

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Strengthening the role of the RMS

Role of RMS issues identified in the ACT EU Master list

Limited reliance

- **Reliance on Part I assessment** by the Reporting Member State (RMS), for both part I and part II review by MSs remains limited

Consolidation

- Role of RMS in **accepting/rejection** of Part I considerations, raising of considerations from EC, phrasing/content of considerations, trust in RMS from all other MSC.
- Clarity required for **role of RMS in consolidation** for both validation and assessment phase.

Workload

- The RMS does not have a **sustainable workload, unbalanced appointment** for being RMS.

Issues identified - Strengthening the role of the RMS

- Key take-away:

Ongoing work required to build trust in the RMS role and to adapt a risk-based approach when MSC

How can CTCG help?

Activities to date

- **CTCG plenary discussions:**

(September 2024)

- RMS selection procedure is based on the sponsor proposal, there is currently no possibility to automatically assign to willing MSC with lowest workshare
    - Should the RMS selection be based on fair workshare only?
- Group suggested discussing the RMS proposal issue with stakeholders to understand why they are only proposing certain MSs as RMS?
- Short-term solution: more MSs should express willingness when they can
    - Future discussions - transparency on MS workload e.g. develop a slot based system?

(February 2025)

- Suggestions to strengthen the role of the RMS:
    - A summary paragraph in AR (outline whether the b/r is positive)
    - Workshops per discipline on how to complete DAR templates
    - Work processes to be updated when MSC vs RMS

How can CTCG help?

Future plans

- **CTCG 2025 Work plan**
  - Lead the CTR collaborate project on effective procedures and to strengthen the role of the RMS for the assessment and supervision of clinical trials.
    - Collaborate workshop (21st March 2025)
      - *Enhancing the responsibilities of the Reporting Member State (RMS) in coordinating the review process, providing clearer guidance, and facilitating communication between involved parties.*

Questions? Comments?