

speed up the assessment of the success of the therapeutic approach.

- Biomedical researchers and clinical scientists located at universities, research institutions or SMEs will be attracted to EATRIS for the support it offers to their research projects. EATRIS will act like a funnel drawing in a multitude of excellent discoveries, select the top ones and translate them for the benefit of the patient.

## Let the EATRIS vision come true

### The Preparatory Phase (2008-2010)

A strong consortium of excellent research centres in the area of translational biomedical research and relevant national and regional research policy makers has gathered to work on this vision of flourishing translational biomedical research in Europe (Figure 2).

The current Preparatory Phase of EATRIS aims at defining the benchmarks to establish a cutting-edge infrastructure for translational medical research, comprehensive training programmes and the requirements for implementation. A business plan will present the financing strategy and the governance scheme of EATRIS. Access conditions, a legal framework and a competitive IP management regime are being drawn up during this phase. The results of the Preparatory Phase will form the basis for the next implementation stage.

### Construction Phase (2011-2015)

During a Construction Phase the different EATRIS sites will see their capacities expanded and a full coverage of the necessary technological facilities established. During this phase will already support a limited number of user projects within the framework of the existing infrastructure in the centres. By the end the EATRIS will be fully operational and offer support on a regular basis.

## ECRIN

### Integrating clinical research in Europe: the European Clinical Research Infrastructures Network



**Jacques Demotes-Mainard, Roxane Brachet, Christine Kubiak**

INSERM, Institut de Santé Publique, PARIS

[www.ecrin.org](http://www.ecrin.org)

### Summary

ECRIN consists of integrating national clinical research facilities into a EU-wide network, able to provide support to clinical research in any medical field, and for any type of clinical research through information and consulting, and through a set of flexible services for the conduct of multinational clinical studies. This distributed infrastructure, based on the integration of competence centres, provides access to clinical research projects after assessment by its scientific board. A team of European correspondents working in the coordinating centre of each national network is the key actor in the provision of consulting and decentralised services. These services are particularly relevant for academic clinical research, especially under circumstances where international cooperation is required (ie. in rare diseases), or for clinical trials sponsored by biotechnology SMEs who often lack the capacity to act as a sponsor in EU-wide studies.

### Introduction

Development of diagnostic and therapeutic innovation, and delivery of improved health care to EU citizens requires clinical research during the whole process extending from understanding the mechanism of disease, genetic studies or identification of biomarkers, clinical development and evaluation, and to post-marketing strategy trials.

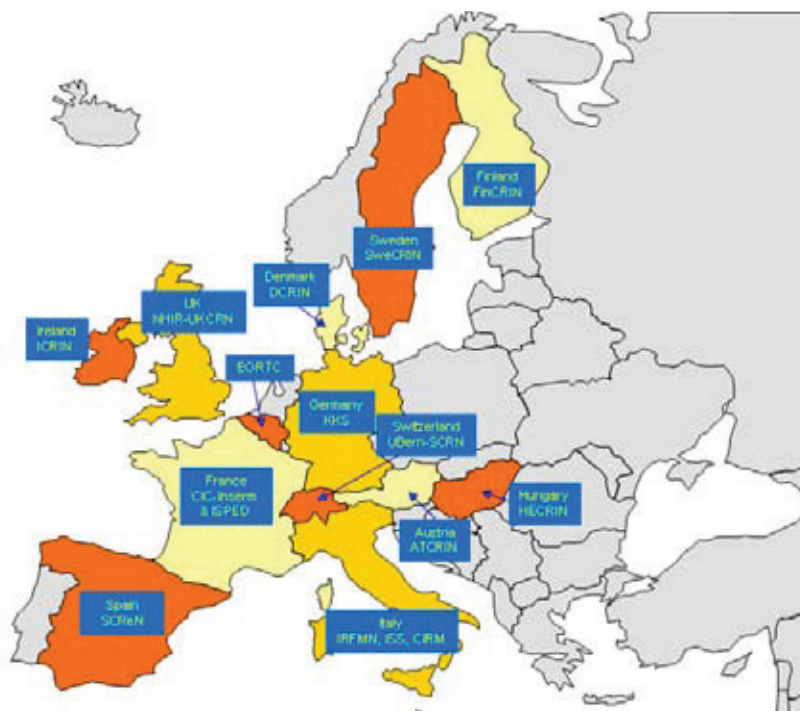


Figure 1: Map of countries participating in ECRIN.

