

ACTIVITY REPORT AND FINANCIAL REPORT





ECRIN-ERIC
Management Office

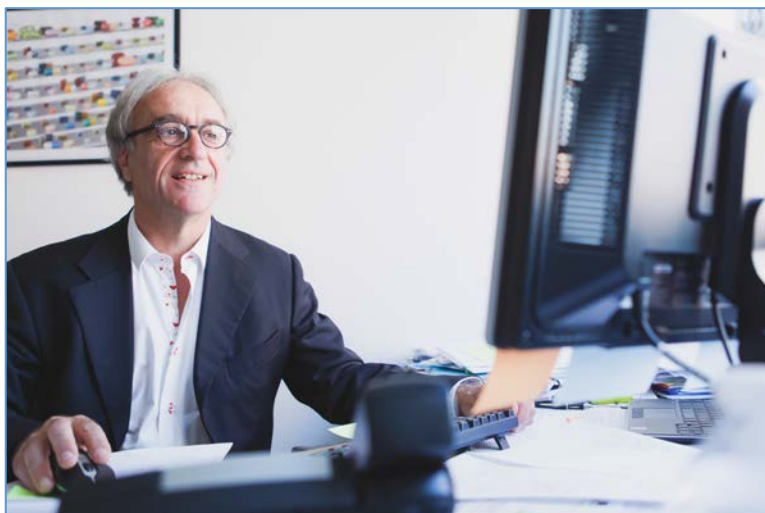
**EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE
NETWORK-
EUROPEAN RESEARCH INFRASTRUCTURE CONSORTIUM
(ECRIN-ERIC)**

Activity Report and Financial Report 2014

TABLE OF CONTENTS

FOREWORD BY DIRECTOR GENERAL JACQUES DEMOTES	3
2014 ACTIVITY REPORT	4
1 EXECUTIVE SUMMARY	4
1.1 Administration	4
1.2 Capacity and infrastructure development.....	4
1.3 Operations	4
1.4 Resources	4
2 MANAGEMENT AND BOARDS.....	5
3 ADMINISTRATION AND COMMON SERVICES	6
3.1 Finance and accounting	6
3.2 Human resource management	7
3.3 Legal affairs.....	8
3.4 Communication.....	9
4 CAPACITY AND INFRASTRUCTURE DEVELOPMENT	10
4.1 QA and certification policy.....	10
4.2 Connection to investigation networks.....	10
4.3 Tools developed in the context of ECRIN-IA.....	10
4.4 Expansion and international partnerships.....	11
4.5 Training	11
4.6 H2020 applications	11
5 ACCESS AND OPERATIONS.....	12
5.1 Access policy	12
5.2 Clinical trial portfolio	12
5.3 H2020 applications	12
2014 FINANCIAL REPORT	13
6 ONGOING RESULTS OF ACTIVITIES.....	13
6.1 Support and revenues	13
6.2 Expenses	13
7 FINANCIAL INCOME	14
8 NET ASSETS.....	14

FOREWORD BY DIRECTOR GENERAL JACQUES DEMOTES



With this ECRIN Activity Report, I am happy to share with you the events and achievements of 2014, a period during which we built foundations and defined strategies for our work in support of multinational clinical trials.

Twenty-first-century medical science requires validation and comparison of increasingly complex preventive, diagnostic and therapeutic solutions, in the context of a more stratified or personalised approach. Clinical trials are critical instruments for fostering

innovation and repurposing approved medicines. Independent clinical trials are also essential for optimising the use of established diagnostic or treatment interventions, containing the costs of healthcare and promoting evidence-based medical practice. International collaboration is required to rapidly access large patient populations, relevant medical expertise and high-quality sites, and to share the cost of trials. However, only a subset of independent trials is currently multinational, pointing to the need for infrastructural support in the management of multinational trials.

ECRIN is the European Strategy Forum on Research Infrastructures (ESFRI) roadmap infrastructure designed to support multinational clinical trials in Europe. ECRIN began its operations by supporting pilot clinical trials during the Framework Programme (FP) 7 preparatory phase (2008–2011), and reaches maturity in 2015 with the completion of the FP7 ECRIN-IA project (2012–2015), designed to strengthen capacity to conduct multinational clinical trials in Europe through the development of specific tools and structuring of user communities. ECRIN achieved ERIC status in 2013 and became a sustainable infrastructure supported by its Member and Observer countries.

