European Clinical Research Infrastructures Network

Presented by Arrigo Schieppati
at the ICORD Meeting
Rome, February 23-25, 2009

ECRIN

European Clinical Research Infrastructures Network

Pan-European, distributed infrastructure providing integrated services to multinational clinical research in the EU:

- access to patients throughout the EU

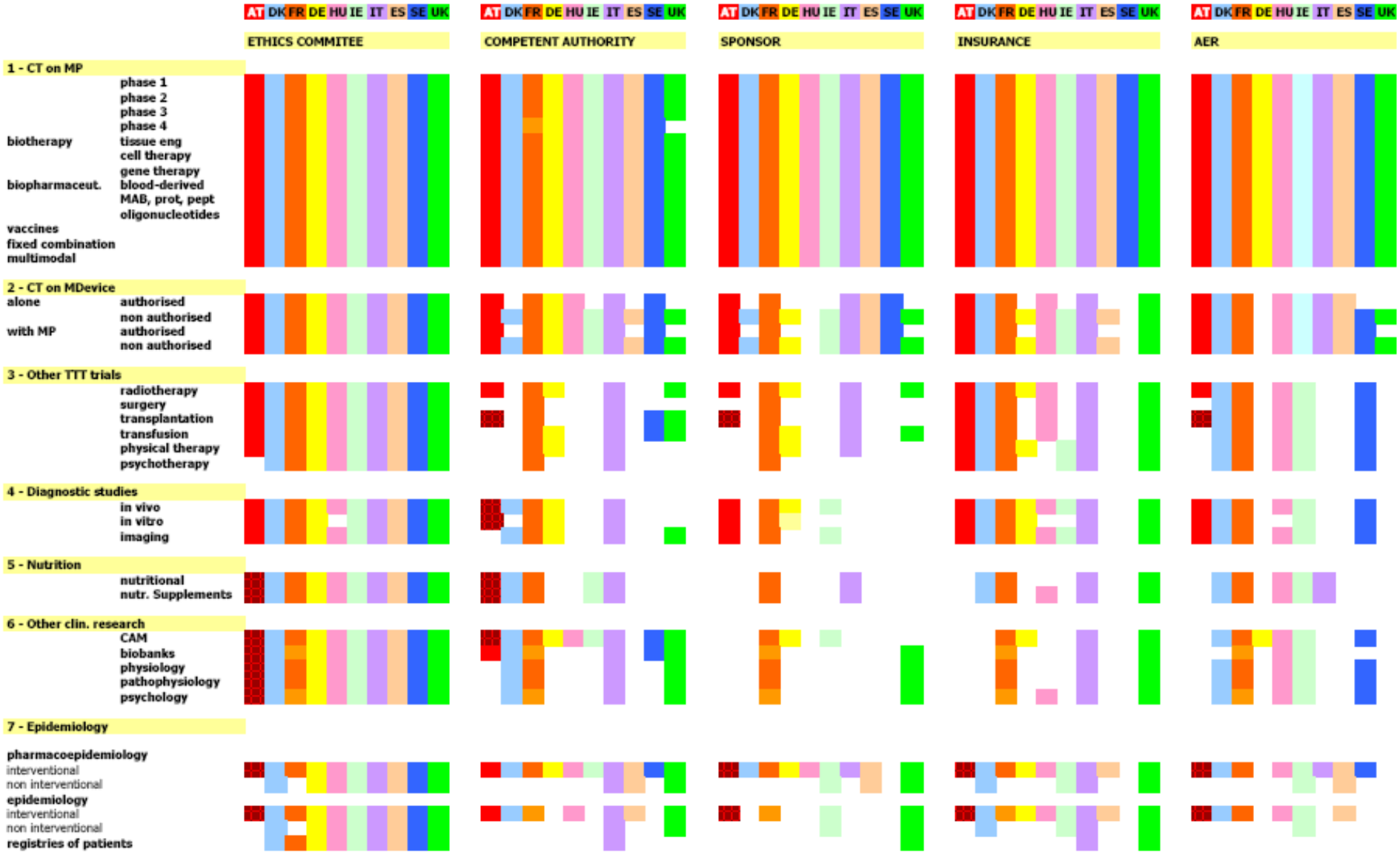
- despite the fragmentation of health and legislative systems

