The role of the coordinating centres for clinical trials (KKS network) and publicly funded trials in Germany

Christoph Coch
Member of Executive Board KKS Network and
Head of Clinical Trial Center Bonn
Institute of Clinical Chemistry and Clinical Pharmacology
University Hospital Bonn
Content of this talk

• Coordinating centre for clinical trials in an academic institution

• Sponsor responsibilities in an academic institution

• Example: Study Center Bonn

• Network of coordinating centres for clinical trials (KKS network) in Germany
  History and structure today

• Publicly funded trials in Germany
Need for a coordinating center for clinical trials in an academic institution!

What is needed for the scientifically and legally sound clinical trial?

...as called for by scientific community and European/National law

- Clinical expertise
- Scientific expertise
- (often) access to patients
- Regulatory/legal expertise
- Trial methodology
- Tools for clinical research, e.g. trial database
- Experience/skills in project management
- Pharmaceutical expertise
- Clinical expertise
- Scientific expertise
- (often) access to patients

investigator responsible

no time/no expertise

Sponsor of trial responsible

Investigator initiated trial

Trial coordinating center

Company sponsored trial: industry

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Structure of a coordinating center for clinical trials

- Project Management
- Monitoring
- Safety Management
- Quality Management
- Biometry
- Data Management
- IT
- IMP handling
- Site Management

Need for an interdisciplinary team:
- Physicians
- Scientists
- Pharmacists
- Statisticians
- Data Manager
- Safety Manager/ Safety Assistant
- Quality Manager
- Clinical monitors
- Clinical Research Assistant
- Study Nurse
Structure of a coordinating center for clinical trials

Essential functions in the beginning

- Director/Management
- Project management
- Biometry
- Quality management

Can be conducted in cooperation/ implemented later

- Data management
- Monitoring
- Safety management
- Training/ education
- IMP handling

Can be implemented later

- Site management
Financing of a coordinating center for clinical trials

- Institution/ Medical faculty
to compensate for services that cannot be financed by external money; e.g. support of fund applications/ trial consulting/ sponsor quality control

- Public funding (general or trial specific)

- Industry funded projects

- Training/ education courses
  investigator training/ study nurse education/ ...
Financing of a coordinating center for clinical trials

Initial BMBF-funding for trial infrastructures*

- Coordinating Centres for Clinical Trials (KKS)
  - 1999-2009, 13 centres
  - 29 Mill. €

- Clinical Trial Centres (site management) (ZKS)
  - 2004-2009
  - 29 Mill. €

- KKS-Network
  - 2004-2009
  - 1.8 Mill. €

- National ECRIN-office
  - 2010-2015
  - 1.2 Mill. €

*German Ministry for Education & Research
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Sponsor responsibilities in an academic institution

Sponsor of investigator initiated trial = medical faculty/ university/ university hospital
e.g. Dean of medical faculty in Bonn

Sponsor = Responsible for initiation/ organisation/ financing of trials with medical
devices and medicinal products according to european/ national law

Sponsor can pass tasks but not responsibility to other parties such as investigator

Before and over course of trial sponsor has implemented quality control
Affiliated with/ attached to a trial coordinating center or separate quality control unit

In Bonn affiliated with trial coordinating center but independent in decision
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SZB: Association of all facilities at the University Hospital Bonn performing clinical trials:

- **Clinical Study Center** of the different departments
- **Clinical Study Core Unit = coordinating center for clinical trials**
  - Institute of Clinical Chemistry and Clinical Pharmacology
  - Institute of Medical Biometrics, Informatics and Epidemiology (IMBIE)
- **Pool Study Nurse**
- **Administrative departments** (legal department, contract management)

Coordinating centre for clinical trials embedded in Infrastructure for clinical research
Study Center Bonn – tasks coordinating center for clinical trials

- Conduct/ support of clinical trials, especially investigator initiated trials at University Hospital Bonn

- Support of clinical trial sites/ investigators at University Hospital Bonn „site management“

- Conduct of early clinical trials in specialized facility „Phase I – Unit“

- Support of translational projects in the research laboratories

- Training and education of staff (GCP training/ AMG course/ MPG course/ lecture series together with BfArM (German competent authority))
Study Center Bonn

Dean of Med. Faculty

Clinical Trial Commission

Clinical Study Center...

Ophthalmology

Med. Oncology

Neuro-Urology

Anaesthesiology

Pulmology

Neuro-Oncology

Surgery

Cardiology

Radiology

Med. Clinic I

Palliative Medicine

Gynaecology

Dermatology

(Pediatric-) Urology

Neuro-Surgery

Early Clinical Trial Unit

Coordinating center clinical trials

Internal Cooperation:
• Administration/ Legal Depart.
• Pool Study Nurse

External Cooperation:
• Pharmaceutical Industry/ CRO
• Authorities (BfArM/ PEI/...)