In 2014, we established the ECRIN-ERIC administration, started recruiting staff and defined our strategy for the coming years, with a focus on users' needs, scientific excellence, efficient coordination and high-quality support to multinational trials. Cooperation and partnership with our national counterparts is a critical focus, as well as the extension of ECRIN-ERIC membership to additional countries to access patients and medical expertise throughout Europe.

Thanks to the work and dedication of our colleagues and collaborators in Europe and globally, we are now positioned to expand our user community and extend our membership and trial portfolio, thereby advancing competitiveness and integration in clinical research.

A handwritten signature in blue ink, consisting of a stylized 'J' followed by a long, sweeping horizontal line that curves upwards at the end.

Jacques Demotes
ECRIN Director General

2014 ACTIVITY REPORT

1 EXECUTIVE SUMMARY

ECRIN is the infrastructure supporting multinational clinical trials in Europe. Its activity includes:

- **Structuring activities**, steered by the Capacity department, including quality assurance (with certification policies for data centres and others), monitoring, regulatory affairs, education and training, partnership with users' networks, expansion and international outreach
- **Access and operations**, coordinated by the Clinical Operations department, providing access to clinical trials through the ECRIN Scientific Board and logistical assessment, and supporting multinational trials through information, consulting and coordinated services

Both activities rely on the contribution of **European Correspondents**, hosted in each national hub, and involved in both the structuring and operations activities. ECRIN-ERIC activities are also supported by an **administrative team**, accessible to both the Capacity and Clinical Operations departments, in charge of financial, legal and communication aspects, and including a secretariat. The whole organisation is steered by the **Director General**.

1.1 Administration

During its first year of activity (2014), ECRIN-ERIC established its legal organisation, opened a bank account, collected the contributions from its Members and started hiring its personnel. Staff recruitment started during summer, and the key collaborators were hired in autumn. ECRIN-ERIC has developed its legal structure:

- Organising its accounting system, taking into account the Member contributions as well as other sources of revenues (FP7, IMI, etc.)
- Developing a capacity for human resource management
- Drafting contracts and partnerships with its national scientific partners and with affiliate partners

1.2 Capacity and infrastructure development

Some of these structuring activities are currently supported by the FP7 ECRIN-IA project (regulation, monitoring, education and training, expansion), however ECRIN-ERIC has launched a second data centre certification campaign and has extended to include new Members (Hungary) and Observers (Czech Republic), while Turkey has also decided to join as an Observer. Other contacts have been made with European countries, as well as with partners outside Europe (Australia, US NIH). ECRIN also applied for H2020 funding for structuring projects.

1.3 Operations

A new procedure and criteria were implemented for access to ECRIN services through protocol review by the Scientific Board. ECRIN is involved in the operational support of 20 trials. ECRIN was involved in more than 30 applications for H2020 and IMI funding in 2014, and some of these new projects were selected and will start in 2015. Two ECRIN-supported trials were published in 2014, one in PLoS one, and the other in the New England Journal of Medicine.

1.4 Resources

Due to delayed registration by the French administration, the contributions (1.3M€ in cash) were collected late and only part of the ECRIN-ERIC staff (3 persons) was hired before the end of 2014, representing only 6 person-months in total.

2 MANAGEMENT AND BOARDS

ECRIN was created as an ERIC based on the Commission Decision (20013/713/EU) of November 29th 2013. An inauguration ceremony was organised on January 30th, 2014 at the French permanent representation in Brussels, in the presence of the Director General of Research and Innovation at DG Research (Robert-Jan Smits), and of national delegates representing the German (Renate Loskill, Head of Division 'Health research', BMBF), Spanish (Antoni Andreu, ISCIII Director General), French (Roger Genet, Director General for Research and Innovation, MESR), Italian (Fabrizio Oleari, ISS President) and Portuguese (Paulo Pereira, FCT Vice-President) governments, as well as Philippe Etienne, French Ambassador at the European Union.

