ECRIN
EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK

What is ECRIN?
What is ECRIN-*Eric* ?

Xavier Carné
Nuria Sanz
Joaquín Saez
Mohammed Ezzeldin
www.ecrin.org

Need for independent clinical trials

Ø ***Clinical trials :***

- development of innovative health products
- exploring new indications for existing drugs
- comparative assessment of efficacy and safety of approved healthcare strategies

Ø ***evidence-based medical practice***

Ø ***international cooperation required:***

- cost
- expertise
- access to patients

Collaboration trend

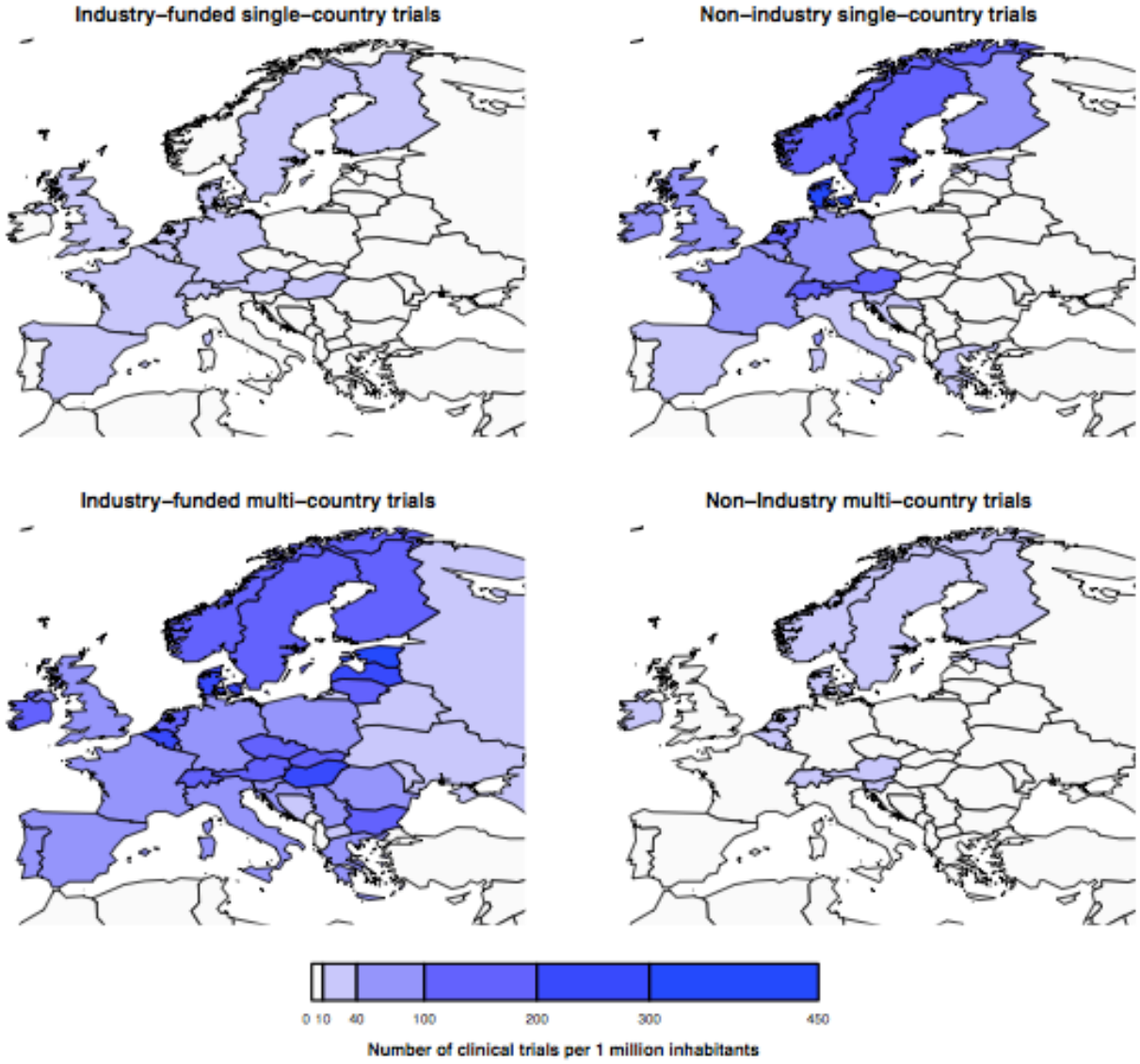
er

Single–country multi–center

Single–continent multi–country

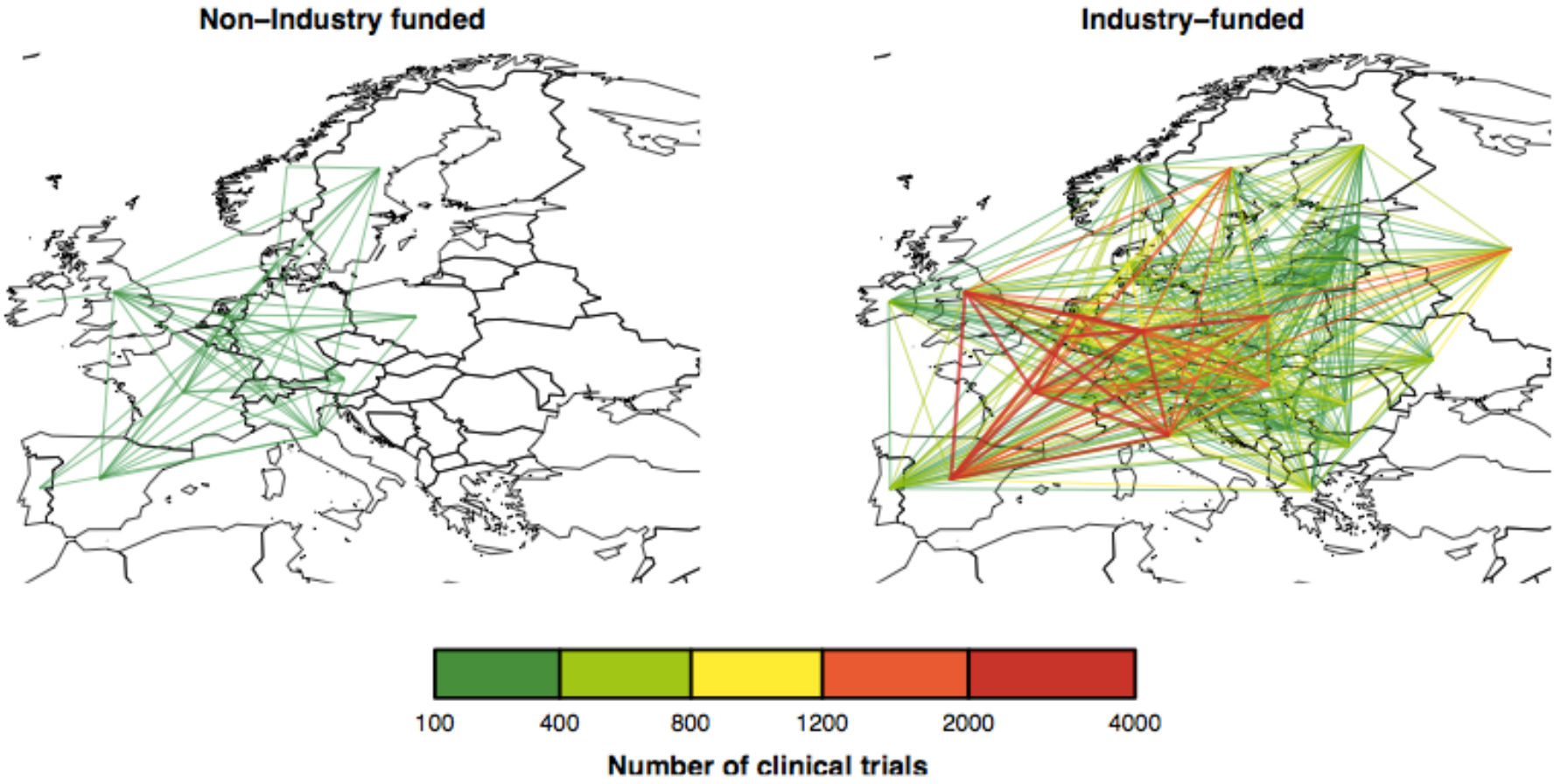
Multi–continent

European collaborative distribution



I Atal Chomali, L Trinquart, R Porcher, P Ravaud
INSERM U1153, Team METHODS, Paris, France

European collaboration network



What is ECRIN?

WHAT IS ECRIN?

- Is the European Clinical Research Infrastructure Network
- Is the European network formed by national networks.

AIMS:

- **Coordination** at the European level of multinational clinical trials.
- **Distributed provision of services** in the conduct ion of multinational clinical projects
- **Operational use and coordination** of existing and experienced national infrastructures with professional staff

Steps towards the constitution of ECRIN-ERIC

- **ECRIN-1** (RKP, 2004-2005) : Identifying bottlenecks (FP6)
- **ECRIN-2** (TWG, 2006-2008) : Development of know-how(FP6)
- **ECRIN-3** (PPI, 2008 - 2011) : Preparatory phase for infrastructure supporting multinational clinical trials in the EU (FP7)
- **ECRIN IA (2012-2015): Translational Access.** The fourth step of the ECRIN programme, funded by the FP7 Infrastructure programme.
- **ECRIN-ERIC**

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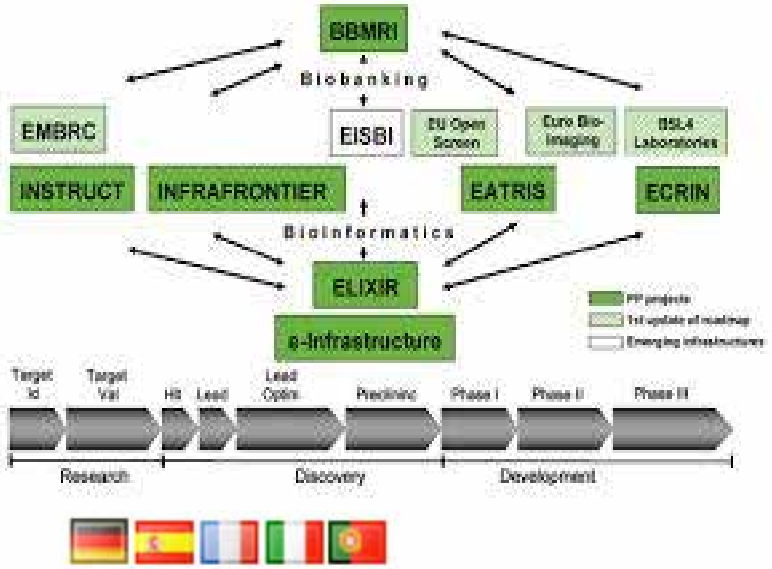


