Core Dossier: opportunities for increasing efficiency and future proofing the CT ecosystem in Europe

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What is the Core Dossier Model ?

- A proposal to optimize the clinical trial ecosystem in the EU by fostering efficiency and consistency in applying for trial approvals.
- A move towards a product development-based approach
- The model focuses on core information regarding an IMP that will be common across trials, including the Investigator Brochure (IB) and the IMP Dossier (IMPD) and associated quality documentation. This information would be cross-referenced to support regulatory activity.
- Extends the established concept of a safety assessing Member State (saMS) to quality assessing Member State (qaMS)
- The core dossier is kept updated throughout the lifecycle of the IMP. Changes or substantial modifications are enacted independently of a specific trial, and updates apply to all ongoing trials referencing that dossier, leading to more efficient regulatory management.
- European institutional knowledge of the IMP is better retained and increases with the development of the product

Principles: Reliance / Referral in the context of core dossier and CTs

Based on following principles:

- **Simplification** through **Harmonization** and **Trust**
- **Reliance** "*if the scientific documentation is approved by one MS, the assessment should be totally or partially relied upon by another MS*"
- **Harmonization**: Need to agree on common (binding) requirements limiting and eliminating the current national flexibility for requirements beyond the CTR.
  - Use concept of saMS for quality documents: quality assessing Member State (qaMS)
- **Efficiency**: Avoid re-submission and re-assessment of already submitted / approved documents revise CTIS+ to create a central repository of trial documents; opportunity to cross-refer to earlier approved documents.

Cross-referencing IMPDs within the current system

- **Does not minimize burden:** requires full overlap between the concerned MS and trial duration between the two trials. In case the referenced trial ends early, a new trial to be referenced is required or the product specific documents and data have to be added via SM, causing unnecessary burden to both sponsor and RMS.
- **Does not lead to reliance***: Even when reference is made to an approved IMPD and the dossier is submitted for a new trial (with non-overlapping MS) new questions arise.
- **Does not enable R&D life cycle management**: submission is done/stored per study, instead of per IMP.

*e.g. there are examples where an RMS1 reviewed the Draft Assessment Report (DAR) issued by a previous RMS for a different trial and endorsed their assessment and had no additional questions. However, RMS1 raised the questions raised by the previous RMS and expected the sponsor to provide the same responses. Additionally, the MSCs raised new questions to answer!

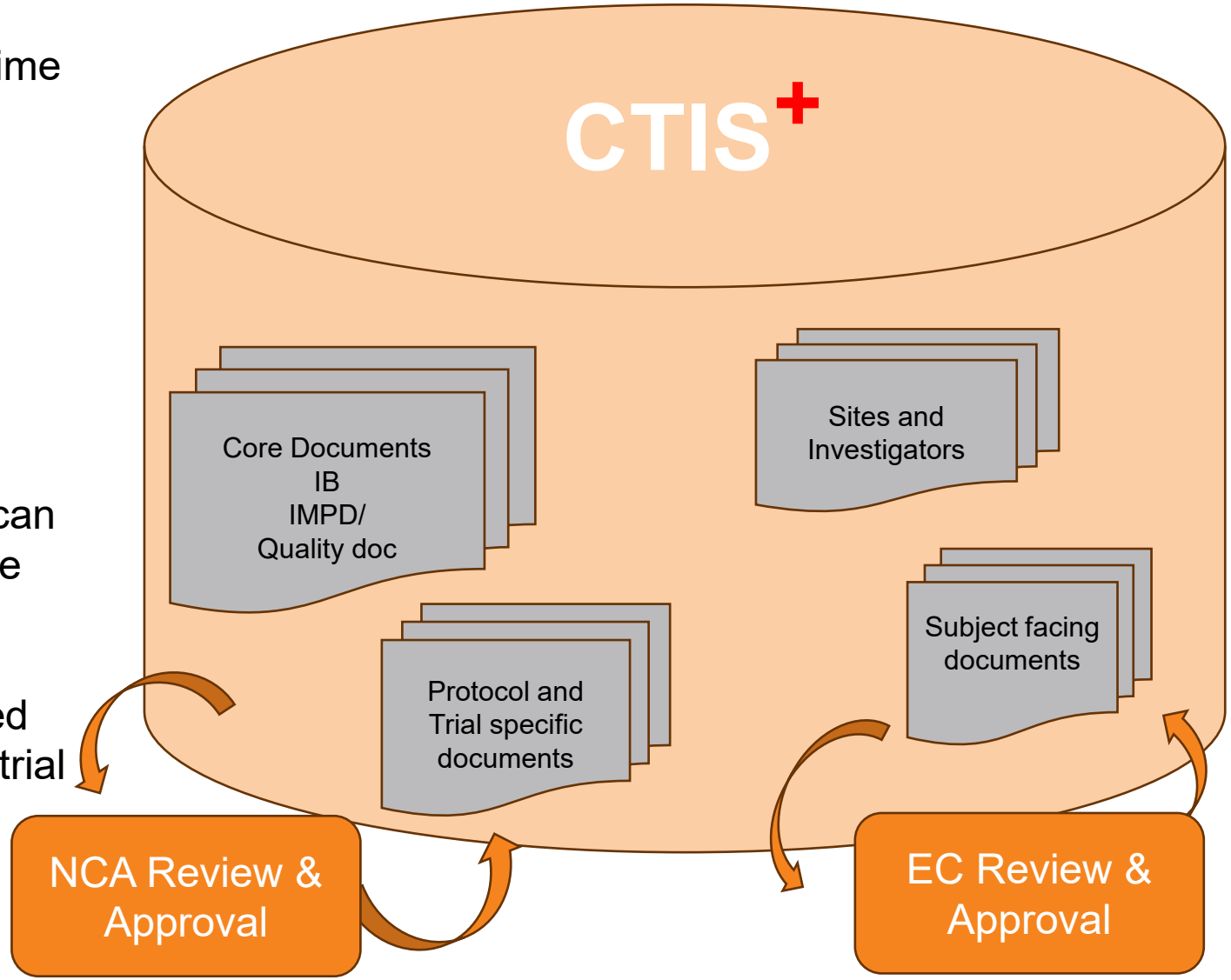
How it could work in practice: Central Clinical Trial Database