On the same day, the Constitutional meeting of the ECRIN-ERIC Assembly of Members (AoM) elected Rafael de Andres (ISCIII, Spain) as the chair of the Assembly of Members, and Filippo Belardelli (ISS, Italy) as its vice-chair. The Assembly of Members appointed Jacques Demotes as the Director General (DG) of ECRIN-ERIC. Subsequently, the AoM met four times face to face and had three teleconferences.

The ECRIN-ERIC Network Committee (NC) elected its chair (Christian Ohmann, Germany), and vice-chair (Emilia Monteiro, Portugal).

The ECRIN-ERIC Steering Committee (SC) is composed of the chair and vice-chair of the AoM, the chair and vice-chair of the NC, and the DG. A particular role for the SC was the recruitment of the Capacity Director and the Clinical Operations Director.

The ECRIN Scientific and Ethical Advisory Board (shared between ECRIN-ERIC and ECRIN-IA, in charge of providing strategic input) had its meeting in Paris (December 1st).

3 ADMINISTRATION AND COMMON SERVICES



ECRIN-ERIC offices at 5 rue Watt, 75013 Paris.

ECRIN-ERIC was registered in April 2014 by the French administrative system. ECRIN was temporarily viewed as an association (SIREN 801933235, VAT FR 91 801933235), while waiting for the creation of a specific administrative category for ERICs by the relevant body, allowing ECRIN to be registered under an appropriate status. The team moved from INSERM headquarters to the new ECRIN-ERIC offices (sublet from INSERM-Transfert, 5 rue Watt, 75013 PARIS) in August 2014.

3.1 Finance and accounting

The financial contributions for 2014 (1.300k€) were received between June 2014 and January 2015. In the meantime, an external accountant and a financial auditor (Commissaire aux Comptes) were selected with the agreement of the AoM.

Discussions were organised with the French Ministry of Higher Education and Research, who was in contact with the Finance Ministry, to clarify the conditions for VAT exemption, upstream and downstream, within and outside France.

Discussions also occurred within the AoM to draft Article 7 of the Rules of Internal Procedure regarding the procurement/sourcing policy. This document was adopted in February 2015, and the procedure will be tested throughout 2015.

3.2 Human resource management



ECRIN-ERIC Core Team, left to right: Mihaela Matei, Legal and Regulatory Officer; Elizabeth Scanlan, Communication Officer; Christine Kubiak, Capacity Director; Jacques Demotes, Director General; Christoph Schuhmacher, Clinical Operations Director; Alicja Szofer-Araya, Administrative Manager; Gustavo Sabino, Quality Assurance Manager.

