

**ECRIN
ANNUAL
REPORT
2016**

TABLE OF CONTENTS

LETTER FROM THE DIRECTOR GENERAL	3
2016 HIGHLIGHTS	4
ECRIN OVERVIEW	5
WHY ECRIN?	7
CLINICAL TRIAL OPERATIONS AND CAPACITY DEVELOPMENT	8
CLINICAL TRIAL PORTFOLIO (CURRENT)	9
STRATEGY	19
ADMINISTRATION AND COMMON SERVICES	19
LOOKING FORWARD: A COMMITMENT TO SCIENCE AND SOCIETY	21
GEOGRAPHIC DISTRIBUTION	22
GOVERNANCE	23
ECRIN PUBLICATIONS IN 2016	24
FINANCIAL REPORT FOR 2016	25

LETTER FROM THE DIRECTOR GENERAL



Dear colleagues and partners,

2016 was an exciting year in many ways. We added a new Member Country (Norway). We became involved in 18 new clinical trials and capacity building projects (set to start in 2017). We received 'ESFRI Landmark status'. And, we introduced a new strategy plan for 2016 to 2019 to identify objectives and challenges to ECRIN's development.

In 2016, the provision of support to multinational, academic clinical trials - covering diverse medical fields and diseases - remained the heart of our activity. In addition, through our ECRIN-On-Board programme, we provided increased support to investigators and sponsors for funding applications on Horizon 2020 (H2020) calls as well as the E-Rare European Research Area Network (ERA-Net) call (repurposing in rare diseases). These applications had relatively high acceptance rates, and a total of 11 ECRIN-supported clinical trials received funding in 2016.

Moreover, we added seven new capacity building projects to our portfolio. We continued to work on ongoing capacity projects such as the H2020-funded CORBEL and Rltrain projects, which were both launched in 2015 and bring together several stakeholders from European research infrastructures (RIs).

Committed to global cooperation, we worked with our many European and international partners to increase collaboration on non-commercial trials. In particular, we made significant progress in laying the groundwork for the Clinical Research Initiative for Global Health (CRIGH) project.

We are proud of what we have achieved with our partners so far, and are aware of the significant challenges that still lie ahead. Among other things, we need to scale up our activities while striving to make the best possible use of our human and financial resources. This report provides an overview of how we used those resources in 2016 to achieve our goals.

We look forward to overcoming obstacles to multinational trials with our outstanding partners in Europe and internationally. Together, we hope to make even greater progress towards more evidence-based medical decisions. We thank you for your interest and continued support.

Sincerely,





MISSION, VISION, VALUES

OUR MISSION

To support the conduct of multinational clinical research in Europe

OUR VISION

To generate scientific evidence to optimise medical practice

OUR VALUES

Healthcare optimisation, health innovation, patient involvement, scientific excellence, ethics, transparency, data sharing, high-quality data, non-profit focus, international cooperation

By managing and supporting clinical trials across borders, connecting scientific networks, and providing investigators and sponsors with tools and other resources, ECRIN aims to enhance the quality of clinical research projects for greater public health impact.

2016 HIGHLIGHTS

WELCOMED A NEW MEMBER COUNTRY, NORWAY, WITH THE NORWEGIAN CLINICAL RESEARCH INFRASTRUCTURE (NORCRIN) AS SCIENTIFIC PARTNER

PROVIDED SUPPORT TO 29 H2020 2016 FULL PROPOSALS, AND 33 LETTERS OF INTENT FOR THE 1ST STEP OF THE 2017 H2020 2-STEP CALLS: SUPPORTED COORDINATORS IN DEVELOPING THE TRIAL MANAGEMENT SECTION OF THE PROPOSAL IN PARTICULAR

BECAME INVOLVED IN 7 NEW MULTINATIONAL CLINICAL TRIAL PROJECTS, INCREASING THE CURRENT TRIAL PORTFOLIO TO 28 ONGOING TRIALS

GRANTED ESFRI LANDMARK STATUS (SEE BOX BELOW)

LAI D THE GROUNDWORK FOR THE LAUNCH OF CRIGH, WITH A PRE-KICK-OFF MEETING IN OCTOBER 2016

CERTIFIED 4 NEW DATA CENTRES IN EUROPE

HELD A MEETING IN HONOUR OF INTERNATIONAL CLINICAL TRIALS DAY (ICTD) 2016 ON PERSONALISED MEDICINE

DEVELOPED A 2016-2019 STRATEGY PLAN

CONTRIBUTED TO EUROPEAN DISCUSSIONS ON THE CREATION OF A POSSIBLE EUROPEAN RESEARCH AREA NETWORK (ERA-NET) FOR CLINICAL TRIALS

SIGNED MEMORANDUMS OF UNDERSTANDING WITH THE FOUNDATION FOR BIOMEDICAL RESEARCH AND INNOVATION (FBRI) IN JAPAN AND THE OSWALDO CRUZ FOUNDATION (FUNDACAO OSWALDO CRUZ, FIOCRUZ) IN BRAZIL

CONTRIBUTED TO 7 ARTICLES PUBLISHED IN 2016

ECRIN IN NUMBERS: 2016

- 40** number of multinational trials in the ECRIN portfolio
- 28** ongoing trials supported by ECRIN in 2016
- 7** average number of countries per ECRIN-supported trial
- 7** Member Countries
- 2** Observer Countries

ECRIN, AN 'ESFRI LANDMARK'

A noteworthy accomplishment in 2016 was the listing of ECRIN as an 'ESFRI Landmark' on the European Strategy Forum on Research Infrastructures (ESFRI) Roadmap 2016, launched on 10 March 2016 in Amsterdam. ECRIN has been listed on the ESFRI Roadmap since 2006.

ESFRI identifies Research Infrastructures (RIs) of pan-European interest meeting the long-term needs of Europe's research communities across scientific areas. ESFRI RIs are facilities, resources or services of a unique nature identified by European research communities to conduct top-level research activities in all fields. The publication of periodically updated ESFRI roadmaps, since 2006, aims to ensure that Europe has excellent RIs, which are accessible to researchers and supportive of scientific advancement and innovation.

The ESFRI Roadmap 2016 distinguishes between 21 'ESFRI Projects', or projects with a high degree of maturity, and 29 'ESFRI Landmarks'. ESFRI Landmarks are RIs that were implemented or started implementation before 2015 and are now considered 'pan-European hubs of scientific excellence, generating new ideas and pushing the boundaries of science and technology'.

The attribution of Landmark status is a major accomplishment for ECRIN as it reflects its valuable and long-term contribution to the European research landscape through the provision of high-quality scientific and managerial services.

ECRIN OVERVIEW

Since its creation in 2004, the European Clinical Research Infrastructure Network (ECRIN) has been striving to overcome the obstacles to multinational trials in Europe. Multi-country trials mean greater access to patients, resources, and expertise, and, in turn, potentially more robust trial results and greater public health impact.

A non-profit intergovernmental organisation with the legal status of a European Research Infrastructure Consortium (ERIC) since 2013, ECRIN offers support for trial preparation, validation and, in particular, implementation/management. It focuses on independent, multinational academic research as well as trials initiated by biotech and medical device small and medium enterprises (SMEs).

