Coordination Centres for Clinical Trials

caBIG-TMF-MediGRID Workshop
23 January 2008
Berlin, Germany

Prof. Dr. C. Ohmann
Coordination Centre for Clinical Trials
Heinrich-Heine-University
Düsseldorf, Germany

Coordination Centres for Clinical Trials

- aim of the presentation -

- perspective of DM- support for clinical trials
- status of DM in the German Coordination Centres for Clinical Trials (KKS-network)
- status of DM in the European Clinical Research Infrastructures Network (ECRIN)
- conclusions and consequences

DM= data management

Perspectives of DM- support for clinical trials

- objectives -

- support of data management and and study workflow
- accomplish regulatory requirements
- improve quality of clinical trials
- increase cost- efficiency

Perspectives of DM- support for clinical trials

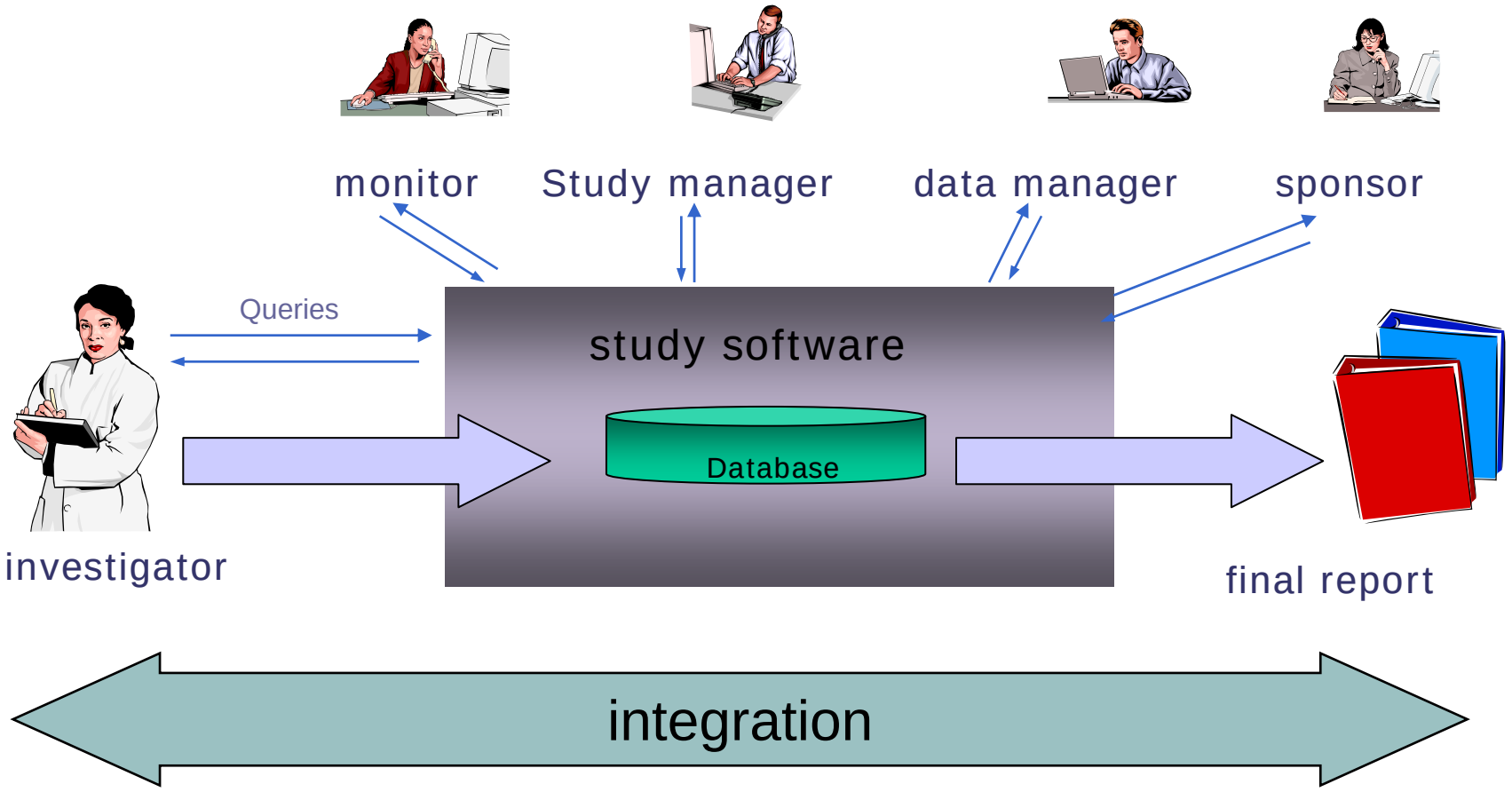
- regulatory requirements -

- EC 2001/ 20/ EG Guideline (04.04.2001)
- EC 2005/ 28/EC Guideline (08.04.2005)
- Arzneimittelgesetz (12. Gesetz zur Änderung des AMG vom 06.08.2004)
- ICH E6: Good Clinical Practice (Mai 1996)
- ICH E9: Statistical Principles for Clinical Trials
- FDA 21 CFR Part 11: Electronic Records: Electronic Signatures (March 1997)
- FDA Guidance for Industry: Computerised Systems used in Clinical Trials (April 1999)
- Annex 11 – European Commission Directive 2003/ 94/ EC