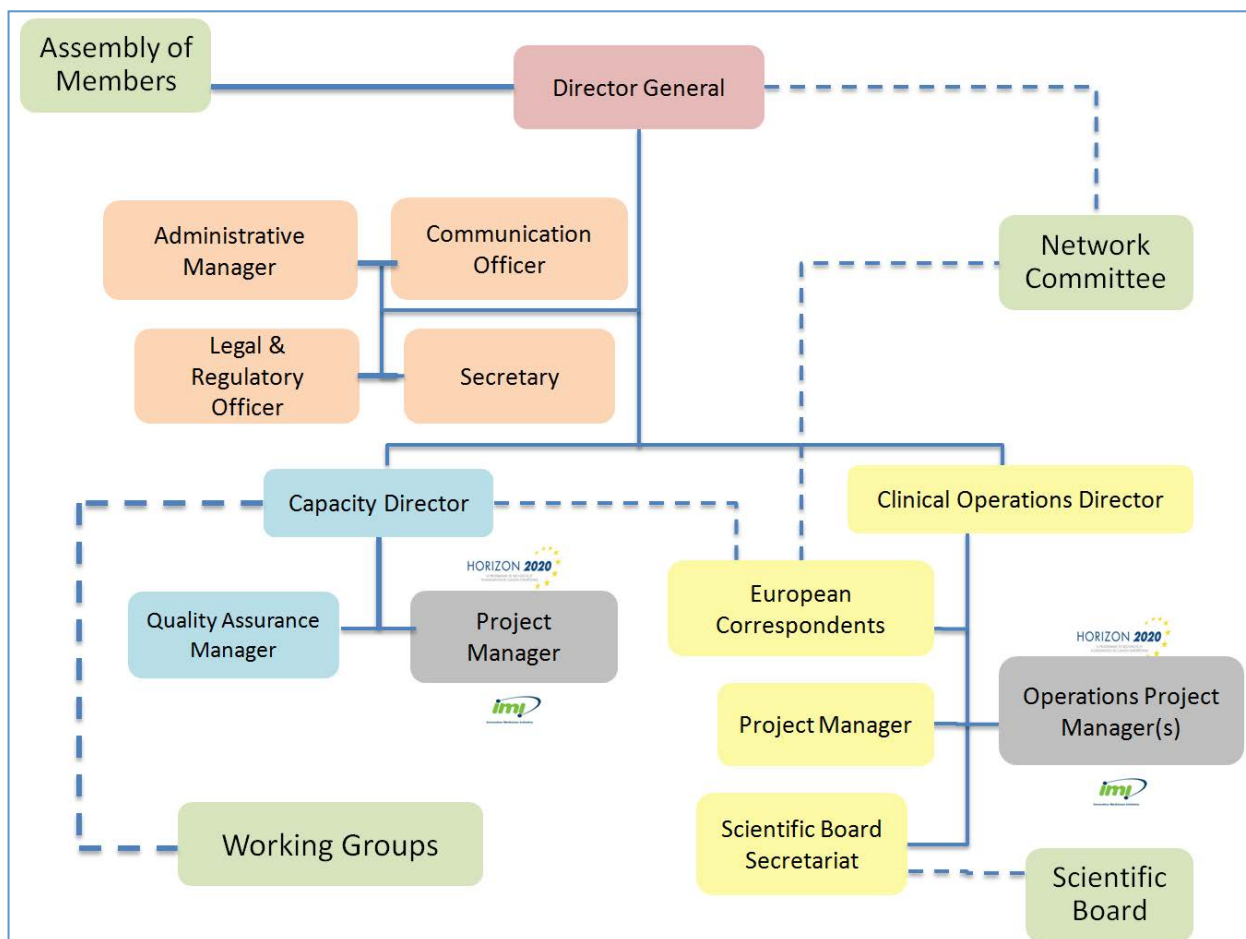
As a public but multinational organisation, ECRIN must employ its staff under the private legislation in France. ECRIN opted for an employment policy based on the framework employment rules (convention collective) of the pharmaceutical industry, as this is the most closely related sector.

Based on the organisation chart adopted in the 2014 work plan, job descriptions were drafted and the recruitment procedure for the Capacity Director and the Clinical Operations Director was started. The final decision was made in September 2014. The Clinical Operations Director was hired in November and the Capacity Director in December.

Other positions were opened and the selection based on analyses of the application dossier. Decisions were made for the following positions:

- Legal and Regulatory Officer (hired October 2014)
- Quality Assurance Manager (hired February 2015)
- Communication Officer (hired March 2015)

The Administrative Manager and Capacity Project Manager were hired in January 2015 following an internal recruitment procedure.



ECRIN-ERIC organisation chart.

Regarding the European Correspondents, the situation in France, where the European Correspondent (hired in January 2015) is a direct employee of the ECRIN-ERIC, is different to the other countries where he/she is employed by a national institution and seconded to ECRIN-ERIC. This may correspond to an in-kind contribution, or to an in-cash payment to ECRIN-ERIC, which is then forwarded to the national employer. However the appointment of the European Correspondent must receive explicit agreement from the ECRIN-ERIC DG.

3.3 Legal affairs

The highest priority in terms of legal activity consisted of finalising a template framework agreement between ECRIN-ERIC and the scientific partners. A template version was developed and adopted by the AoM in November. However, signing the framework agreement with each country is still a difficult adaptation exercise, as this requires taking into account the organisation of the national partner (network and hub), the presence or absence of a legal status or of a consortium agreement and the status of the European Correspondent (seconded or direct employee, etc.). For this purpose, a task force was set up, chaired by the Capacity Director (upon request of the Network Committee), supported by the Legal Officer, and we expect the first framework agreements to be signed by Q2 2015. This is essential as it defines the interfacing between ECRIN-ERIC and the national scientific partner, the position of the European Correspondent, and will help defining the status of the national partner regarding its participation in H2020 or IMI projects.

