



ERIEC

Evaluation of Research Infrastructures

EVALUATION REPORT OF ECRIN-ERIC
(EUROPEAN CLINICAL RESEARCH
INFRASTRUCTURE NETWORK-EUROPEAN
RESEARCH INFRASTRUCTURE
CONSORTIUM)

**Made on behalf of the European Research
Infrastructure Evaluation Consortium (ERIEC)**



ERIEC

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Under the decree No.2014-1365 dated 14 November 2014,

¹ The president of Hcéres "countersigns the evaluation reports set up by the expert Committees and signed by their chairman." (Article 8, paragraph 5);

² The evaluation reports "are signed by the chairman of the experts committee". (Article 11, paragraph 2).

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Introduction

1 / Characterisation, stakes and context of the evaluation

The origins of ECRIN are in the progressive creation since 1992 of a French network of Clinical Trials Units (CTUs) and of a network of CTUs (*Koordinierungszentren für Klinische Studien* or KKS) in Germany since 1999. The period 2004-2006 saw European funding (FP6 health program¹) for design and tool development for pan-European research infrastructures (RI) for support of multinational clinical trials. The results of these initial efforts led to the assimilation of the idea of a European clinical trials infrastructure into the ESFRI² roadmap in 2006. A FP7 preparatory phase from 2008 to 2011 (capacity program) was followed by further funding between 2012 and 2015 for integrated activity projects. An ESFRI ex post assessment was carried out in 2014 but has not been published and therefore was not used for the committee's mandate.

ECRIN is a platform that evolved during the period up to 2013 with attribution, at that stage, of ERIC status. In 2013, ECRIN comprises participating member states and a central hub located in Paris. Five nations participated in the creation of ECRIN-ERIC (France, Germany, Spain, Italy and Portugal). They were joined by Hungary in 2014, Norway in 2016, and the Czech Republic and Ireland in 2018. There are also three observer countries, Switzerland (since 2015), Slovakia (since 2018) and Poland (since 2019). Observer countries do not finance the central core team (hub) but do finance their national CTU networks and most of their European correspondents (EuCos).

ECRIN's 2019 provisional budget amounts to €5,4M. It consists of activity generated income, mainly from competitive grants (60%), and on member and observer annual contributions (40%).

ECRIN has 34 staff operating within its structures. 17 are ECRIN employees working from a Parisian hub. Seventeen European Correspondents (EuCos) work in member countries, who by and large pay their salaries as part of their contribution.

This evaluation report deals exclusively with ECRIN's activity undertaken with the legal status of an ERIC between 2013-2019.

This report is divided into 3 domains, documented through 14 standards preceded by this introduction and ended with general conclusions and recommendations.

- Domain 1 – Positioning and strategy of the ERIC
- Domain 2 – Governance and management
- Domain 3 – ERIC activities

2 / Context of the evaluation

The ECRIN evaluation is the first of an ERIC and is carried out by a European consortium of national evaluation agencies (ERIEC³). HCERES (FR) (who with ANVUR-(IT) and AEI (ES) were ERIEC members at the time of evaluation) acted as the ERIEC Evaluation Leader and oversaw the evaluation from its preparatory phase to the production of the final evaluation report, which included a restitution with ECRIN-ERIC before conclusion. The full methodology for the evaluation follows the terms of reference approved by ERIEC members; ERIEC also selected expert members of the Evaluation Committee. The evaluation focuses on the period 2013-2019, which is consistent with the framework of ECRIN-ERIC's strategic trajectory. A self-assessment report (SAR), written according to ERIEC's terms of reference, complemented by interviews, constituted the evidence on which the Evaluation Committee based its recommendations.

ERIC⁴ is a legal status, created at the European level, to allow the development, installation and operation of pan-European research infrastructures as not-for profit public bodies.

¹ European Commission's 6th framework programme for research and technological development.

² European strategy forum on research infrastructures.

³ www.eriec.eu or www.eriec-evaluation.eu

⁴ Reference publications UE : JOL206 du 8.8.2009, p.1 ; JOL326 du 6.12.2013, p.1 ; COM(2014)460 final.

Positioning and strategy of the ERIC

1 / Positioning and missions

The primary mission of ECRIN⁵, made explicit in ERIC's statutes, is the facilitation, coordination and management of multinational clinical trials in Europe. There were good reasons for developing such an European entity, especially in relation to collecting cohorts of sufficient size to be competitive with large nation states such as the USA and China, where large cohorts are much easier to generate and manage.

Strategic leadership to deliver the vision is provided by the Director general (DG) who oversees the ECRIN hub and also a team of EuCos who coordinate centres and units in their home countries. In parallel, scientific leadership of each approved trial is provided by the proposing clinical scientists (PIs).

The slow increase in ECRIN membership is not encouraging as ECRIN's mission also includes raising clinical trial infrastructure standards throughout Europe, especially in countries that have not had the means or resources to prioritise clinical research in their health policies. The current members all have a culture and expertise in clinical research and clinical trials, though some, who are strong in the area have not joined, *e.g.* the Netherlands.

ECRIN activities need to be of a standard sufficient to convince national health ministries of the added value provided by evidence-based medicine, standardised protocols and procedures for clinical trial activity in providing attractive innovation and development conditions for the international scientific community and pharmaceutical industries.

The EuCos system may need reinforcement, especially in terms of standardising the present variety of contractual links to the ECRIN hub. The composition of the Assembly of members may also need adjustment. To create a European health area of equal quality throughout its component nations the Assembly needs sufficient weight to interface with national political health agendas so that the aim can be progressed more quickly and efficiently.

Member state representatives had a number of constructive observations. A representative from a country strong in clinical research said that assessment of added value is difficult because of a history of good prior investment in clinical trials by his country. However, he especially appreciated technical added value and good consortium information. An observer country representative is looking to ECRIN to provide education, certification and facilitation of a strong national network capable of attracting other countries to create trial consortia. Trial guidelines, procedural harmonisation and raising standards were considered important ECRIN functions. What the national representatives felt is missing is a clinical management tool that will help in coordination – this is an in-progress ECRIN project – and also simple and nationally acceptable processes for exchanging best practice. One country stated that the procedure of self-assessment adopted by ECRIN is an effective and potent force for harmonisation.

However, the Committee felt strongly that a quote made by one national representative is worthy of consideration in future strategic thinking: "...my worst nightmare is that there is an ECRIN and nobody uses it".

The Committee feels that the strategy of waiting for nations to join ECRIN may need to be replaced by a policy of more active advocacy and lobbying at a variety of medical and political levels. The role of a pan-European science platform with legal status is to focus on the area of scientific interest it facilitates. However, the Committee agrees with comments that account should also be taken of structural needs in the European eco-system of clinical research in general. The need to move to compatible legislations, to support clinician-investigator development, to create an international community with similar standards of clinical research and to promote the idea that this activity is also a fundamental component of translational medicine and therefore of health care provision needs more pro-active promotion.

Thought might be given to generalising such an effort in conjunction with European partners focused on other components of the translation pipeline.

⁵ <https://www.ecrin.org/sites/default/files/ECRIN%20statutes/Statutes%20ECRIN%20EN.pdf>

2 / Institutional strategy

To benefit from ECRIN, a clinical trial must be proposed by investigators from at least 2 participating nations, so establishing, with ECRIN, a trial consortium. Partner countries outside Europe have been included in this number, but a majority must be European. A guiding principle is responsiveness to investigator demands, a bottom-up approach to initiation of tractable scientific ideas and development of clinical trial protocols. Once a trial's aims are validated and cohort characteristics are identified, ECRIN, as a full consortium member, provides services to it and facilitates management centrally. ECRIN also oversees, in a classic hub and spoke organisational model, the coordination of component national clinical trial centres and units of the consortium through the activity of its EuCos.

Membership fees are mainly based on national population sizes. The fees constitute a relatively stable proportion of ECRIN's income, which finances shared activities and resource development. ECRIN promotes observational studies and randomised controlled clinical trials (RCTs) and assessments of procedural interventions. Member state funding is currently €2.2M per annum. This is supplemented by peer-reviewed grants, which vary in amount (the maximum grant received to date is €8.0M) and are obtained from European funding programmes, national research funds and some private sources. No commercially funded trials are undertaken – industry is regarded as having developed a capacity for multinational trial management internally or by outsourcing to commercial CROs. Fifty-seven trials were started in the review period, 17 have finished and 40 are in progress. This represents 54% drug trials and 18% trials on procedural interventions; paediatric trials represent 25% of ECRIN's portfolio. New molecules are examined for efficacy, but a considerable proportion of work is done on repurposing older agents (50%).

There are 34 ECRIN staff – 17 in member countries⁶ and 17 in the Paris hub. Typical functions include clinical operations, quality control and IT units. Current resources offered to consortia include a database of regulatory and ethical requirements and issues, an analysis toolbox, a toolbox for data sharing. There is an active infrastructure development unit, with currently 20 projects including development of a process for data centre certification. A library of policy documents and guidelines – a portfolio of processes for ECRIN members – is accessible through the web. Given the European plethora of national rules involved, ECRIN has an important function in providing support for arranging international trial sponsorship. Direct ECRIN support services include a) trial preparation, design and planning, b) methodological, logistical and ethical review, c) implementation through coordinated project management and operational services.

Effective risk management is now monitored by a set of key performance indicators (KPIs) which feeds into annual work plans. A process of regular management discussions and reviews is in place for hub staff and EuCos. ECRIN is in effect a meta-network mainly providing services, so its main job is coordination.

The DG is very positive about the competence and devotion of his team members to continuous strategic development. He identified the main variables that constrain ECRIN's ability to optimise strategy as 1) an insufficiently stable budget to guarantee quality control in all countries in the range of activity supervised, especially in relation to CTUs and data management; 2) a business model that remains unclear because of a complete dependency on the number of member states and 3) the policy of waiting for bottom-up initiatives in relation to trial proposals.