Industry standard:
GAMP Guide for the validation of Automated Systems, Version 4

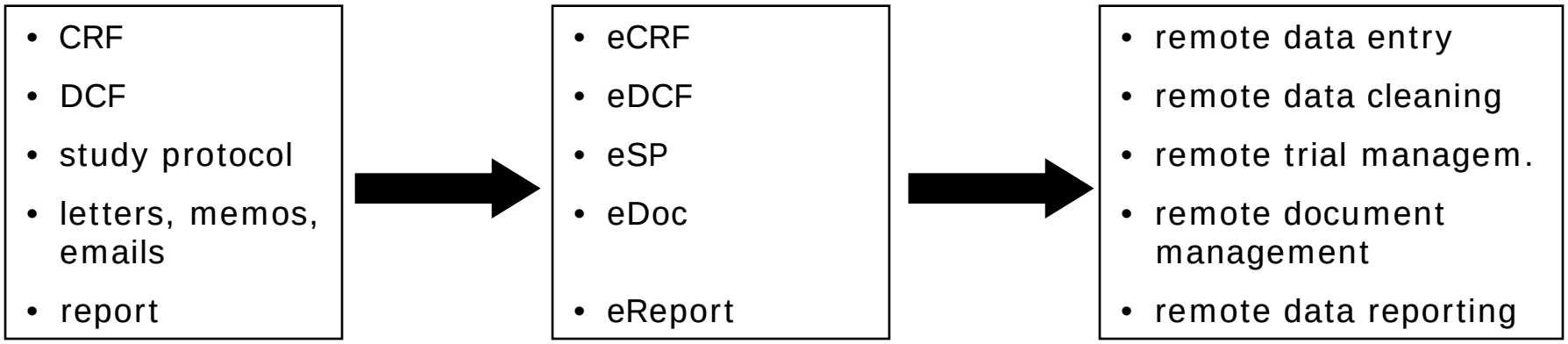
Perspectives of DM- support for clinical trials

- information flow/user roles -



Perspectives of DM- support for clinical trials

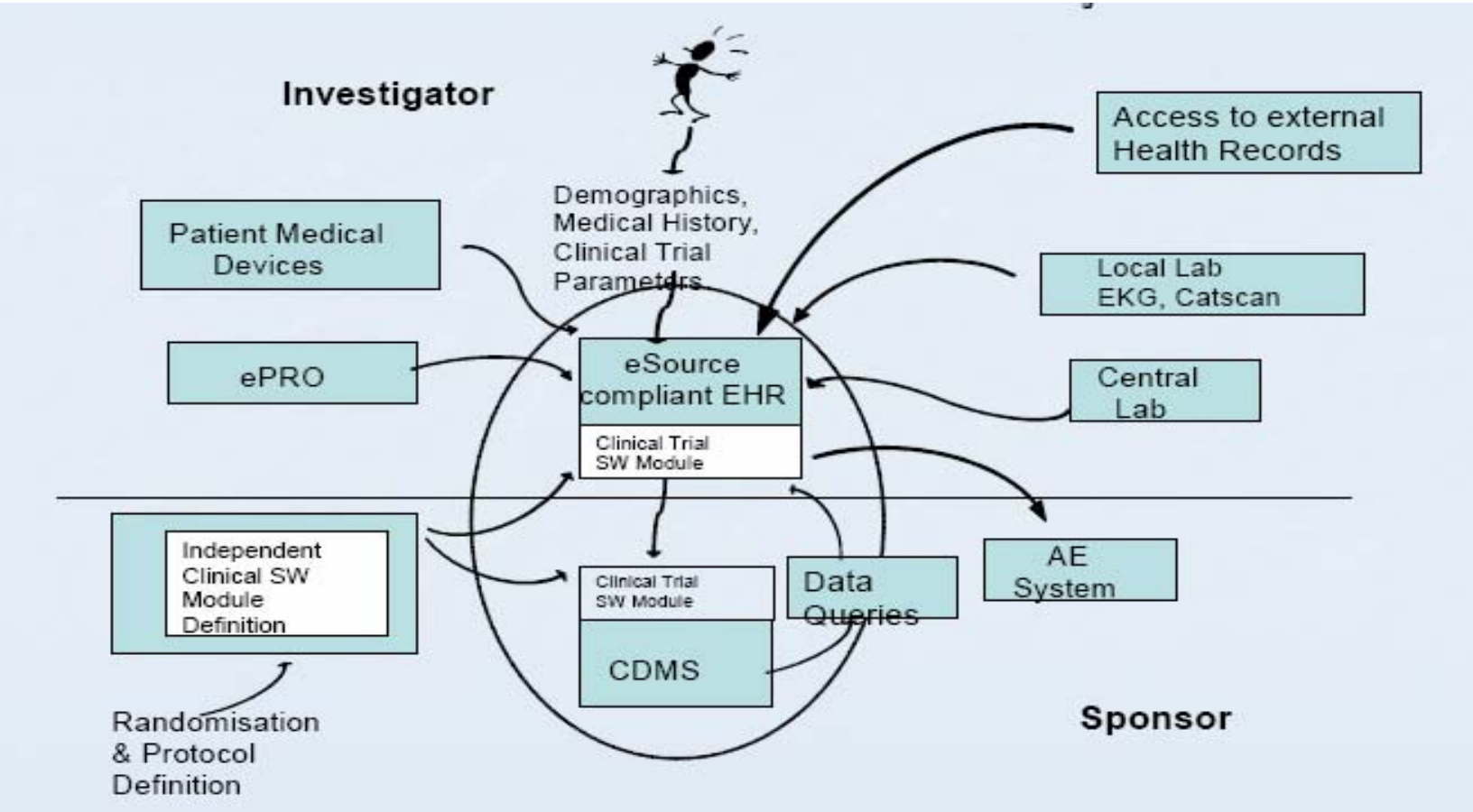
- paper-based versus remote -



CRF= case report form
DCF= data cleaning form
e= electronic

Perspectives of DM- support for clinical trials

- the vision* -



**eClinical Forum and PhRMA EDC/eSource Taskforce: The future vision of electronic health records as eSource for Clinical Research, Vers. 1.0, 2006*

German Coordination Centres for Clinical Trials

- objectives-

- initiating, planning and performing innovative and competitive international trials
- supporting drug regulatory and scientific-driven *("investigator initiated")* trials
- harmonizing quality management to establish international standards *(e.g. GCP)*
- improving education related to scientific and organizational aspects of trials
- long-term establishment of the centres with university and pharmaceutical industry support