- support to sponsors in multinational studies

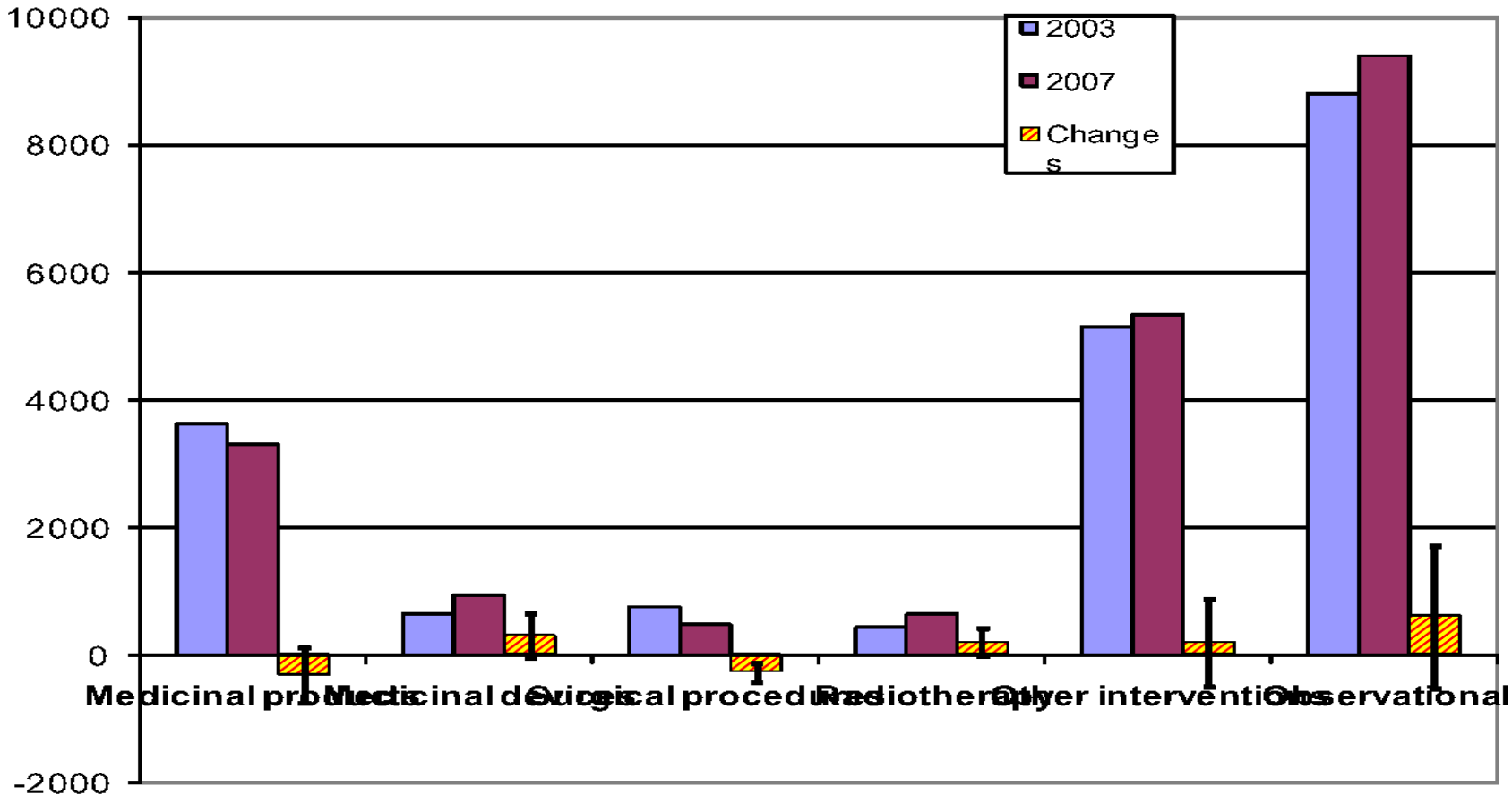
European Clinical Research ECRIN Infrastructures Network