A question that needs to be posed is why more trials are not proposed. Is it because of inadequate communication? Is the added value of ECRIN real and if so, is it recognised? Does a service provider and management coordinator justify more than acknowledgment in published papers? **At this stage, a further analysis may be needed of the institutional strategy for attracting new members.** As the European Commission representative said "A cautious facilitating bystander approach probably hasn't been successful. There's a need to get more proactive and mechanistic considerations – membership and access to transnational collaboration - need to be jazzed up." Another member representative added "Data management advances suggest a way of expanding CTU networks and RCTs generally".

The Scientific and Ethical board representatives also had some interesting observations about possible impediments to engagement with ECRIN by the clinical trials community. Before 2018, there was a 10-person external Scientific Board that made recommendations based on the final submitted protocol about whether to provide operational services to a trial. Since 2018 the project synopsis is submitted to the Collaboration committee, chaired by the Head of the clinical operations unit, which makes decisions whether to accept or decline collaboration for the for the design and planning phase. a submission. Once the application is approved, the pre-final protocol is submitted to the Peer-Review committee, which consists of 6 external members and *ad hoc* experts if needed. There is no budgetary justification mechanism but suggestions for

⁶ Some member countries have two EuCos.

protocol amendments can be made. The issues are whether there is added complexity and hence time taken to decision that dissuades potential applicants. Secondly, whether ECRIN inclusion as a full member of a consortium is essential for trial approval. This issue is discussed further in the section on governance (see page 7).

Representatives of the national science partners illustrated the advantages of ECRIN to countries with fewer prior resources. Portugal has clearly benefitted. It decided to include clinical research as a priority in its national strategic plan. Subsequent participation in ECRIN led to the development of clinical research in the country. Portugal has published an academic article describing the creation of the national CTU network that resulted. Their representative stated that it was a major advantage to deal with countries with greater experience in clinical research and to belong to a community of countries actively involved in such research. Portugal chose to channel investment to universities for the creation of academic CTUs. The Czech Republic, Hungary and Ireland confirmed this case study with their experiences on joining ECRIN. Indeed, Ireland is now considering application for data centre certification. Future challenges were identified including Hungary's proposal for a new ECRIN funding regime to make it less vulnerable to H2020 style grant dependency and for the creation of a professional network to share organisational best practice among European countries.

Such activities could be pursued, and approaches exploited further in the future.

3 / Strategy of alliance and partnerships

Recruitment of new ERIC members has been slow and largely restricted to northern Europe where there is a more developed clinical trial infrastructure and culture. The process for recruitment is a problem, but no policy other than personal networking is presently proposed. The ECRIN leadership feels that a pan-European organisation with obligatory membership would not work and that the current concept of a network of networks is supported by good quality assurance in those countries that have joined. Some areas such as oncology clearly do not engage with ECRIN at all, apparently because they feel they have the experience and knowhow to do things on their own. An opinion expressed by more than one interlocutor is that clinical scientists and infrastructure people do not understand or talk to each other sufficiently.

This is an area of ECRIN's mission that may be worth expanding.

As an ERIC, ECRIN is committed to making Europe a single area for clinical research. The critical difficulties that need to be answered are 1) how to attract more clinician-scientist investigators (PIs), 2) whether to engage with European professional societies to maximise efficiency (*eg*, a contract with the European Vision Institute for vision related trials has been signed), 3) is harmonisation of procedures by working with an array of European scientific societies practical (*e.g.*, cooperation with the European stroke organisation has proved very beneficial), and 4) would recruitment be improved by identification of thematic priorities, or by thematic calls?

Internationally, the concept of a translational pipeline - from bench to bedside to trial and translation with final evaluation by economists - has evolved over a decade, with considerable contributions to this idea from Europe. **ECRIN might consider whether its responsibilities in this pipeline could now be viewed in the context of a more integrated European network than its positioning suggests at present. This idea could be explored with other ESFRI partners (*e.g.*, EATRIS⁷, BBMRI-ERIC⁸, *etc.*) perhaps as an exercise in building capacity generally in this area.** The ESFRI representative even suggested that if 3 roadmap entities were able to make a proposal along these lines, it would be well received. Also, for possible consideration, is whether to explore public-private funded collaborative projects and/or trial coordination, which could provide new opportunities to advance ECRIN's aims. The recent implication of extra-European countries in trial consortia is a good experiment in the Committee's opinion and coordination with global health initiatives especially so. The European Commission representative also clearly stated that "...expansion to extra-European countries to have a wider international focus" could be a good way to go. The French governmental representatives also commented on the move to an extended pipeline concept, suggesting that the present isolated working of ECRIN is problematic. Nevertheless, the French are totally committed to supporting ECRIN type activity, even though only two CTUs constitute the French ECRIN network amongst their national network of 23 clinical investigation centres.

The Network committees have a role in establishing alliances. Its members represent national CTU networks contributing to ECRIN trials. They especially advise the Assembly of members about national priorities and strategies and the fit or otherwise within ECRIN proposals. One problem is the individual history of a country's

⁷ European infrastructure for translational medicine

⁸ Biobanking and Biomolecular Resources Research Infrastructure.

links with ECRIN, that is, the presence or not of a pre-existent CTU network. National political issues arise in this context, especially in relation to pharmacovigilance, cross-border data exchange and data management. New member countries may be keen to adapt their structures to ECRIN, but national ministries are very influential and may not agree. Two examples of this type of problem provided to Committee members included the Scandinavian countries, which have their own clinical trial organisation that is independent of ECRIN, and Belgium.

A strategic approach to the issue of legislative heterogeneity is needed but difficult to imagine at present.

Governance and management

1 / Functional and geographical organization

Framework agreements are established between ECRIN and its national scientific partners. These define the nature and conditions of collaborations and provision of services, as well as the obligations of each party. One part of the management and services provided by ECRIN is centralized in the hub, the other is devolved to the partner nation state networks. This organization, based on the principle of subsidiarity, developed during ECRIN-ERIC's preparatory phase is designed to maintain a balance of well-defined responsibilities between ECRIN's supra-national core team in Paris and its national partners. With health care being a national responsibility in the EU, national laws and rules of national CTU network organization are respected, while fostering further networking between nation states, so ensuring coordination is made possible at a European level.

At the end of the review period, ECRIN is now composed of a 17-person core team interacting with 11 decentralised national networks. The centre facilitates international coordination and management, it also makes possible the provision and distribution of common services. It is principally concerned with developing common research strategies, guaranteeing uniform quality and management and generalising a common approach to procedural developments for activities such as pharmacovigilance. The decentralised spoke structure of 11 national networks comprises in total more than 80 CTUs. The geographical distribution of national operational structures managing clinical trials that contribute to a European effort requires strong coordination to be efficient and robust. To ensure the link between these groupings of national CTU networks and the central core team, 17 EuCos are positioned and work geographically within their nation states. Their activity is coordinated at weekly meetings with the core team chaired by the ECRIN Head of clinical operations.

The EuCos are in charge of implementation of ECRIN project-related activities in their respective countries. They are key actors in guaranteeing efficient operational activities related to ECRIN projects with which their countries are engaged. In particular, they are involved in obtaining regulatory and ethical authorisations and also in study monitoring. The Committee met the EuCos during its visit and was impressed by their enthusiasm, understanding and commitment to their difficult and complex missions.

The organization of ECRIN is complex because European nation states develop their own policies and manage their own health systems. Although the overall ECRIN structure is somewhat complicated as a result, the coordination of international projects appears effective.

A major issue for ECRIN's future is the attractiveness of the present organisation, especially in relation to recruitment of more nation states and an increase in the number of projects managed. Anomalies the Committee found included, for example, the fact that two countries with major clinical research profiles (the United Kingdom and the Netherlands) are not ECRIN members nor do they plan to become so in the future. Also, many countries with more limited clinical research experience and resources do not join ECRIN even though integration would help to quickly raise their clinical trial capacity and profiles.

The organization of clinical research carried out by CTU networks in each member state is clearly heterogeneous. In some countries, such as Germany and Spain, pre-existing, well-organized national networks bring together a majority of publicly funded CTUs. In other countries, such as France, the national network represents only a small proportion of the country's clinical research strength, as exemplified by an impressive number of *Centres d'investigations cliniques* (CICs) located in academic hospitals. Exchanges with French representatives of the Ministries of research and of health suggest that sometimes, the way policy decisions are made and coordinated at a national level can lead to sub-optimal national governance of clinical research.

European research is very effective and has overcome many impediments to pan-European cooperation and collaboration. One potential solution is to treat clinical research (including clinical trials) as research rather than health care, thus permitting faster and more efficient homogenisation of rules and regulations in this area.

In addition, the Committee has the impression that ECRIN is weakly connected to clinical research professionals individually and with professional medical associations, both general and specialty oriented. This probably explains the absence of whole medical specialties in the ECRIN portfolio (*eg*, oncology). PedCRIN is an example of a successful pioneering ECRIN project resulting from thinking out of the box. It relies on the bottom-up needs and ideas arising from professional links and has, in a short time, attracted a significant increase in the number of paediatric collaborations.

The Committee suggests that ECRIN explore this approach in relation to its activities more generally.

The Committee recommends that these issues be discussed with interlocutors that organise the agendas at European Council level to raise awareness that a major strength of European health care for improving citizen well-being is not being effectively exploited.

2 / Governance

In summary, ECRIN was initially funded by the European Commission as a component of the ESFRI roadmap. In the period before ERIC status was granted a platform structure was adopted. ERIC status consolidated a hub and spoke model of organisation. This consists of a distributed component comprised of member states with EuCos, associated with a core team in a central hub located in Paris. The governance is designed so that the nation states and central core team are governed effectively and efficiently.

Each national partner is responsible for the constitution and development of its own network of CTUs. The size and number of CTU networks varies from member state to member state. Each national network has its own governance determined by political funding considerations and at ground level by senior PIs who propose and manage collaborative clinical trials. PIs are responsible for generating ideas for clinical trials that require an international dimension to be viable and credible. The network of networks contributing to an accepted ECRIN trial is coordinated by the core team whose function is to provide services and to manage the meta-network so constituted.