KKS Netzwerk
Koordinierungszentren für Klinische Studien

German Coordination Centres for Clinical Trials*

- objectives-

Coordination Centre for Clinical Trials with paediatric module

associated member

- **Coordination Centre for Clinical Trials**
  (12 centers, 1999-2007, 30 Mill. €)
- **Paediatric Network (PAED-NET)**
  (6 centers, 2005-2008, 2,6 Mill €)
- **Surgical Network (CHIR-NET)**
  (6 centers, 2006-2008, 1,8 Mill. €)
- **National Coordinating Office for the Coordination Centres for Clinical Trials**
  (1 office, 2004-2007, 1 Mill €)
- **Clinical Trial Centers**
  (6 centers 2007-2015, up to 48 Mill €)
- **Integrated Research and Treatment Centers with a clinical trial unit**
  (up to 10 centers, 2007-2017, up to 250-500 Mill €)

KKS Netzwerk
Koordinierungszentren für Klinische Studien

**funded by German Ministry for Education and Research (BMBF)*

German Coordination Centres for Clinical Trials

- supporting structures -

- permanent working groups
  (training/education, quality management, biometry/data management)

- central office in Cologne

KKS Netzwerk
Koordinierungszentren für Klinische Studien

German Coordination Centres for Clinical Trials

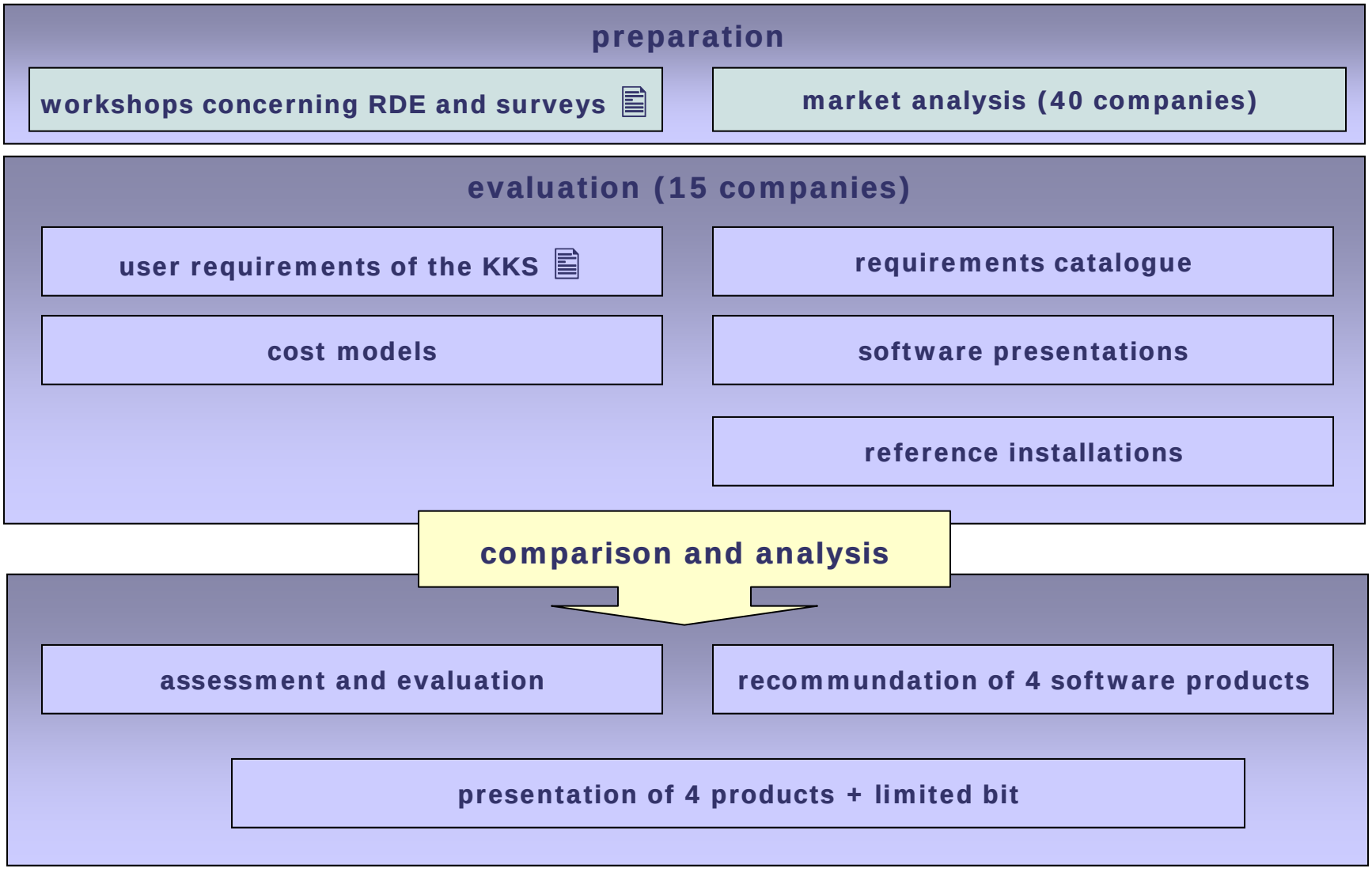
- framework for IT-support of DM -

- implementation of commercial and professional software products with industry standard already in use *(no own develeopment)*
- standardized process for software evaluation, implementation, validation and evaluation
- purchasing of 2-3 software products with different functionality *(small, large EDC systems)*
- limited ressources *(personel, hardware, software)*
- close cooperation with the Telematikplattform e.V. and the Working Group „Data management“ of the KKS-network

KKS Netzwerk
Koordinierungszentren für Klinische Studien

German Coordination Centres for Clinical Trials

- software selection process* -



*supported by Telematikplattform e.V., Berlin , Germany

German Coordination Centres for Clinical Trials

-software products used* -

eResNet	MACRO	PhOSCo
■ eDataManagement ■ eDataEntry ■ eStudyConduct ■ eResearchComm. ■ eSafetyNet	■ Study Definition ■ Web Data Entry ■ Web Data Review ■ System Managem. ■ Libary Management	■ Trial Recorder ■ Trial Builder ■ Trial Monitor ■ Trial Server ■ (Open Source Licence)
KKS Düsseldorf KKS Leipzig KKS Halle	KKS Köln KKS Marburg KKS Freiburg KKS Mainz KKS Münster KKS Dresden KKS Heidelberg	KKS Tübingen/now CenTrial) (experiences in KKS Düsseldorf and KKS Halle)

*SecuTrial™ used additionally at KKS Berlin

*supported by:

KKS Netzwerk
Koordinierungszentren für Klinische Studien

TMF Telematikplattform für Medizinische Forschungsnetze e. V.