Complete set of trial documents submitted at the time of the first trial of an IMP:

- Protocol / trial specific documents
- Core Documents (IB, IMPD and GMP / Quality docs)
- Ethics documents (ICFs, contracts)
- Investigator details*

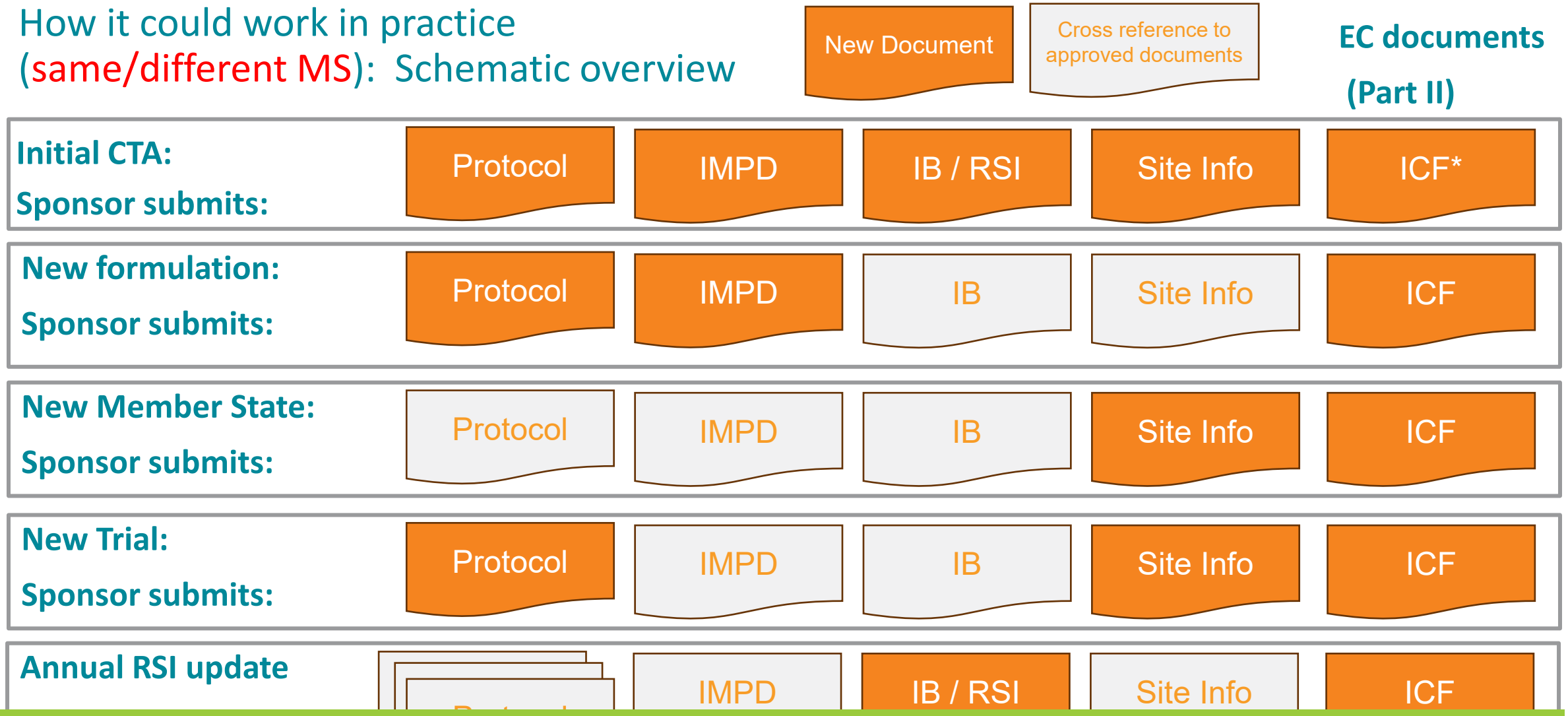
Stored in individual database spaces allows cross referencing. Alternatively, another EMA database can be used. Multiple trials** can refer to the same core information