Governance of this complex structure is provided by the following committees:

- The Assembly of members is made up of one representative *per* member state, who meet together twice a year. This is the ultimate ECRIN decision-validating and budget-monitoring body. It can also serve to promote harmonization of a heterogeneous set of national procedures and regulations governing CTU networks across participating European states and their collaborators. Members of the Assembly are national state appointees.
- The Steering committee is an important body of the Assembly composed of two of its members (chair and vice-chair) and two senior clinical scientists (chair and vice-chair of the Network committee). The DG joins them as head of the ECRIN hub. It supervises the management of ongoing clinical projects.
- The External scientific and ethical advisory board is composed of eight members. Its purpose is to provide recommendations and advice on all topics related to ECRIN governance and its research activities. The Committee received little or no information about its structure, composition or working during the assessment period.
- The Network committee represents the national scientific partners, that is, the national CTU networks. It consists of one senior representative from each collaborating national CTU network, in practice this is usually the national network coordinator. The national network(s) also host a national EuCo. The Network committee is a key player in the organization as it provides input to the DG on all ECRIN activities.
- The Scientific board selects projects for ECRIN support. This structure has evolved over time in compliance with scientific evaluation policies of succeeding European programs (FP6, FP7, H2020) that have funded a considerable part of the clinical research work. Before the constitution of an ERIC, the Scientific committee was composed of 11 members (6 external and 5 internal) with 6 methodologists also associated ad hoc. Its purpose was to offer additional expertise to that provided by EU Scientific program committees, especially in relation to study methodology and feasibility. With changes in H2020 assessment procedures, including methodological criteria, and demands for the provision of more rapid responses to investigators there also arose a need to deal with constraints arising from grant call timetables and budget setting processes. A change was therefore implemented such that two new committees, the Collaboration and Peer-review committees, replaced it.
- The Collaboration committee is charged with providing rapid answers to new proposals for clinical trials based on a preliminary synopsis. Currently 45% of such answers are positive, 35% are negative and 20% lead to a request for clarification. It is composed of 6 members, the DG, the Head of clinical operations, a medical expert, the Operations director, a EuCos representative and the chair of the Peer-review committee. The chair is the Head of clinical operations, a member of the core team. All members are appointed by the DG.
- The Peer-review committee reviews each pre-selected project in depth, especially the methodological aspects and suggests design improvements as required, based on the final submitted protocol. It is composed of 6 external members of which 3 are methodologists, again appointments are made by the DG.

The main components of governance do not elicit any particular comments. They are appropriate for implementing ECRIN's primary aim, which is that of developing a platform for international, European clinical

research. There is some evidence for promotion of clinical research in European countries where it was relatively underdeveloped (eg, Hungary, Czech Republic). The Network committees are seen to play an important role in this regard. Exchanges at the level of the Assembly of members could also substantially promote harmonization of European rules and standardisation of procedures and data management, especially if appropriate messages could pass to national political decision-makers. In this regard it is not clear who appoints the members and who they report to about their activities.

However, the Committee has questions about project selection. It is certainly necessary to respond to applicant investigators rapidly, but the composition of the Collaboration committee may influence the decisions. Various types of conflict of interest may arise and must be prevented. Also, ECRIN as an institution takes on the role of a full collaborating partner in any successful collaborative project. Is this necessary as authorship is claimed by this status? It is not clear that the criteria for authorship are justified and so clinician-scientists may find this state of affairs off-putting. Full acknowledgment rather than authorship may be adequate where the idea and writing are initiated and done by scientists, albeit using the ECRIN platform?

3 / Quality policy

ECRIN-ERIC is a network of national networks that implicate different organisational cultures, regulation systems, clinical trial experiences and maturity amongst its partners. An effort to harmonize working procedures is therefore needed within such a heterogeneous environment. The existence of a common, well-known and shared quality policy is a key element to add value and credibility to the organisation.

The management team has been aware of this need since 2016. Three “life-threatening” challenges were identified in ECRIN’s SAR. These were quality, attractiveness and expansion⁹. The ECRIN executive management team has made great efforts to respond effectively to the various challenges it identified, in an attempt to promote and improve quality within the organization.

Quality governance is managed through the ECRIN Quality and Risk council created in 2017 to evaluate risks and overall performance and to decide on quality priorities through an annual management review meeting. The Quality and Risk council is chaired by the Head of quality and information systems and is composed of the ECRIN DG, the Operations director, the Head of clinical operations, the Head of administration and finance and the EuCo co-ordinator, the latter two as supervisors of processes. *Ad hoc* members are appointed as needed.

ECRIN employs people with an adequate, extensive knowledge of both quality management systems and biomedical research infrastructures, which undoubtedly constitutes an important and necessary resource. ECRIN has included key people in the elaboration of policies and standard operating procedures (SOPs), which has resulted in improved performance and served to spread knowledge about the importance and content of the quality management system (QMS).

ECRIN has formalised its commitment to quality by preparing for ISO 9001/2015 certification, expected in 2020. If certification is achieved, ECRIN’s international recognition will undoubtedly improve, as will its visibility as a high-quality organization, so allowing it to face future challenges more effectively. For potential scientific collaborators and new recruits amongst nation states, certification will provide objective evidence of significant added value that makes the objective of homogenising European clinical trial quality an achievable ambition.

However, despite this enormous effort, ECRIN-ERIC faces several further challenges. The requirements of the certification process and the timetable of procedural deadlines are very demanding. Without added personnel, this activity may limit ECRIN’s ability to carry out day-to-day operations and to manage new problems or establish organisational corrective and preventive actions (CAPA).

The QMS is focused on and limited to ECRIN activities. National partners, due to the principle of subsidiarity, potentially remain on the outside of such quality policies unless experience at the European collaborative level leads to their adoption nationally. ECRIN has in its aims expansion and growth to a greater number of countries, but also to add new areas of clinical research, both of which will entail an increase in complexity and the need for further resources to keep the QMS up to date.

The Committee recommends that during the ISO certification process ECRIN considers the possibility of external support, or an increase of personnel in the quality and information system department. The

⁹ ECRIN-ERIC SWOT, 2016 strategic plan.

Committee also recommends exploring ways of assuring quality standards in new national partners by facilitating specific training and support for improving quality as a service.

4 / Communication

The extension, growth, recognition and influence of ECRIN as a point of reference in the framework of European clinical research infrastructures depends, among other factors, on an adequate and extensive communication plan. This is especially important since attribution of ERIC status in 2013. It is clear that as integration of the components of the drug discovery pipeline proceeds, ECRIN will need to participate in a yet more complex competitive clinical research environment.

Communication activities began in 2015 with a single person as communication officer. Current activities are focused on the creation of different communication tools and the organization of internal and external meetings. Presently, there is an ECRIN web page and other elements have also been developed (templates, brochure(s) updated approximately once *per* year, general PowerPoint presentations, *etc.*). In terms of social media, ECRIN has a Twitter account with over 550 followers (May 2019) and a LinkedIn account with nearly 450 followers. Since 2016, a newsletter has been sent to more than 1,000 external stakeholders, (as of May 2019 the number of subscribers is 1,140).

However, the organization itself identifies that there is still little visibility of ECRIN as a key element in collaborative European clinical research¹⁰. Recently, a strategic communication plan was designed¹¹. In this plan, it is stated that *“A major strategic weakness is the lack of a roadmap for communications activities, and it is the desire of senior management (DG) to improve our communications and to make ECRIN more visible, which this strategy plan aims to address”*. This strategy includes parts for internal and external communication as well as objectives, targets and key messages and has a budget of €80,000.

Certainly, an annual communication plan is a new step forward to improved visibility. However, there remain weaknesses and risks that bear consideration.

The extensive scope of communication objectives proposed, especially externally (for instance - *build visibility and awareness of ECRIN among key groups; strengthen ECRIN's reputation of reliability, professionalism and quality, etc.*) makes it difficult to assess achievements or their impact. Yet such assessments are critical to guide future decisions on which external communication activities should be promoted and which stopped.

The Committee advises specifying objectives more concretely to allow for their quantification and proposing goals, milestones and deliverables to be achieved at the end of each phase of the plan. The communications plan needs to become a living policy document. An important part of any communication plan will be the interaction and engagement with patient associations and lobby groups.

It is not easy to identify who is responsible for each activity and target in the communication plan. It is obvious that communication cannot depend only on the communications officer. It is a common activity that implicates all of ECRIN's staff members and at every level of activity.

It is advisable for the communications officer to attempt to identify and establish relationships and responsibilities relevant to promoting internal and external components of the plan.

Finally, the limited number of direct contacts between local network communication managers and ECRIN's communications officer is a major difficulty that needs to be addressed. It speaks also to the Committee's perception that the resources devoted to communication at all levels from local CTUs to national ministerial cabinets need to be reviewed.

The Committee supports positively the recent establishment of a set of objectively measurable KPIs to reflect process efficiency and progress. This is an important management tool that we suggest will be especially useful in assessing implementation of a complete communications plan.

The Committee also recommends establishment of close lines of communication between ECRIN's communications officer and those in National Partner communication units to promote efficient information dissemination to national popular and scientific media as well as to collaborating clinician scientists.

¹⁰ ECRIN-ERIC self-evaluation report, 2019.

¹¹ ECRIN-ERIC communications strategy, 2019.

5 / Multi-annual prospective analysis

The work is composed of clinical trials and capacity building projects that are financed by a mix of funding streams, some of which involve direct distribution of money to partners. Solutions to this complex governance/administrative situation have evolved and are updated and monitored annually within the constraints of a longer-term strategic plan, as described above. The management team (re-)drafts the plan after discussion with member states before submitting it to an annual joint retreat with national members and their networks for approval.