German Coordination Centres for Clinical Trials

- status of software use -

From 10 centers participating in a survey*:

- 10 Clinical Data Management Systems *(clinical trial software)* in routine use *(Macro: 6, eResNet: 3, SecuTrial: 1)*
- 7 centers with own installation, 3 with APS
- 10 centers with RDE- support
- 10 centers QM- system with SOPs
- 7 external DM- audit
- 3 centers internal DM- validation

KKS Netzwerk
Koordinierungszentren für Klinische Studien

**ECRIN survey, 2007*

German Coordination Centres for Clinical Trials

- additional IT- support -

area	software	status
safety	Vigilance One™ Safety Net™	software purchased and implemented in the KKS *(supported by Telematikplattform e.V., Berlin, Germany)*
project management	Projectile™	software purchased and implemented in several KKS *(mainly hosting)*
document management	Enterprise Content Management™	purchased, will be implemented
MedDRA- coding	own development	under development, pilot available
randomisation	TENALEA *(EU-project)*	under development, pilot available

KKS Netzwerk
Koordinierungszentren für Klinische Studien

German Coordination Centres for Clinical Trials

- summary -

- major progress in DM of clinical trials with the support of the German Ministry of Education and Research (BMBF) and the Telematikplattform e.V.
- implementation of GCP- compliant DM in a number of clinical trial centres with professional software tools and adequate quality management
- routine application of clinical trial software, partly with remote data entry, mainly in investigator-initiated trials
- ongoing activities with respect to additional software tools *(e.g. safety, project management)* and harmonisation/standardisation *(e.g. CDISC, XML supported by the Telematikplattform e.V.)*

KKS Netzwerk
Koordinierungszentren für Klinische Studien

European Clinical Research Infrastructures Network

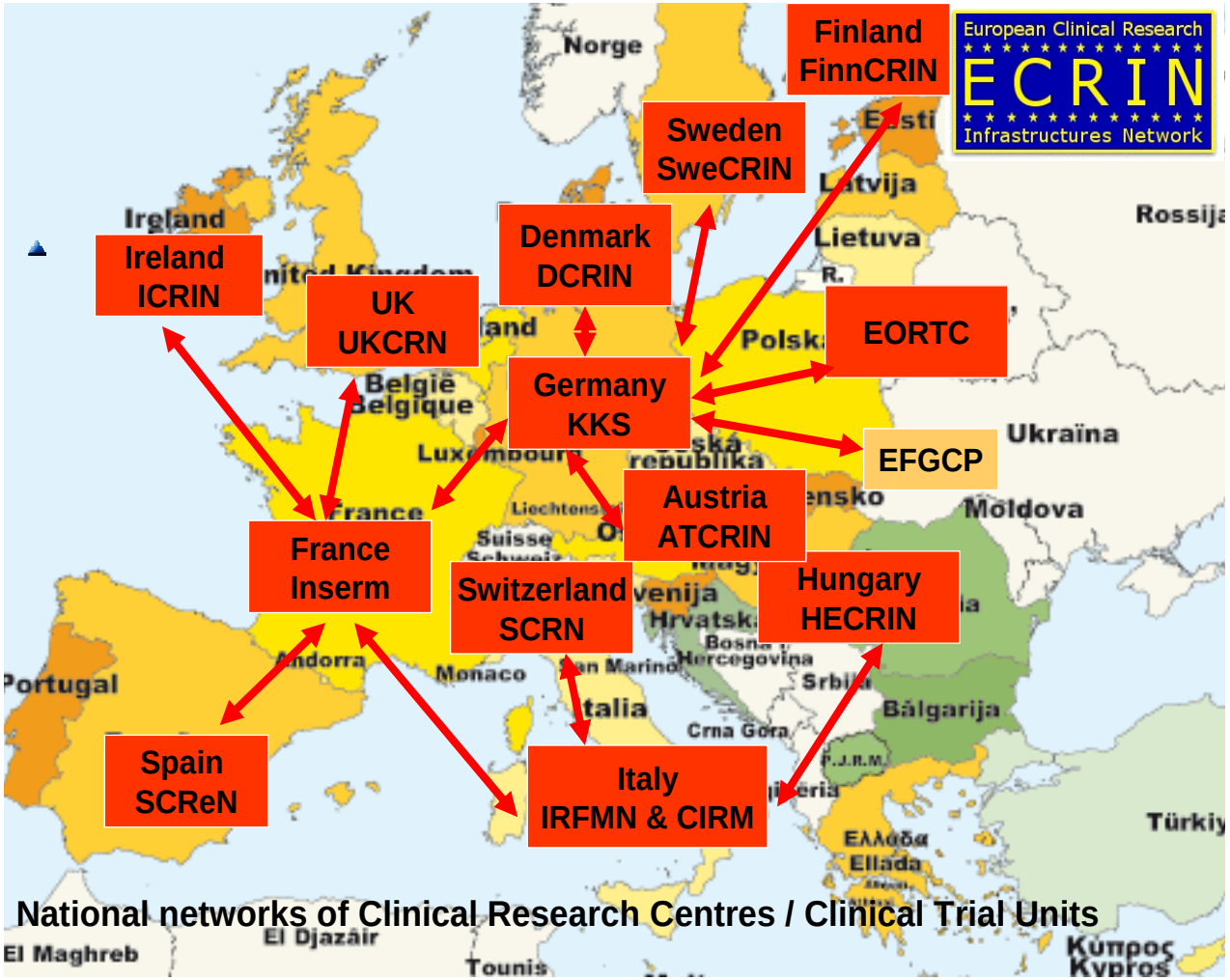
- aim -

ECRIN is designed to bridge the fragmentation of clinical research in Europe through the interconnection of national networks of clinical research centres and clinical trial units*