COMMISSION IMPLEMENTING DECISION

of 29 November 2013

on setting up the European Clinical Research Infrastructure Network (ECRIN) as a European Research Infrastructure Consortium (ECRIN-ERIC)

(2013/713/EU)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Council Regulation (EC) No 723/2009 of 25 June 2009 on the Community legal framework for a European Research Infrastructure Consortium (ERIC) [1], and in particular point (a) of Article 6(1) thereof,

Whereas:

(1) The Federal Republic of Germany, the Kingdom of Spain, the French Republic, the Italian Republic and the Portuguese Republic requested the Commission to set up the the European Clinical Research Infrastructure Network (ECRIN) as a European Research Infrastructure Consortium (ECRIN-ERIC).

The French Republic has been chosen by the Federal Republic of Germany, the Kingdom of Spain, the Italian Republic and the Portuguese Republic as the Host Member State of ECRIN-ERIC.

The measures provided for in this Decision are in accordance with the opinion of the Committee established by Article 20 of Regulation (EC) No 723/2009,

HAS ADOPTED THIS DECISION:

Article 1

1. The European Clinical Research Infrastructure Network as a European Research Infrastructure Consortium named ECRIN-ERIC is hereby established.

2. The Statutes of ECRIN-ERIC are set out in the Annex. These Statutes shall be kept up to date and made publicly available on the website of ECRIN-ERIC and at its statutory seat.

3. The essential elements of the ECRIN-ERIC Statutes for which amendments shall require approval by the Commission in accordance with Article 11(1) of Regulation (EC) No 723/2009 are provided for in Articles 1, 2, 3, 11, 12, 14, 15, 19 and 20.

Article 2

This Decision shall enter into force on the third day following that of its publication in the *Official Journal of the European Union*.

Done at Brussels, 29 November 2013.