Framework agreements or Memorandums of Understanding (MoUs) with affiliate partners were also drafted but not finalised (except for a MoU with Therapeutic Innovation Australia). There will be three distinct situations, namely MoUs with international partners, framework agreements with data centres and agreements with pan-European investigation networks (for example the European Vision Institute).

Contracts were made with insurance companies for various purposes:

- Insurance for the office
- Insurance for the management team
- Travel insurance
- Professional liability Insurance

Finally, the Rules of Internal Procedure were drafted over the course of 2014 and adopted by the AoM in July, except for Article 7 on procurement policy, which needed additional discussion and was eventually adopted in February 2015. ECRIN-ERIC is a partner in a H2020 project on innovation procurement (Pro4VIP) that was submitted in 2014, successfully evaluated and starts in Q1 2015.

3.4 Communication

Communication activities remained limited in 2014, mostly due to the absence of the Communication Officer, hired in March 2015. The website, database, brochures and newsletter development were therefore postponed to 2015. Communication activities mostly consisted of meetings, including the inauguration meeting in Brussels on January 30th, and the annual meeting and international clinical trial day in Luxembourg May 19-20th. Other meetings were organised by ECRIN-ERIC on IT solutions for clinical trials (Düsseldorf, May), and on cloud and SaaS for clinical trial data management (Brussels, October). About 35 communications were given in 2014 on various aspects of ECRIN-ERIC activities.

ECRIN was a partner in the FP7 ECRAN project (www.ecranproject.eu) on communication with patients and citizens on clinical trials. ECRAN was terminated in September 2014, and ECRIN is committed to hosting the ECRAN website content following the development of its updated website.

4 CAPACITY AND INFRASTRUCTURE DEVELOPMENT

The objective of the Capacity department is the development and upgrade of tools and procedures that support high-quality, multinational trials, promote the structuring of, and the connection to disease-oriented European investigation networks, contribute to improvement of the organisation of national scientific partners, foster adhesion of new members and observers and promote international cooperation. In 2014, a significant number of actions of the capacity programme were supported by the FP7 ECRIN-IA funding. The Capacity Director was hired in December 2014.

These actions are supported by the network of European Correspondents, and require close coordination with the Clinical Operations department to meet the expectation of ECRIN-supported projects.

4.1 QA and certification policy

A major event in 2014 was the launch of the second pilot data centre certification campaign, with a dissemination of the call for application in June and a deadline in August. Applications were limited to one per Member or associated country (at the time of the launch of the call) to limit the number of audits. Applications were analysed by the IT certification board, auditors trained, the audits started in November 2014 and the last centre will be audited in April 2015. Based on this experience, an updated set of specifications will be drafted and a new campaign launched in 2015.

This initiative also questions the general quality assurance policy of ECRIN, including whether a certification process could also be proposed for the clinical trial units acting as the final service provider for ECRIN-supported trials. This will be further discussed in 2015.

The job position for the Quality Assurance Manager was published in October and the QA Manager was recruited in February 2015. In addition, a transnational working group on QA with QA experts from various countries will be activated.

4.2 Connection to investigation networks

ECRIN provides a generic, disease-agnostic capacity for the management of multinational trials. Nevertheless, establishing partnerships with disease-oriented investigation networks has a considerable added value as they represent potential users requesting ECRIN support for multinational trials they have initiated, and they also provide ECRIN with efficient and pan-European investigation capacity.

In 2014, development of pan-European investigation networks and hubs on rare diseases, medical device and nutrition happened in the context of the ECRIN-IA project. ECRIN was simultaneously involved in the FP7 ROAMER project establishing a roadmap for research on mental health in Europe, which was an opportunity to promote connection with this community. The participation of ECRIN in the IMI New Drug for Bad Bugs (ND4BB) programme, and more specifically in the COMBACTE project, is also an opportunity to liaise with investigation networks specialising in infectious diseases. Other contacts were established, including with the European Stroke Organisation (ECRIN is involved in two stroke trials), and a framework agreement with the European Vision Institute – Clinical Research (EVI.CR) is being prepared.