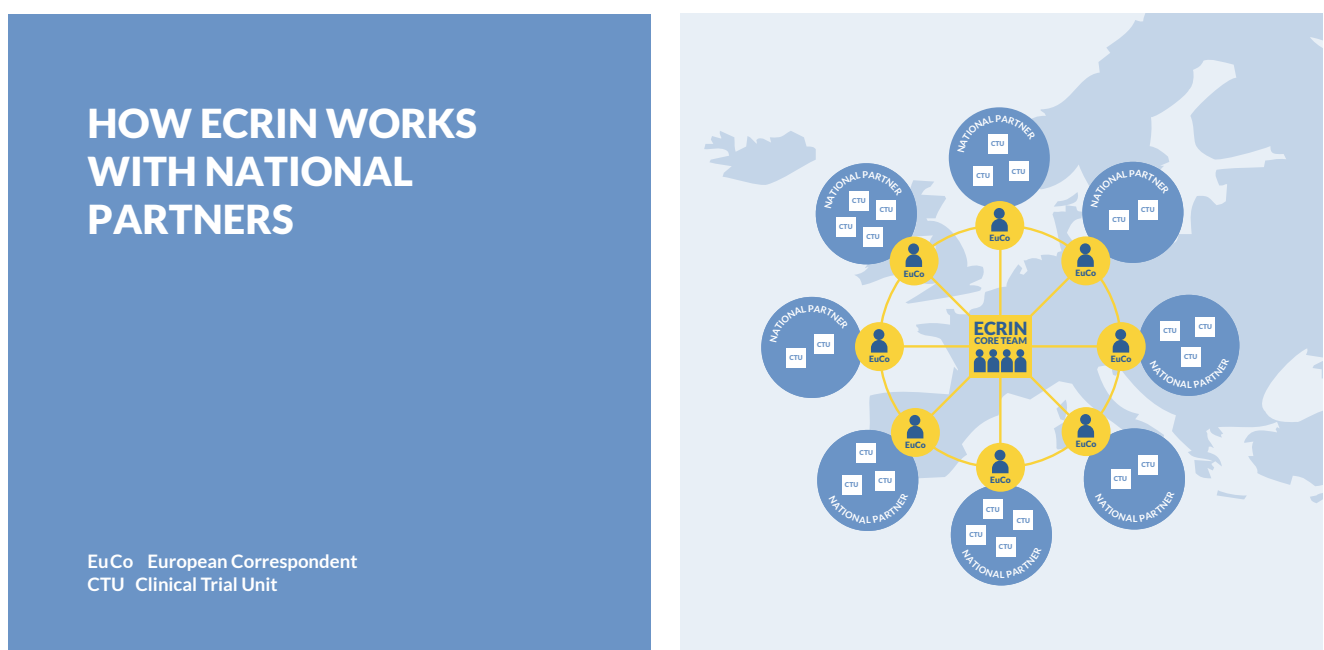
In addition, ECRIN contributes to capacity building projects aiming to establish shared services in biomedical areas and to foster international cooperation in non-commercial trials.

ORGANISATION

ECRIN's organisational model is based on country membership. In 2016, it had seven Member Countries (France, Germany, Hungary, Italy, Norway, Portugal and Spain) and two Observer Countries (Czech Republic and Switzerland).

Each country hosts a European Correspondent (EuCo) who is seconded to ECRIN by the national scientific partner (i.e. network of academic clinical trial units (CTUs) and/or clinical research centres (CRCs) located at or affiliated to national universities and hospitals). EuCos are clinical research experts with extensive knowledge of the national and European clinical research landscape; they manage the clinical trial portfolio and coordinate with the national scientific partner with support from the Paris-based Core Team.

The image below shows how ECRIN works with its national partners.



ECRIN'S EUROPEAN CORRESPONDENTS (EuCos)

How do ECRIN's EuCos provide support to investigators, sponsors and other parties during the funding application phase and trial implementation (the heart of ECRIN's activity)?

Your Partner for Funding Applications

ECRIN's EuCos act as the intermediary between the sponsor and service providers (i.e., national networks and CTUs) in different countries, ensuring smooth coordination, communication, organisation and support throughout the funding application process. They can advise on anything from ethical/regulatory requirements to trial insurance, and can provide a logistical assessment of project plans.

Facilitating Trial Management

During trial implementation, EuCos, in close collaboration with the Paris-based Core Team, ensure proper organisation and follow-up until trial completion (this will depend on the scope of ECRIN's services). They play an active role in reassuring stakeholders that all the necessary steps are being taken to successfully implement the trial. In particular, EuCos act as the link between ECRIN and the sponsor's team and assist with issues relevant to the sponsor/CTUs.

A Collaborative Network

ECRIN's EuCos across Europe collaborate closely, providing each other with essential information and support during the development and implementation of clinical trials, as well as for related activities.

FUNDING

ECRIN is funded by the contributions of its Member and Observer Countries. These funds are primarily dedicated to supporting the organisation and developing its core competencies.

In addition, ECRIN receives funds from European funding bodies (Horizon 2020, Innovative Medicines Initiative – IMI, or other sources) that cover specific activities carried out as part of multinational clinical trials or capacity building projects.



WHY ECRIN?

MULTI-COUNTRY TRIALS: IMPORTANCE AND CHALLENGES

Clinical trials are an essential step in evaluating the efficacy and safety of innovative treatments, exploring new indications for authorised drugs, and comparing the efficacy and safety of approved healthcare strategies.

International collaboration is important for clinical research, as it maximises access to patients and leads to faster results. It also enables the sharing of medical and scientific expertise, tools, procedures and costs; increases the applicability of research findings; reduces duplication; and enhances methodological standards. The evidence from multinational trials can support enhanced health policy-making, optimal resource use, and improved patient care across borders.

Despite the advantages of multinational trials, only a very small percentage of academic trials involve more than one country; however, a significant number of industry trials are multinational, especially when they involve countries with small and medium-sized populations. In Europe, the relative scarcity of multinational academic trials can be explained, in part, by restrictions with current cross-border funding options. Other general barriers to multi-country collaboration include different legal, regulatory and ethical requirements; difficulties in locating CTUs; and linguistic, insurance, contracting, and managerial and administrative issues.

Due to these obstacles, investigators may forgo multinational trials in favour of trials conducted in a single centre, or in multiple centres within one country. This limits the scope of research and reduces its potential impact on global public health.

THE ECRIN ADDED VALUE AND IMPACT

By providing investigators with essential resources and expertise, ECRIN aims to help them overcome barriers to the development and implementation of multinational clinical trials. ECRIN links investigators, sponsors and CTUs across countries, facilitating dialogue and coordination between parties, and, ultimately, leading to more effective trials.



Q&A: MEMBERSHIP BENEFITS AND ELIGIBILITY FOR ECRIN SUPPORT

Q. What services do Member Countries receive?

A. ECRIN Member Countries can benefit from the full range of ECRIN services for multinational trial preparation, protocol evaluation and/or trial management. Advice and information are freely provided by the ECRIN Core Team and EuCos. Trial management services are provided at not-for-profit rates for academic investigators and sponsors.

Q. Are all trials in Member and Observer Countries automatically eligible for ECRIN support?

A. No. To be eligible for ECRIN support, projects must involve at least two Member or Observer Countries; the protocol and trial plans must be reviewed and approved by ECRIN.

Q. Can ECRIN support a trial that is coordinated by a country that is not a Member or Observer?

A. Yes, ECRIN can provide support services even if the trial's coordinating country is not a Member or Observer, provided that the project involves at least two Member and Observer Countries. In this case, one of ECRIN's EuCos or the Core Team is assigned to the trial.