Comparison of national requirements

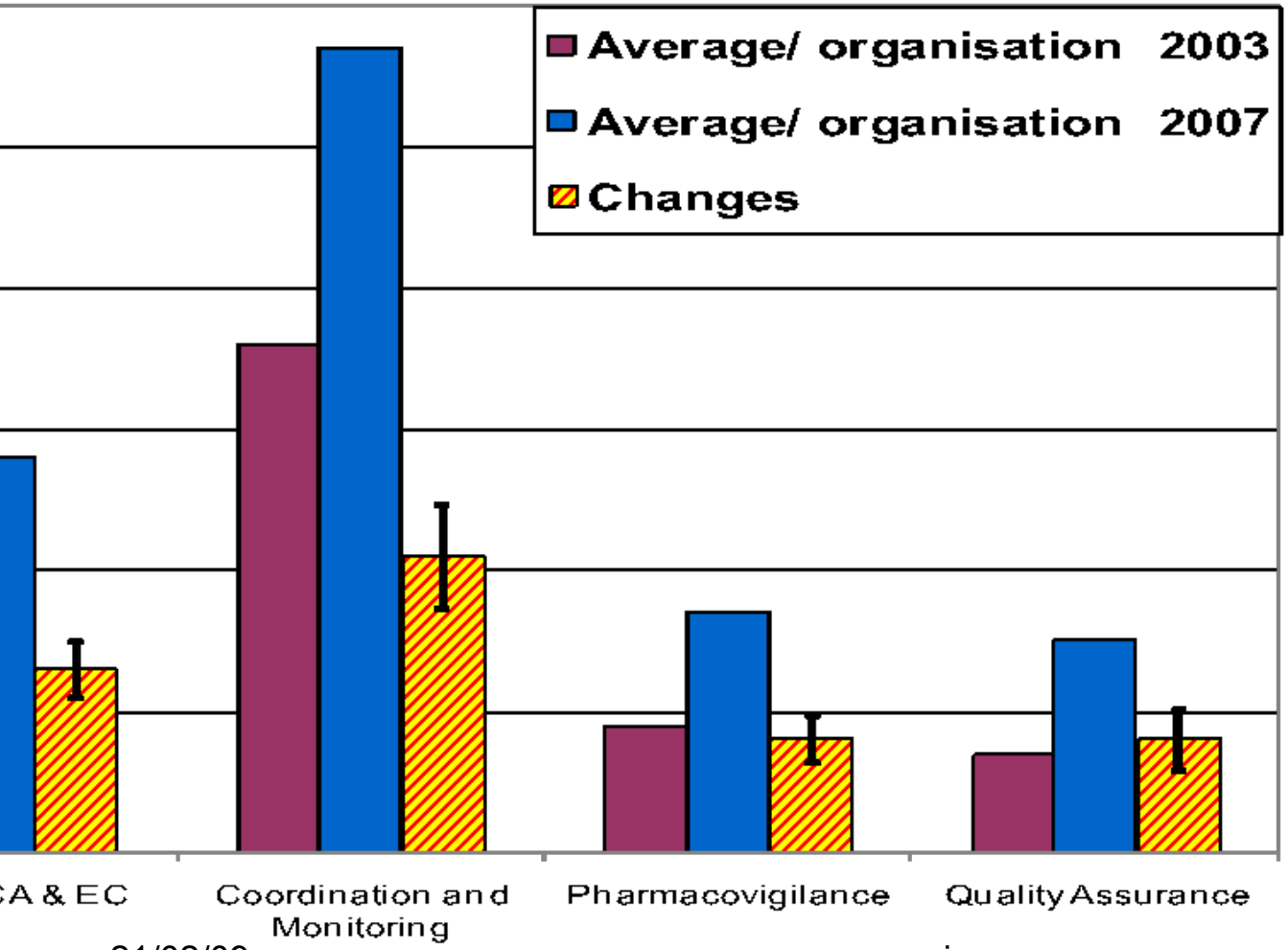
EC CA sponsor insurance AER

