Academic trials and the challenge of sponsor responsibility

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Clinical Trials Center Cologne
Legal Situation

- **2001: DIRECTIVE 2001/20/EC**
  - The European „Clinical Trials Directive“

- **2004: The 12th amendment of the German Drug Law (AMG)**
  - National implementation of the Directive 2001/20/EC

- **2005: RL 2005/28/EG**
  - The European „GCP-Directive“
Relevance for Investigator Initiated Trials (IITs)

- Legal definition of „Sponsor“ and „Clinical Trial“
- Legal implementation of Good Clinical Practice (GCP)

→ German Drug Law (AMG) became binding for IITs
Sponsor...

- ... is a natural or legal person who assumes responsibility for the commissioning, organization and financing of a clinical trial on human beings.

[AMG § 4 (24)]
Sponsor for IITs

- Institution (University, Hospital)
- Investigator (rare!)
Challenges for the Academic Institution

- Defined roles and responsibilities
- Controlled delegation
- Quality management (GCP)
- Know how (law, background, methodology)
- Resources (human and financial)
- Risk management
Cologne Sponsor Model

- University (Rector)
- CTCC
- Coordinating Investigator (CI)

Sponsor
Executive institution of the sponsor
Sponsor's representative

QAU
Delegation of sponsor duties

**CTCC**
- General organisation
- Proof for sponsorship
- Surveillance of trial conduct

**CI**
- Financing
- Data management
- Monitoring
- Insurance
- Protocol / ICF
- Pharmacovigilance
- Applications / approvals

**Third Parties**
- As appropriate
Proof for Sponsorship: GCP Check

- Protocol, ICF, IMPD (SmPC),
- Financing, contracts
- Insurance
- Investigational medicinal product (IMP release)
- Involvement of other countries and trial sites
- Pharmacovigilance
- Monitoring-concept
- Delegation of tasks to third parties, contracts and qualification

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Surveillance of Trial Conduct

- Audits according to a risk-based audit program
- Control samples of monitoring reports
- Annual trial status reports from sponsor’s representatives (CI)
Risk-based Auditprogramm

- 3-4 audits per year
- System- and on-site- audits
- Focus of Audit:
  - Fulfillment of assumed Sponsor duties
  - GCP-Compliance
- Criteria/Raster (e.g.):
  - AMG / MPG Trial
  - multicenter
  - phase I
  - Low Monitoring extent
Reporting Line of Quality Assurance Unit
Experiences I

- 52 applications for University sponsorship
- 36 trials accepted (5 international)
  - All with subsequent improvement
- 16 remaining
  - In preparation, cancelled or postponed (financing, organisation, other reasons)
Experiences II: Audit Findings

- CI (trial conducting unit)
  - Roles and responsibilities unclear
  - Missing approval processes
  - Clinical monitoring low, follow up and consequences of findings missing
  - ...

- Trial
  - ICF incorrect
  - SAE not reported or delayed
  - Delay in documentation
  - Violation of in- and exclusion criteria
  - ...

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Side step: Support by CTCC

- **Know How:**
  - IIT manual
  - Academy (basic and advanced training)
  - QM-Coaching: establishment of quality management in the CI’s facility (i.e. SOP & contract templates, audit action plan)

- **Service Provider:**
  - Services of all aspects of a clinical trial (methodological and medical)
Acceptance and Financing of the Cologne Sponsor Model

- High acceptance
  - by public and corporate financiers of IITs as well as authorities!!

- Financing:
  - 2 FTE (1 Medical Faculty, 1 funded by Federal Ministry of Education and Research)
  - Sustainability by project-specific take over of audit costs (planned)
Summary

- The Cologne Sponsor Model provides...
  - ... a “risk-based” system
    - ... with a combination of central management, control and support
    - ... and of decentral measures
  - ...that offers a sensible option for fulfilling the legal and GCP requirements for the academic environment.
Thank you for your attention

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Perspective / International Trials

- Analogous delegation model
  - *Allocation of entire* sponsor duties
  - *One* national organizational unit

- Synergies with ECRIN in international Trials
CTCC: Clinical Trials Center Cologne

Managing Board

Quality Assurance (QAU)

Methodological Division

Medical Division
CTCC Services

Methodological Division
- Project Management
- Data Management
- SAE / SUSAR Management
- Monitoring
- IT
- Quality Management (i.e. coaching)
- Training Academy

Medical Division
- "Translational research"
- Site Management
- IT Medicine