The recent development of therapeutic innovation is mainly based on biopharmaceuticals and on personalized treatments, on pharmacogenetics and toxicogenetics, on the use of biomarkers, and requires access to large populations of patients, enabling clinical trials adapted to these new therapeutic strategies with a need to focus on specific patient subpopulations (1-5). Further, a very large number of rare diseases are without effective interventions. In addition, the quality of clinical trials and other clinical investigations, the quality of clinical and biological data, and the rate of enrolment of patients into clinical trials are all requiring urgent improvements. Hence, the quality of the clinical research infrastructure is one of the main factors determining the competitiveness of European clinical research. European academic research (6), as well as the pharmaceutical and biotechnology research and development need an efficient, integrated, and professionalized organization of clinical research, based on competence centres able to provide efficient support through a consistent set of services for clinical trials. Infrastructures supporting clinical trials, data management, quality assurance, monitoring, ethics, and regulatory submissions are required for improving the quality and raising the credibility of data. An integrated,

EU-wide infrastructure allows the conduct of multinational studies in Europe, taking advantage of the EU population and competencies, unlocking latent expertise and patients currently scattered across the EU member states.

### ECRIN: a three-step project

The European Clinical Research Infrastructures Network (ECRIN) is designed to improve the capacity of the European Union to perform high-quality clinical research, and to promote innovative pharmaceutical and biotechnology development as well as development of other interventions (7). This integrated clinical research infrastructure bridges the fragmentation of clinical research in Europe through the interconnection of national networks of clinical research centers and clinical trial units. ECRIN participants are currently Austria, Belgium, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Spain, Sweden, Switzerland, and the United Kingdom (Figure 1). ECRIN plans extension to other existing national networks in other member states, and stimulates the set-up of new national networks for further connection through its capacity building programme.

Coordinated by the National Institute of Health and Medical Research in France (INSERM), ECRIN

started with a first project (2004-2005), funded by the European Commission under the FP6 Health programme, and helped identify bottlenecks to multinational collaboration (mostly the poor capacity of academic institutions to act as sponsors in multinational studies) and define a strategy for provision of services (mostly support to sponsors across the borders) (8 -10)

This conclusion served as a basis for the second phase of the ECRIN project (2006-2008, FP6 Health Programme) in which transnational working groups prepared guidelines and procedures to support clinical studies in any medical field, in any patient population, and for any type of study.

These working groups covered: interaction with ethics committees, interaction with competent authorities and regulatory requirements, adverse event reporting, data management, study monitoring, and quality assurance.

In its third step (2008-2011, FP7 Health priority - Infrastructures programme), ECRIN enters into the preparatory phase of the European strategy forum on research infrastructures (ESFRI) roadmap infrastructures. During this current third phase, the team of European Correspondents, a specialised staff located at the coordinating centre of each national network (Figure 2), provides decentralised support to multinational studies through a set of flexible services to investigators and sponsors (interaction with ethics committees, with competent authorities and support on regulatory submissions, in adverse event reporting, in drug dispensing, in the circulation of blood and tissue samples, in study monitoring). ECRIN also provides centralized services, including data management through accredited data centres.

ECRIN may also help with consulting and practical information on ethical and regulatory requirements, insurance, centre selection, cost evaluation, and funding opportunities during the preparation of the clinical research project.

An independent scientific board is in charge of providing access to ECRIN, based on a set of eligibility and acceptance criteria (see [www.ecrin.org](http://www.ecrin.org)).

### Impact and users

ECRIN has a substantial impact on the structuring of clinical research in the European Union, through the debate on the *legislative framework* for clinical research in the EU by contribut-

ing to the discussion on the 2001/20/EC Directive (12, 13) and to the FP7 ICREL (Impact on Clinical Research of European Legislation) project (14). ECRIN also promotes the active participation of patients and citizens, and transparency in clinical research, and has launched the *International Clinical Trials Day* (each 20th of May, see [www.jameslindlibrary.org](http://www.jameslindlibrary.org)) as a yearly communication event on the challenges raised by clinical research. In addition, ECRIN initiated, with the other ESFRI-biomedical research infrastructures and the pharmaceutical companies as participants, the FP7 Innovative Medicines Initiative (IMI) (15, 16) EMTrain project to develop a pan-European education platform ([www.emtrain.eu](http://www.emtrain.eu)).

Such an integrated infrastructure will benefit mainly the academic scientific community but also SMEs or pharmaceutical companies, and public-private partnership programs, as well as series of projects developed by disease-oriented scientific networks. As access to patients is a limiting factor, ECRIN will promote research on rare diseases, improving diagnostics and treatment strategies. This will enable translation of medical innovation into healthcare, hence to the benefit of patients and citizens.