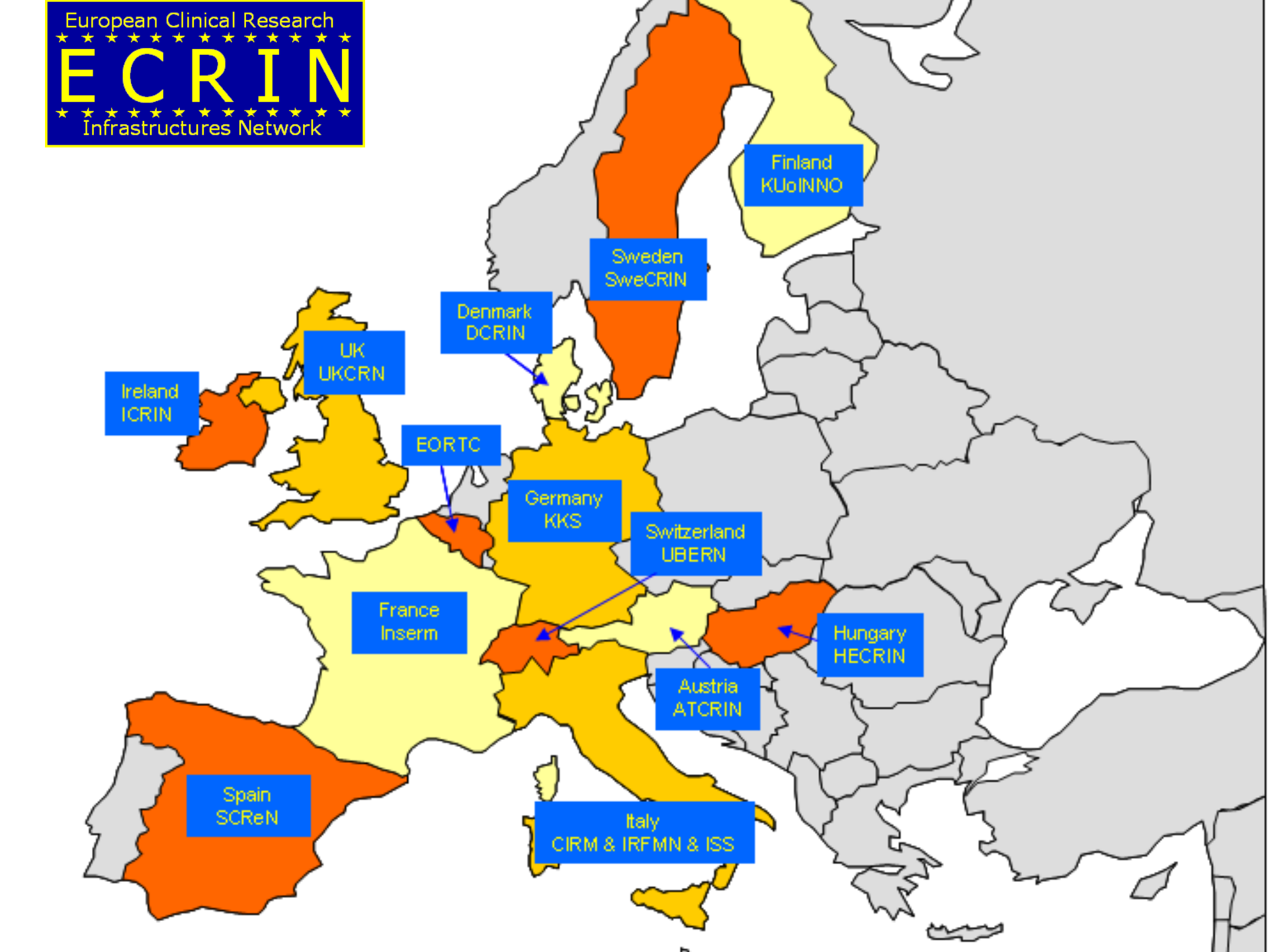


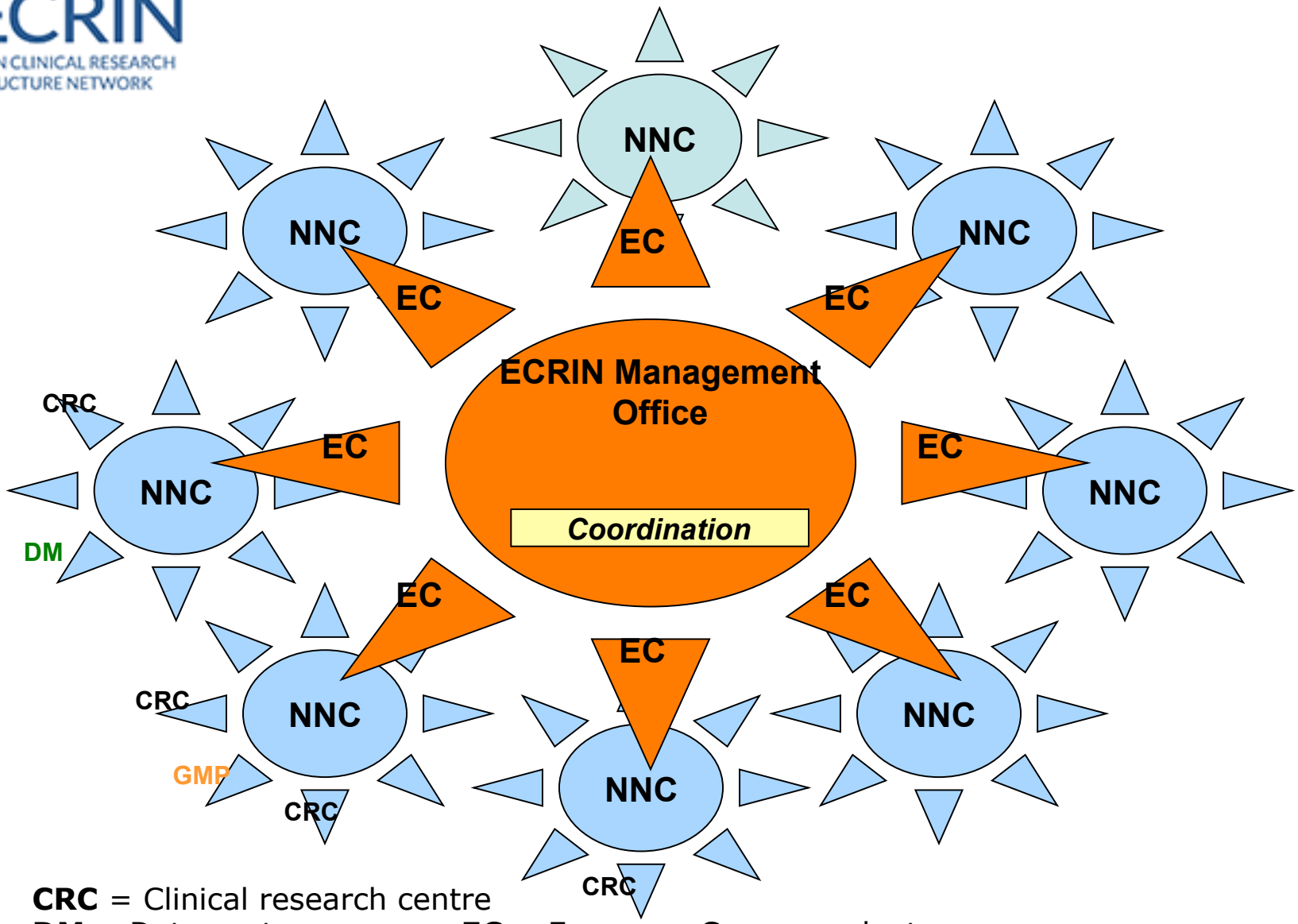
CTs performed before and after the CTD implementation