For the Commission

The President

José Manuel BARROSO

ECRIN-ERIC Members and Scientific Partners

Strategy - maturation

ECRIN-*ERIC* Member Countries

ECRIN-*ERIC* Member Country Representatives (Assembly of Members)

National Scientific Partners ECRIN-*ERIC* (Network Committee)

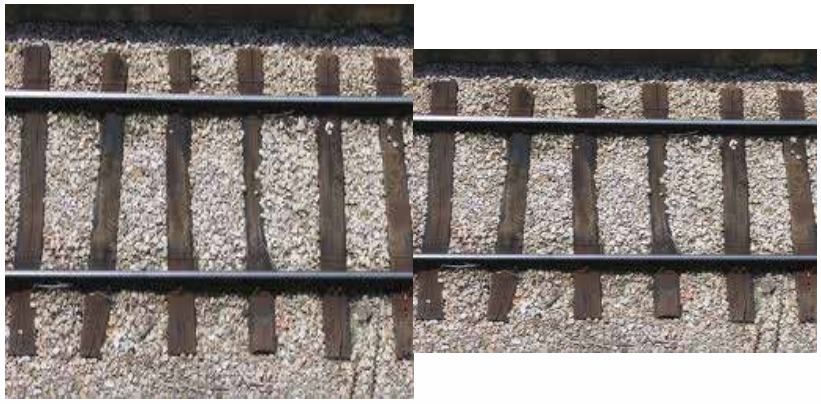
Steering Committee

Multinational clinical trials

Ø updated infrastructure

Ø high impact projects

Ø interoperability



Ø appropriate funding

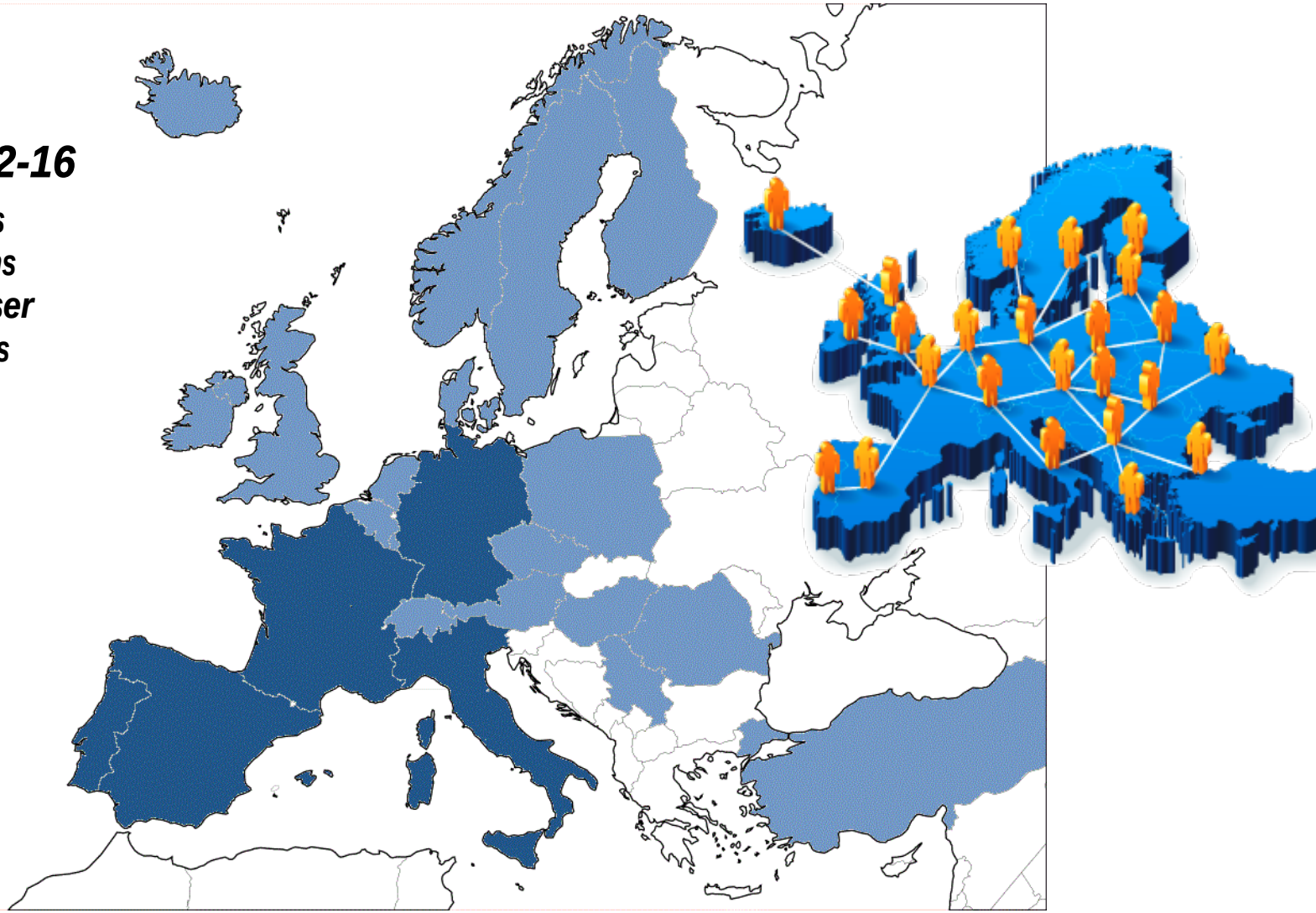
ECRIN ERIC 2013

ECRIN IA 2012-16

23 countries
567M citizens
Structuring user communities

ECRIN-ERIC
5 countries
266M citizens