The Assembly of members as a governing body has comments on the positioning of ECRIN as a European body. Its representatives emphasised the complexity of the national membership model but acknowledged that it was not conducive to membership of less well-off countries. Membership is a political decision depending on national political priorities for health and research. The result is that to be a member, a country needs to have developed some prior clinical trial capacity. As one representative stated "...*the mandate precludes solidarity*". In this regard the DG feels a crucial issue obstructing member state recruitment is the cost of creating a national network of CTUs and/or clinical investigation centres. One solution he proposes is to introduce a set of rules and internal admission procedures to homogenise and assure a standard of operational quality throughout member states, which the Committee endorses.

A second issue raised by the Assembly of members is that in 2018 the EU decided to stop funding of international clinical trials. This is flagged as a major risk with a potential political result that fewer new drugs may become available for European Union citizens. Some form of lobbying from ERIC member states is needed to modulate this decision in relation to ECRIN's activities. It was also pointed out that as a VAT-excluded ERIC, ECRIN cannot carry out commercial or for-profit activity by law, except within tight constraints. Private-public projects are possible but need to be carefully structured. This view was echoed by the French ministerial representative. Rationalisation of rules consequent on changes in the way drugs are discovered and brought to the clinic will be needed.

The Committee felt that for the coming years the Assembly of members needs to become more heavyweight so as to be able to influence EU nation states in promoting expertise in national and especially international clinical trials. Europe is historically strong in pharmaceutical research and development. Pharmaceutical companies represent a major EU industry that generates employment and wealth whilst also improving citizens' health and well-being. **A dialogue between industry and academia leading to action plans to facilitate construction of an imaginative R&I pipeline are needed.** The Committee agreed with the DG that the Assembly of members in its present constitution may be over-defensive, tending to avoid tensions and hence not as pro-active as it needs to be. However, a positive element is the reported commencement of collaborations and other interactions with other ESFRI structures to enable a more inclusive and interactive provision of integrated services in the clinical trial domain. **ECRIN could play an influential role here and high-level lobbying is needed to begin to make this happen.**

As stated, various actions and objectives, including simplified procedures for acceptance and constructive ways of preventing refusal, are becoming available. The acceptance level in applying for H2020 EU grants is approximately 20% which compares favourably with the 5-10% success rate generally. However, what will happen if ECRIN applications increase in volume? Is there institutional reticence because the chances are that this attractive and efficient success rate may fall as a result? The Committee wondered why other funding routes had not been identified. Even pharmaceutical companies have not-for-profit foundations that might be exploitable, especially in relation to capacity building.

In general, though planning clearly goes on in the minds of a strong leader and a coherent leadership group, **pluri-annual planning will need some further development and formalisation. The planning process needs to be more inclusive and should include patient input. It needs documentation and dissemination with aggressive attempts to get national political buy-in and improved recruitment of nations and PI initiated projects. The annual review should contribute to a living document, up-dating and describing the strategy and its evolution clearly to the research community. Communication needs to be beefed up and good practice disseminated. The tendency to being inward looking should be modulated by looking at best practice in other areas that have developed excellent clinical trial networks independently of ECRIN, for example in the cancer field.** ECRIN has made a very productive attempt, even if somewhat serendipitously, with such an approach through the establishment of a highly impressive PedCRIN project. The French government has developed an impressive clinical investigation centre network that involved national investment. Germany's networks are highly effective and efficient, if more heterogeneous in funding terms. Lessons for helping other nations must surely also be available from these and other similar experiences in Europe.

6 / Support and assistance services

ECRIN commits initially to invest in clinical trial planning and design as a “free” collaboration, by investing national financial contributions and then commits to provide operational services at not-for-profit cost when project funding is obtained. Competing on the international Clinical research organisation (CRO) market is not seen as a priority because ECRIN’s ERIC status legally places certain limits on ‘economic’ activities¹², which would presumably require a second accounting system without VAT exemption.

The ECRIN annual work plan and provisional budget are prepared in October each year for discussion in November with the Network committees and adoption in December by the Assembly of members. In addition to the annual work plan, a prospective triennial budget plan was produced for the 2018-2019-2020 period. The revenues generated by national member state annual contributions are relatively stable and easily predictable. The revenues generated by clinical research projects are far more difficult to estimate as they depend on published calls of interest, the probability of ECRIN participation, the estimated success rate and many other poorly predictable factors. Therefore, successful (or unsuccessful) applications impact ECRIN’s work plan and strategy significantly.

ECRIN’s financial sustainability depends on revenues generated by member and observer contributions. These contributions made up approximately €2.2M in the 2019 provisional budget¹³, 40% of the total, and enabled ECRIN to invest in the early steps of trial planning and design. Participation in projects, which contributes about €3.3M, or 60% of the total, is for services to multinational clinical studies, mostly redistributed to participating national partners acting as final services providers, and for infrastructure development projects. ECRIN has adopted a mixed model of collaboration/service provision that follows the above-described three-step process, where steps 1 and 2 are provided as a free-of-charge collaboration and step 3 is provided as services at not-for-profit cost.

Operational services for the management of multinational clinical studies are also provided and the costs, charged to the sponsor, are mostly redistributed to the national partners. Typically, for a H2020-funded clinical trial receiving a €6M grant, ECRIN management services account for 5% - 10% (about €400,000) of the budget. The majority (6%, €360,000) is redistributed to the national partners acting as final service providers, and only a very limited amount (1%, €40,000) is retained by ECRIN to cover service coordination tasks performed by its network of EuCos and the core team¹⁴.

Independently of participation in financial and scientific reporting of projects, ECRIN also produces an annual report summarizing the activity of its infrastructure and its financial situation. This document is validated by the Assembly of members and is formally sent to the EU Commission, Directorate-General for research and innovation (DG RTD), before the end of June every year. Therefore, the budgetary organization seems well balanced and meets the strategic goals of the organisation.

Nevertheless, there are several issues worth addressing. The organisation has one post responsible for managing human resources and budget control, admittedly supported by an external accountant and outside auditors. Employee contracts are managed through an external law firm, which also supports ECRIN in other human resource management issues. In addition to overseeing ECRIN’s ongoing budget, this employee supports EuCos in the preparation of contractual grant application packages. With receipt of a grant, the responsibility for preparing service provider contracts for ECRIN’s activities is added. The same employee is responsible for payments to service providers. ECRIN has a contractual relationship with the research sponsor only, not with the PIs. Payments to PIs are made through the sponsor. ECRIN has a simple computerised accounting tool, but lacks a more sophisticated computerised financial management system. There is an initiative to purchase specifically tailored software for this purpose. The Committee welcomes this initiative, which will facilitate more effective and efficient management.

Currently, the main source of funding for multinational clinical trials is H2020. However, H2020 halted support for new clinical trials in 2018. Twelve trials started in 2017, seven of which were funded by H2020 calls, two by ERARE3 (the ERA-Net on rare diseases launched a call for re-purposing trials in 2016), and three by PedCRIN. Conversely, only two trials started in 2019. This represents a major risk to ECRIN.

The Committee therefore recommends that ECRIN should explore ways of constituting a wider portfolio of research funding opportunities, such as joint oncology clinical trial grants, industrial partnership grants, early

¹² Article 3§4 of ECRIN-ERIC’s status states that: “ECRIN-ERIC shall pursue its principal task on a non-economic basis. However, it may carry out limited economic activities, provided that these are closely related to its principal task and that do not jeopardise the achievement thereof.”

¹³ SAR, page 34.

¹⁴ SAR, page 35.

development research funding sources and so on. Creative and out of the box thinking is needed to identify multiple financial support opportunities for multinational PI-initiated clinical research. The Committee believes an inclusive approach to international trials is a better approach for the future than concentrating on specific, limited areas. There is an opportunity by cooperation and interaction to create something bigger than the parts. The argument is analogous to the one about integrating the components of the whole translation pathway rather than dicing it into component parts that have difficulty exchanging with each other.

In the ECRIN SAR, there is a section discussing clinical trials budgets funded mainly from H2020. The initial research budget quoted in the report is not necessarily the final budget and ECRIN does not appear to have accurate and up to date information regarding the actual budget amounts received. In addition to the awarded grant amount, the relative budget amount dependent on research objectives needs to be reported, *eg.*, recruitment goals. **The Committee recommends that the latest research status should be mentioned in reports and accordingly, the budget status in both open recruitment studies as well as the closed ones.** These details are significant from budgetary and organizational flow management perspectives.

ECRIN employees have been recruited since September 2014, following assumption of ERIC status. ECRIN is composed of three operational units: clinical operations, quality management with information systems, and infrastructure development. There is also a management team that is supported by common services namely administration, finances, human resource management, legal and regulatory expertise, and communication. ECRIN-ERIC has 34 employees; 17 are core team and 17 EuCos. Three out of 17 EuCos are direct employees of ECRIN-ERIC, the others are funded nationally, which can cause problems of accountability. All recruitment is based on international dissemination of job descriptions *via* sites including Euraxess, NatureJobs, *etc.*, followed by interviews of shortlisted candidates. Manpower is well-trained and works professionally according to SOPs per job description.

The management of clinical trial services is the primary task of EuCos whose work is coordinated by the EuCo located in the coordinating country. This EuCo acts as the interface between investigators, the sponsor, and ECRIN. The other EuCos act as the interface between ECRIN and their collaborating national partner's networks of CTUs. This activity is supervised and monitored by the clinical operations unit in the ECRIN core team, and also takes advantage of core team resources, namely contracting and financial management. It is estimated that a EuCo can manage 4 to 5 projects as a coordinating EuCo.

The national representatives to ECRIN (Assembly of members) feel that the services provided to them enhance their research capabilities and they are satisfied with the support services and the training they receive. Overall, the personnel are professional, committed to ECRIN's goals, with considerable overall job satisfaction. Training programs, especially summer schools, have been cited as an important professional activity that contributes to connections between people from different cultures and environments. There seems to be proper investment in this area.

The Committee recommend that EuCos gradually become direct ECRIN-ERIC employees, given the centrality of their role in managing and coordinating studies at national and international levels.

