EU Recommendations on Decentralised Elements in Clinical Trials

Annual workshop of the European network of paediatric research at the EMA (Enpr-EMA)
10 October 2023, Amsterdam, The Netherlands

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CTCG vice-chair

Recommendations on decentralised elements in CTs
from European Medicines Regulatory Network (EMRN)

RECOMMENDATION PAPER ON DECENTRALISED ELEMENTS IN CLINICAL TRIALS: Published Dec 14th 2022 on Eudralex Vol. 10

DCT Recommendation paper

Direction of EMRN harmonisation

National provisions overview

Member state specific provisions, where national legislation does not currently allow for alignment

First step towards EMRN harmonised DCT approached
Best practice for EU CT authorisation and inspection
Updated as knowledge and experience evolve

Broad cross-functional collaboration for DCT recommendations

Link: DCT recommendations published in Eudralex Vol. 10 – EMRN document

European Commission
Regulations, Directives and guidances
- CT: EudraLex Volume 10

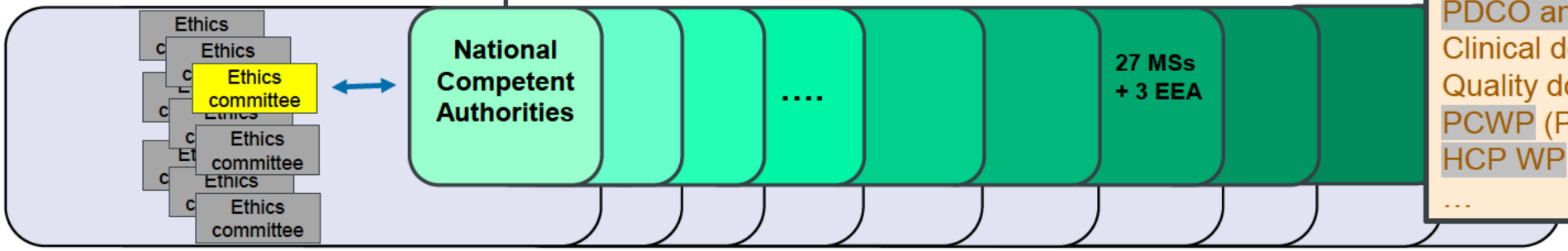
CTEG and CTAG (clinical trials experts)
Medical Device and IVD area
…

HMA
Heads of Medicines Agency
Collaboration between National Competent Authorities (NCAs)
- Guidance documents

CTCG (clinical trials coordination group)

EMA
European Medicines Agency
Coordinate authorisation of medicinal products
- Guidance documents, Scientific advice, CTIS

CHMP (Marketing authorisation)
SAWP (scientific advice)
GCP IWG (GCP inspectors)
MWP (methodology, data experts)
Non-clinical WP (safety)
PDCO and Enpr-EMA (paediatrics)
Clinical domain
Quality domain
PCWP (Patients and consumers)
HCP WP (Health care professionals)
…



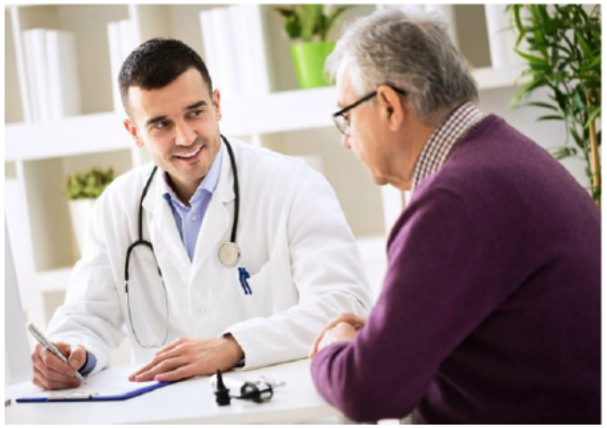
Decentralised elements (DCT)

The DCT approach seeks to take advantage of the technological progress and introduce new methodologies to make clinical trials more easily accessible and participation more convenient for trial participants.