Sustainable infrastructure

4 countries about to join



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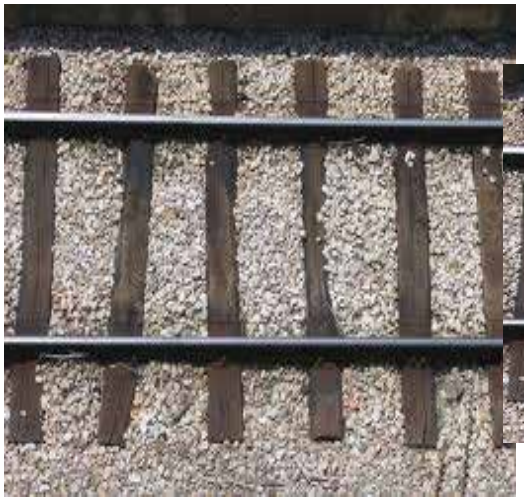
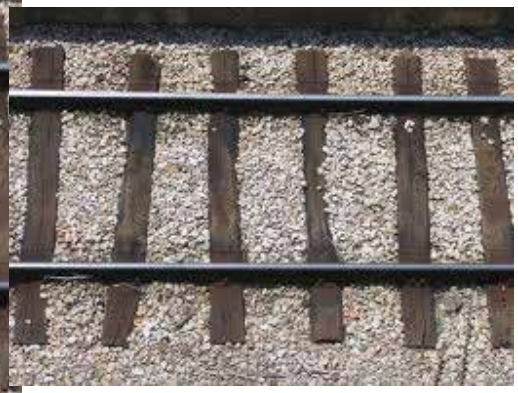
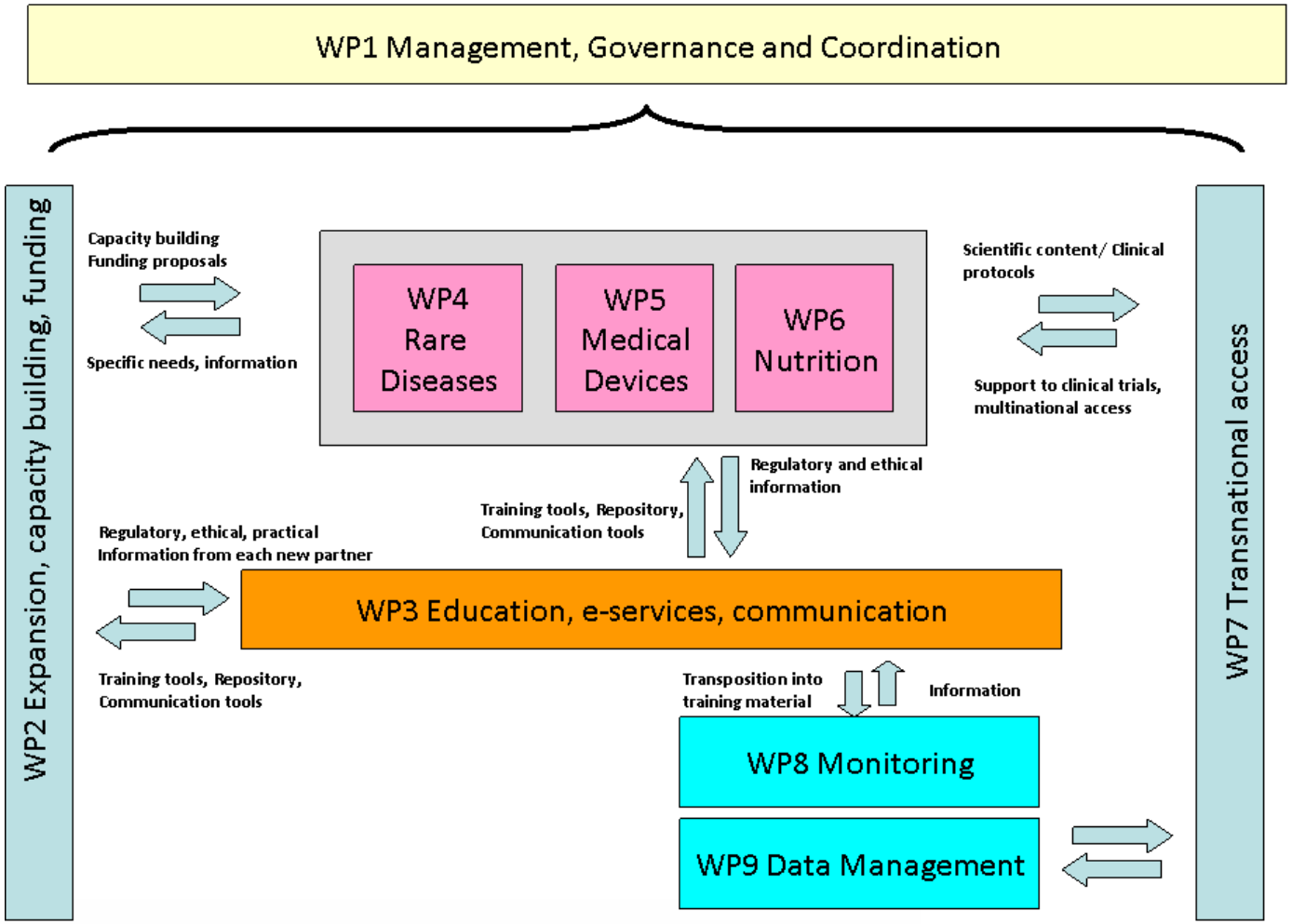
Capacity: developing an updated infrastructure, and interoperable tools and procedures





ECRIN-IA (2012-16): structuring pan-European investigation networks



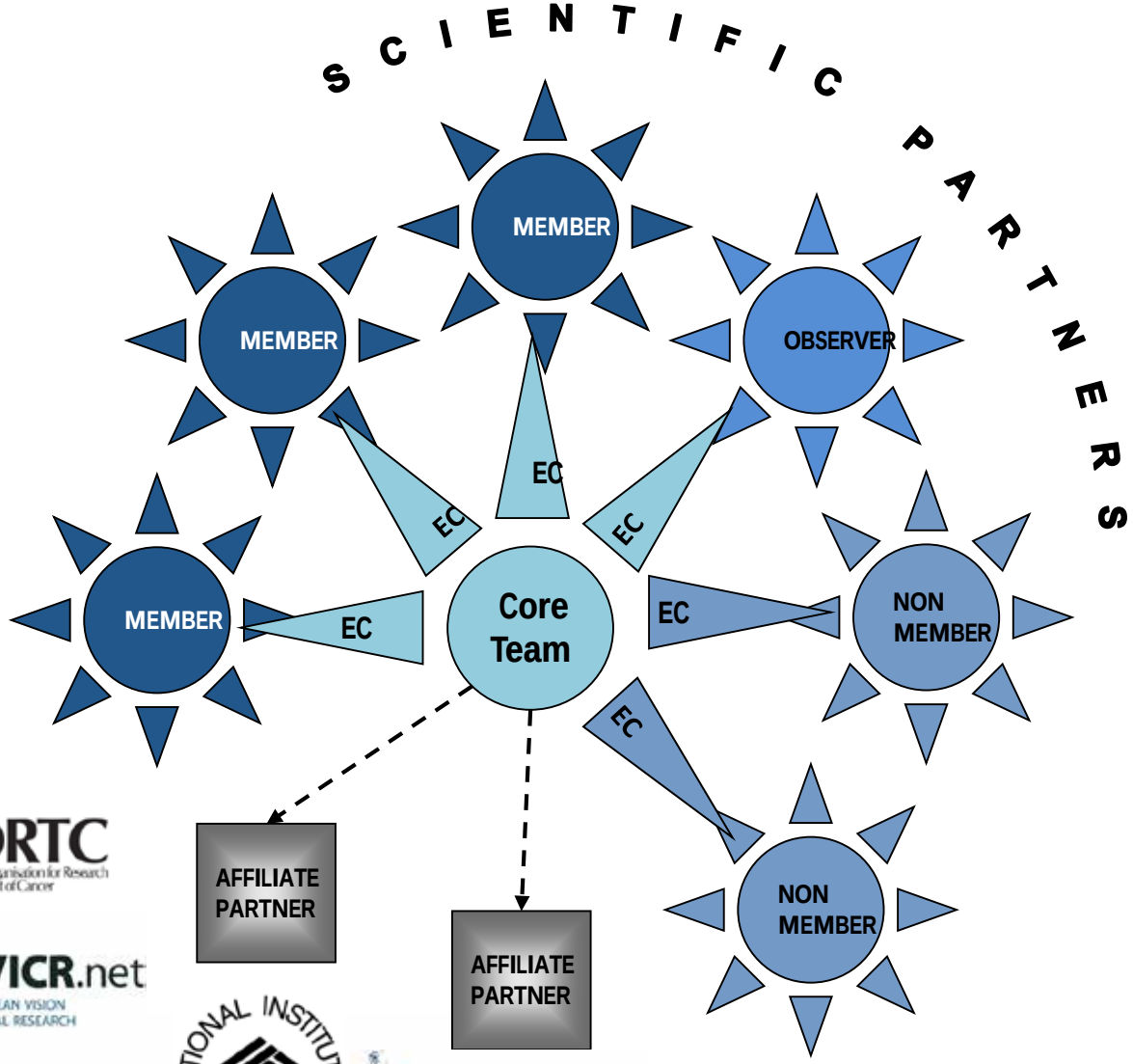
ECRIN-ERIC and its partners

- **ECRIN ERIC**
- **not-for-profit organisation**

- **Scientific Partners (national networks & hubs)**

- ***framework contracts on***
  - provision and costs of services
  - quality assurance