EU 7FP, Capacities-Research Infrastructures, INFRA-2007-2.2.1.18, No. 211738

European Clinical Research Infrastructures Network

- partners -



National networks of Clinical Research Centres / Clinical Trial Units

European Clinical Research Infrastructures Network

- historical development -

- **ECRIN-1** (2004-2005) :

  identifying bottlenecks

- **ECRIN-2** (2006-2008) :
  design of the infrastructure

- **ECRIN-3** (2008 ->) : ESFRI roadmap
  preparation, construction and operation of the infrastructure supporting multinational clinical trials in the EU

- in line with expectations of FP7

  'Innovative Medicines Initiative'

European Clinical Research ECRIN Infrastructures Network

European Clinical Research Infrastructures Network

- aim of ECRIN 3* -

flexible, integrated services (one-stop shop) in the conduct of multinational trials

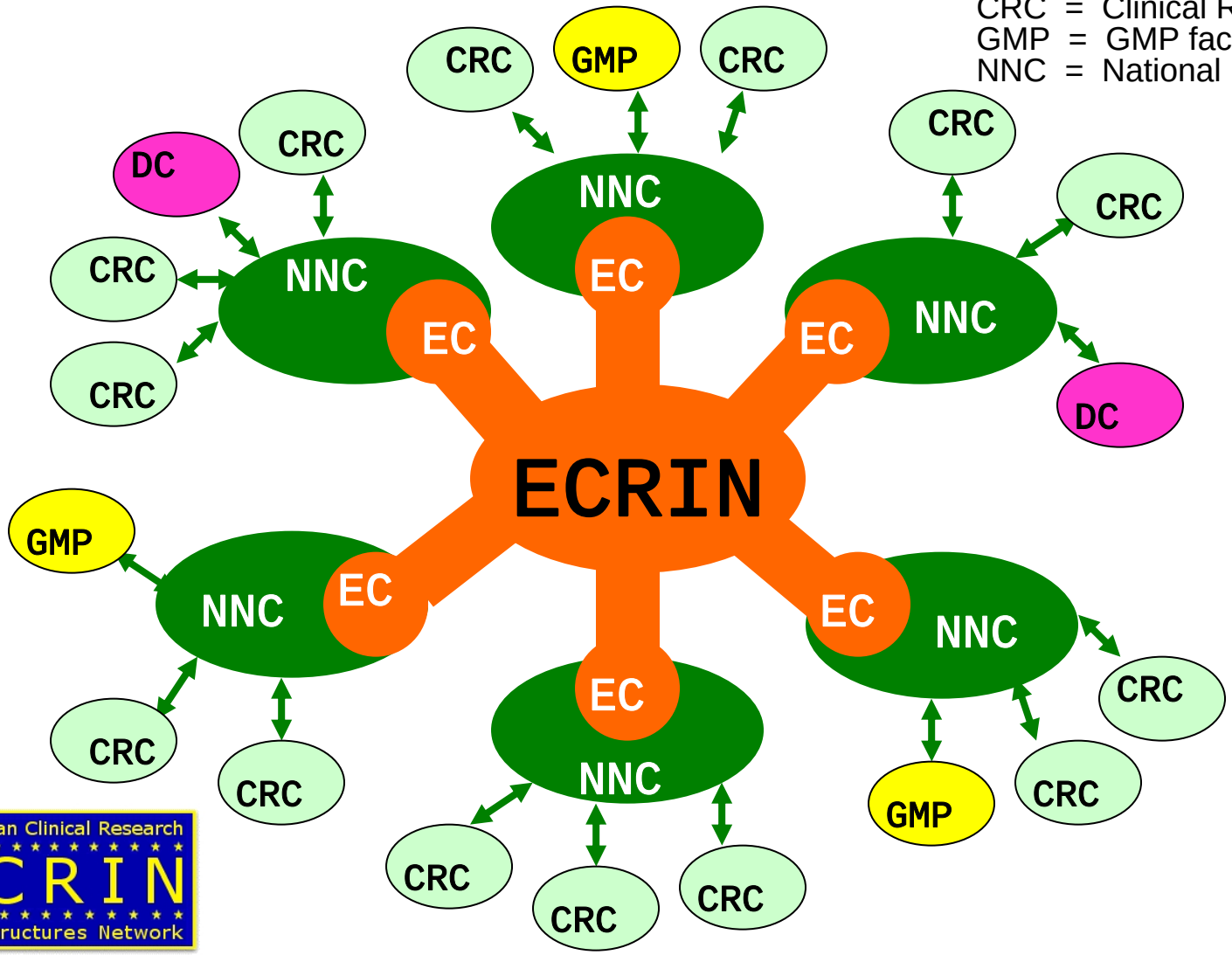
1 - interaction with ethics commitees
2 - interaction with competent authorities, regulatory affairs
3 - drug dispensing
4 - adverse event reporting
5 - data management
6 - study monitoring
7 - management of biological samples

*associated partner:

European Clinical Research Infrastructures Network

- infrastructure of ECRIN 3 -

DC = Data Centre
EC = European Correspondent
CRC = Clinical Research Centre
GMP = GMP facility for biotherapy
NNC = National Network Coordination