4.3 Tools developed in the context of ECRIN-IA

The ongoing ECRIN-IA project supports the development of common tools and procedures for multinational trials, including a regulatory database, a database for outcome measures, methodological recommendations, a toolbox for risk-adapted monitoring, and will make the upgraded version of the EORTC data management tool (VISTA) available to the ECRIN community as a software as a service (SaaS). All these tools will be finalised and disseminated in 2015.

4.4 Expansion and international partnerships

Expansion of the ECRIN-ERIC membership is a crucial activity, partly supported by the ECRIN-IA project that will terminate in December 2015. Afterwards, there will no longer be any formal link with the 23 countries of the ECRIN-IA consortium.

In January 2014, the ECRIN-ERIC was composed of five Member countries (DE, ES, FR, IT, PT). Over the course of 2014, three additional countries decided to join: the Czech Republic as an Observer (in July 2014), with a hub in Brno, Hungary as a Member (in November 2014, however official Membership is pending reception of official documents) with a hub in Pecs and a national partner having a legal personality (HECRIN), and Turkey as an Observer with a hub in Izmir (the formal application is however still pending). Contacts were made with other countries, and the year 2015 will be critical to maintain the scientific partnership with the ECRIN-IA countries and for the expansion of the distributed infrastructure.

As mentioned earlier, contacts were made with international partners. A collaboration MoU was signed in May with Therapeutic Innovation Australia. Other contacts were also made or reinforced over the course of 2014, in particular in the context of the set-up of implementation groups to follow-up the OECD initiative to foster international cooperation in non-commercial clinical trials.

4.5 Training

Although ECRIN is not a teaching organisation, training is part of its quality and interoperability policy. ECRIN may contribute through provision of training material (on regulation, on methodology), and through harmonised guidance for national training programmes. This is, for instance, the contribution of ECRIN to the IMI-EMTRAIN project, where ECRIN drafted a strategy document to promote a European approach for the training and careers of biomedical research and development professionals – the operators of research infrastructures. More specifically, ECRIN also published, together with IMI-PharmaTRAIN, a syllabus for clinical investigator certification (CLIC), with a basic GCP training, a more advanced investigator training and a third-tier programme for coordinating investigator in independent multinational trials. ECRIN will organise such a training in 2015, and 2014 was an opportunity to run a local pilot in France.

4.6 H2020 applications

The 2014 H2020 infrastructure calls (deadline September) was an opportunity to participate in consortia applying for funding for structuring activities. A joint project on training infrastructure managers was accepted (RITRAIN), and the large cluster project (CORBEL) involving all of the 12 ESFRI biomedical research infrastructures also got a positive funding decision (15M€).

5 ACCESS AND OPERATIONS

ECRIN started supporting some pilot trials during the FP7 ECRIN-PPI project in 2010. This helped understanding of the issues and bottlenecks, refining of the organisation and upgrading the tools. This experience of conducting the management of multinational, independent trials is essential for the progressive improvement of ECRIN capability and efficiency, which is an ongoing process.

The ECRIN-ERIC Clinical Operations Director was hired in November 2014. His major tasks are coordinating and supervising the activity of the European Correspondents, liaising with investigators and user communities, and interfacing with the Scientific Board during the protocol review procedure.

5.1 Access policy

Access to the ECRIN services is based on scientific excellence as assessed by a protocol review by the Scientific Board (SB). In 2014, the Scientific Board composition, procedure, criteria and role were revisited to improve the attractiveness of ECRIN. This change was discussed with the Scientific Board, then within the Network Committee and eventually adopted by the AoM in April. Following this new procedure, the SB has an advisory role, is composed of 10 permanent members (including a patient representative) and requests methodological peer-review to a panel of affiliated methodologists. This reduces the timelines for scientific evaluation, and allows discussion with the investigator to clarify critical points.

In 2014, a total of 10 trial protocols were reviewed by the Scientific Board.

5.2 Clinical trial portfolio

These new trials increased the size of the ongoing clinical trial portfolio, in the range of 15 to 20 ongoing trials in 2014 (also due to the five trials selected by ECRIN-IA WP7 in 2013, activated in 2014). In turn, the expected contribution to the IMI COMBACTE trials was cancelled because of the termination of the GSK '322 development.