- ***single contract with sponsor***
- ***PIC 948646712***



Data centres

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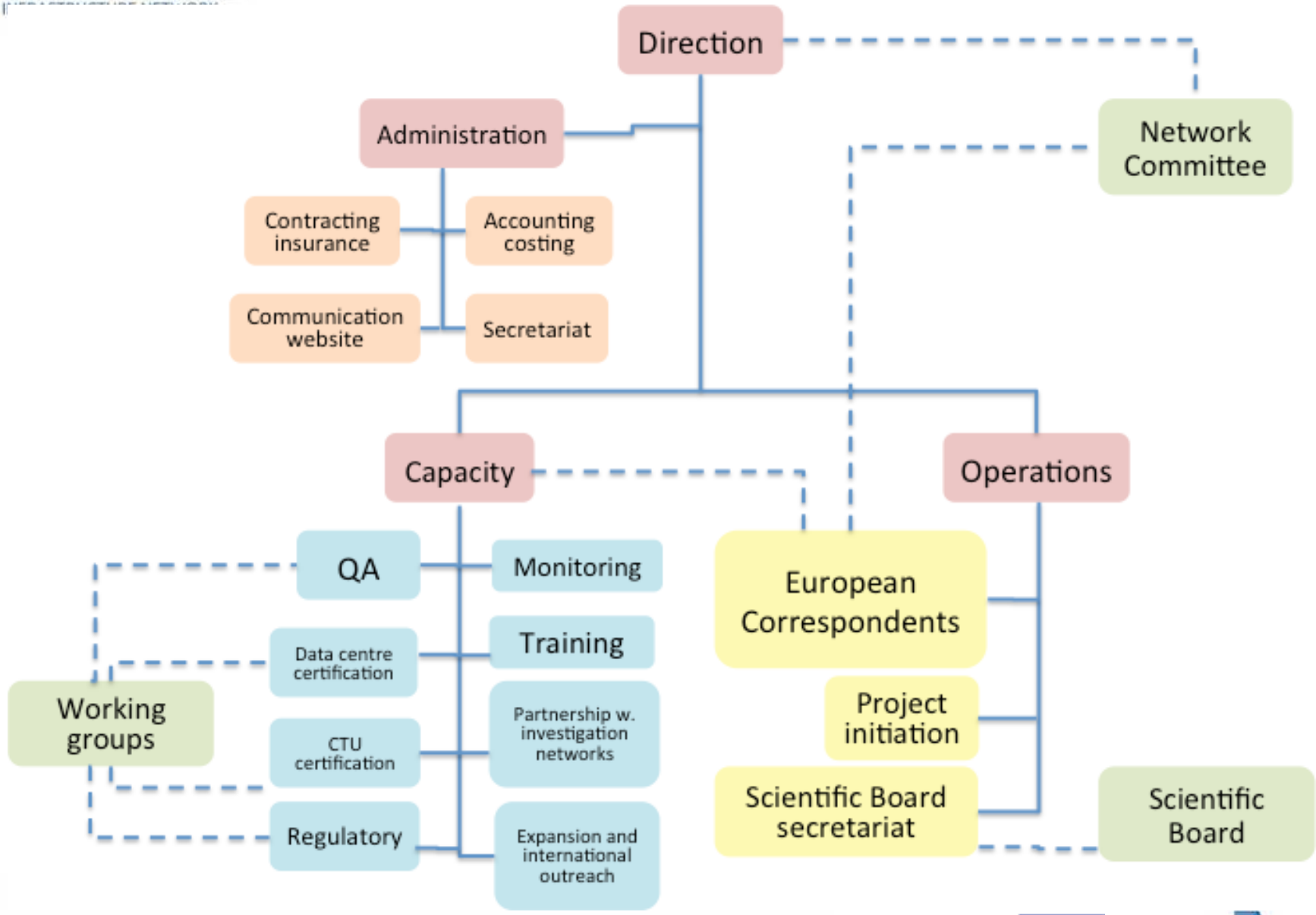