European Clinical Research ECRIN Infrastructures Network

European Clinical Research Infrastructures Network

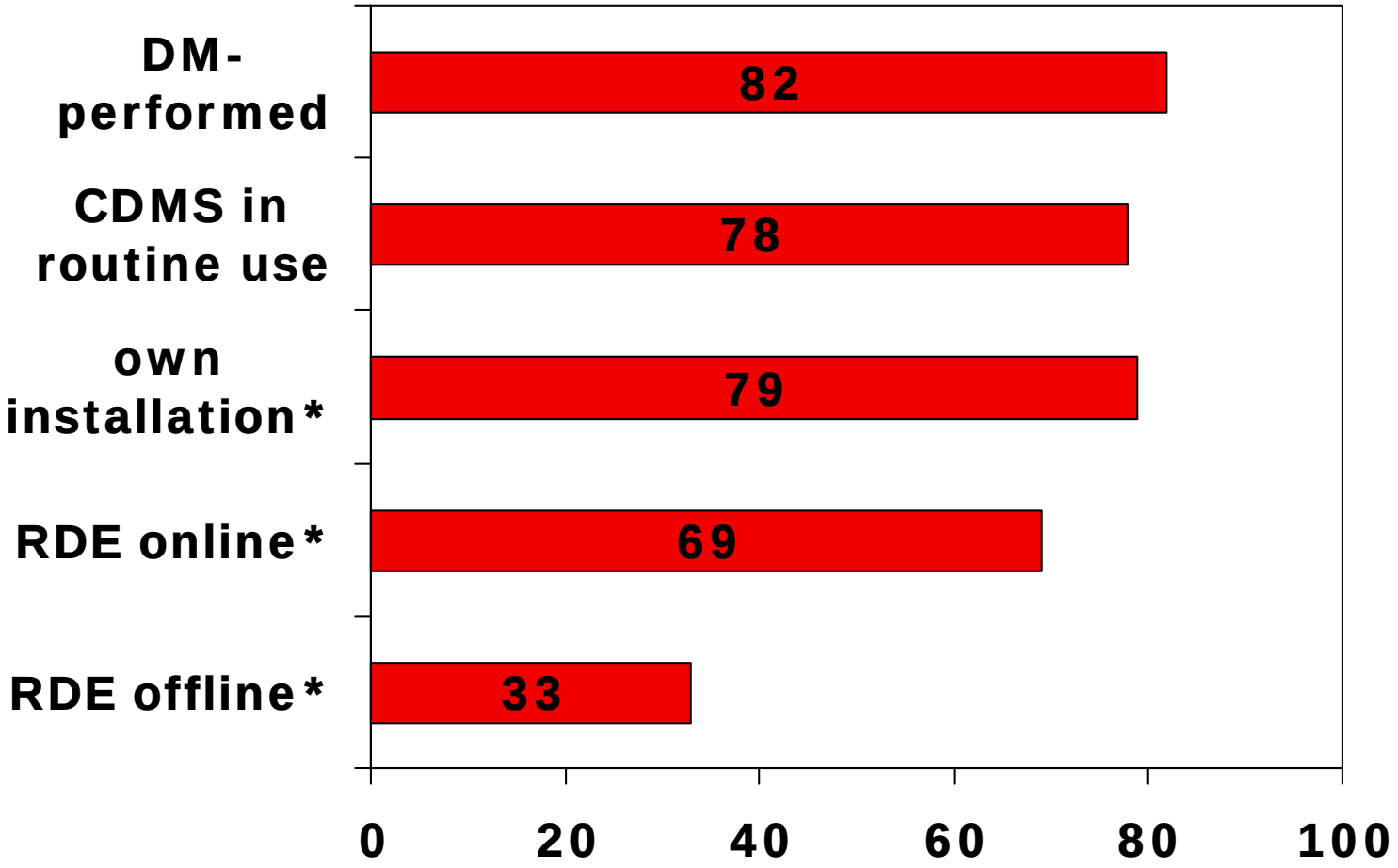
-survey on data management*-

No	country	questionnaire	
		send out	filled in
1	Denmark	12	10
2	EORTC	1	1
3	France	66	18
4	Germany	12	10
5	Ireland	8	4
6	Italy	23	19
7	Spain	8	5
8	Sweden	18	2
9	UK	19	9
total		167	78