Two ECRIN-supported trials were published in 2014, one was a phase I trial for a recombinant intranasal pertussis vaccine (Thorstensson et al, PLoS one 2014, Volume 9, Issue 1, e83449), and another showed that the threshold for blood transfusion in septic shock should be 7g/l rather than 9g/l haemoglobin (Holst et al, NEJM 2014, 10.1056/NEJMoa1406617). Altogether, by end of 2014, four ECRIN-supported projects were therefore published, including one in PLoS one and three in the New England Journal of Medicine.

5.3 H2020 applications

The Clinical Operations department, ECRIN core team and European Correspondents were actively involved in the preparation of H2020 (and IMI) applications for multinational clinical trials, particularly PHC 13 and PHC 18 calls. A total of 33 H2020 applications involving ECRIN were submitted, and four H2020 applications were selected for funding in 2014 – a success rate of 12%, significantly higher than the 3-4% overall success rate.

A new role for the SB was explored during the first H2020 application: between the first and second round of application, investigators were invited to send their protocol to the SB secretariat who asked affiliated methodologists to review the trial and make suggestions when relevant. This was the first ECRIN service during the application process. Only four projects used this support proposed by the ECRIN SB, of which two were funded and one was placed on the reserve list, which is far above the mean success rate for the second round.

2014 FINANCIAL REPORT

Under article 13 of the statutes, the statements of activities of ECRIN shall be presented to the Assembly of Members accompanied by a report on the financial management over the past year.

This report is presented below.

ECRIN's statement of activities is showing a net assets-ending of 1,137,590 € composed as follows:

Description	Amount
Ongoing results of activities	1,134,363
Financial income	4,107
Exceptional income	-
Taxes based on financial gains	-880
Net assets-ending	1,137,590

6 ONGOING RESULTS OF ACTIVITIES

Here is the analysis of the results of activities:

6.1 Support and revenues

The financial contributions of the members (the method of calculating is defined according to the statutes) can be payable in two different ways:

- In cash
- In kind especially by employee leasing services in the contributing countries

The earnings are exclusively composed of financial contribution paid in cash by the members. The amount for 2014 is €1,299,998

For better information, contributions in kind have been included in the account "evaluation of the contributions in kind". The amount is €450,000

On the statement of financial position accounts, the grant receivables shows an amount of €238,626 which corresponds to the contribution balance to be paid by the contributing countries. A deposit was made in January 2015.

6.2 Expenses

They concern supporting services expenses and are essentially composed of:

- Salaries, payroll taxes, incidental expenses €46,878
- Fees "Scientific Board" €48,000
- Offices (rents and charges) €43,329
- Fees (lawyer, auditor, consultant...) €16,821
- Mission expenses, removal costs € 7,894

Due to the late start of activities by ECRIN, the expenses that show in the accounts correspond to part of the year.

In fact, the following elements should be noted:

- The first employee was hired 1st October
- The rents under INSERM-Transfert contract started 1st August

Remaining statement of financial position includes:

- Deferred revenue: € 100,000
The balance of contributions in kind, which amount of €100,000 is to be paid back. The reimbursement was effective beginning 2015.
- Payroll taxes payables: €23,211
- Trade payables: €49,709

They are corresponding to invoices either issued or provisioned in the 2014 accounts for an amount of €49,709

7 FINANCIAL INCOME

The financial result shows a gain of €4,107.

Financial products and cash gain deposited on savings accounts. A part of these financial revenues are submitted to state tax. This tax shows on the account for an amount of €880

8 NET ASSETS

The net assets ending of ECRIN are €1,137,590 and comes exclusively from the statement of activities accounts of past financial year 31st December 2014, as it has been noted in this analysis.

We propose to record this net assets ending 31st December 2014, as unrestricted net assets in net asset accounts.

Contact

Director General: Jacques Demotes | jacques.demotes@ecrin.org

Clinical Operations Director: Christoph Schuhmacher | christoph.schuhmacher@ecrin.org

Capacity Director: Christine Kubiak | christine.kubiak@ecrin.org

Notes