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KKS-Network: members

7 KKS-sites promoted by BMBF program 1999

20 KKS-sites 2016
KKS-Network: Objectives

- Harmonising of nationwide quality standards and work processes.
- Initiating and implementing of synergistic effects between academic trial units (*e.g. in case of acquisitions or methodological and technical developments*)
- Developing standardised curricula for certified training programmes.
- Increasing visibility, acceptance and influence of academic clinical research (*e.g. interaction and networking with bodies, politicians, policy makers*)
- Strengthening the academic profile of clinical trials
- Improving the range of services towards comprehensive project management
KKS-Network: Structure

Consortium since February 2005:

- General Assembly
- Executive Board
- Central Office
- Managing Directors

National Committees / Expert Panels / Medical Associations

ECRIN

Global Science Forum of the OECD

Expert Panels

- Education and Training
- Quality management
- Data management
- Biometry
- IT
- Site Management
- Monitoring
- Project management
- Vigilanz/SAE-Management
- Sponsor responsibility

Task Forces

- Master Contract Templates
- Cost Calculation
KKS-Network: Activities

• KKS-Network coordination by a central office (Berlin)

• Regular meetings of the General Assembly, the KKS/ZKS-directors, the expert panels and task forces

• Workshops/ symposia for internal and external participants

• Purchase of software to be used by all KKS/ ZKS-sites

• Obtaining legal advice

• Communication, public relations and media work

• Regulatory, scientific and political networking on a national and international basis

• Infoservice for members
KKS-Network: Expert panels

**Topics**

- Education
- Quality management
- Data management
- Biostatistics
- Information technology
- Project management
- Site management
- Pharmacovigilance
- Monitoring

**Results (examples)**

- Harmonised SOPs
- Curricula & certification of courses
- Discussion of specific topics
- Recommendations for members
- Sharing best practice
- etc.
KKS-Network: Activities (examples)

Papers

GCP-compliant digital archiving of paper-based patient records of clinical trial subjects: a key issues paper


Comments

Comment: on the draft by the European Parliament regarding A regulation on the protection of individuals with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation, referred to hereinafter as the GDPR)

taking into account the draft by the European Commission
in conjunction with the
Netzwerk der Koordinierungszentren
für klinische Studien (KKS-Netzwerk)
Network of the Coordinating Centres for Clinical Trials

Panels

Chairing expert panel on insurance in clinical trials *(results to be included in the German Drug Law)*

Projects

ADAMON

Adaptiertes Monitoring

Prospective cluster-randomized investigation into strategies adapted on a study-specific basis for on-site monitoring in conjunction with additional quality assurance measures.
KKS-Network: Membership

- Target: Slow and controlled growth
- Critical mass of applicants available
- Standardised procedure defined in SOPs
- New members need to share the objectives of the KKS-Network
- Two-phase admission for new members:
  - associated membership for 1 year
  - full membership after successful external audit (*structure, work processes*)
- Annual membership fee: 15.000,- €
KKS-Network: Employees

Employees (N)

Year

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<thead>
<tr>
<th>Typ of Course</th>
<th>Courses (N)</th>
<th>Participants (N)</th>
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<tr>
<td>Investigator</td>
<td>400</td>
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<tr>
<td>Study nurse</td>
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<td>Coordinating Investigator</td>
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<td>540</td>
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<tr>
<td>Medical device</td>
<td>11</td>
<td>202</td>
</tr>
</tbody>
</table>

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ECRIN national office: Structure/activities

- part of KKS-Network central office
- home of the European Correspondent (and other related staff)
- structuring work between KKSN and ECRIN
  - establishing processes for interactions between KKS-Network and ECRIN
  - implementing cooperation of KKS-Network experts for ECRIN
  - introducing expertise/tools available in the KKSN into ECRIN
  - building infrastructure to meet criteria for ECRIN data centre certification
- first contact point for sponsors interested in cooperating with ECRIN
  - fostering participation of other ECRIN countries in IITs initiated in Germany – and vice versa
  - coordinating service provision from ECRIN for trials with sponsors from Germany
Financing of trial

Clinical trials in which the KKS-Network is responsible for central tasks:

Industrial sector 54%
German Federal Ministry of Education and Research 14%
German Research Foundation 7%
European Union 1%
German Cancer Aid 5%
Other public institutions 12%
Faculty 10%
State government 1%
Unknown: 7%

Multiple answers are possible
As per September 2011
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Public funding options in Germany

- Local funds of the medical faculties, e.g. in Bonn
  - small pilot trials

- German Research Foundation
  - regular funding programme; calls for phase III clinical trials
  - reduced focus on early clinical trials
  - research grants

- BMBF (German Ministry for Education and Research)
  - regular funding programme for clinical trials; depending on calls
  - via German Centers for Health Research (not open for every hospital)

- Societies/ Associations: e.g. German Cancer Aid

- Federal Joint Committee („gemeinsamer Bundesausschuss“)
  - Innovation committee - Innovation fund (§ 92b Abs. 1 SGB V)
    (Health insurances/ Hospitals/ Ministries)
    Support of healthcare research
  - Clinical trials with off-label use of medicinal products used (funding of medicinal products and procedure; SGB V § 35c)

...many investigator initiated trials are funded by pharma industry, but via individual contracts no general fund
Thank you very much!

...and why all these efforts? Because the patients will appreciate it!

„I stopped taking the medicine because I prefer the original disease to the side effects“