CLINICAL TRIAL OPERATIONS AND CAPACITY DEVELOPMENT

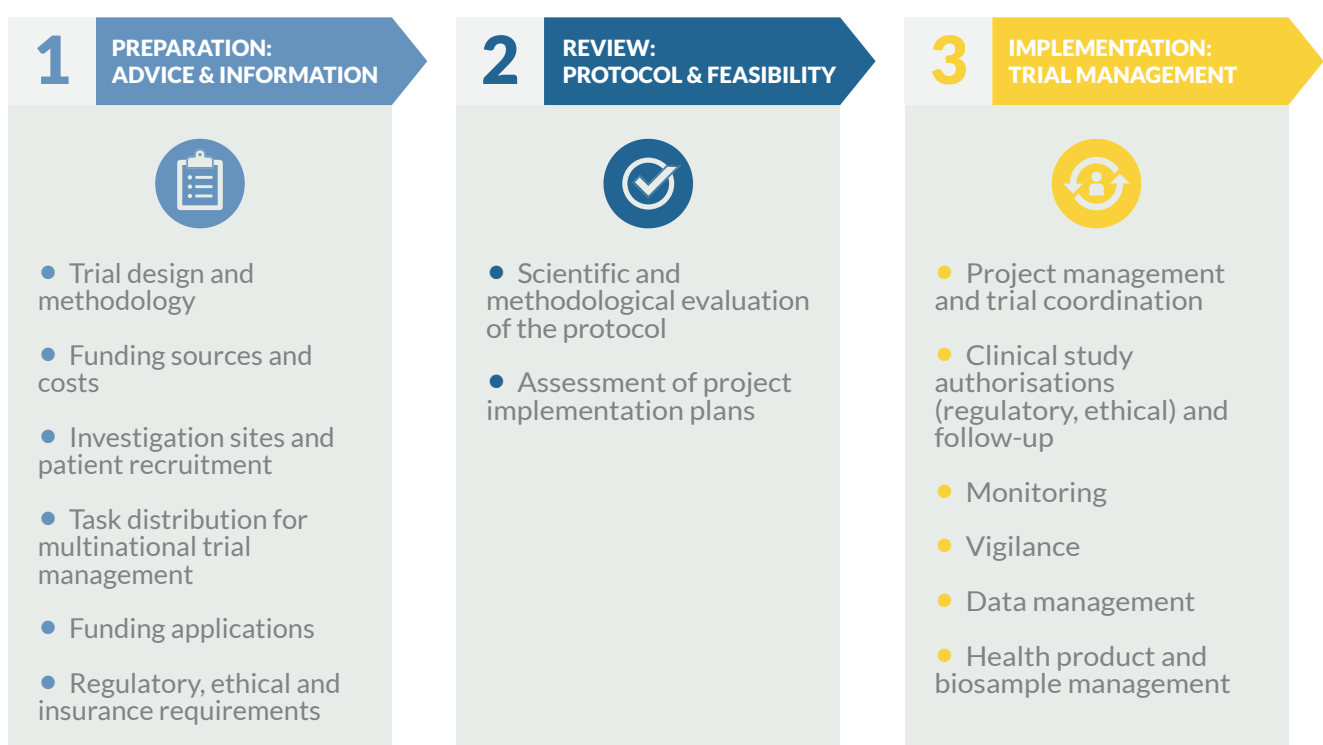
OVERVIEW

In 2016, ECRIN continued to focus on clinical trial operations and capacity development. Its main activities included: support to clinical trials; tools development; interactions with investigators; expansion of membership and international partnerships; quality assurance; and capacity building projects. This section provides an overview of each activity and an update on progress made throughout the year.

SUPPORT TO MULTINATIONAL CLINICAL TRIALS

ECRIN's support to multinational clinical trials is three-fold. It can provide support to investigators and sponsors in ECRIN Member and Observer Countries for the preparation of EU funding applications, and subsequently the validation of study protocols. Provided that projects meet ECRIN's eligibility criteria, it can also offer various trial management services, accompanying investigators and project coordinators from recruitment to scientific publication.

The image below provides a closer look at specific ECRIN services for the development and implementation of trials.



PREPARATION/PROTOCOL REVIEW: FUNDING APPLICATION SUPPORT

In the preparation phase, ECRIN can give input on the different aspects of funding applications such as work package architecture, potential impact, management, governance, consortium composition, and multinational clinical trial management. ECRIN can also advise on the types of available (European) funding and how to go about applying. Moreover, EuCos can provide information on the facilities that have the capacity and services needed to manage the trial, as well as on investigator sites and networks in their countries. They ensure that the CTUs selected for the study are an appropriate fit, both in their country and in other European countries.

Also in the preparation stage (or in parallel to protocol review), EuCos can assess the practicality of trial plans in each country and give suggestions and alternatives to ensure that the trial runs smoothly. Finally, ECRIN can provide methodological consulting and an independent review of study protocols. This evaluation is done by ECRIN's Scientific Board, which is composed of clinical research and methodology experts.

In 2016, ECRIN proposed more comprehensive support to investigators and sponsors for funding applications. This was achieved in part through the ECRIN-On-Board (EoB) initiative, which involves early support on the protocol (with independent review from ECRIN's independent Scientific Board) and consulting on the logistical/operational aspects of project design.

While the majority of support was provided for H2020 calls, ECRIN also assisted with applications to the E-Rare ERA-Net call for repurposing clinical trials in rare diseases. In 2016, 11 projects went through the EoB initiative. In all, of the 30 (H2020/IMI) projects submitted, seven new multinational clinical trial projects involving ECRIN as a partner were funded in 2016:

- 6 H2020 SC1 projects: 4 on chronic diseases (HIVACAR, LIVERHOPE, PAPA-ARTIS, PROOF) and 2 on regenerative medicine (ORTHOUNION, RESPINE)*
- 1 trial funded by the Innovative Medicines Initiative 2 (IMI 2) programme (MACUSTAR)*
(In addition, ECRIN is involved in new projects funded by the E-Rare-3 ERA-Net.)

* See below for details on these trials

The total number of ongoing clinical trials (all funding sources) in ECRIN's portfolio thus increased to 28 in 2016. A total of 33 Letters of Intent were also submitted in 2016 to two-stage 2017 calls, of which 11 were invited to submit a full proposal.

IMPLEMENTATION: TRIAL MANAGEMENT SERVICES

In the project implementation phase, ECRIN offers investigators and project coordinators various trial management services. Through its national partners (networks of CTUs), ECRIN can perform project management (central and local); handle submissions to regulatory and ethics authorities in participating countries; provide on-site monitoring in the different countries; and conduct local pharmacovigilance tasks. ECRIN can also provide centralised activities such as data management (through its certified data centres) and central pharmacovigilance. In addition, it can assist with (national or multinational) trial insurance and medicine and sample handling across countries.

TOOLS

ECRIN's support to multinational clinical trials is not limited to funding application advice or management services alone. ECRIN recognises that to be successful, countries need the right tools to design and conduct robust multinational trials. For this purpose, it develops and maintains freely accessible common tools.

In 2016, ECRIN continued to develop the tools that were originally developed as part of the ECRIN Integrating Activity (ECRIN-IA) project¹. One example is the CAMPUS database (campus.ecrin.org) which provides regulatory and ethical information on 22 European countries for studies on medical devices, medicinal products for human use, and nutrition. CAMPUS can be used to locate country-specific competent authorities and ethics committees, consult the summary of requirements for each country, compare country information, and browse related documents (e.g. regulations and guidelines).

Other tools that continued to be available to users were a risk-based monitoring toolbox, an outcome measure database for medical devices, and a mapping of nutrition centres.



¹ECRIN-IA was funded by European Union Framework Programme 7 (grant agreement no. 284395). Involving 23 countries and covering three main areas of expertise (rare diseases, medical devices and nutrition), it brought together diverse stakeholders to build capacity and tools for multinational clinical trials in Europe (ESCALE, IMPACTT, MENAC, POEM vs LHM, and RESCUE ESES). Originally planned for four years (2012 to 2015), the clinical trials work package was extended until 2017.

Note: the “**” symbol designates the trial coordinating country; the “\$” symbol refers to projects funded in 2016 and starting in 2017.

ADIPOA2^I (Clinical Trial of Autologous, Adipose-Derived Mesenchymal Stromal Cells (ASCs) in the Treatment of Mild-to-Moderate Osteoarthritis, OA): ADIPOA2 aims to assess the safety and efficacy of autologous (patient-derived) ACSs in the treatment of advanced OA of the knee. ECRIN provides support for project management, regulatory and ethical submission, data management, monitoring and pharmacovigilance in this phase 2b study.

Countries: France*, Germany, Ireland, Italy, Netherlands, United Kingdom

Medical field: Orthopaedics / cell therapy

AETIONOMY^{II} (Taxonomy of Neurodegenerative Diseases: Observational Study in Alzheimer's Disease and Parkinson's Disease): AETIONOMY aims to validate the mechanism-based taxonomies of Alzheimer's and Parkinson's disease for two biomarkers for each disease. ECRIN provides support for regulatory and ethical submission, as well as monitoring.

Countries: France*, Germany, Spain, Sweden

Medical field: Neurology

BETA3_LVH^{III} (A multi-center randomized, placebo-controlled trial of mirabegron, a new beta3-adrenergic receptor agonist on left ventricular mass and diastolic function in patients with structural heart disease): ECRIN continued to support the implementation of this phase 2b trial, which aims to evaluate mirabegron (a new β 3-specific agonist) over 12 months as add-on to standard treatment compared to standard treatment alone.

Countries: Austria, Belgium*, France, Greece, Germany, Italy, Poland, Portugal, United Kingdom

Medical field: Cardiology

BIOCHIP^{IV} (Clinical Trial for the Regeneration of Cartilage Lesions in the Knee (NosetoKnee2): BIOCHIP aims to investigate the efficacy of an engineered cartilage transplant (N-TEC) in comparison to a cell-activated matrix (N-CAM) for the treatment of articular cartilage lesions in the knee. ECRIN is a work package leader and is involved as well in regulatory/ethical submission and monitoring.

