Learnings and findings from implementation of ICH GCP E6 addendum

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The Clinical Trial Unit (CTU): what is it?

- Support function for academic trials sponsored by Oslo University Hospital (OUH) or others
- Local, regional, national, international studies
- Many drug trials, but also other interventional studies
- It is not mandatory to use the CTU

The CTU is not a CRO*/ARO**

*: Contract Research Organisation
**: Academic Research Organisation

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Sponsor responsibility and task split

	The Devisions where the clinicians are located	The CTU
Responsibility	√	
Tasks (example):		
Protocol	√	
Correspondance with authorities	√	
Informed consent document	√	
Pharmacovigilance	√	
Project leadership	√	
Monitoring		√
Data management		√
Statistics		√
Health Economics		√

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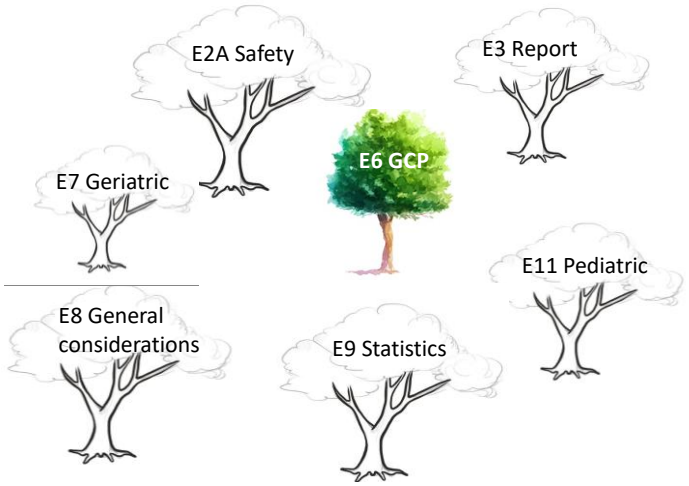
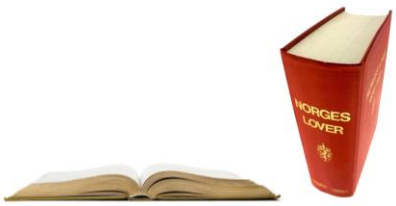
GCP never stands alone





Directives

Eudralex volume 10

Reflection papers, CTFG recommendations…

Regulation(s)

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GCP in our setting: what is it all about?

Patient safety, integrity and well-being

Data integrity

Providing results that can change or confirm clinical practice

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ICH GCP E6 addendum: Old news?

Mainly <u>underlining</u> some aspects of GCP

E.g.
Responsibility for checking on delegated tasks

No deletions

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What did ICH GCP E6 addendum bring?

Quality Management System and Risk Evaluation

Focus on Data and Electronic Systems

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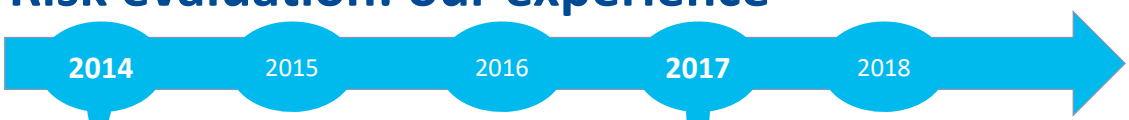
Risk evaluation: our experience



The CTU did risk assessments based on a guideline developed by NORM, a Nordic academic monitoring network
Focus: what would be controlled by a monitor?

It became part of the hospital's quality system

So the researcher became responsible for the risk evaluation process, but most often facilitated by the CTU

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Risk evaluation today

Our template is a mixture of:

- a checklist for tasks to be done mainly before start-up
- risks that might occur mainly during the conduct and closing of the study and that need to be mitigated

Difficult to quantify the analysis part (probability, consequence, detectability) and find tolerance limits

Important to make it as simple as possible

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Risk assessment tool

RISIKOVURDERING

EUdraCT nummer:	
0	
Dato og versjon for risikovurdering:	
Protokoll navn	0
Sponsor	0
Deltakere	
Sentre evaluert	0

RISIKO NR	BESKRIVELSE AV MULIG RISIKO	SANNSYNLIGHET (lav,middel,høy)	KONSEKVENS (lav,middel,høy)	RISIKO FOR IKKE Å AVDEKKE (lav,middles,høy)	AKSEPTERES RISIKOEN? (J/N)	BEHOV FOR TERSKELVERDI	HVORDAN SKAL RISIKOEN HÅNDTERES?	KONTROLLERES AV (Skriv inn eller velg fra rullegardin)
1								
2								
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prøver, dagbokføring, bruk av legemidler