Workload before and after CTD implementation




European Clinical Research
ECRIN
Infrastructures Network
Finland
KUoINNO
Sweden
SweCRIN
Denmark
DCRIN
UK
UKCRN
Ireland
ICRIN
EORTC
Germany
KKS
Switzerland
UBERN
France
Inserm
Hungary
HECRIN
Austria
ATCRIN
Spain
SCReN
Italy
CIRM & IRFMN & ISS



CRC = Clinical research centre
DM = Data centre **EC** = European Correspondent
GMP = GMP facility for biotherapy **NNC** = National Network Coordination

Scientific Partners

INSERM, France
Heinrich Heine Universitaet Duesseldorf, Germany
Consorzio Italiano per la Ricerca in Medicina, Italy
Rigshospitalet Copenhagen, Denmark
Istituto Mario Negri, Italy
Hospital Clinic i Provincial Barcelona, Spain
Karolinska University Hospital, Sweden
Medical Research Council, Hungary
Dublin Molecular Medicine Centre, Ireland
University of Leeds, UK
EORTC, Belgium
Medical University of Vienna, Austria
Universität Bern, Switzerland
Kuopio Innovation, Finland

Associated Partners

- EFGCP, Belgium,
- Telematikplattform, Germany
- Ministère de la Recherche, France
- Ministère de la Santé, France
- Agency for Science, Technology and Innovation, Denmark
- Science Foundation of Ireland,
- Department of Health, UK
- Ministry of social affairs and health, Finland
- Bundesministerium für Wissenschaft und Forschung, Austria
- Vinnova, Sweden
- Ministerio de Educacion y Ciencia, Spain
- Federal Science Policy Office, Belgium
- TEKES, Finland

Funding Organisations (ministries, research councils)

- Bundesministerium für Bildung und Forschung, Germany
- Health Research Board, Ireland
- Spanish Medicines Agency and Medical Devices, Spain
- Instituto de Salud Carlos III, Spain
- Medical Research Council, UK
- Istituto Superiore di Sanita, Italy

ECRIN, a distributed infrastructure for clinical trials in the EU

- ECRIN-1 (RKP, 2004-2005) :
  Identifying bottlenecks

- ECRIN-2 (TWG, 2006-2008) :
  Design of the infrastructure

- ECRIN-3 (PPI, 2008 - 2011) :
  ESFRI roadmap infrastructure supporting multinational clinical trials in the EU

Mission Statement

Vision

ECRIN is the European infrastructure for clinical research, facilitating clinical research in the European Union, taking advantage of its population size and of its high healthcare standards, and improving quality and transparency for the benefit of patients, citizens and healthcare systems.

Mission

This multinational and distributed infrastructure makes the European Union an integrated area for clinical research, unlocking latent scientific potential, spreading best practices and highest quality standards, thus fostering the attractiveness of Europe for clinical research and increasing the competitiveness of European biomedical research for academic institutions, small- and medium-sized enterprises, and health industry.

Mission Statement

Aims

To achieve this goal:

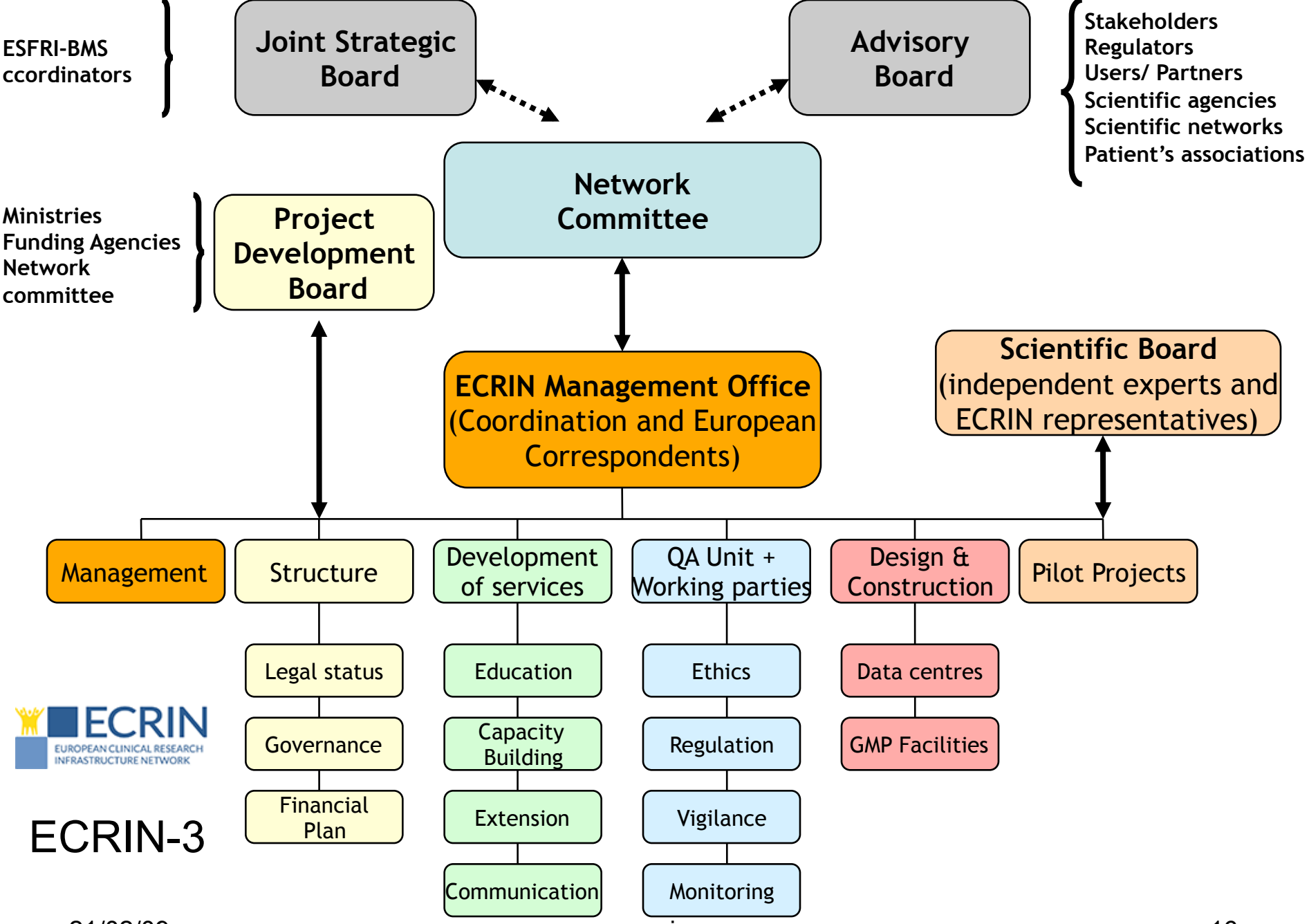
- ECRIN provides integrated 'one-stop shop' support to investigators and sponsors in multinational clinical research projects, for any category of clinical research, in any disease area, particularly in rare diseases where multinational collaboration is a critical success factor.
- ECRIN promotes the development of national networks of clinical research centres and clinical trial units with professional staff and data management tools, implementing high quality standards in the conduct of clinical studies.
- ECRIN promotes education and training, as well as mobility programmes between countries, between preclinical and clinical research, and between academia and industry.
- ECRIN facilitates the connection of disease-oriented networks across borders.

Mission Statement

- ECRIN promotes sound, unbiased methodology ensuring optimal protection of trial participants and high ethical standards.
- ECRIN promotes availability and EU integration of funding to clinical research projects.
- ECRIN promotes harmonisation of national legislation on clinical research and the development of a European regulatory framework providing optimal protection for the trial participants and minimal obstacles to medical institutions, through requirements adapted to the risk of the individual trial.
- ECRIN promotes transparency and optimal use of data through public registration of clinical studies, transparent reporting, and the development of public repositories for clinical study data.
- ECRIN promotes the active participation of patients in clinical research, through their involvement in every step including the initiation and design of clinical studies.

Mission Statement

- ECRIN promotes communication on the challenges raised by clinical research with patients, families, citizens, ethics committees, competent authorities, academic and industry sponsors, news media, national and EU policy makers, and other stakeholders.
- ECRIN acts synergistically with the other EU biomedical infrastructures involved in preclinical research and biobanking, promoting common strategies, shared procedures and interoperable data, thus providing a comprehensive support to biomedical science in the EU.
- ECRIN plans extension to all the EU member and associated states, develops partnership with clinical research infrastructures in other world regions, and with developing countries through its capacity building programme.