Pan-European structuring of biomedical research

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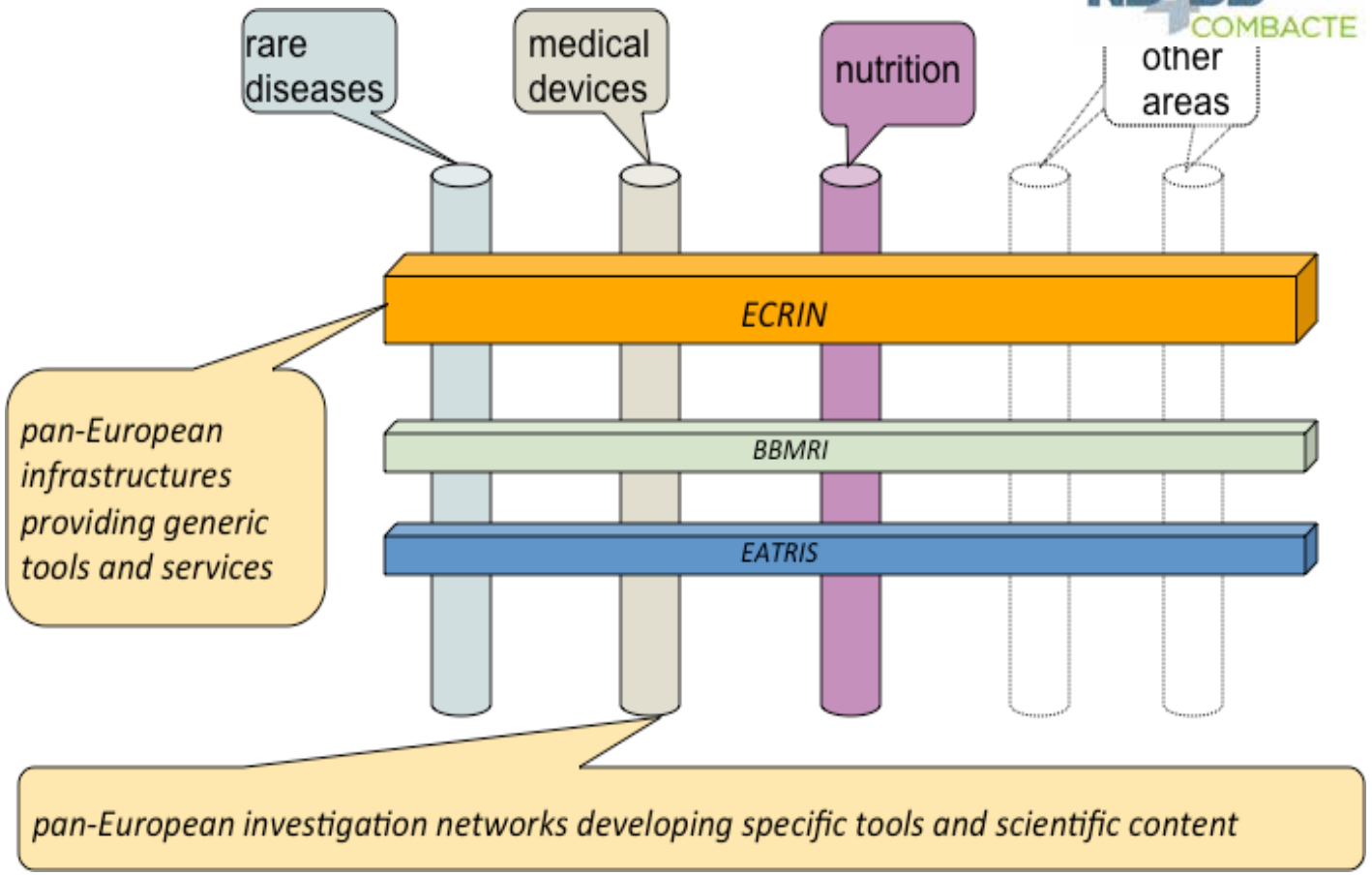
ROAMER

ND4BB COMBACTE



InnoRARE MuO

EU-OPENSCREEN
Chemical keys for life's locks

BBMRI
Biobanking and Biomolecular Resources Research Infrastructure

EATRIS
European Infrastructure for Translational Medicine

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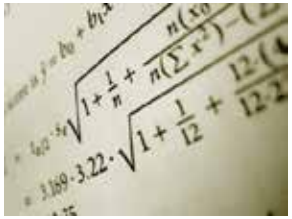
Future perspectives for clinical research: forward looking 'think tank'

- Statistical methodology



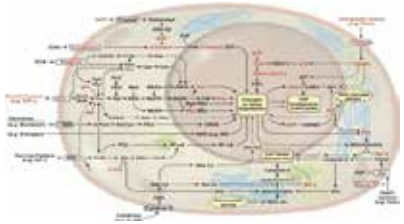
- Use of healthcare data, data quality
- Patient registries, trials nested in cohorts

- Transparency and optimal use of data

- Integration of high throughput data (genomics, imaging)

- Disease taxonomy and stratified medicine
- Personalised medicine

- Sanitary Systems
  - expert systems optimising personal healthcare strategies
  - modeling trials to select design



OECD Global Science Forum

Facilitating International Cooperation in Non-Commercial Clinical Trials

OCTOBER 2011

www.oecd.org/sti/sci-tech/49344626.pdf

Follow-up / implementation

- WG on infrastructure and funding
- WG on investigator training and certification
- WG on accreditation of ethics committees
- WG on patient involvement
- WG on comparative effectiveness research
- WG on regulation

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Operations: support to multinational clinical trials

How does ECRIN support multinational trials ?

Ø **Information and consultancy during the preparation of the trial**

- Information on regulatory and ethical requirements
- Information on sites and participant recruitment
- Information on clinical trial units
- Information on insurance
- Information on cost and funding opportunities
- Information on contracting
- Adaptation to local context
- Methodological support

Full protocol

Scientific evaluation

Logistical assessment

Contract with sponsor

Ø **Services during the conduct of the trial**

- Interaction with competent authorities and ethics committees
- Support with insurance contracting
- Adverse event reporting
- Monitoring
- Data management
- Investigational medicinal product management
- etc.

ECRIN certification policy

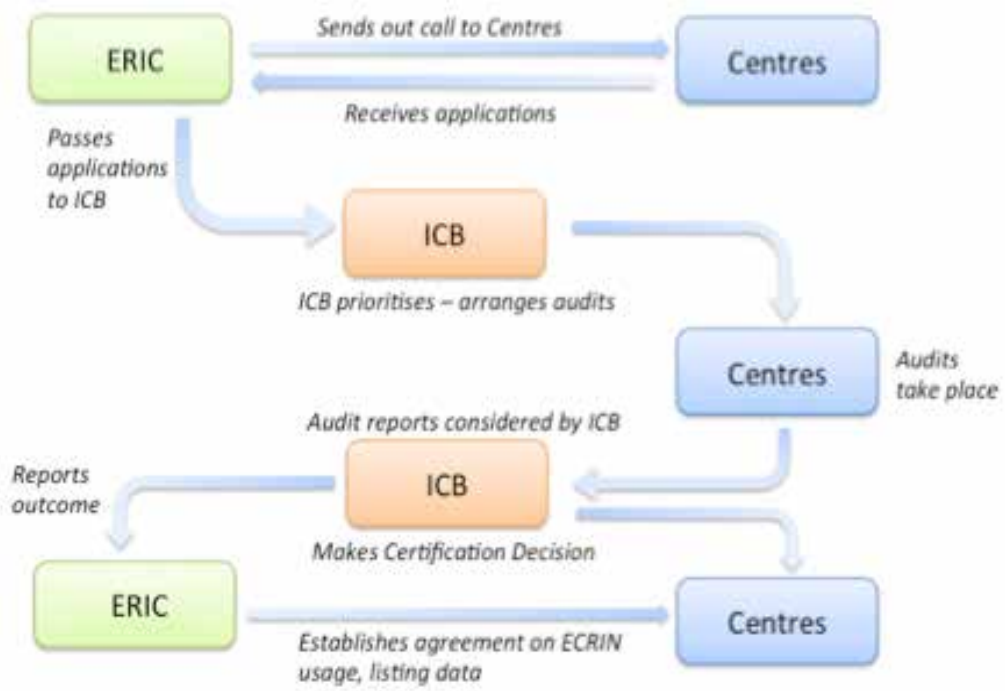
Ohmann et al. Trials 2011, 12:85
http://www.trialsjournal.com/content/12/1/85

TRIALS

RESEARCH Open Access

Standard requirements for GCP-compliant data management in multinational clinical trials