Countries: Croatia, Germany, Italy, Switzerland*

Medical field: Orthopaedics / cell therapy

BIO-RAIDS^V (Biomarker Evaluation in Advanced Stage Cervical Cancer by an International Working Group. Tumor Stages (1B1 - 4)): This study aims to identify predictive biomarkers of standard treatment response using an integrative approach combining exome sequencing, proteomics and tumour micro environment analyses. ECRIN is involved in regulatory/ethical submission and monitoring.

Countries: Belgium, France*, Germany, Moldova, Netherlands, Romania, Serbia

Medical field: Oncology

^I ADIPOA2 has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 643809.

^{II} AETIONOMY has received funding from the Innovative Medicines Initiative (IMI) under grant agreement number 115568.

^{III} BETA3_LVH has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 634559.

^{IV} BIOCHIP has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 681103.

^V BIO-RAIDS has received funding from the European Union's 7th Framework Programme for research and technological development under grant agreement number 304810.

DISCHARGE^{VI} (Diagnostic Imaging Strategies for Patients with Stable Chest Pain and Intermediate Risk of Coronary Artery Disease: Comparative Effectiveness Research of Existing Technologies): This trial hypothesizes that coronary computed tomography (CT) is superior to invasive coronary angiography (ICA) for major adverse cardiovascular events in a given population. ECRIN provides support for monitoring.

Countries: Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany*, Hungary, Ireland, Italy, Latvia, Lithuania, Netherlands, Portugal, Romania, Serbia, Spain, United Kingdom

Medical field: Cardiology

ESCALE^{VII} (Efficacy Study of Antimicrobial Catheters to Avoid Urinary Infections in Spinal Cord Injured Patients): ESCALE aims to make a comparison between the use of antiseptic silver alloy-coated silicone urinary catheters and the use of conventional silicone urinary catheters in spinal cord injured patients to prevent urinary infections. ECRIN's role includes monitoring, pharmacovigilance and project management.

Countries: Italy, Netherlands, Portugal, Spain*, Turkey

Medical field: Infectiology / medical device

EUROHYP-1^{VIII} (Cooling Plus Best Medical Treatment Versus Best Medical Treatment Alone for Acute Ischaemic Stroke): This study seeks to determine if systemic cooling to a target temperature of 34 to 35°C, started within six hours of symptom onset and maintained for 24 hours, improves functional outcome at three months in patients with acute ischaemic stroke. ECRIN is involved in monitoring.

Countries: Belgium, Bulgaria, Croatia, Czech Republic, Denmark, France, Germany*, Greece, Hungary, Ireland, Italy, Netherlands, Norway, Poland, Romania, Spain, Sweden, Turkey, United Kingdom

Medical field: Neurology

FAIR-PARK II^{IX} (Conservative Iron Chelation as a Disease-Modifying Strategy in Parkinson's Disease): FAIR-PARK II aims to demonstrate an effect of deferiprone (DFP) on the course of PD (including both disease modifying and symptomatic effects). ECRIN is in charge of pharmacovigilance, regulatory and ethical submission and monitoring.

Countries: Austria, Czech Republic, France, Germany, Netherlands, Portugal, Spain, United Kingdom

Medical field: Neurology

HIVACAR^X (Evaluating a Combination of Immune-based Therapies to Achieve a Functional Cure of HIV Infection): The main goal of HIVACAR, a proof-of-concept phase IIa clinical trial, is to obtain a functional cure for HIV (i.e., control of viral load to levels below the threshold of 50 copies/ml and maintenance of high CD4+ T-cell count after discontinuation of antiretroviral therapy) thanks to effectively targeting residual virus replication and viral reservoirs.

Countries: Belgium, Canada, Denmark, France, Germany, Spain, United States

Medical field: Infectious diseases (AIDS)

^{VI} DISCHARGE has received funding from the European Union's 7th Framework Programme for research and technological development under grant agreement number 603266.

^{VII} ESCALE has received funding as part of the ECRIN-IA project from the European Union's 7th Framework Programme for research and technological development under grant agreement number 284395; additional funding is provided by Fundacio la Marata de TV3.

^{VIII} EUROHYP-1 has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 278709.

^{IX} FAIR-PARK II has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 633190.

^X HIVACAR has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 731626.

IMPACTT^{XI} (Efficacy Study of IgY (Antibody Against Pseudomonas) in Cystic Fibrosis Patients): This study aims to prolong the time to reinfection with Pseudomonas aeruginosa after successfully treated acute or intermittent infection. ECRIN's support role includes regulatory and ethical submission, monitoring, pharmacovigilance, and advice.

Countries: Austria, Belgium, France, Germany*, Hungary, Italy, Poland, Spain, Sweden

Medical field: Pneumology / rare diseases

LIVERHOPE^{XII} (Simvastatin and Rifaximin as New Therapy for Patients with Decompensated Cirrhosis): This ECRIN-supported project aims to evaluate a novel therapeutic strategy for patients with cirrhosis. In particular, LIVERHOPE will include two randomized double-blind trials to investigate safety, tolerability and efficacy of combination of simvastatin plus rifaximin in patients with decompensated cirrhosis in five countries. ECRIN is involved in data management and trial management.

Countries: France, Germany, Italy, Spain*, United Kingdom

Medical field: Gastroenterology / hepatology

MACUSTAR^{XIII} (Dry age-related macular degeneration: Development of novel clinical endpoints for clinical trials with a regulatory and patient access intention): MACUSTAR aims to develop novel clinical endpoints for clinical trials with a regulatory and patient access intention in patients with intermediate age-related macular degeneration (iAMD). Additional objectives are to characterise visual impairment in iAMD and its progression, as well as identify risk factors for progression to late stage AMD.

Countries: Belgium, Denmark, France, Germany*, Italy, Netherlands, Portugal, United Kingdom, United States

Medical field: Ophthalmology

MEDIT-AGEING^{XIV} (Investigating the Impact of Meditation Training on Mental Health and Wellbeing in the Ageing Population): MEDIT-AGEING involves a randomised multicentre clinical trial (RCT) in patients with subjective cognitive decline (SCD) at risk for Alzheimer's disease to assess the short-term effects of a standardised meditation intervention vs. active control on behavioural measures. ECRIN is involved in pharmacovigilance, regulatory and ethical submission, and monitoring.

Countries: France*, Germany, Spain, United Kingdom

Medical field: Neurology

MENAC^{XV} (A Randomised, Open-label Trial of a Multimodal Intervention (Exercise, Nutrition and Antiinflammatory Medication) Plus Standard Care Versus Standard Care Alone to Prevent/Attenuate Cachexia in Advanced Cancer Patients Undergoing Chemotherapy): This phase 3 study aims to prevent the development of cachexia early on rather than providing treatment late in the disease trajectory.

Countries: Norway*, Switzerland, United Kingdom

Medical field: Medical oncology / nutrition

^{XI} IMPACTT has received funding from the European Union's 7th Framework Programme for research and technological development under grant agreement number 261095; it has received additional funding from another FP7-funded project, ECRIN-IA under grant agreement number 284395.

^{XII} LIVERHOPE has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 731875.

^{XIII} MACUSTAR has received funding from the Innovative Medicines Initiative (IMI) under grant agreement number IMI2IOUT/2016-03697.

^{XIV} MEDIT-AGEING has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 667696.

^{XV} MENAC has received funding as part of the ECRIN-IA project from the European Union's 7th Framework Programme for research and technological development under grant agreement number 284395.

NISCI^{XVI} (Antibodies against Nogo-A to enhance plasticity, regeneration and functional recovery after acute spinal cord injury, a multicentre European clinical proof of concept trial): NISCI is a double-blind, placebo-controlled trial to test the efficacy of antibody therapy against Nogo-A (a protein inhibiting axonal growth) to improve motor outcome and quality of life of tetraplegic patients. ECRIN's role involves regulatory and ethical submission, as well as monitoring.