- **Home health visits** to the trial participant's home and teleconsultation,
- **Electronic informed consent** procedures with remote consent.
- **Direct shipment** of investigational medicinal products (IMPs) to trial participants home

- Flexibility for trial participants
- Less direct interaction between investigator and trial participants

Focus of EMRN DCT recommendations



Opportunities ⟷ **Challenges**
manage and mitigate

- Trial participant-centred and risk-based approach
- Investigator and sponsor oversight
- Reliable and robust data fit for purpose

EMRN DCT recommendations - Content

1. Introduction, scope and **general considerations**
2. **Clinical trial oversight**: roles and responsibilities
3. **Informed consent process**
4. **Delivery of medicinal products** and administration at home
5. Trial related **procedures at home**
6. **Data collection and management** including defining and handling **source data**
7. **Trial monitoring**

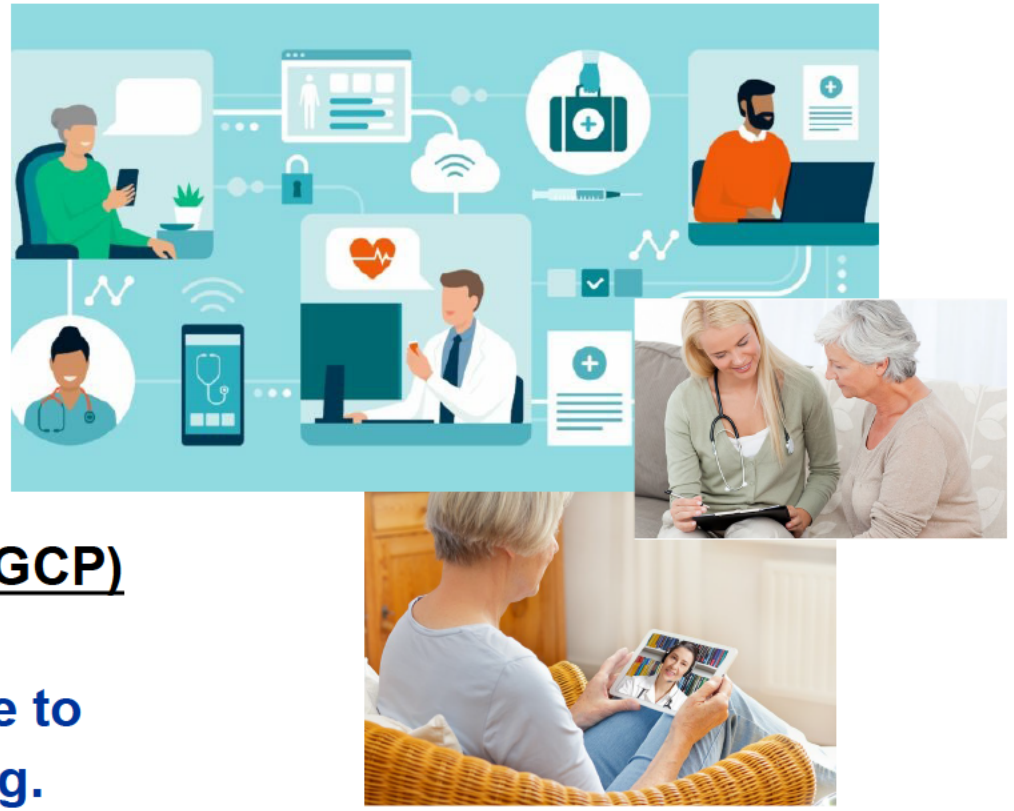
Clinical trial oversight - challenges

↓ On site visits

↑ Involvement of service providers

↑ Use of electronic systems

↑ Amount of incoming data: wearables, home nursing, patient reported outcomes, etc.



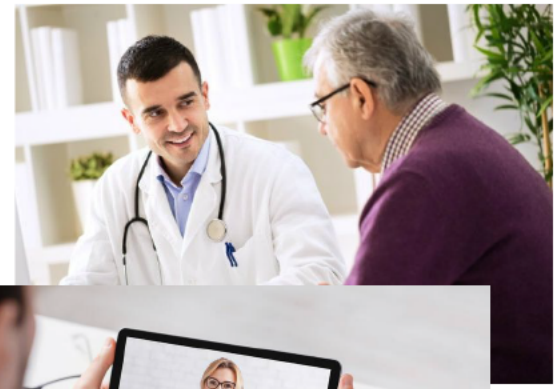
More tasks delegated - responsibilities same (ICH E6 GCP)

Mitigate: **Ensure that sponsor and investigator are able to keep oversight on trial paticipant safety and well-being.**

Clinical trial oversight: Clear roles and responsibilities

- → **Document** which tasks are conducted at what place, when, and by whom and how oversight is maintained.
- → Clear **communication plan** between the different parties involved: sponsor, investigator, participants, service providers.
- → Trial **participants informed** on information flow and how to make contact for acute safety concern, device malfunction or other questions.