Christian Ohmann[1*†], Wolfgang Kuchinke[1†], Steve Canham[2†], Jens Lauritsen[3], Nader Salas[4], Carmen Schade-Brittinger[5], Michael Wittenberg[5], Gladys McPherson[6], John McCourt[7], Francois Gueyffier[8], Andrea Lorimer[9] and Ferràn Torres[10] for the ECRIN Working Group on Data Centres



- Certification of data centres
  - Pilot 2011/12
  - First campaign 2014

- Towards certification of clinical trial units ?
  - Ad-hoc working group:
    - ü opportunity
    - ü specification
    - ü procedure
    - ü cost - resources

ECRIN Scientific Board Criteria and Recommendations

ELIGIBILITY CRITERIA

1 - Multicentre trial run in at least two European countries.
2 - Rules for transparency:
    a) Commitment to register the trial in a public register before inclusion of the first participant, for example on www.clinicaltrials.gov.
    b) Commitment to publish results irrespective of findings.
    c) Commitment to make raw anonymised data sets available to the scientific community upon request to the sponsor or principal investigator one year after the trial is completed (last follow up of the last patient) or, for registration trials, when registration is completed or the development is discontinued.
3 - Declaration of conflicts of interest.
4 - Commitment to fairly describe the contribution of ECRIN and its national partners in the publications

EVALUATION CRITERIA

Projects having already undergone scientific evaluation are invited to provide previous evaluation reports

1 - Rationale for the trial - including the choice of the experimental intervention and the comparator - based on extensive and up-to-date review and analysis of relevant clinical and preclinical data.
2 - Suitable overall trial design appropriate to the clinical question.
3 - Clinical relevance for patients and public health.

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RECOMMENDATIONS

1 - Relevant patient population (inclusion and exclusion criteria), setting, and duration of treatment and follow up.
2 - Randomised superiority design is preferable for benefit assessment, rather than non-inferiority.
3 - Use of the best available comparator.
4 - Primary outcome measure most suitable for patient and public health's interests. Outcome measures for efficacy and safety clinically meaningful for the patient.
5 - Adequate sample size with supporting calculation. Sample size calculation based on the primary outcome measure, and power calculation for secondary outcomes.
6 - Adequate recording of adverse events.
7 - Adequate strategies to reduce or control possible biases, for example central randomisation; blinding of all parties (at least assessors, statisticians); intention-to-treat analysis for efficacy in superiority trial; blinded conclusions drawn before breaking the allocation code; and interpretation of, and decision to publish results, independent of funding source.
8 - Description of potential risks and how to handle them, including involvement of and charter for independent data monitoring and safety committee.
9 - Description of governance structure of the project including responsibility for coordination, data analysis, and independent monitoring.
10 - Involvement of pertinent patient organisation (if available) or patient representatives in the protocol design.

ECRIN Scientific Board

Core Members

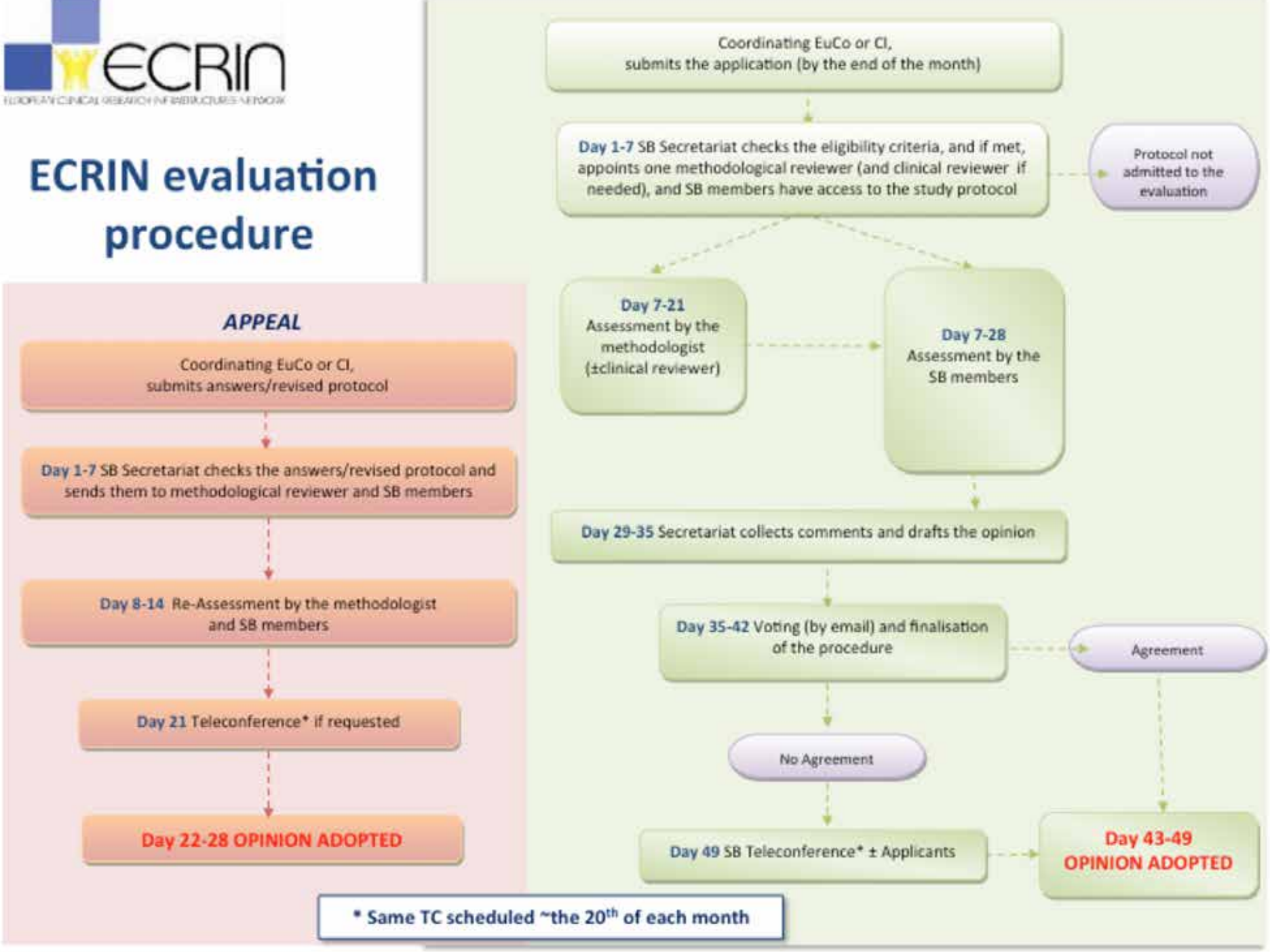
- Silvio Garattini
- Xavier Carné
- Christian Gluud
- Miguel Viana Baptista
- Armin Koch
- Jordi Linares (orphan drugs)
- Michael Hiesmayr (nutrition)
- Eric Vicaut (medical device)
- Emad Shash (cancer)
- *Kim Wever (patient)*