Countries: Czech Republic, Germany*, Italy, Spain, Switzerland

Medical field: Neurology

ORTHO UNION^{XVII} (ORTHOpedic randomized clinical trial with expanded bone marrow MSC and bioceramics versus autograft in long bone nonUNIONS): ECRIN provides trial management services to this clinical trial that aims to assess clinically relevant efficacy of an autologous advanced therapy medicinal product (ATMP) with good manufacturing practice (GMP) multicentric production. This will be achieved through a randomised, controlled, three-arm clinical trial under GCP, versus bone autograft, gold-standard in fracture non-unions.

Countries: France, Germany, Italy, Spain*

Medical field: Orthopaedics / rheumatology

PAPA-ARTIS^{XVIII} (Paraplegia Prevention in Aortic Aneurysm Repair by Thoracoabdominal Staging with 'Minimally-Invasive Segmental Artery Coil-Embolization': A Randomized Controlled Multicentre Trial): PAPA-ARTIS is a phase II trial to demonstrate that a staged treatment approach can reduce paraplegia and mortality dramatically. identify risk factors for progression to late stage AMD.

Countries: Belgium, Denmark, France, Germany, Italy, Netherlands, Poland, Spain, Sweden, Switzerland, United Kingdom, United States

Medical field: Neurology

POEM vs LHM^{XIX} (Endoscopic Versus Laparoscopic Myotomy for Treatment of Idiopathic Achalasia: A Randomized, Controlled Trial (POEM rcpmt)): This study aims to compare short and long-term feasibility, safety and efficacy of peroral endoscopic myotomy (POEM) with laparoscopic Heller myotomy (LHM) in the treatment of achalasia. ECRIN provides support for pharmacovigilance and monitoring.

Countries: Belgium, Czech Republic, Germany*, Italy, Netherlands, Sweden

Medical field: Gastroenterology / rare disease / surgery trial

PRECIOUS^{XX} (Prevention of Complications to Improve Outcome in Elderly Patients with Acute Stroke): PRECIOUS aims to find out whether a pharmacological strategy to prevent complications after stroke can reduce the risk of death or long-term disability^{XXI}. ECRIN's support roles include coordination and monitoring.

Countries: Estonia, France, Germany, Hungary, Italy, Netherlands*, Norway, Poland, United Kingdom

Medical field: Neurology

^{XVI} NISCI has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 681094.

^{XVII} ORTHO UNION has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 733288.

^{XVIII} PAPA-ARTIS has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 733203.

^{XIX} POEM vs LHM has received funding as part of the ECRIN-IA project from the European Union's 7th Framework Programme for research and technological development under grant agreement number 284395.

^{XX} PRECIOUS has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 634809.

^{XXI} PRECIOUS will recruit 3,800 patients in 80 hospitals, and patients aged 66 years or older will be randomised to a strategy to prevent complications in the first four days of their hospitalisation, or to standard care.

PROOF^{xxii} (Penumbral Rescue by Normobaric O=O Administration in Patients With Ischaemic Stroke and Target Mismatch ProFile: A Phase II Proof-of-Concept Trial): The PROOF project seeks to demonstrate that NBHO (high-flow 100% oxygen at >45 L/min via a non-rebreather mask, or FiO₂=1.0 for intubation/ventilation) reduces infarct growth from baseline to 24 hours compared to standard treatment if administered at 3 hours after onset of anterior circulation IS, in patients with proximal vessel occlusion and salvageable tissue at risk.

Countries: Belgium, Czech Republic, Finland, France, Germany*, Spain, Sweden, Switzerland
Medical field: Neurology

RESCUE ESES^{xxiii} (A Randomized European trial of Steroids versus Clobazam Usage for Encephalopathy with Electrical Status Epilepticus in Sleep): The aim of this study is to establish which treatment is best for children with ESES syndrome. ECRIN provides support for regulatory and ethical submission, monitoring, pharmacovigilance and project management.

Countries: Belgium, Bulgaria, Denmark, Finland, France, Germany, Italy, Netherlands*, Romania, Spain, United Kingdom
Medical field: Neurology / rare diseases / paediatrics

RESPINE^{xxiv} (REgenerative therapy of intervertebral disc: a double blind phase 2b trial of intradiscal injection of mesenchymal stromal cells in degenerative disc disease of the lumbar SPINE unresponsive to conventional therapy): RESPINE aims to assess, via a multicentre, randomised, controlled, phase 2b clinical trial including 112 patients with DDD, the efficacy of an allogenic intervertebral mesenchymal stem cell (MSC)-based therapy.

Countries: France*, Germany, Ireland, Italy, Spain
Medical field: Orthopaedics / rheumatology

SABATO^{xxv} (Staphylococcus Aureus Bacteremia Antibiotic Treatment Options): This multicentre, open-label, randomised controlled trial aims to demonstrate that an early switch from intravenous to oral antimicrobial therapy is non-inferior to a conventional 14-days course of intravenous therapy regarding efficacy and safety. ECRIN's support role includes advice and information, monitoring, local pharmacovigilance, and regulatory and ethical submission.

Countries: Germany*, Netherlands, Spain, United Kingdom
Medical field: Intensive care

SECURE^{xxvi} (Secondary Prevention of Cardiovascular Disease in the Elderly Trial): The purpose of this study is to evaluate the efficacy of a polypill strategy containing aspirin (100 mg), ramipril (2.5, 5 or 10 mgs), and atorvastatin (40 mgs) compared with the standard of care in secondary prevention of major cardiovascular events in elderly patients with a recent myocardial infarction. ECRIN supports local pharmacovigilance.

Countries: Czech Republic, France, Germany, Hungary, Italy, Poland, Spain*
Medical field: Cardiovascular

^{xxii} PROOF has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 733379.

^{xxiii} RESCUE ESES has received funding as part of the ECRIN-IA project from the European Union's 7th Framework Programme for research and technological development under grant agreement number 284395; it has received additional funding from the Wilhelmina Research Fund, Dutch National Epilepsy Fund (NEF).

^{xxiv} RESPINE has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 732163.

^{xxv} SABATO has received funding from DFG (Deutsche Forschungsgemeinschaft).

^{xxvi} SECURE has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 633765.

STRONG TREAT (Multiple Versus Single Dose of Ivermectin for the Treatment of Strongyloidiasis): The aim of this study is to define the most effective dose schedule of ivermectin to cure strongyloidiasis. ECRIN's support role includes advice and information, monitoring, and data management.

Countries: Belgium, Italy*, Peru, Spain, United Kingdom

Medical field: Infectious diseases / vaccines

TRIHEP 3 (A Comparative Phase 2 Study Assessing the Efficacy of Triheptanoin, an Anaplerotic Therapy in Huntington's Disease): This study asks whether the administration of triheptanoin can effectively improve Huntington's disease as assessed by MRI, in vivo spectroscopy and clinical evaluation. ECRIN's support ranges from regulatory and ethical submission to monitoring.

Countries: France*, Netherlands

Medical field: Neurology / rare diseases

VISION-DMD^{xxvii} (Phase 2 Clinical Trials of VBP15: An Innovative Steroid-like Intervention on Duchenne Muscular Dystrophy): This project aims to assess the safety and toxicity (phase 2a) and safety and efficacy (phase 2b) of the orphan drug VBP15 in ambulatory boys with Duchenne muscular dystrophy (DMD). ECRIN provided support for project start-up and is responsible for various components of the phase 2b study including regulatory management.