Informed consent process

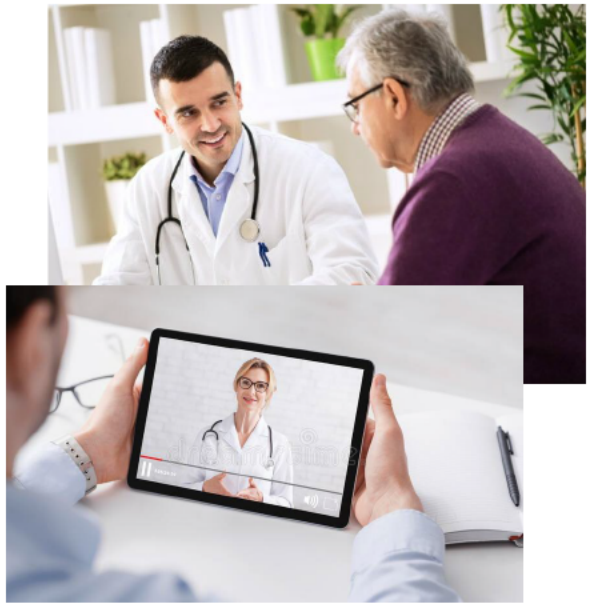


Hybrid forms – many shapes:

- Informed consent interview: remote video or physical on-site
- Patient information (leaflet): paper, digital or video
- Signature: electronic or ‘wet ink’ by post

National provisions overview with country specific requirements

Informed consent process



Participant-centered approach: Tailor to trial and population

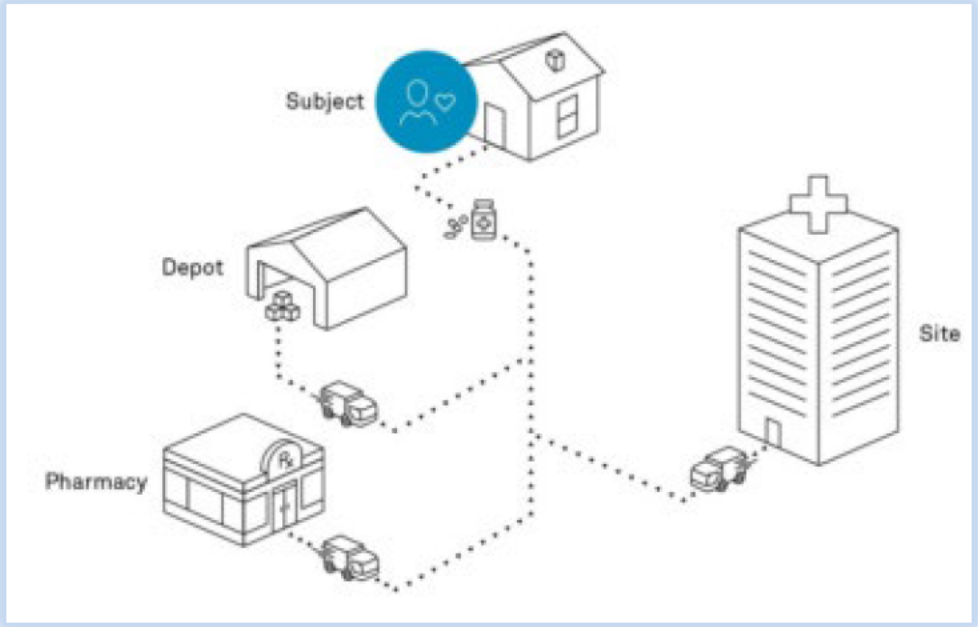
→ ICH E6: **trial participants fully informed** and able to ask questions.

→ **Step-by-step description** of procedure including selection and evaluation of eligibility. This in general, includes a **physical meeting**.

Remote interview may be justified depending on vulnerability of trial population, knowledge on efficacy/safety profile and complexity of trial.

Informed consent not only of ethical and legal importance: good communication between investigator and trial participant creates mutual trust and promote trial compliance

Delivery of medicinal products and administration at home



Basic principles:

→ The **investigator request and initiate shipment** of investigational medicinal product (IMP)

→ **Feasibility** with regard to storage conditions and administration? Clear instructions to participants.

→ Highly restricted access to trial participants contact details.

- From the sponsor/manufacturer by distributor
- From pharmacy of investigator's site
- From a local pharmacy (close to participant's home)

National provisions overview with country specific requirements

Many national provisions due to national pharma legislations.

General considerations for use of DCT elements

General medical rules to protect trial participant's safety should be upheld, in particular when patients are separated from their traditional care centers.

Trial specific rationale: depending on trial population, its disease, type of assessment and characteristics of investigational medicinal product (IMP) including its stage of development and efficacy/safety profile.