Finally, the ECRIN self-assessment report states that one human resources risk factor is career development. **The Committee supports the future development of a formal program aimed at retention of professional manpower to palliate this risk.**

7 / Data management

There is no widely accepted published interpretation of what good clinical practice (GCP) compliance means for IT and data management in international clinical trials research. Aware of this state of affairs, ECRIN in the framework of a FP7 ECRIN project, decided to develop a set of quality standards and requirements. These requirements have been used as a basis for the selection and certification of recognised ECRIN data centres. Certification lasts 4 years.

The ECRIN data centre certification programme was launched in 2011. In 2012, there were 139 'essential' standards; in 2015, the number of standards fell to 129 and in the last version (version 4.0, approved in 2018) there are 106 standards. The standards are grouped into three domains: general standards, data management standards and IT standards. Only a third of participating centres received certification immediately. The other two thirds required some initial corrective action with the production of documentary evidence of change, or even a new audit.

Currently, 13 European centres are certified, of which 3 will be evaluated upon completion of their first 4-year period of accreditation. Two centres were certified in 2012 (KKS Dusseldorf, Germany; Uppsala Clinical

Research Centre, Sweden, whose certification had lapsed), five centres in 2015 (EUCLID, Bordeaux, France; The clinical trial unit, Freiburg, Germany; Mario Negri Institute for Pharmacological Research, Milano, Italy; GIMEMA Foundation, Roma, Italy; Association for Innovation and Biomedical Research on Light and Image, Coimbra, Portugal), three centres in 2016 (UPCET, Lyon, France; IZKS Mainz and KKS Marburg, Germany) and finally, three centres in 2018 (KKS Dresden, Germany; KKS Heidelberg, Germany; and *Ospedale pediatrico bambino gesu*, Italy).

This process has had a major impact since requests for collaboration and certification have been received from outside Europe, *eg*, Japan and Korea. Also, European nation states have incorporated ECRIN standards into their “good professional practice” manuals, *eg*, France, Switzerland and Germany.

Therefore, it can be stated that ECRIN has a real world, validated model of certification of data centres for international clinical trial research, which is being exported outside Europe. This activity increases ECRIN's visibility and recognition as a model supportive organisation for international and incidentally, national clinical research and clinical trials.

However, the Committee believes there may be issues that need future consideration. Firstly, the number of ECRIN certified data centres is small. There are only 11 of a total of more than 80 CTUs distributed among ECRIN member and observer countries. Indeed, after 7 years, more than 85% of units remain uncertified. Secondly, the distribution of certified data centres is very unequal, so that of the 11 certified, 5 are in Germany, 2 in France, 3 in Italy, 1 in Portugal.

Apparently, there is no relationship between the number of projects (current or past) and the number of ECRIN-certified data centres. According to available information, countries such as Spain, the United Kingdom, Norway and Denmark (the last three do not belong to ECRIN but have had collaborating CTUs in several ECRIN projects), have no ECRIN-certified data centres.

Finally, ECRIN-certification is not required for a data centre to take part in an ECRIN clinical trial. It may be desirable to stipulate this as a requirement of ECRIN participation in any international trial, or at least that any proposed validated model for centralised data management is compatible with the ECRIN quality standard.

The Committee recommends considering a pro-active policy of promoting the accreditation of at least one data centre in each ECRIN member state. It may also be worthwhile promoting or requiring certification of a data centre in those non-ECRIN countries that want to participate in an ECRIN-managed European research project.

8 / Intellectual property

The Committee met no one responsible for this area during its visit and the topic was not substantially dealt with in the self-assessment report or other documents. Our conclusion is that there is no significant intellectual property generated and no opportunity for generating revenue streams in this manner.

ERIC activities

1 / Service provision to users

Multinational clinical trials have a major added value, as they provide faster access to patients and medical expertise. ECRIN was designed to support academic, and small and medium-sized enterprise (SME) sponsors through the provision of multinational trial management services. The services proposed by ECRIN to facilitate multinational trials are provided to sponsors, not to PIs. These include services for interaction with competent authorities and ethics committees, multinational monitoring, data management, data management certification via the centre certification program, pharmacovigilance and multinational project management. These trial management services are provided by CTUs and the role of ECRIN consists of coordinating and synchronising that services are delivered simultaneously in each country to support multinational clinical trials.

Challenges pertaining to trial management services, *i.e.*, supporting the sponsor, are country-specific, but with little disease-specificity. Conversely, the challenges for investigator-initiated, project-specific networks are highly disease-specific, but with little national specificity. As underlined previously, ECRIN provides services to academic and SME sponsors, rather than to PIs. Most studies are multinational interventional RCTs. A majority of these publicly funded trials are post-marketing authorisation trials sponsored by academic organisations or SMEs. The questions they explore are relevant for medical agencies (national and EMA¹⁵) and control of market access. ECRIN does not directly support investigation, neither through a site infrastructure providing study nurses nor logistical support for patient recruitment and investigation.

Prior to the start of a trial, support in study planning, design, funding, peer review of the protocol, and risk assessment is free of charge. Thereafter, operational services are provided to the clinical study at not-for-profit cost. Operational services for multinational trial management include obtaining ethical and regulatory authorisations in each participating country, multinational data management by one of the ECRIN-certified data centres, pharmacovigilance, reporting of adverse events at a pan-European level, project management services, and study monitoring in each participating country.

ECRIN is not the direct service provider. Instead, it delegates provision of these services to multiple CTUs in the national partner networks. ECRIN coordinates these services through its EuCo network, with the EuCo located in a sponsor's and PI's country acting as the trial coordinator. Some of these services are decentralised, meaning they have to be delivered simultaneously by local CTUs in each of the participating countries, which requires a high level of coordination, standardisation and synchronisation. Decentralised services include interactions with ethics committees and competent authorities, support for insurance contracting, interaction with data protection and any other regulatory bodies. It also includes study monitoring; requiring the involvement of local monitors after appropriate training. Other distributed services such as bio-sample shipment and investigational medicinal product management, may be delivered upon request by national partner CTUs.

Other services are centralised, meaning they have to be delivered by one single centre for the whole trial, which also requires coordination and interoperability across borders. Centralized services include data management, which is typically performed through an ECRIN-certified data centre; pharmacovigilance, which is usually carried out by the study sponsor. However, some academic and SME sponsors also request such services, for example, surveys demonstrate user and national partner interest for data and pharmacovigilance centre certifications. Multinational project management may also be requested when a sponsor lacks experienced resources. Other potential services include support in drug conditioning, labelling and dispensing.

ECRIN's service provision model for multinational academic PI-initiated trials most often meets its objectives. The model is based on independent, government-supported CTUs that allow PI-initiated clinical trials to be conducted at a high-level operative and regulatory level with relatively low trial costs. The Quality assessment director added to ECRIN-ERIC's core team in the last two years has brought significant added value to these services.

Despite this enormous effort, ECRIN-ERIC faces several further challenges. The peer review that ECRIN provides prior to the start of a study is not a peer review in the traditional sense, but more of an operational assessment of the study. **This should be more clearly understood.** The timeline to initiate a clinical trial - the research-initiation process in the model under consideration - is relatively long and depends on excellent collaboration at the operational level by each CTU. **Training is needed to improve efficiency of this process.**

¹⁵ European Medical Agency.

The ability to purchase one clinical trial insurance policy per multinational project should be considered, which remains compatible and in strict accordance with regulation policies of all participating countries in a study, so that separate policies for each country as is customary today can be avoided and the process of trial initiation made significantly more efficient.

Data management is an essential service tool for conducting clinical research, especially in multinational studies. **With a view to streamlining and facilitating this area, the Committee suggests the establishment of an ECRIN-based core data management system that is adaptable to specific studies according to their protocols and can be used as a uniform and validated tool. If used by all member centres for all trials, a significant shortening of timelines and provision of uniform data management services is to be expected.** However, the Committee does not suggest that such a system should replace existing, local and national, validated research data management systems already satisfactorily in use.

Pharmacovigilance is a complex service, especially in multinational investigator-initiated studies. **The Committee recommends mandating 2-3 experienced CTUs to provide an acceptable template for a high-quality service for use in all ECRIN trials.**

2 / Results monitoring, analysis and qualification

ECRIN has developed a series of open-access tools, made available to user communities to facilitate the planning and design of clinical trials. Most of these tools were developed in the context of collaborative projects supported by EU funding, including the ECRIN-TWG¹⁶, ECRIN-PPI¹⁷ and ECRIN-IA¹⁸ projects. In particular. These tools include:

- A regulatory and ethical database named “Campus”¹⁹ that provides information on ethical and regulatory requirements for clinical trials on medicinal products, medical devices and nutrition covering over 22 European countries;
- Methodological guidance on study design: A series of publications describing the main challenges relevant to trial design, with a particular focus on rare diseases, medical devices, and nutrition;
- A risk-based monitoring toolbox, with standardised solutions for risk-adapted monitoring plans. The toolbox describes validated options available for risk assessment and study monitoring to help PIs and sponsors prepare their monitoring plans. In addition, it provides guidance on trial design and methodology including a data centre certification program.

Other tools are being developed to meet user needs and to adapt services to emerging technologies and methodologies in clinical research²⁰.

Whether centralised or decentralised, the services are coordinated, synchronized and overseen by ECRIN, but delivered by ECRIN national partners who act as the final service providers. This reflects an implementation of the subsidiarity principle that might otherwise be breached if ECRIN were to directly deliver services for activity in the health area. This solution raises the question of how to ensure that the quality of service provision is maintained, if delivered by national partners. Currently each CTU provides a self-assessment sheet to demonstrate its ability to deliver decentralised services. For centralised services, a policy of data centre certification was introduced in 2011, which currently identifies 106 criteria that together ensure compliance with ICH-GCP²¹, FDA²² and European data management requirements. A data centre certification board is established, and auditors are trained. Presently, audit campaigns (3 auditors for 3 days per centre) are held yearly, following an annual call for applications. Thirteen centres are currently certified. One of the major objectives of this project is to build on the successful experience of certification to improve quality assessment in ECRIN-supported clinical studies.