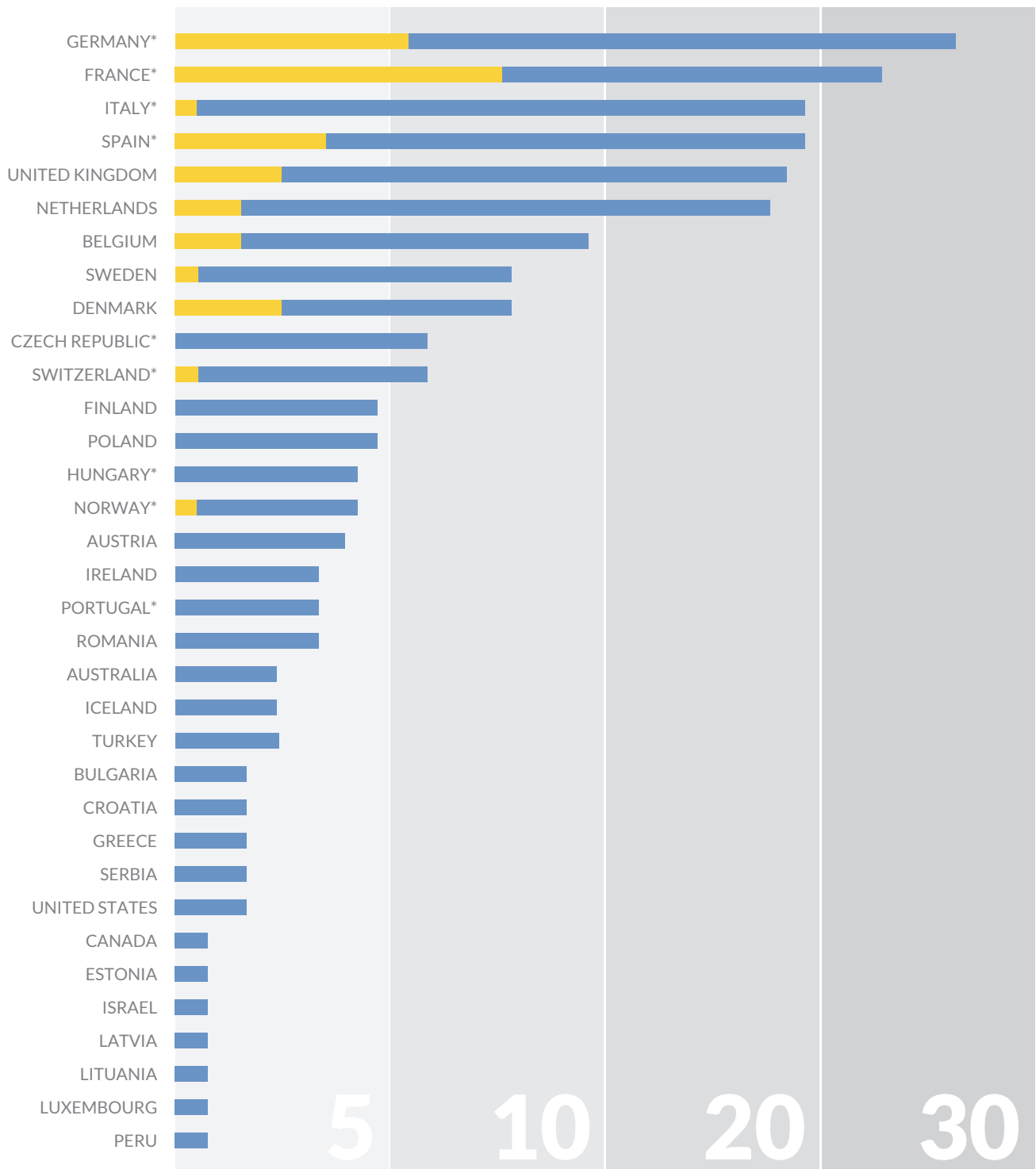
Countries: Australia, Belgium, Czech Republic, Denmark, France, Germany, Israel, Italy, Netherlands, Poland, Spain, Sweden, Turkey, United Kingdom*

Medical field: Neurology / rare diseases / paediatrics

^{xxvii} VISION-DMD has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 667078.

OVERVIEW OF ECRIN CLINICAL TRIAL PORTFOLIO

ECRIN is involved in information, advice and management services for 40 trials (28 ongoing or in preparation), with an average of seven countries per trial.