Involve patient organisations and investigators:

→ **implementation according to trial participant and investigator needs**

National provision overview

Please see relevant footnotes for responses marked with an asterisk. A footnote may be raised even though no response is given.	AT	BE	BG	CY	CZ	DE BfArM	DE PEI	DK	EE	EL	ES	FI	FR	HR	HU	IE	IS	IT	LI	LT	LU	LV	MT	NL	NO	PL	PT	RO	SE	SI	SK
The shipment and hand-out of IMPs from pharmacies. This is currently not included in the recommendation paper but may be relevant in next version of the RP.																															
Q9: Is it possible to deliver or dispense authorised IMPs directly to trial participants from pharmacies not associated with the clinical trial sites? This include authorised investigational medicinal products not used according to their SmPC.	Yes *	No *			No *	Yes		Yes *	No *	No *	No *	No *	No *	No *	Yes			*		No *			No	Yes *	Yes *	No *	No *	No *	Yes *	*	Yes *
Q10: Is it possible to deliver or dispense non-authorised IMPs directly to trial participants from pharmacies not associated with the clinical trial sites?	No	No *			No *	Yes		No *	No *	No *	No *	No *	No *	No *	Yes			*		No *			No	Yes *	Yes *	No *	No *	No *	Yes *	*	Yes *
The eConsent process, in relation to RP section 3.																															
Q11: Is a physical face to face meeting between the trial participant and the PI or a member of the research team always mandatory during the consent procedure (even if the rest is conducted remotely)?	No	No			No *	Yes *		No *	*	*	No *	No	No *	No *	Yes *	No		No *		No			No	No *	No	No	Yes *	No	No	*	No
Q12: Is it possible to use electronic signatures instead of wet ink? If yes, please specify in the footnotes which eIDAS category is expected for the electronic signature.	Yes *	Yes *			Yes *	Yes *		Yes *	Yes *	*	Yes *	Yes *	Yes *	Yes *	Yes *	Yes		Yes *		Yes *			Yes	Yes *	Yes *	*	Yes *	Yes *	Yes *	*	Yes *
Trial participant oversight and home visits, in relation to RP section 2 and 5.																															
Q13: Is it possible for the PI to delegate tasks under their responsibility to a qualified (for the delegated task) external healthcare provider?	Yes	Yes *			Yes *	Yes *		Yes	Yes *	Yes *	Yes *	Yes	Yes *	Yes	Yes *	Yes		Yes		Yes *			Yes	Yes *	Yes *	*	Yes *	Yes *	Yes *	Yes	Yes
Q14: Certain tasks/procedures carried out at home may require supervision of the investigator (a physician). Is it allowed for the physician to supervise remotely?	Yes	Yes *			No *	Yes *		Yes	*	*	*	Yes	*	Yes *	Yes *	*		Yes		Yes			Yes	Yes *	Yes	*	Yes *	No *	Yes *	*	No
Trial Monitoring using remote access to source data, in relation to RP paper section 7																															
Q15: Is remote access to the medical records allowed by the monitor or auditor?	Yes *	No *			No *	Yes *		Yes *	*	No	*	Yes	Yes *	No *	Yes *	Yes *		Yes *		Yes *			Yes	Yes *	*	*	*	No	No	No *	No

IMP delivery directly to trial participant

Mandatory physical F2F meeting

Electronic signature

Next steps

→ **Update national provision overview** on regular basis.

→ Collect experience: **tracker** of decentralised elements in clinical trials.

→ Update references for new guidances/guidelines:

- **EMA-GCP IWG Guideline on computerised systems and electronic data in clinical trials (europa.eu)**, *Applicable since 7 September 2023*
- *IWG* Q&A: Good clinical practice (GCP) | European Medicines Agency (europa.eu) *Q D3: Considerations on direct remote access to identifiable personal and health data in a clinical trial, June 2023*

→ Topics on parking lot: GDPR, clinical trial site vs satellite sites, specific populations

Decentralised Clinical Trials in Paediatric population

Summary of feedback

- engagement of children/youths and their parents/legal guardians in the development and implementation of the clinical trials
- role family members/parents/legal guardians in case of children (e.g. on training digital tools)
- home visits in case parents are divorced or children stay at grandparents
- central (coordinated) or decentral participation should be an option
- facilitation informed consent process in case person can not hear and/or see
- inclusivity of persons (minors) with a significant handicap
- remote assent and consent procedure for minors and their legal representative(s)
- IMP delivery at home: child proof packaging /additional instructions around crushing medication or additives to mask taste
- trial procedures at home: blood draws can be challenging (appropriate trained staff and experience with children
- .....

Thank you for your attention

Want to [illegible]

- **Internal DCT MS learning and exchange meeting** May 24th [illegible] (3h) https://vimeo.com/844197779?share=copy

- **ACT EU multi-stakeholder meeting** on DCT Oct 4th 2022 (video and slide[illegible]