ECRIN is aware of the importance of making information and tools relating to research procedures available for PI-initiated studies. Such tools have and are being developed. Articles on this subject can be found on ECRIN’s website. This is an important service and a contribution to the clinical research community. Further, quality control tools have been developed in recent years. One of these is CTU validation, another control of quality assurance and organisations. This year, 14 audits have been performed, with the core team quality assurance manager training auditors. In the last two years, many SOPs have been added to the ECRIN portfolio. These procedures facilitate professional homogeneity at an organisational level and thus are also a

¹⁶ ECRIN Transnational Working Groups, FP6 2006-2008, grant agreement n°037199.

¹⁷ ECRIN Preparatory Phase for the Infrastructure, FP7 2008-2011, grant agreement n°211738.

¹⁸ ECRIN Integrating Activity, FP7 2012-2017, grant agreement n°284395.

¹⁹ <http://campus.ecrin.org/> (accessed September 3rd, 2019).

²⁰ See section “Development trajectory” on next page, and ECRIN’s self-assessment report.

²¹ The International Conference on Harmonisation (ICH) guideline for Good Clinical Practice (GCP).

²² The United States Food and Drug Administration.

basis for effectively controlling quality. Organisational computing, project and budget management procedures are work in progress, which the Committee welcomes.

Despite these many efforts, there remain professional differences between the various CTUs at national and organisational levels.

The monitoring plan and monitoring quality are not sufficiently clear. The Committee recommends the development of tools for the regulation and validation of multinational monitoring in the ECRIN hub-and-spoke model. The Committee suggests that these tools are developed within the CTU model to guarantee uniformity and high standards.

3 / Development trajectory

The digital revolution presents challenges for data management especially in the era of big data, with opportunities for data reuse and novel analytical techniques to deal with complexity. This issue is being closely monitored and indeed the EU has made innovative advances in response to the opportunities presented over the last decade (for example, The European research strategy for data management, compliance with FAIR²³ principles and involvement in the development of the ESOC²⁴ project). Legislative constraints related to personal data privacy (eg, GDPR²⁵) limit what may be possible. However, the ability to integrate data from different levels of spatial resolution and functional specialisation into multidisciplinary biomedical research programs and the perspectives these advances present for personalised medicine pose fascinating challenges for ECRIN. The pace of the revolution also poses specific issues concerning the concept of European research infrastructures organised structurally and administratively into ERICs.

Since its creation, ECRIN is primarily a service infrastructure dedicated to international clinical trials, carried out by publicly-funded investigators or SME's.

Member states partly finance the organisational infrastructure. Budget balance is ensured by investigators who remunerate ECRIN for services provided from grants on a cost only basis. Therefore, ECRIN is heavily dependent on European institutional funding of clinical trials, though supplemented by minor philanthropic and other contributions. In 2018, the European H2020 program decided to stop funding clinical trials. This decision threatens the financial sustainability of ECRIN and represents a threat to its future development.

ECRIN is facing this challenge in a number of ways. It is developing partnerships with networks of investigators in niche areas such as rare diseases, paediatrics, infectious diseases, neuroscience and vaccine production. It is developing new tools and approaches for clinical research, such as data reuse and multimodal data management. It has initiated international collaborations and provides a secretariat for the Clinical research initiative for global health (CRIGH), whose aim is to serve as a support structure for world-wide international collaboration on clinical research for the benefit of patients, healthcare professionals, and health systems. As an ERIC, ECRIN cooperates with BBMRI-ERIC, IMI and EATRIS (also ERICs) to begin development of integrated biomedical research programs along an extended and integrated translational pipeline. It also offers its skills more widely by committing itself to participation in a rapidly increasing number of "structuring" projects funded by the European Commission (C4C²⁶, CORBEL²⁷, ECRAID-Plan²⁸, EJP RD²⁹, EOSCLife³⁰, EOSCHub, EOSCpilot, the ERIC Forum, EuLac-PerMed³¹, ID-EPTRI³², RISCAPE³³, RITRAIN³⁴, RI-VIS³⁵, SYNCHROS³⁶, TB-MED, TRANSVAC2, XDC³⁷). ECRIN's contribution to these multifarious activities tends, for obvious reasons, to be small if not minimal.

²³ Findability, accessibility, interoperability, reusability.

²⁴ European stroke organisation conference.

²⁵ General data protection regulation (EU regulation n°2016/679).

²⁶ Conect4children.

²⁷ Coordinated research infrastructures building enduring life-science services.

²⁸ European clinical research alliance on infectious diseases.

²⁹ European joint program on rare diseases.

³⁰ European open science cloud.

³¹ Cooperation of Europe (Eu), Latin America and Caribbean countries (Lac) for personalized medicine (PerMed).

³² European paediatric translational research infrastructure.

³³ Research infrastructure landscape.

³⁴ Research infrastructure training program.

³⁵ Research infrastructures visibility.

³⁶ Synergies for cohorts in health: integrating the role of all stakeholders.

³⁷ Extremal data cloud.

This strategy, designed to guarantee ECRIN's future financial stability, inevitably leads it away from its core mission of a clinical research infrastructure providing services. The Committee had no clear recommendation how to resolve this ambivalent strategic posture, especially as it might incidentally increase and widen ECRIN's visibility, so helping recruitment of new nation state members and also of PIs with innovative research proposals. The Committee feels both of these are critical to achieving ECRIN's aims.

Ultimately, the Committee feels that the increasing need for multidisciplinary and integrated scientific approaches to drug discovery, to changes in medical care and to the evaluation of novel solutions to diseases will pose questions about how international infrastructures incorporated as separate ERICs will evolve. How might they be encouraged and stimulated to cooperate intensively and seamlessly in the prosecution of modern biomedical research? Is it reasonable to conceive of an immutable ERIC model, without possibility of evolution to allow for fusions, takeovers, changes in governance or accommodation of new disciplines, for example economics or social science? The dynamism of modern biomedical research and of the healthcare sector in general does not square well with a one size fits all legal entity to support efficient and agile responses to future health challenges.

A high-level strategy discussion, involving decision makers, needs to be had at a European level.

Conclusion

The ECRIN-ERIC research infrastructure was established as and ERIC in 2013, following a long maturation process in the framework of the ESFRI roadmap, beginning in 2006. It aims to coordinate a large number of clinical research trials between ERIC members and to expand the coverage of such trials across Europe.

ECRIN started with a few members and has grown at a slow pace, to reach a membership of 9 full members and 3 observers. The reasons for this slow accession rate exercised the Committee and a number of recommendations have been made to ECRIN in this regard. However, the Committee also points out that recruitment and accession are two components of the process of ECRIN enlargement. A better understanding by funding agencies and EU member states of ECRIN-ERIC's role is needed as is a more dynamic and inclusive ECRIN communication strategy.

Clinical research trials are only a component of the overall landscape of life sciences applied to health, ECRIN-ERIC will need to act in partnership with other EU funded sectors (biology, translational medicine, economic sciences and so on in the future).

The organisational model based on a central hub coordinating EuCos located in member countries interfacing with national CTUs seems efficient. The overall management benefits from strong leadership. The leadership style is inclusive and motivating. As ECRIN enlarges devolution of responsibility in key areas may be needed and a more collegiate approach adopted. The organization should not forget to prepare modern succession plans for top-level management positions that are compatible with EU recruitment policies.

ECRIN's activities are numerous and diverse with high levels of competence shown by the scientific actors. The introduction of paediatric trials to ECRIN's perimeter has had perhaps unexpected beneficial effects from which interesting lessons are being learned. This bodes well for the further evolution of ECRIN-ERIC in a more integrated and cooperative international clinical trial environment.

1 / Strengths

- A compact, efficiently run service structure for investigator-initiated international clinical research
- A committed and satisfied workforce
- An agile, responsive and prospectively oriented work plan devoted to improving the quality of international clinical research services
- A program that promotes clinical research provision and quality assurance in European countries
- A program consistent with a research infrastructure on the ESFRI roadmap

2 / Weaknesses

- Slow recruitment of nation state members, for a variety of reasons, that could otherwise lead to harmonisation of a PI-initiated European clinical research effort
- A restricted funding scope and a heterogeneous multinational network of CTUs
- A relatively poor communication policy for the promotion of the advantages for clinical research provided by ECRIN in services and in cost terms
- Inadequate lobbying at the national decision-making level to promote the implementation of ECRIN at a Europe-wide level
- At present, the essential actors (the EuCos) are not all full-time ECRIN employees

3 / Recommendations

- To explore models for engagement of the scientific community in initiating new research, for example the PedCRIN project
- To invest more in interacting with other European research infrastructures in the domain of biomedical research
- Take advantage of alternative funding opportunities, for example, private-public projects with the pharmaceutical industry
- Keep abreast of advances in technical and service requirements for clinical research, for example big data analysis and distributed data management

List of symbols

B

BBMRI Biobanking and biomolecular resources research infrastructure

C

C4C Conect4Children

CIC *Centre d'investigation clinique* (French clinical investigation centre)

CORBEL Coordinated research infrastructures building enduring life-science services

CRIGH Clinical research initiative for global health

CTU Clinical trial unit

D

DG Director general

DG RTD European Commission's Directorate-General for research and innovation

E

EATRIS European infrastructure for translational medicine

ECRAID European clinical research alliance on infectious diseases

ECRIN European clinical research infrastructure network

ECRIN-IA ECRIN integrating activity

ECRIN-PPI ECRIN preparatory phase for the infrastructure

ECRIN-TWG ECRIN transnational working groups

ECTRIMS European committee for treatment and research in multiple sclerosis

EJP RD European joint programme on rare diseases

EMA European medical agency

EPTRI European paediatric translational research infrastructure

ERIC European research infrastructure consortium

ERIEC European research infrastructure evaluation consortium

ESOC European stroke organisation conference

ESFRI European strategy forum on research infrastructure

EuCo European correspondent

EuLac PerMed Cooperation of Europe (Eu), Latin America and Caribbean countries (Lac) for personalized medicine (PerMed)