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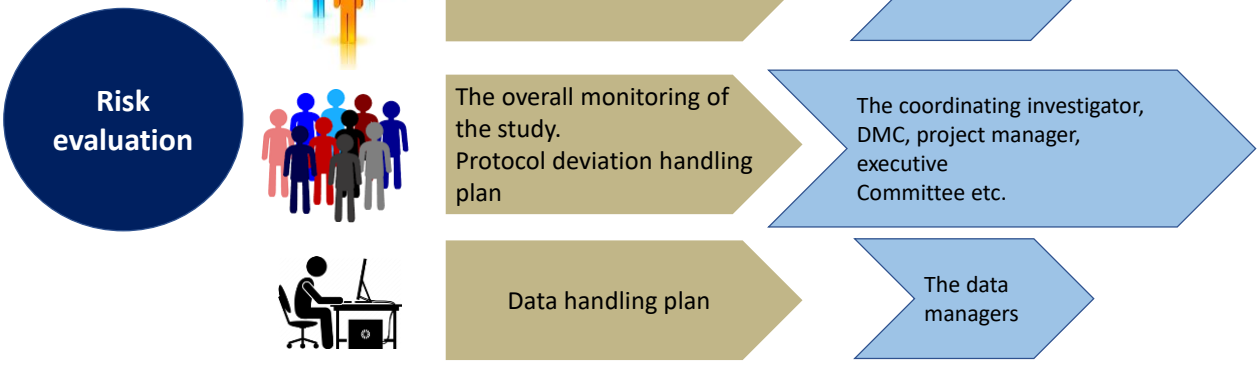
Involvement in the risk assessment process



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Learnings and findings

Make it useful

Must be adapted to the academic setting:

- The overall safety risks are usually smaller than in industry studies
- The risks are usually related to competence and capacity of trial staff

Uncertain if the researcher follow up on the risk assessment

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Data and electronic systems

One of the two main pillars of GCP is data integrity

still GCP gives very few details about data

Chapter 8 of GCP (essential documents) does not mention a data handling plan or report, or a statistical analysis plan

But requirements for electronic systems is a start

Central monitoring is important

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Data Management in academic settings

Not clearly defined as a role and GCP did not promote it, but…

ECRIN has now a certification system for data management centers (2011)

ECRIN
EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK

The CTU at OUH was certified by ECRIN in July 2019

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We still need to inform about Data Management to those not using our services

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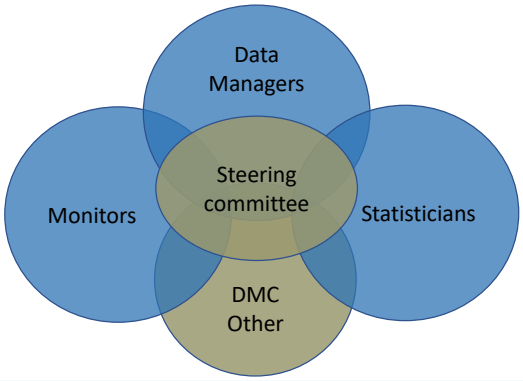
Back to risk-based monitoring

- Does ICH GCP addendum require a monitor?
- It requires risk-based monitoring.



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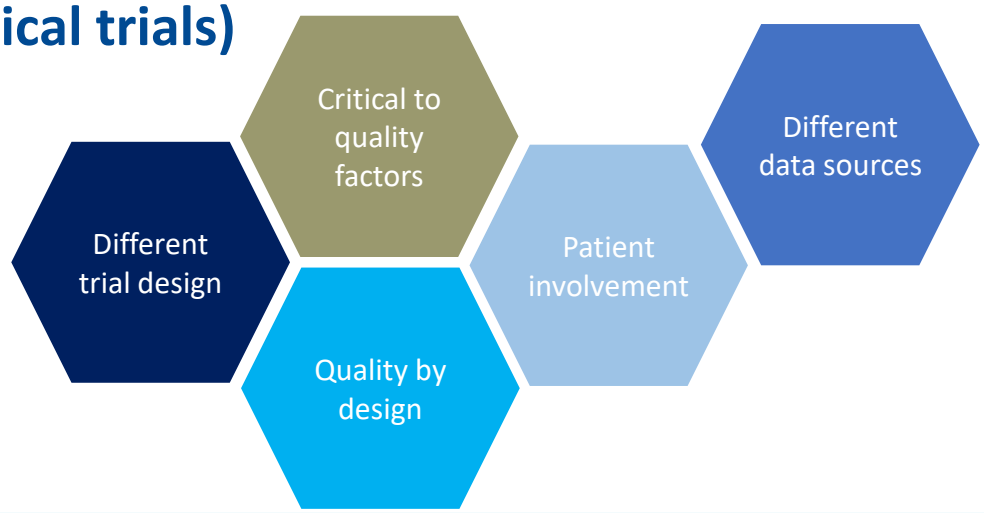
ICH E8 R1 draft (General considerations in clinical trials)



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ICH GCP E6 R3; looking forward to

- Proposed Annex 2: Non-Traditional Interventional Trials and/or data sources
  - Pragmatic trials
  - Real world data sources
- Proposed Annex 3: Non-Traditional Trial Designs
  - Observational studies
  - Patient registries (R-RCT?)

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Thank you for your attention

References

- Baigent C, Harrell FE, Buyse M, et al. Ensuring trial validity by data quality assurance and diversification of monitoring methods. Clin Trials. 2008;5:49-55.
- Sheet N, Wilson B, Benedict J et al. Evaluating Source Data Verification as a Quality Control Measure in Clinical Trials. Therapeutic Innovation & Regulatory Science. 2014, Vol. 48(6) 671-680

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