ECRIN
EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK

ECRIN-3

Flexible, integrated services in the conduct of the study

- Decentralised
  - 1 - interaction with ethics committees
  - 2 - interaction with competent authorities
  - 3 - participant recruitment and investigation
  - 4 - drug dispensing
  - 5 - circulation and storage of blood and tissue samples
  - 6 - study monitoring
- Centralised
  - 7 - adverse event reporting
  - 8 - data management – data centres
  - 9 - GMP manufacturing of biotherapy products

Information and consulting during the preparation of the study

- Practical information
  - 1 - Ethical requirements
  - 2 - Regulatory requirements
  - 3 - Insurance
  - 4 - Centre selection
  - 5 - Cost evaluation
  - 6 - Funding opportunities
- Methodology
  - 7 - Systematic review, meta-analyses, and trial sequential analyses
  - 8 - Methodology, protocol design
  - 9 - Biostatistics
  - 10 - Data safety and monitoring board

Access to the services: eligibility and acceptance

Access to the infrastructure is given by the Scientific Board

Two-step evaluation process

1 – Eligibility, based on a synopsis, helps the investigator to look for a sponsor, for funding, and/or to write the full protocol.

2 – Acceptance, based on the full protocol, once funding is secured and the sponsor identified.

Parallel assessment of feasibility, logistics and funding is performed by the ECRIN coordination

Final decision / ECRIN Network Committee.

Scientific board

- Silvio Garattini (chair)
- Colin Baigent,
- Jean Pierre Boissel,
- Christiane Druml,
- Ralph Edwards,
- Christian Gluud,
- Walter Lehmacher

  (plus Richard Sylvester as a biostatistician for cancer projects)

- *Secretariat: Vittorio Bertelé*

Eligibility and acceptance

- The **eligibility criteria** are:
  - Rationale based on up-to-date systematic reviews.
  - Multicentre project run in at least two EU countries.
  - Clinical importance and/or marked impact on public health.
  - Justified design, e.g., in case of efficacy assessment:
    - Randomised superiority trials
    - Adequate sample size
    - Hard outcome measures (i.e., relevant to patients).
  - Reasonable indications of feasibility.
  - Potential funding.
  - CV of the coordinating investigator.

Eligibility and acceptance

- The **acceptance criteria** are:
  - Involvement of pertinent patient associations in the protocol design.
  - Methodological suitability, i.e., study design correctly fits with research question.
  - Governance structure of the project including responsibility for data analysis and external monitoring.
  - Description of potential risks and handling of such risks, including involvement and charter for independent data monitoring and safety committee.
  - Funding sources.
  - Rules for transparency
    - Registration of the trial.
    - Commitment to publish irrespective of results.
    - Access to database once the study is completed.
    - Conflicts of interest.

Roles and responsibilities in the provision of services

- Services are provided by the network of ECRIN European Correspondents (EC)
- The ECRIN EC in the country hosting the sponsor / principal investigator (coordinating EC) is in charge of coordinating the services to the clinical study.
- In each country, he will be supported by the national EC who will either carry-out by himself, or delegate to his/her national network, the tasks assigned by the coordinating EC.
- The role of the ECRIN Coordination consists of organising an efficient and coordinated workflow between the national networks and ECs, of maintaining a quality assurance system, of managing the overall infrastructure, but not of coordinating each individual study.

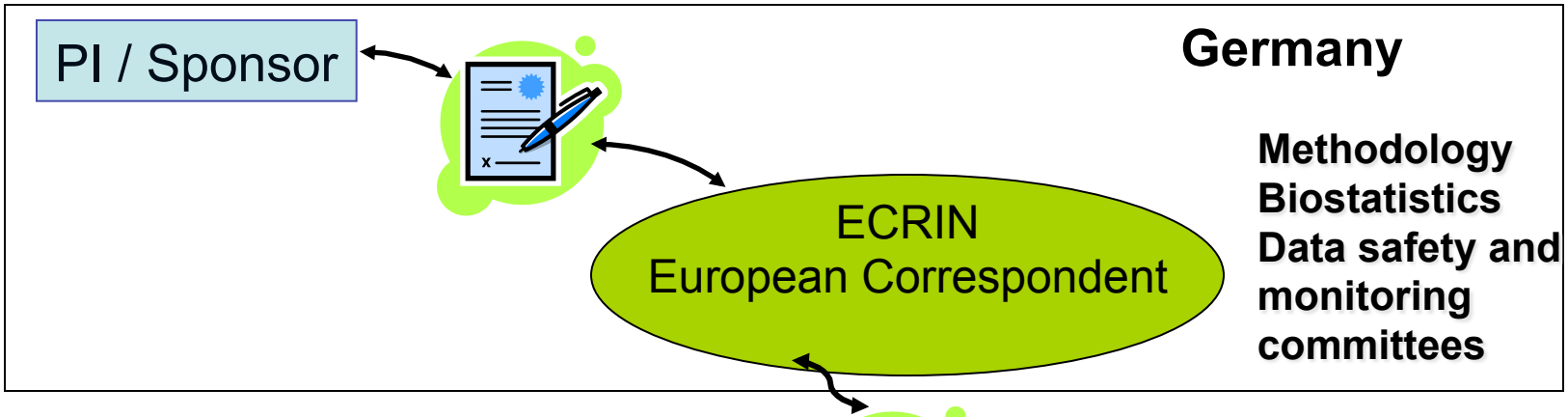
Preparation of the project, submission and contracting