*survey, 5/2007

European Clinical Research Infrastructures Network

- DM performed by ECRIN centres* -



*only centers/ units with CDMS in routine use (n=61), survey, 5/2007

European Clinical Research ECRIN Infrastructures Network

European Clinical Research Infrastructures Network

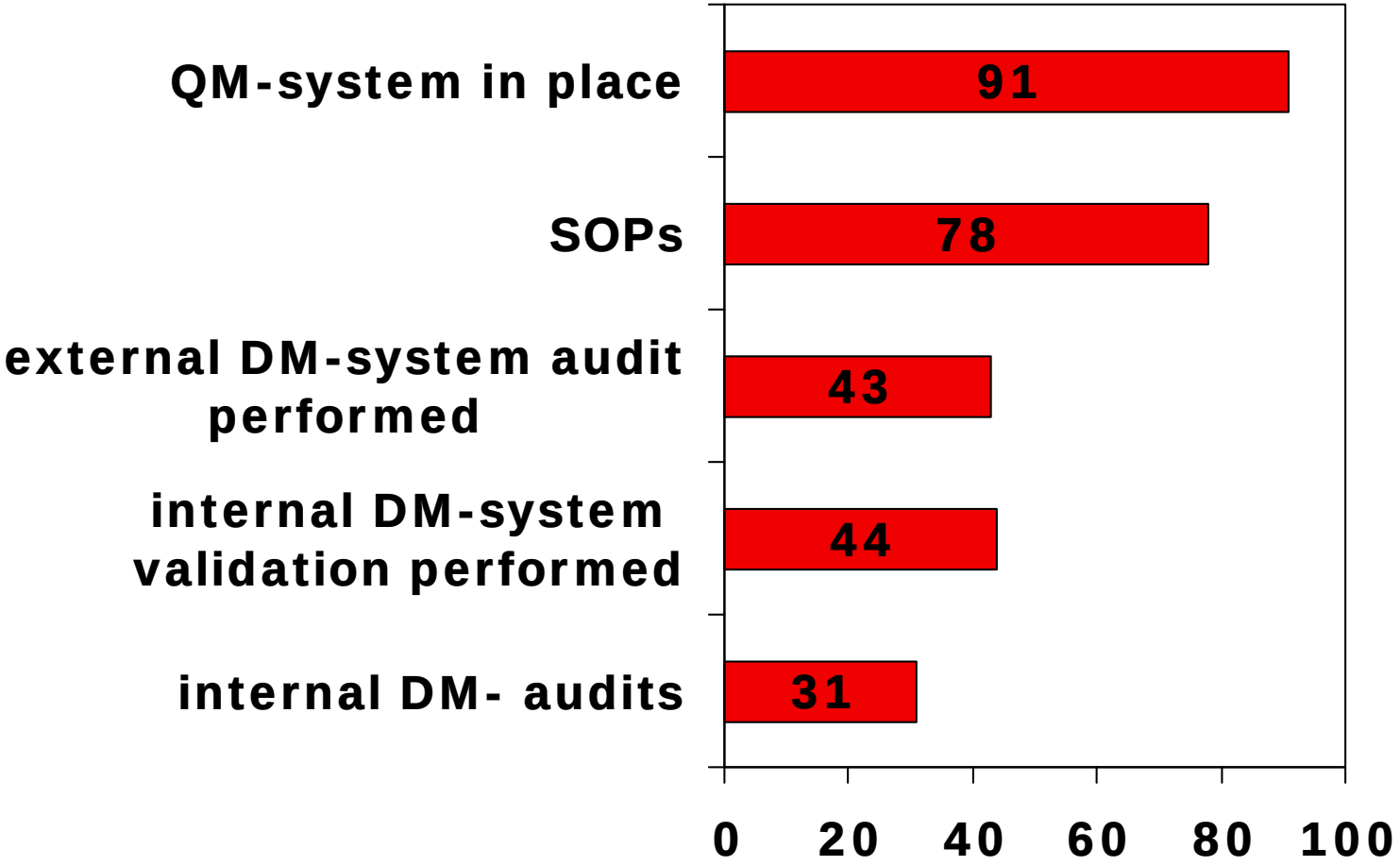
- software in use for DM* -

product name	
commercial	**open source**
Macro™ (n=12+2)	GCP base™ (3)
eResearchNetwork™ (3)	PhosCo™ (1+1)
SAS™-based (3)	Psy Grid™ (1)
Capture System™ (2)	Epidata™ (1)
ECTrial™ (2)	
CliniInfo™ (1)	
SecuTrial™I (1)	
Clin Trial™ (1)	
Epidata™ (1)	
Unknown (3)	

centres with CDMS in routine use (n=61), survey, 5/2007

European Clinical Research Infrastructures Network

- QM and audits -



*only centers/ units performing DM (n=64), survey, 5/2007

European Clinical Research ECRIN Infrastructures Network

European Clinical Research Infrastructures Network

-critical issues identified in the survey -

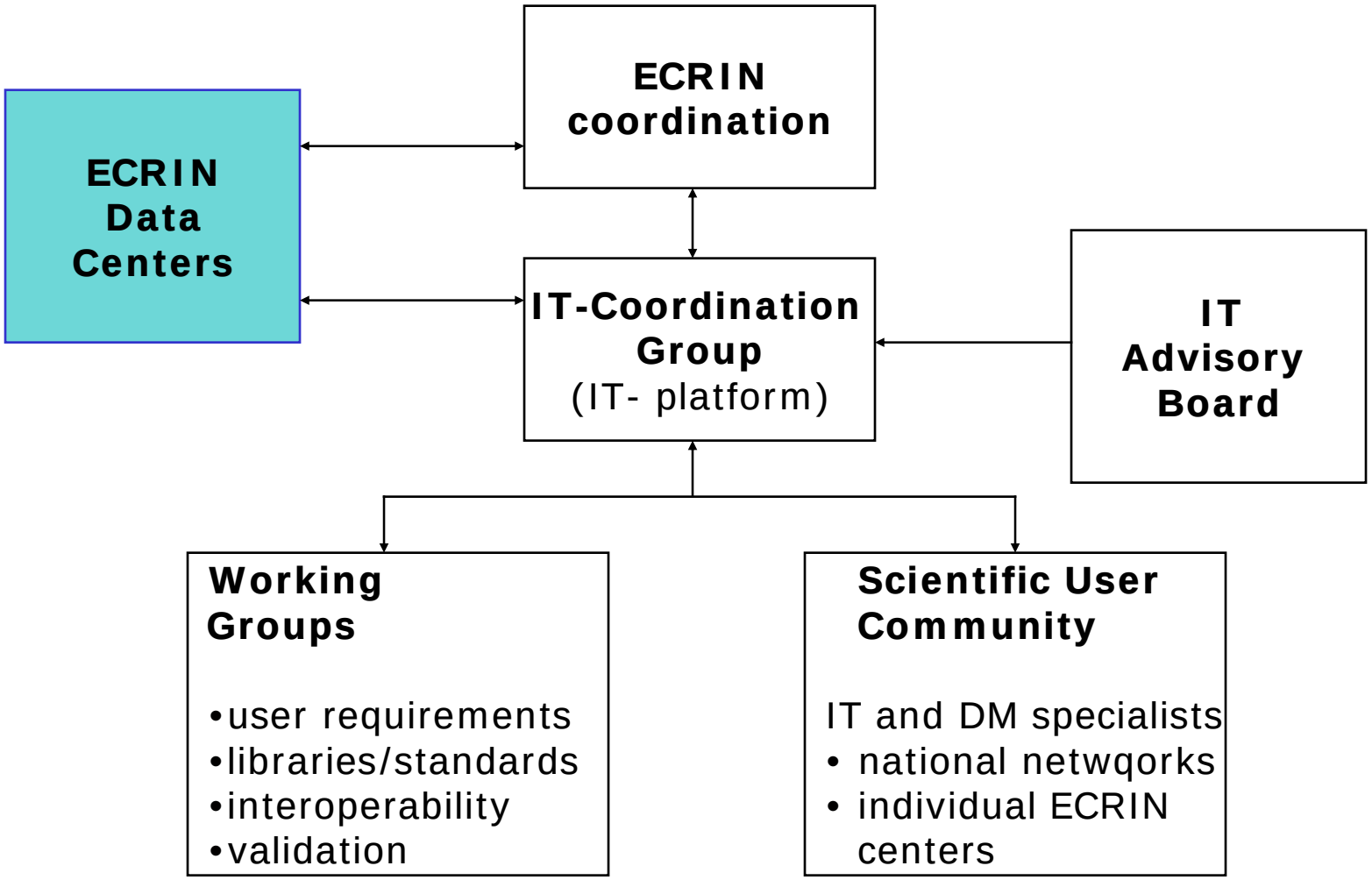
- major experience and professional infrastructures only available in a limited number of clinical trial units *(e.g. in Germany, France, UK)*
- software heterogeneity with the necessity to buy, implement, validate and use all these different systems
- no widespread use of alternative software tools *(e.g. open source)*
- majority of trial units with own local computing center and own installation, rarely cost efficient solutions *(e.g. application service providing)*
- deficits with respect to quality management *(e.g. system validation, external audits)*