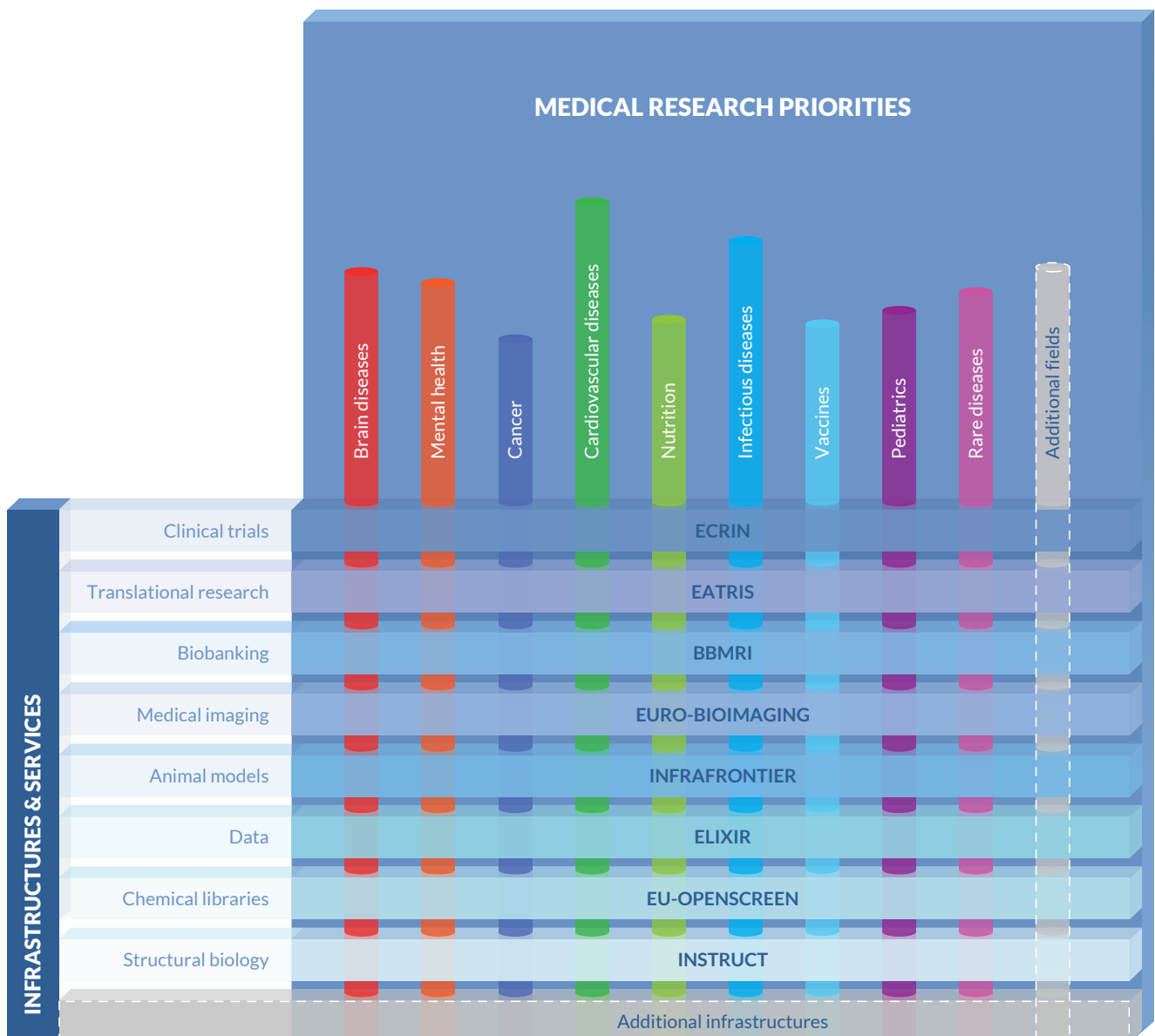
■ COORDINATING COUNTRY

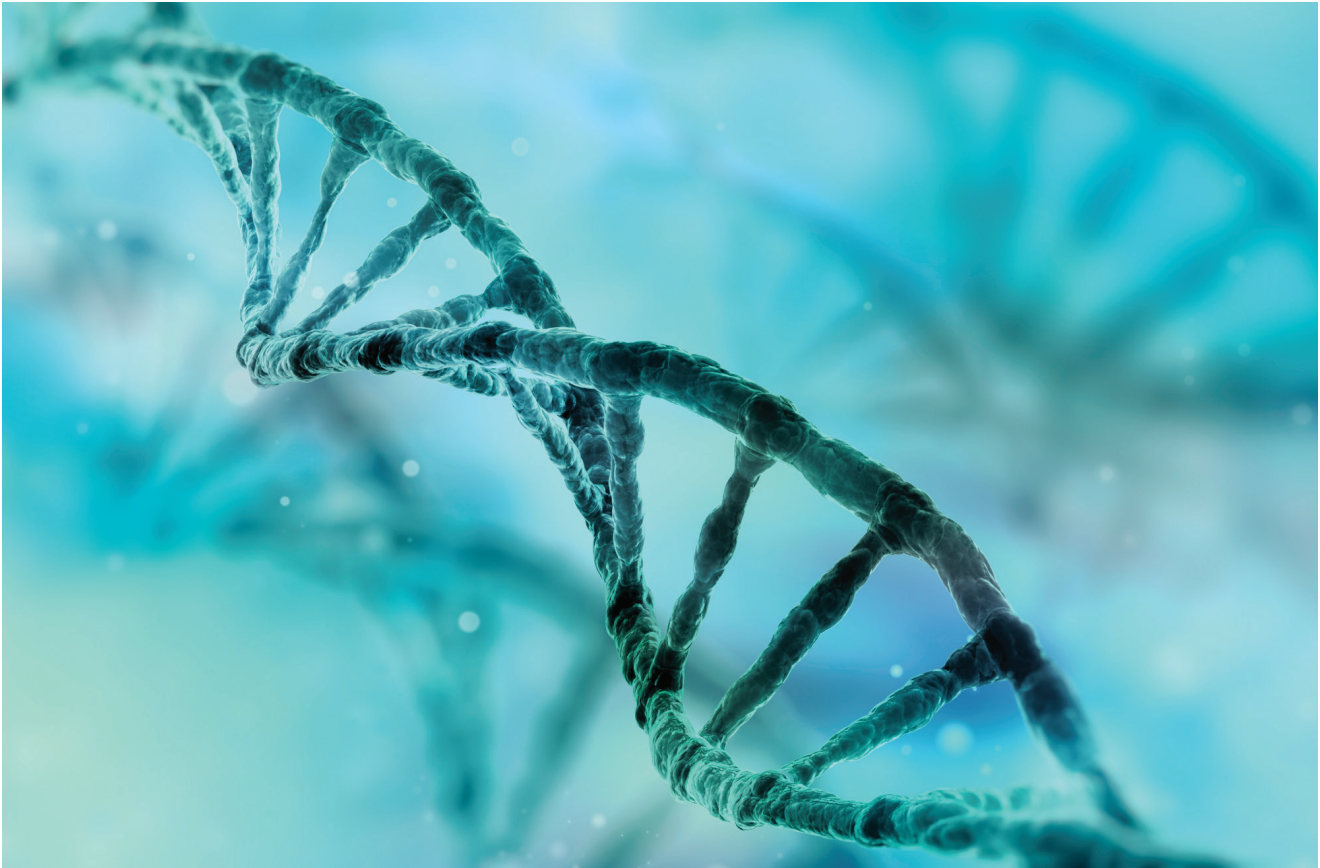
■ PARTICIPATING COUNTRY

*ECRIN MEMBER OR OBSERVER COUNTRY

CAPACITY BUILDING PROJECTS

In addition to supporting trials themselves, ECRIN is an active player in European capacity building projects related to clinical research. Such projects typically involve other European research infrastructures (RIs) working across a wide range of medical fields and offering diverse services (see illustration). The goal of these partnerships is to link RIs to develop tools, services and/or resources for the benefit of medical research communities and, ultimately, patients.





In 2016 ECRIN continued to be involved, as a work package leader or participant, in various H2020 projects including CORBEL and Rltrain (see full list in box below).

- 4 projects funded by the H2020 infrastructure unit:
 - Paediatric Clinical Research Infrastructure Network (PedCRIN, coordinated by ECRIN)
 - European Research Infrastructures in the International Landscape (RISCAPE)
 - European Network of Vaccine Development and Research (TRANSVAC2)
 - European Open Science Cloud (EOSC) pilot
- 1 Marie Curie project: Methods in Research on Research (MiRoR) (kick-off in 2016)
- 1 European & Developing Countries Clinical Trials Partnership (EDCTP) project: Trials of Excellence in Southern Africa II (TESA-II) (to prepare and conduct a certification audit of a data centre for malaria trials in Mozambique)
- Clinical Research Initiative for Global Health (CRIGH), a global consortium funded through the contributions of its Members (pre-kick-off meeting in October 2016, official launch 2017)

CAPACITY BUILDING PROJECTS (CURRENT) /1

Note: the "S" symbol refers to projects funded in 2016 and starting in 2017.

CORBEL^{xxviii} This H2020 project aims to establish shared services between the European Strategy Forum on Research Infrastructures Biological and Medical Sciences Research Infrastructures (ESFRI BMS RIs)–which includes ECRIN–for the biomedical research community. ECRIN is in charge of the third work package (WP3), involving the development of common tools to be used by biomedical research institutions to develop innovative prevention, diagnostic, and treatment solutions.

As part of CORBEL WP3, ECRIN is also leading the Medical Infrastructure/Users Forum (MIUF), which brings together medical research infrastructures and communities to:

- Identify needs of medical research communities in terms of infrastructure and services
- Drive the development of tools and services by the infrastructures
- Share a consistent strategy for the structuring of medical research in Europe, avoiding duplication and gaps

CRIGH^S: CRIGH is the first global initiative to address the wide range of obstacles to global cooperation in clinical research, facilitating multi-country trials. It will seek to optimise clinical research programmes in participating countries, to develop global standards on clinical research, and to promote the take-up of innovative methodology and technologies. This will be achieved through six projects: infrastructure and funding, global core competencies, research ethics, patient involvement, comparative effectiveness research and socio-economic impact, and regulatory awareness. CRIGH is self-funded through member contributions.

Learn more: www.crigh.org

ECRIN-IA^{xxix} Involving 23 countries and covering three main areas of expertise (rare diseases, medical devices and nutrition), the ECRIN Integrating Activity (ECRIN-IA) project brings together diverse stakeholders to build capacity and tools for multinational clinical trials in Europe (ESCALE, IMPACTT, MENAC, POEM vs LHM, and RESCUE ESES). Originally planned for four years (2012 to 2015), the clinical trials work package was extended until 2017.

EOSCpilot^{xxx} Funded by H2020, the European Open Science Cloud for Research Pilot Project (EOSCpilot) project will support the first phase in the development of the European Open Science Cloud (EOSC). It will aim to reduce fragmentation between data infrastructures by working across scientific and economic domains, countries and governance models; and improve interoperability between data infrastructures by demonstrating how data and resources can be shared. ECRIN is involved in the work package on policy, and in particular is the lead, along with BBMRI, on the sub-task on drivers and constraints for ethics.

EuroStemCell^{xxxi} A H2020-funded project, the European Consortium for Communicating Stem Cell Research (EuroStemCell) unites 33 partner institutions, which collectively represent >400 stem cell research groupings across Europe. The goal is to provide trusted high-quality information on stem cells accessible to citizens and stakeholders across Europe, through support and further development of the multi-lingual European Stem Cell Information Portal (www.eurostemcell.org).

^{xxviii} CORBEL has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 654248.

^{xxix} ECRIN-IA has received funding from the European Union's 7th Framework Programme for Capacities - Research Infrastructures under grant agreement number 284395.

^{xxx} The EOSCpilot has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 739563.

^{xxxi} EuroStemCell has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 652796.

CAPACITY BUILDING PROJECTS (CURRENT) /2

PedCRIN^{xxxii}: The Paediatric Clinical Research Infrastructure Network (PedCRIN) brings together ECRIN and the European Paediatric Clinical Trial Research Infrastructure (EPCTRI) to develop capacity for multinational paediatric clinical trials. Launched in January 2017, the project will last four years and includes six work packages (WPs): 1) Project coordination and implementation of management decisions, 2) Definition of the PedCRIN business strategy and governance structure, 3) Development of tools specific for paediatric and neonatal trials, 4) Provision of operational support to select pilot trials, 5) Communication targeting user communities, 6) Ethics.

Learn more: www.pedcrin.org

RISCAPE^{xxxiii}: Also funded by H2020, the European Research Infrastructures in the International Landscape (RISCAPE) project will provide a comprehensive, peer-reviewed international landscape analysis report on the position and complementarities of the major European research infrastructures (RIs). To achieve this, RISCAPE will establish close links with a stakeholder panel representing the main user groups of the report and will collaborate closely with RI projects and initiatives. The report is intended to inform the EU strategic RI development and policy. ECRIN is leading work on biomedical sciences and will draft the landscape analysis report in the biomedical sector.