### References

- 1 Innovation or Stagnation? Challenge and Opportunity on the Critical Path to New Medical Products. <http://www.fda.gov/oc/initiatives/critical-path/whitepaper.html>
- 2 Zerhouni E. The NIH Roadmap. *Science* 302 :63-72 (2003).
- 3 Zerhouni E. Translational and clinical science – time for a new vision. *NEJM*, 353 :1621-1623 (2005)
- 4 The Royal Society. Personalised medicines : hopes and reality. September 2005, pp 1-52. Access through <http://www.royalsoc.ac.uk/document.asp?id=3780>
- 5 Rawlins MD. Cutting the cost of drug development ? *Nature Rev. Drug Discov.* 3 :360-364 (2004)
- 6 Remuzzi G, Schieppati A, Boissel JP, Garattini S, Horton R: Independent clinical research in Europe. *Lancet* 364: 17232-6 (2004).
- 7 Demotes-Mainard J, Ohmarm C : European Clinical Research Infrastructures Network : promoting har-



Figure 2: Organisation of the network

monisation and quality in European clinical research. *Lancet* 2005; 365, 107-108.

- 8 Demotes-Mainard J, Chêne G, Libersa C, Pignon JP : Clinical research infrastructures and networks in France : report on the french ECRIN workshop. *Thérapie*, 60:183-199, 2005.
- 9 See reports and comparative analyses on [www.ecrin.org](http://www.ecrin.org)
- 10 Demotes-Mainard J, Ohmann C, Gluud C, Chene G, Fabris N, Garattini S, Carné X, Lafolie P, Collet JP, Crawley F. European Clinical Research Infrastructures Network Meeting report : 'Towards an integration of clinical research infrastructures in Europe', Brussels, Feb 14-15th, 2005. *Int J Pharm Med*, 19:43-45, 2005.
- 11 Krlježa-Jeric K, Chan A-W, Dickersin K, Sim I, Grimshaw J, Gluud C for the Ottawa Group. [Principles for international registration of protocol information and results from human trials of health related interventions: Ottawa Statement \(part 1\)](#). *BMJ* 2005;330:956-8.
- 12 EC-EMA conference on the Operation of the Clinical Trials Directive, Oct.2007, London.
- 13 ESF-EMRC Consensus Conference Investigator-Driven Clinical Trials, Sep. 2008, Strasbourg.
- 14 ICREL conference on Impact on Clinical Research of European Legislation, Dec. 2008, Brussels <http://www.efgcp.be/Conference>.
- 15 Donnelly F, Jehenson P. European Technology Platform on Innovative Medicines. *Int J Pharm Med*, 19 :153-161 (2005).
- 16 The Innovative Medicines Initiative (IMI) Strategic Research Agenda: Creating Biomedical R&D Leadership for Europe to Benefit Patients and

1 <http://bmj.bmjournals.com/cgi/content/extract/330/7497/956>

## ELIXIR

### Data for Life: from information to the Medicines and Bio-industries of the Future



**Andrew Lyall**

ELIXIR Project Manager,  
European Bioinformatics  
Institute (EBI), Hinxton, UK

[www.elixir-europe.org](http://www.elixir-europe.org)

In May 2007 EMBL was awarded a Framework 7 grant of 4.5 Million Euro to run the Preparatory Phase of a project called ELIXIR of which Professor Janet Thornton, Director of EMBL-EBI is the coordinator. The purpose of ELIXIR is to construct a sustainable infrastructure for biological information in Europe. The purpose of the Preparatory Phase is to make the plan for the construction phase which will follow.

ELIXIR is one of six bio-medical projects that are part of the European Strategic Forum on Research Infrastructures (ESFRI) Roadmap. It is very significant that bio-medical projects are part of the ESFRI Roadmap as this is the first time that it has been recognized at this level that biology needs infrastructures in the same way that the physical sciences do. This is necessary because the nature of biological research is changing due to the availability of new high-throughput technologies such as next-generation sequencing.

Biology is changing from an activity engaged in by individuals and small groups to one in which large coordinated projects will make a much larger contribution. The intensive nature of the new technologies means that teams of peoples are required to generate the data and then other teams to process and understand it and to translate that understanding into improvements in healthcare and so on. This in turn is going to need to be a change in the way in which the infrastructure for biology research is funded. This is because the new technologies, as well as being extremely powerful, require much more substantial capital investment than did previous technologies. In particular, they produce vast