European Clinical Research ECRIN Infrastructures Network

**survey, 5/2007*

European Clinical Research Infrastructures Network

- ECRIN 3: ECRIN data centres -



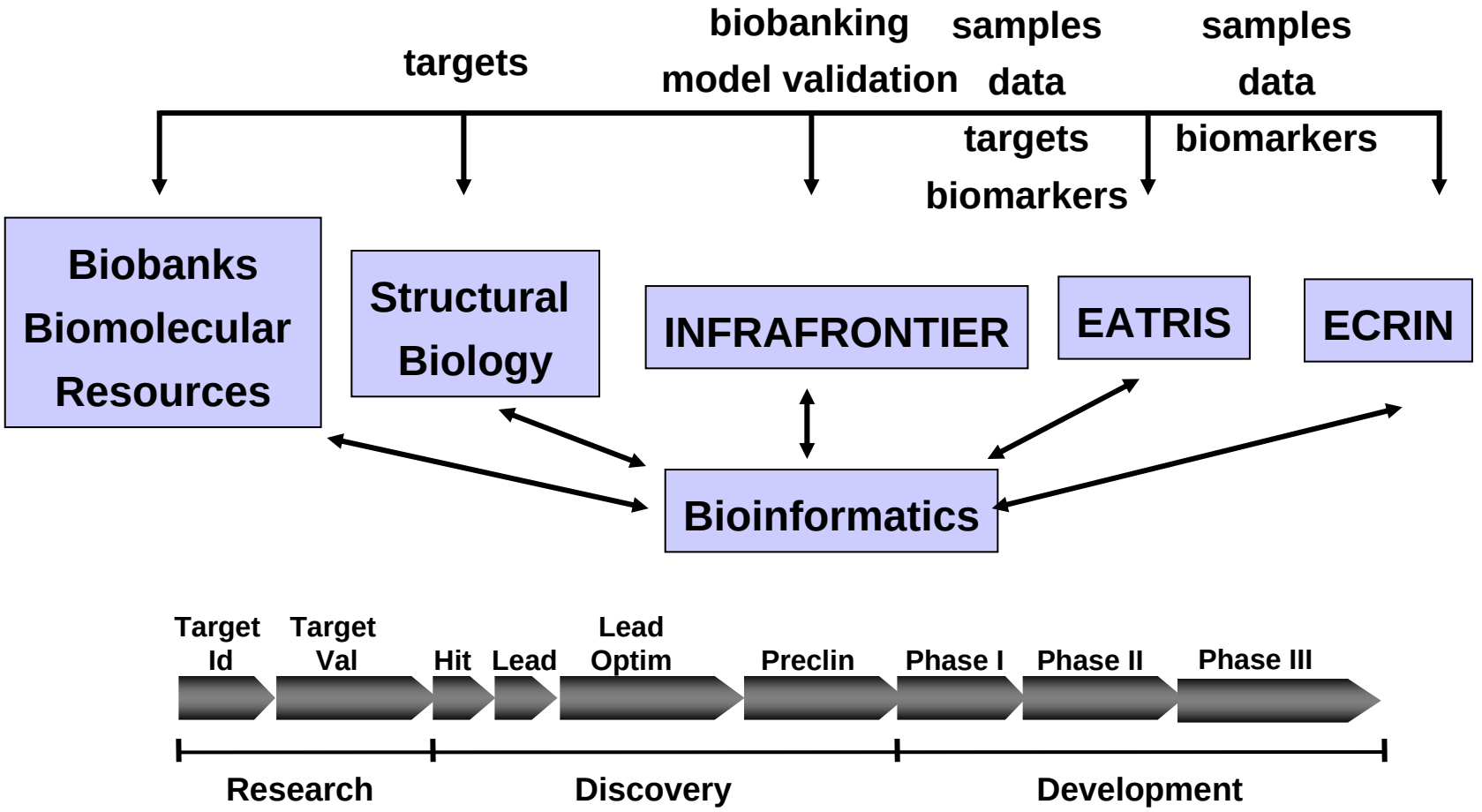
European Clinical Research Infrastructures Network

- IT-coordination group -

- initiation and coordination of platform activities/coordination and steering of working groups
- strategic planning of IT activities and infrastructure
- evaluation and mediation of tools and frameworks for software evaluation, software development, system validation
- evaluation and recommendation of standards and complying tools
- evaluation and accreditation/certification of ECRIN data centers, audits of certified centers

European Clinical Research Infrastructures Network

- synergies with other ESFRI* infrastructures -



*European Strategy Forum for Research Infrastructures, funded by FP7

Conclusions and consequences

- tremendous progress with respect to DM in clinical trials in some countries *(e.g. Germany)*
- core business of GCP-compliant DM adequately performed by selected and qualified clinical trial units/trial centres
- some activities with respect to harmonisation, standardisation and integration *(supported by Telematikplattform e.V.,Germany)*, however, not systematic and on a project by project basis
- no general and comprehensive IT- concept for networked clinical research to direct planning, development and use of software tools

Conclusions and consequences

- areas not or inadequately tackled so far -

- harmonisation of quality management in DM
- harmonisation and standardisation *(e.g. data dicitionaries, case report forms)*
- integration/interoperability of software tools
- primary and secondary use of EHR *(electronic health record)* for clinical research
- IT- support for study management and workflow
- use of eSOURCE and electronic signature
- integration of additional functionality *(e.g. randomisation, „mobile computing“)*
- etc.

Conclusions and consequences

There is a strong necessity for a general and comprehensive IT-conception for networked clinical research

- based on existing experiences and results *(e.g. caBIG, BRIDG)*
- to achieve longterm data integration and interoperability based on standardised, systematic, molecular and open approaches
- in order to support planning, development and use of IT- tools on a cost- efficient basis