F

FAIR Findability, accessibility, interoperability, reusability

FP6 6th framework programme for research and technological development

FDA United States food and drug administration

G

GCP Good clinical practice

GDPR General data protection regulation

H

H2020 Horizon 2020

HCERES *Haut Conseil pour l'évaluation de la recherche et de l'enseignement supérieur*

I

ICH-GCP International conference on harmonisation guideline for good clinical practice

IMI Innovative medicines initiative

K

KKS *Koordinierungszentren für Klinische Studien*
 KPI Key performance indicator

P

PI Principal investigator

Q

QMS Quality management system

R

RCT Randomised controlled clinical trial
 RISCAPE Research infrastructure landscape
 RITRAIN Research infrastructure training programme
 RI-VIS Research infrastructures visibility

S

SAR Self-assessment report
 SMEs Small and medium-sized enterprises
 SOP Standard operating procedure
 SYNCHROS Synergies for cohorts in health: integrating the role of all stakeholders

V

VAT Value added tax

X

XDC Extreme data cloud

Observations of the Director general



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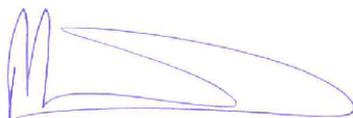
Dear Dr Robert,

Many thanks to the evaluation panel and to the consortium of evaluation agencies for their involvement in this external and independent ECRIN-ERIC evaluation process. These recommendations will be discussed with ECRIN national partners and the governance boards, and taken into account in the preparation of the next strategy plan, of the corresponding work plan and budget plan, in the development of new partnerships and the participation in collaborative projects.

Below you will find a few observations and comments on the suggestions proposed in the evaluation report.

We agree with the dissemination of the evaluation report together with these observations on the ERIEC and HCERES websites.

Kind regards



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Observations of the ECRIN-ERIC Director General on the evaluation report

The comments and recommendations from the evaluation report target critical strategic issues for ECRIN, its governance and partnerships, and for the clinical research ecosystem in Europe. These insightful suggestions will be considered in the future strategic decisions of ECRIN.

○ **Expansion to new countries**

Although ECRIN-ERIC now covers 350 millions European citizens (and potential patients), representing 70% of EU population (80% in case of Brexit), expansion to new Members (and Observers) is a slow and difficult process, with no one-size-fits-all solution. An efficient expansion policy requires visibility and attractiveness for the scientific community, a bespoke and well-targeted message to the policymakers including figures on the return on investment, delivered at the right time with regards to the national political context. Some countries have established a national roadmap for research infrastructures including clinical research, others have not. Clinical research is supported by ministries of research or innovation in some countries, and ministries of health in other, with weaker links with the ESFRI delegates. Some countries have developed specific funding mechanisms and national infrastructures for academic clinical research, others have not (particularly in central European countries). Countries also differ by their population size, by their level of economic development, and by their scientific maturity and priorities. Arguments driving the decision to join ECRIN should therefore be tailored as the reasons for joining, the added value and return on investment, in the short- and the long-term, differ between countries. In addition, joining ECRIN mostly results from an internal political decision. For instance Poland decided in 2019, as part of a national policy promoting a research- and innovation-based economy, to create *de novo* a medical research agency, dependent on the Ministry of Health, including a department for clinical research with a very significant budget allocated to non-commercial trials, and this was immediately followed by the decision to join ECRIN.

As pointed to by the evaluators, communication with national policymakers is critical, however it is often difficult to identify the right contact (depending on the country, the key contact may be the scientific community, the central administration, or the politicians) and the right timing for interaction. Creating a marketplace where all the research infrastructures would meet national science policymakers to make them aware of the potential added value of membership, and to establish contacts with the right partners for further negotiations would be a major step towards pan-European expansion of ESFRI infrastructures. If such a marketplace is not organized by the EU Commission nor by ESFRI, this should be done by the ERIC themselves in the context of the ERIC-Forum.

ECRIN currently restricts its membership to countries eligible to H2020, as this represents the main funding source for multinational trials, which makes sense for an organization whose mission is primarily the operational support to multinational trials. ECRIN however strongly promotes international cooperation in the development of common tools and standards for clinical research, through its involvement in the Clinical Research Initiative for Global Health (CRIGH, where ECRIN acts as the co-secretariat), a follow-up of the OECD recommendation on the governance of clinical trials.

○ **Communication**

As discussed above, strategic communication is critical for the success of ECRIN expansion, and also for many other critical science policy decisions: on the funding of multinational trials, on the content of the Horizon Europe programme and the role of research infrastructures in supported projects, on other funding sources, on the partnership with the industry, on partnerships with medical specialty communities, on international cooperation. Until now the ECRIN communication was mostly directed towards national partners and users' communities to raise the visibility and attractiveness of ECRIN for investigators and sponsors. As pointed to by the evaluators, ECRIN should now adopt the communication policy of a mature organization. A revisited communication strategy plan will be discussed to develop a strategic communication targeting European policymakers (EU Commission, Parliament, IMI, ESFRI etc) possibly through resources shared with BBMRI and EATRIS. Approaching investigator communities is another priority - this should in particular be achieved through coordinated messages delivered through ECRIN national partners' communication offices, through systematic

participation in conferences of learned societies, and through stable partnerships with medical specialty networks. This renewed communication should also target the other key stakeholders (patients, regulators, health authorities, funders, national policymakers, and the health industry).

- **Visibility of ECRIN contribution**

The evaluation report raises the question of academic competition vs. cooperation in the biomedical research community, suggesting that requesting authorship would make some investigators reluctant to involve ECRIN. In fact ECRIN never requests authorship, this decision is left to the investigators based on the nature of ECRIN contribution, in particular in the design and planning phase and in the provision of operational services. The eligibility criteria for access to ECRIN services only include a “commitment to fairly describe the contribution of ECRIN and its national partners in the publications”. In practice the ECRIN contribution is mentioned in the ‘acknowledgements’ (but some journals restrict acknowledgements to funding bodies), or in the ‘methods’ section, or sometimes as a co-author. The current authorship rules and academic reward in the biomedical research community appear poorly adapted to highly cooperative research conducted by large consortia involving multiple scientific and technical contributors. The particle physics community signs papers by alphabetical order, promoting participation in large cooperative projects rather than signature as first or last author. The raising involvement of research infrastructures in the biomedical field should lead to discuss renewed authorship and evaluation rules, better taking into account all the contributions to large-scale and complex research projects (and avoiding slicing reports into multiple articles). Journal editors, research evaluation agencies and ESFRI should be involved in such a discussion, as the infrastructure contribution to the methodology, technology, quality and reproducibility of research should be made more visible, without competing with the users/researchers developing the scientific content. Appropriate recognition is also critical for the academic career of infrastructure staff, and for their evaluation. Interestingly one of the first KPIs for research infrastructures proposed by ESFRI is the number of publications based on the research performed using the facilities/resources of the RIs. This issue extends beyond authorship, as investigators may sometimes view the research infrastructure as competing for a budget share within the consortium - a point of view detrimental to the quality and reproducibility of research. Cultural changes in the scientific community are needed, and incentives promoting cooperation rather than competition, as well as technical solutions, should also be promoted. For instance the European Research Council (ERC) grant awardees may benefit from a substantial additional budget (not competing with the research budget) to purchase scientific equipment or access research infrastructures.

- **Funding multinational trials**

Availability of funding for multinational trials clearly represents a limiting factor for ECRIN’s expansion and activity. The discontinuation of H2020 funding for multinational trials in 2018 and 2019 showed the dependence of ECRIN on this funding mechanism, and led ECRIN to explore new funding strategies, including private or charity funding. However most of the investigator-initiated trials in Europe remain national trials, funded by national grants, which is suboptimal with regards to patient recruitment, access to medical and scientific expertise, robustness of results and generalisability. National funding could be used to support multinational trials, either when cross-border funding is allowed, or through a ‘virtual common pot’ mechanism (ERA-Net on rare diseases, on personalized medicine, on neurodegenerative disorders, or possibly the creation of an ERA-Net for clinical trials). ECRIN must therefore strive to convince both the EU Commission and the national funding bodies of the major added value of multinational clinical research - why to create an infrastructure supporting pan-European trials if there is no funding available for multinational trials ? ECRIN will organize a workshop on funding clinical research with EU and national funders, exploring funding solutions, and sharing best practice on the evaluation process by funding agencies, taking into account not only the scientific value, but also the budget and logistical aspects, to ensure optimal use of the funding allocated to clinical research.

As suggested by the evaluation report, a strong endorsement of such a need for funding to multinational trials by the national governments participating in the Assembly of Members should contribute to find

appropriate solutions, through their strong link with the national and European decision-making process: promoting H2020 or IMI funding for multinational clinical research, promoting an ERA-Net on clinical trials, or promoting cross-border use of national funds. More generally, ECRIN should leverage on the government representatives at its Assembly of Members, who should also be able to foster harmonization through the promotion of coordinated national policies, and through coordinated input to the EU Commission and to the Council on various components of the clinical research ecosystem in Europe, such as the discussion on new Regulations (Clinical Trial Regulation, Medical Device Regulation, General Data Protection Regulation etc) and their national implementation, the harmonisation of practice in ethics committees, the better alignment of clinical trial insurance requirements, the revision of the ICH guidelines, the harmonization of regulatory framework for clinical trials without health products, etc.

