Coordination Center for Clinical Studies
KKS Charité
Quality management in clinical research

How could a network facilitate quality management of an academic sponsor?

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1990ies and ICH GCP:
• Increasing complexity for clinical trials and decreasing numbers of non-commercial clinical trails
• Insufficient quality of clinical trials results (data and timelines)
• Insufficient knowledge of methods for clinical trials in the academic community

→ Within the framework of a funding programme of the German Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung — BMBF) in 1999/2000 and 2002

→ 12 Coordinating Centres for Clinical Trials at the medical faculties of university hospitals.
→ Implement a nationwide quality campaign at academic sites
→ Establish the same standards all over Germany.

→ KKS Network, allowing a harmonised approach and the effective use of synergies

*KKS: Koordiationszentrum für Klinische Studien = Coordination Center for clinical Studies
**ZKS: Zentrum für Klinische Studien = Center for clinical Studies
KKS Network

- **17 Members:** Centres for Clinical Trials in university hospitals throughout Germany (approximately 600 staff members)
- Independent institutions, connected to their universities
- Support for all types of clinical trials (with medicinal products, medical devices, or epidemiological studies) in phases I to IV on all medical indications
- All relevant services, from study design to preparing the final trial report
- Partner of ECRIN in Germany
- Cooperation among the members in several projects (e.g. monitoring)
Coordination Center for Clinical Studies

**KKS Charité**

funded by the Federal Ministry of Education and Research from 2002 to 2008

part of the Charité Center for Therapy and Research

Services: project management, regulatory affairs, study planning, biostatistic, data management, QA/QC, monitoring, study nurses, (pharmco)vigilance, reporting
## Legally required activities depending on the study type

<table>
<thead>
<tr>
<th>Study type</th>
<th>Example</th>
<th>Regulatory framework</th>
<th>Regulatory Affairs</th>
<th>Biometry</th>
<th>pCRF/eCRF</th>
<th>Data management</th>
<th>Monitoring</th>
<th>Vigilance</th>
<th>Study Nurse</th>
<th>Coordination</th>
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<td>Interventional</td>
<td>- Drugs(^1) (Phase I – IV)</td>
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1. also ATMPs, biotechnologically produced drugs, tissue preparations, etc.
2. Case-Control-Studies, Cohort Studies
3. Post-Marketing Studies
4. Post Authorization Safety Studies
5. non interventional
6. if necessary notification only
7. if compliant with ICH-GCP, but not legally required for non-interventional studies

### Scope of performance depends i.a.:
- study type/ duration
- number of sites/ patients
- data volume
- …
Quality in a clinical trial

Quality in clinical research may be defined as...

- Reliability and credibility of information providing an answer to a scientific question

- Compliance of the trial process with defined requirements (ICH-GCP, national regulations)
### Project management: Quality Planning

<table>
<thead>
<tr>
<th>Phase</th>
<th>Sponsor</th>
<th>Staff</th>
<th>Co-Sponsor</th>
<th>QA / QC</th>
<th>Study site</th>
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<tr>
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<td>Project Outline</td>
<td>Submission EC/CA</td>
<td>Selection of partners</td>
<td>Audit</td>
<td>Staff (qualification, experience)</td>
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Aim: Quality improvement

- **Cooperation between the KKS**
  - but which standards have to be applied?

- Implementation of concerted SOPs within a federal structure
- All members of the KKS-Network committed themselves to implement the concerted SOPs **unchanged** into each QM system.
- **Working Group QM**: Representatives of each KKS developed a collection of harmonized SOPs.
- **Harmonization process** of the SOPs ➔ improves the cooperation within the CTC network considerably especially for multicenter trials.
All SOPs developed by the CTC network are accessible on the TMF homepage for all interested parties free of charge.
Problems and gaps

- Variabel QM systems and infrastructure
- Increasing topics and issues
- Issues concerning sponsor overall responsibilities (delegation gap)
- Processes during study conduct at study sites
- Maintainance of SOP system
• Various QM systems and infrastructure ➔ introducing designated paragraphs intended for local specification


• Processes during study conduct at study sites ➔ SOP-templates dealing with all operational processes during clinical trials at study sites/SMOs.

SOPs für Prüfzentren / Site Management Organisationen:
- PZ-GE01 - SOP-Erstellung für Prüfzentren und SMOs*
- PZ-GE02 - Personalschulung*
- PZ-QS01 - Vorbereitung auf Audits und Inspektionen*
- PZ-SD01 - Studienvorbereitung*
- PZ-SD02 - Einschluss und Beendigung einer Studienteilnahme*
- PZ-SD03 - Dokumentation von Patientendaten*
- PZ-SD04 - Archivierung von Unterlagen im PZ*
- PZ-SD05 - Patientenaufklärung
- PZ-SD06 - Umgang mit SAEs
- PZ-SD07 - Abbruch einer klinischen Prüfung*
- PZ-VG01 - Bearbeitung von Studienanfragen – Feasibility
- PZ-VG02 - Studienkalkulation inkl. Identifikation des studienbedingten Mehraufwandes*
- PZ-VG03 - Vertragsgestaltung*
Good SOPs are prerequisites but not sufficient …

➔ Expert panels with the mission:

• Development of standards
• SOPs
• Support
• Discussion on impact of regulations and laws
Expert panels in the KKS network

- Training programmes
  Contents of training programmes, curricula

- Data management
  Data management processes

- Biostatistic
  Processes for biostatistics, methods

- Quality management
  SOPs, quality standards

- Site management
  Study conduct, organisation of sites

- IT
  IT infrastructure

- Vigilance
  SAE Management, (pharmaco)vigilance infrastructure, processes

- Project management
  Study preparing, study documents, CTA, archiving

- Monitoring
  Standards, ADAMON,
Working Group Sponsor responsibilities

- Issues concerning sponsor overall responsibilities (delegation gap) ➔ Working group sponsor responsibilities

- ICH –GCP: 5.7 Allocation of Responsibilities

Prior to initiating a trial, the sponsor should define, establish, and allocate all trial-related duties and functions.

➔ Organisation of an academic sponsor

➔ SUPERVISION OF DELGATED TASKS
Sharing experience

Reliability and credibility of information providing an answer to a scientific question

- Documentation and data quality
  - Data generation ➔ standards
  - Data center certification program (ECRIN)
  - Software ➔ supervision of site performance; central monitoring
Problems

- More or less acceptance of KKS by their university hospitals
- Economic pressure
- Competition among KKS (funding of projects)
- Various infrastructure (comparability of systems)
- Maintainance of developed SOPs
KKS Network and his impact on quality

• Development of standards
• Impact through lobbying: discussion on new legal regulation (e.g. EU regulation) and their feasibility in non commercial clinical trials
• Improvement of the understanding of potential risks and problems in clinical trials
• Think tank ➔ expertise and quality improvement
Thank you for your attention

et

Merci beaucoup pour l’invitation

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