Secretariat Vittorio Bertelé

Panel of methodologists

- Janbernd Kirchner
- Philippe Ravaud
- Ferran Torres
- Walter Torri
- Altamiro Costa Pereira
- Janus Jakobsen
- Marina Maggini

ECRIN evaluation procedure



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydroxyethyl Starch 130/0.4 versus Ringer's Acetate in Severe Sepsis

Anders Perner, M.D., Ph.D., Nicolai Haase, M.D.,
Anne B. Guttormsen, M.D., Ph.D., Jyrki Tenhunen, M.D., Ph.D.,
Gudmundur Klemenzson, M.D., Anders Åneman, M.D., Ph.D.,
Kristian R. Madsen, M.D., Morten H. Møller, M.D., Ph.D., Jeanie M. Elkjær, M.D.,
Lone M. Poulsen, M.D., Asger Bendtsen, M.D., M.P.H., Robert Winding, M.D.,
Morten Steensen, M.D., Pawel Berezowicz, M.D., Ph.D., Peter Søe-Jensen, M.D.,
Morten Bestle, M.D., Ph.D., Kristian Strand, M.D., Ph.D., Jørgen Wiis, M.D.,
Jonathan O. White, M.D., Klaus J. Thornberg, M.D., Lars Quist, M.D.,
Jonas Nielsen, M.D., Ph.D., Lasse H. Andersen, M.D., Lars B. Holst, M.D.,
Katrin Thormar, M.D., Anne-Lene Kjældgaard, M.D., Maria L. Fabritius, M.D.,
Frederik Mondrup, M.D., Frank C. Pott, M.D., D.M.Sci., Thea P. Møller, M.D.,
Per Winkel, M.D., D.M.Sci., and Jørn Wetterslev, M.D., Ph.D.,
for the 6S Trial Group and the Scandinavian Critical Care Trials Group*

N Engl J Med, June27, 2012, DOI: 10.1056/NEJMoa1204242

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest

Niklas Nielsen, M.D., Ph.D., Jørn Wetterslev, M.D., Ph.D., Tobias Cronberg, M.D., Ph.D., David Erlinge, M.D., Ph.D., Yvan Gasche, M.D., Christian Hassager, M.D., D.M.Sci., Janneke Horn, M.D., Ph.D., Jan Hovdenes, M.D., Ph.D., Jesper Kjaergaard, M.D., D.M.Sci., Michael Kuiper, M.D., Ph.D., Tommaso Pellis, M.D., Pascal Stammet, M.D., Michael Wanscher, M.D., Ph.D., Matt P. Wise, M.D., D.Phil., Anders Åneman, M.D., Ph.D., Nawaf Al-Subaie, M.D., Søren Boesgaard, M.D., D.M.Sci., John Bro-Jeppesen, M.D., Iole Brunetti, M.D., Jan Frederik Bugge, M.D., Ph.D., Christopher D. Hingston, M.D., Nicole P. Juffermans, M.D., Ph.D., Matty Koopmans, R.N., M.Sc., Lars Køber, M.D., D.M.Sci., Jørund Langørgen, M.D., Gisela Lilja, O.T., Jacob Eifer Møller, M.D., D.M.Sci., Malin Rundgren, M.D., Ph.D., Christian Rylander, M.D., Ph.D., Ondrej Smid, M.D., Christophe Werer, M.D., Per Winkel, M.D., D.M.Sci., and Hans Friberg, M.D., Ph.D., for the TTM Trial Investigators*

N Engl J Med, November 17, 2013, DOI: 10.1056/NEJMoa1310519

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ECRIN trial portfolio

	AT	B	CH	CZ	DK	FIN	FR	D	H	IS	IRL	IT	LUX	NL	NO	PL	P	RO	SR	SP	S	TR	UK
LEAN																							
6S																							
CHILDINN																							
TTM																							
PRECARDIA																							
EuroHYP																							
IMPACTT																							
SafeBoosC																							
STRONG TREAT																							
TRISS																							
EORTC 40091																							
TINN 1																							
SABATO																							
TINN 2																							
RESCUE ESES																							
H11																							
POEM vs LHM																							
ESCALE																							
NeoVitaA																							
ECLIPSE																							
NICO																							
Total	5P	8P	6P	3P	5C, 5P	5P	6C, 5P	5C, 7P	3P	3P	2P	1C, 11P	1P	1C, 10P	6P	3P	2P	2P	1P	2C, 10P	11P	2P	1C, 10P

P = Participating countries

C = Coordinating Country

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Number	Topic. Call Number	ACRONYM	Coordinating Country	Participating Country	CE Outcome
1	PHC 13-2014	ID-THERA	ES	UK, BE, FR, NL, CH, ES	Invited to second stage
2	PHC 13-2014	ASTUTE	ES	BE, CH, DL, Fi, ES	Invited to second stage
3	PHC 13-2014	SPHERE	ES	ES, FR, DE	Invited to second stage
4	PHC 13-2014	HaptoAID	ES	IL, UK, FR, IT, DE, ES	Invited to second stage
5	PHC 17-2014	SYMPTOMS	FR	FR, IT, BE, DE, CH, Canada	Invited to second stage
6	PHC 17-2014	RETREAT-FRAIL	FR	FR, IT, ES, PO, FI, NL, UK	Invited to second stage
7	PHC 5-2014	PROFET	FR	FR, BE, DE, RS, CH, IT, TR, PO, ES, UK	Invited to second stage
8	PHC 13-2014	INDERM	FR	FR, GR, UK, NL, SE, DK, DE, IT, ES, BE	Invited to second stage
9	PHC 13-2014	IMACS	FR	FR, UK, DE TBC	Invited to second stage
10	PHC 13-2014	FAIRPARK II	FR	FR, IT, UK, PT, ES, CZ, DE, AT, NL	Invited to second stage
11	PHC 5-2014	STRATOSPHERE VTE	FR	FR, DE, NL, ES	Invited to second stage
12	PHC 17-2014	PRECIOUS	NL	NL, UK, It, Nor, Fr, Hu, Ge, Po, Est.	Invited to second stage
13	PHC 1-2014	CVD-Epigen	FI	FI, NO, DE, NL, Israel, US	Invited to second stage
14	PHC 5-2014	Atherorisk	FI	FI, DE, NL, Israel, US	Invited to second stage
15	PHC 6-2014	PREVENT	FI	FI, SE,FR, UK, IT, AT, NL, ES, DE	Invited to second stage

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Funding multinational clinical trials ?

Funding mechanisms for multinational clinical trials

- National funding
- ERA-nets – JPIs ?
- European Union
- IMI and industry
- International, charities

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Muchas gracias