- Projects seeking access to ECRIN will benefit from a free support of the European Correspondent in the country hosting the sponsor / principal investigator (coordinating EC) to prepare the application. This support in the preparation may include collection of information from the other ECs and national networks, from the ECRIN coordination, and from the relevant ECRIN working groups (ethics, regulation, vigilance, monitoring).

- The contact with the Scientific Board is achieved through its secretariat, and preliminary discussion with the secretariat may help refine the proposed project upstream to submission to the Board.

- Once the project is agreed by both ECRIN and the sponsor, a task delegation contract is prepared and signed between ECRIN and the sponsor in order to define the selected services, the cost of these services, and their respective roles and responsibilities in the conduct of the clinical study.

Consulting / Information



Germany

Methodology
Biostatistics
Data safety and monitoring committees

France

ECRIN Correspondent
+ National Coordination

Ethical requirements
Regulatory requirements
Cost evaluation
Funding opportunities
Insurance
Proposal of centres

Spain

ECRIN Correspondent
+National Coordination

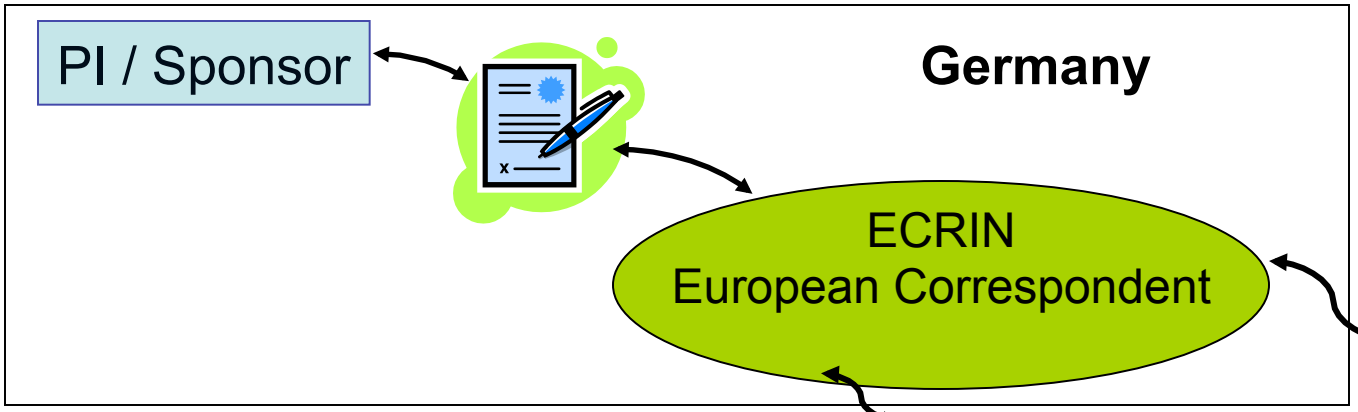
Ethical requirements
Regulatory requirements
Cost evaluation
Funding opportunities
Insurance

UK

ECRIN Correspondent
+National Coordination

Ethical requirements
Regulatory requirements
Cost evaluation
Funding opportunities
Insurance

Set up and management



Centralised services

Data Centre

Vigilance

Decentralised services

France

ECRIN Correspondent + National Coordination

Coordinate or perform:
- **Preparation of documents**
- **Submission EC, CA, other authorities**
- **Insurance process**
- **Management IMP**
- **Management of samples**
- **Monitoring**

Spain

ECRIN Correspondent +National Coordination

Coordinate or perform:
- **Preparation of documents**
- **Submission EC, CA, other authorities**
- **Insurance process**
- **Management IMP**
- **Management of samples**
- **Monitoring**

UK

ECRIN Correspondent +National Coordination

Coordinate or perform:
- **Preparation of documents**
- **-Submission EC, CA, other authorities**
- **Insurance process**
- **Management IMP**
- **Management of samples**
- **Monitoring**