Addition of new elements e.g. new protocol; revised IB/ RSI, new Member States /sites etc. during the trial conduct allows **parallel evaluation** (if required).



*Cross EU db available for all sponsors
**Incl. Investigator Initiated Studies

How it could work in practice (same/different MS): Schematic overview



The core dossier concept addresses addition of MS and subsequent trials with non-overlapping CMS – the scientific assessment remains valid, and no re-assessment is required

Initial analysis of implications on CTR text and systems

Important considerations and articles, but no apparent major blocks:

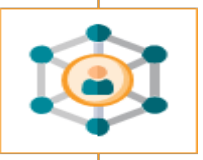
- Single portal for submission: Article 5(1)
- Reliance: Art 4 (EC also review Part I), Art 6 (all cMS jointly review), art 14 (additional MS may disagree). saMS implementing act could be replicated for quality documents.
- Substantial Modifications: art 2(2)13 and Q&A Q3.5 (definition refers to decision on previous modification). No provision for SM for core dossiers, but also no block.
- CTIS: need to change business rules that block submission if another SM is ongoing

current text does not prevent sponsors being able to submit under a core dossier model. Smaller adjustment may be needed. Challenge may be in CTIS business rules.

Enabling the Core Dossier Model

- Define “core dossier” (IMPD, GMP, IB, RSI) as reusable across trials/modifications
- Establish central repository in CTIS for core dossier storage and referencing
- Update CTR & CTIS guidance to enable parallel submissions using core dossier
- Make reliance/referral mechanism default; objections only on major safety/legal concerns
- Enable lifecycle management: approved modifications auto-apply to linked trials
- Introduce qaMS model for quality docs, harmonizing assessments across MS
- Provide user guidance, templates, and training for core dossier implementation

Positive impact for all stakeholders



- **Patients:** Potential for faster access to innovative treatments through more efficient trial approval processes, reducing delays in drug development.
- **Trial Sponsors:** Reduced administrative workload and improved efficiency in managing trial submissions and approvals. Makes it easier for Academic sponsors to cross refer to product information.
- **Regulatory Authorities:** Authorization processes more streamlined, more effective resource allocation and oversight. Can leverage the already established saMS concept and use for quality assessment (qaMS). Enables a life-cycle approach to IMPs and centralises document / knowledge management
- **Clinical Trial Sites :** A standardized submission process simplifies protocol approvals and operational logistics, facilitating trial commencement.
    - **Enables more harmonised global submission process and increases the attractiveness of EU/EEA as a trial destination by enabling "better, faster, smarter clinical trials"**

Questions for discussion

- Would you be supportive of this proposal, or a version of it?
- Do you foresee any major roadblocks?
- Do you agree with the potential positive impact?
- Who are the key stakeholders we would need to engage with?
- How can the MSP AG support moving towards this approach
- Can we use the proof of concept of the safety module in CTIS to pilot product-based submissions in 2026?
- What are the next steps?

Thank You