- **Heterogeneity of national partners**

The evaluation report points to the heterogeneity of the national partners. Depending on the country's history, economic status, population size, past investment in clinical research, role of hospitals vs. universities, regulatory and ethical practice, medical expertise and equipment, scientific excellence and maturity, the organisation and performance of the national clinical research infrastructures are highly variable when they join ECRIN. In turn ECRIN promotes their development and the convergence of the clinical research systems across the partner countries, which represents a long-term investment. This is reflected in the Framework Agreement signed between ECRIN and each national partner, describing the operational services that it is committed to deliver. This Framework Agreement also includes self-assessment sheets assessing the quality, resources and capacity of the national partner. ECRIN proposes a capacity building programme, including short term visits, and appropriate training sessions. The data centre certification programme is also designed to raise quality and promote common standards across ECRIN national partners¹.

- **Alliance with BBMRI and EATRIS**

As suggested in the evaluation report, discussions were recently initiated with BBMRI and EATRIS to consider the creation of an alliance of medical research infrastructures (with the provisional acronym AMRI). This alliance would create an integrated service pipeline for health innovation, with a critical mass of staff, partners and competencies. Two external factors acted as strong incentives for considering such an alliance. The General Data Protection Regulation pushes BBMRI, EATRIS and ECRIN to work together (in particular in the context of the European Open Science Cloud) to propose both technical and ethical/data protection solutions for the secondary use of personal and sensitive health data and biosamples. On the other hand, personalized medicine research programmes typically include a stratification cohort and a validation cohort, with multi-omics analysis of biosamples, a translational step to select the treatment options to be tested in each patients' cluster, and multi-arm trials to test these treatments. The recently funded H2020 PERMIT project, coordinated by ECRIN, will address this personalized medicine pipeline and represents *de facto* the first AMRI project, establishing methodological standards for personalized medicine research. The IMI EU-PEARL is another critical project for the alliance, through the development of four multinational platform trials. The AMRI has now to discuss strategic questions: should we start with the development of common tools and standards ? or provide an integrated operational service pipeline for health innovation ? or should we

¹ The evaluators suggested to have at least one data centre certified in each Member and Observer country. This would be of course an ideal status, however the centres cannot obtain the certification if they don't meet the requested level of excellence and quality. This is the reason why training sessions are organised to prepare the centres for future application and certification audits. Another comment suggests that the certification of data centres in non-Member countries would be an incentive to join. Our feeling is the opposite, it would rather be an incentive for the current Members to leave ECRIN. ECRIN has a very open policy in terms of provision of operational services, as it supports trials in non-Member and non-Observer countries as far as two Member or Observer countries are involved. For this reason, it is necessary to keep a real added value for ECRIN Membership, and this certification programme, exclusively offered to Members, is one of them.

first focus on personalized medicine projects ? or on the support to the secondary use of multinational data and samples ?

These questions should also be discussed with national partners and with the Assemblies of Members of the three RIs. In any case, the AMRI offers opportunities for ECRIN, BBMRI and EATRIS, in particular in terms of provision of new services, attractiveness for new users communities, partnership with medical specialties, partnership with industry. This also raises some challenges, as the current geographical coverage of the three RIs only partially overlaps, as the current missions of the three RI are not aligned, as some national partners or governments may be reluctant, and as only ECRIN has human resources in-country². Sharing this resource, as well as further integration as a federation or even as a single entity will also be part of the discussion. This alliance could be an opportunity to share other expertise (including a common expert on strategic communication, expertise in data science, data protection, data management etc), and possibly to improve our geographical coverage if governments agree to participate in the whole AMRI.

- **Partnership with industry**

The AMRI also represents an opportunity to establish a strong partnership with the health industry. ECRIN is involved in a significant number of IMI-funded projects to develop tools, and to provide solutions for their sustainability after completion of the project. This could be amplified in the Horizon Europe Health Partnership, extending the public-private partnership towards the health industry as a whole (and not only the EFPIA companies). This partnership will be open to the medical technology sector, including large and small companies. In the context of the new medical device Regulation (745/2017), medical device SMEs will have to conduct randomized trials and will need an operational support, and ECRIN proactively develops such competency. Although ECRIN cooperates for many years with the industry for the development of common tools, this operational support to SMEs on medical device, diagnostics or biotherapy would represent a new development, also building on the contribution of EATRIS expertise on the innovation pipeline and the market access.

- **Partnership with pan-European medical specialty networks**

The evaluation report highlights the value of the PedCRIN model for a win-win cooperation with medical specialties' investigation networks. In such a win-win distribution of roles, ECRIN provides generic trial management services to the sponsor, whereas specialised investigation networks focus on support to investigators on-site (resources to support investigation and recruitment such as study nurses and specific equipment), and through pan-European investigators' networks generating the scientific content and providing access to patients. This arrangement allows cross-fertilization across disciplines in Europe through the rapid spreading of new technologies and methodologies – patient stratification through big data and machine learning has moved from cancer to psychiatry. This cooperation model clearly optimises the use of resources and competencies, taking advantage of existing research infrastructures to build pan-European investigators' communities, avoiding duplication and fragmentation while promoting pan-European cooperation in the initiation and conduct of clinical trials and in the development of appropriate tools.

² Having all the EuCos as direct employees, as suggested by the evaluation report, is seen as an ideal scenario for ECRIN, however there are financial obstacles (some countries pay the local contribution 'in kind'), and employment rules still differ between EU countries.

Organisation of the evaluation

The evaluation of ECRIN-ERIC was performed from June 25th to 27th, 2019.

The evaluation Committee experts carried out 24 interviews over 2 days, including the first with the Director general and his team, and the last with him alone. Domain 1 of the report – Positioning and strategy of the ERIC – is based on written documents and interviews with:

- ECRIN member representatives;
- European Commission representatives;
- members of the Scientific board;
- representatives of the Network committees;
- the Chair of the Assembly of members;
- representatives of the relevant French ministries;
- an ESFRI Board representative.

Domain 2 of the report – Governance and management – is based on written documents and interviews with:

- the Director of operations;
- the Head of the legal and regulatory service;
- the Head of administration, finance and human resources;
- the Leader of the data centre certification project;
- the Head of quality and information technology management;
- the Accountant;
- the Head of communications.

Domain 3 of the report – ERIC activities – is based on written documents and interviews with:

- the Head of clinical operations;
- the Manager of the PedCRIN project;
- two sets of national EuCos;
- managers of infrastructure and service development projects.

Evaluation committee

The external expert Committee was chaired by:

Prof. Richard Frackowiak, Emeritus professor at University College London (UCL – United Kingdom) and Titular professor at the *École Polytechnique Fédérale de Lausanne* (EPFL – Switzerland). Prof. Frackowiak is a neurologist specialised in brain imaging. He was Dean of UCL's Institute of neurology (1998-2002), Vice-Provost of the UCL (2003-2009), Head of Department of cognitive studies at the *Ecole Normale Supérieure* (2004-2009), and Scientific advisor to INSERM's³⁸ chairman and CEO (2007-2014). In 1994, he established the Wellcome Trust centre for neuroimaging where he developed new techniques for magnetic resonance imaging. Subsequently, Prof. Frackowiak headed the CHUV's³⁹ Department of clinical neuroscience (2009-2015). In 2013, he co-directed the Human Brain Project, one the 4 FET⁴⁰ flagships, the largest scientific projects ever funded by the European Union. Prof. Frackowiak's work has been honoured by numerous prizes, including the Ipsen, Wilhem Feldberg and Klaus Joachim Zulch prizes.

The following experts participated in the evaluation:

Mrs. Alizia Ackerstein, Clinical oncology division clinical trials research manager at Chaim Sheba medical center (Israel). Mrs Ackerstein has an extensive career that spans over 30 years in the field of life sciences and clinical oncology, starting at the Hadassah University Hospital in Jerusalem, where she served for 16 years. In 2006, she joined Novartis Pharmaceuticals as an oncology clinical research manager. She was in charge of managing multi-phasic clinical trials – both local and regional – specializing in investigator-initiated trials. In 2010, she returned to a hospital-oriented clinical setting, where she is now responsible for managing, recruiting and supervising more than 130 active phase I-IV clinical trials.

Prof. Angel Asúnsolo del Barco, Associate professor at University of Alcalá (UAH – Spain), and affiliate faculty to the Department of epidemiology & biostatistics (Graduate School of Public Health & Health Policy, City University of New York). Specialist in both preventive and legal medicine, Dr Asúnsolo studied clinical research at Harvard Medical School and management science at Pompeu i Fabra University and at IESE Business School. He has successfully combined these areas in his career. He has been member of the governing board and permanent commission of the Spanish Public Research Consortium in Epidemiology and Public Health (CIBERESP, 2011-2013), Dean of medicine (2013-2014) and Director of academic quality at UAH (2014-2015). Currently, he is Deputy director of the Department of surgery, medical and social science (2016-) and member of the Ramón y Cajal Health Research Institute (IRYCIS).

Prof. Hervé Le Marec, Emeritus professor of cardiology and hospital practitioner at University of Nantes (France). For 10 years, Prof. Le Marec was managing the French *Institut du Thorax* and its research unit that he cofounded (2006-2016). Before, he was chairing of Nantes University's Medical commission (2003-2009) and was heading the Cardiological and Vascular Diseases Clinic (2004-2009). He was awarded the Paul Binet prize of the Medical Research Foundation and the Daniel Herman prize of the French Institute for his work related to valvular diseases. In 2018, he was appointed Special advisor to the French Minister of health.

Dany Vandromme, scientific advisor, and Amaury Barthet, project officer, represented the HCERES, acting as ERIEC Evaluation Leader for the ERIEC consortium.

The evaluation concerns the situation of the ERIC for the period from 2013 to the evaluation date.

The CVs of experts can be found at the HCERES website (URL <http://www.hceres.fr/MODALITES-D-EVALUATIONS/Liste-des-experts-ayant-participe-a-une-evaluation>).

³⁸ *Institut national de la santé et de la recherche médicale* – French National Institute of Health and Medical Research.

³⁹ *Centre hospitalier universitaire vaudois* – Lausanne University Hospital.

⁴⁰ Future and emerging technology.

The evaluation reports of European research infrastructures under the umbrella of ERIEC are available at: www.eriec.eu



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