RItrain^{xxxiv}: The Research Infrastructures Training Programme (RItrain) aims to develop a flagship training programme enabling research infrastructures (RIs) across all domains to gain expertise on governance, organisation, financial and staff management, funding, intellectual property (IP), service provision and outreach in an international context. ECRIN is involved in work packages on project management; definition of competencies required by RIs; and continuing professional development for managers of RIs.

TRANSVAC2^{xxxv} (European Vaccine Research and Development Infrastructure): TRANSVAC2 is the follow-up to TRANSVAC, the European Network of Vaccine Research and Development funded by European Union Framework Programme 7, FP7. TRANSVAC2 will support innovation for both prophylactic and therapeutic vaccine development based on a disease-overarching and one-health approach, thereby optimising the knowledge and expertise gained during the development of both human and animal vaccines. ECRIN is leading the work package on clinical trial support.

^{xxxii} PedCRIN has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 731046.

^{xxxiii} RISCAPE has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 730974.

^{xxxiv} RItrain has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 654156.

^{xxxv} TRANSVAC2 has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 730964.

PROJECTS COMPLETED IN 2016

PRO4VIP^{xxxvi}: ECRIN contributed to this H2020 project, which aimed to: create a European-wide network of procurers; define a common innovation procurement roadmap in the short and long term; and define the public procurement of innovation procedure(s) that best meet needs and support the early detection and screening of functional low vision conditions, or would support the provision for low vision services. ECRIN was involved in work packages on information management, online engagement/dissemination, and resources for decision-making and the media.



^{xxxvi}PRO4VIP received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 645584.

QUALITY MANAGEMENT

Upgrading the quality management system (QMS) used within ECRIN and by its national partners continued to be an essential task in 2016. In particular, a workshop including representatives from ECRIN national partners was organised in Paris on 3 November 2016 to discuss 'Which ECRIN approach to promote quality in clinical research'. Objectives were to examine the best ways to promote quality in the provision of support from ECRIN and ECRIN partners in multinational clinical research; to ensure that research is as efficient and effective as possible; and to use the conclusions of the workshop to help shape ECRIN's own strategy for supporting quality initiatives, whether that is in developing quality standards, creating training materials and programmes, supporting units in gaining certification, or running ECRIN's own qualification programmes.

DATA CENTRE CERTIFICATION

Another key activity in 2016 was Data Centre Certification, part of ECRIN's quality programme. Following successful audits in 2014 and 2015, applications were invited in 2016 from CTUs within the national networks of ECRIN Member Countries (France, Germany, Hungary, Italy, Norway, Portugal, Spain) who wished to become an ECRIN certified data centre. The goal in 2016 was to select and audit one centre from each of these countries. The certification process in 2016 was funded by ECRIN, so there were no fees for centres selected for an audit.

Certification decisions were based on the results of a two- to three-day, on-site audit of a centre's systems and procedures, led by an independent Certification Board. The visits evaluated compliance with the ECRIN data standards, which were revised in January 2016 (download here: bit.ly/2m7uMGs). Compliance confirms a centre's capacity to provide appropriate and effective data management services for multinational, randomised controlled trials (RCTs) and ECRIN-supported trials.

ECRIN's Independent Certification Board certified four CTUs as high-quality data centres in 2016: Clinical Pharmacology and Therapeutic Trials Service HCL, Laennec Faculty of Medicine in Lyon, France; Interdisciplinary Centre for Clinical Trials (IZKS) in Mainz, Germany; AIBILI Data Centre in Coimbra, Portugal; and KKS Marburg (an independent facility of the Medical Faculty of the Philipps-University Marburg) in Marburg, Germany. All four institutions will be certified until 2020.

ECRIN's partners outside of Europe also expressed interest in the data centre certification programme. In particular, ECRIN's Japanese partner, the Foundation for Biomedical Research & Innovation (FBRI), asked for audits and certification of data centres in Japan. A similar request was made by ECRIN's Korean partner, Korea National Enterprise for Clinical Trials (KoNECT), for data centres in South Korea. To explore these possibilities, ECRIN's Director General visited both countries from August to September 2016, and discussions have continued.



CONNECTION TO INVESTIGATION NETWORKS

ECRIN provides support to multinational trials regardless of the type of disease being investigated. However, it values the establishment of partnerships with disease-specific networks, as they represent potential users of ECRIN support services and provide ECRIN with efficient and pan-European investigation capacity.

In 2016, ECRIN maintained its relationships with pan-European investigation networks and hubs on rare diseases, medical devices and nutrition (developed as part of the ECRIN-IA project). Links were also strengthened with investigator communities on paediatrics and ophthalmology.

EXPANSION OF MEMBERSHIP

The expansion of ECRIN membership was a key priority in 2016, and progress was made in attracting new countries. Norway joined ECRIN as a Member early in the year. The scientific partner is the Norwegian Clinical Research Infrastructure (NorCRIN, www.norcrin.no/in-english). NorCRIN's aim is to facilitate clinical research by supporting the many complex elements of this type of research, such as study design, the application process, trial conduct, and good clinical practice (GCP) reporting. The main objective is to strengthen and simplify the collaboration within all categories of clinical research in Norway. The Ministry of Health and Care Services in Norway initiated the founding of NorCRIN, and Trondheim University Hospital (St. Olavs Hospital) is responsible for coordinating and operating the network.

Additional countries, particularly among those which had been involved in the ECRIN-IA project, expressed strong interest in joining as well and discussions continue with these states.



INTERNATIONAL PARTNERSHIPS AND MULTINATIONAL COLLABORATION

Not just focused on Europe, ECRIN seeks to facilitate multinational clinical research on a global level. This work is in line with the Organisation for Economic Co-operation and Development (OECD) initiative to foster international cooperation in non-commercial trials.² This initiative was the launching pad for the ECRIN-led Clinical Research Initiative for Global Health (CRIGH), a capacity building project which was pre-launched in Paris from 12 to 13 October 2016. Bringing together research institutions globally, CRIGH aims to serve as a support structure for international collaboration on clinical research for the benefit of patients, healthcare professionals, and health systems.

In terms of bilateral cooperation, ECRIN signed memorandums of understanding in July 2016 with the Foundation for Biomedical Research and Innovation (FBRI) in Japan and the Oswaldo Cruz Foundation (Fundacao Oswaldo Cruz, FIOCRUZ) in Brazil. These partnerships are significant in that they expand ECRIN's geographic reach to Asia and South America, respectively. ECRIN's other international partners include the Korea National Enterprise for Clinical Trials (KoNECT), Therapeutic Innovation Australia Ltd (TIA), and the National Center for Advancing Translational Sciences (NCATS) at the National Institutes of Health (NIH).

Also in 2016, ECRIN contributed to discussions with European and international partners on issues related to multinational clinical trials such as funding. For example, ECRIN was part of a European Commission (EC) workshop entitled 'Multinational cooperation on clinical trials reflections on a potential ERA-NET Cofund', held on 15 December 2016. The objective of the meeting was to provide grounds for the EC and the Societal Challenge (SC) 1 Programme Committee to consider including the topic of an ERA-NET cofund on multinational independent clinical trials and translational research in the work programme 2018-2020 of the H2020 SC1 (Health, Demographic Change and Wellbeing). The rationale for this is that independent multinational trials face continued funding challenges compared to industry trials (of which 30% are multinational, compared to 3% of independent ones). While certain funding mechanisms now exist for independent multinational trials, there is still a need for additional funding. An ERA-Net could complement national funding and contribute to solving some of the main problems of clinical trials, such as patient/subject recruitment, and could provide sufficient regulatory expertise and common evaluation procedures, among others.

² An OECD Global Science Forum (GSF) initiative started in 2008 with the aim of fostering international cooperation in non-commercial trials, leading to a report in 2011, followed in 2012 by the "OECD Recommendation on the Governance of Clinical Trials".

STRATEGY

To ensure our sustainable development, while providing the highest quality trial and project management services possible, we finalised a new strategy plan in 2016 for the period from 2016 to 2019. For this purpose, a SWOT (strengths, weaknesses, opportunities, and threats) analysis was first conducted. Three major challenges were identified:

- 1 ENSURING** the quality of tools and services; the quality of data; the quality of methodology and the robustness of results; and quality in the organisation.
- 2 INCREASING** ECRIN's attractiveness to expand its participation in multinational clinical studies. This requires demonstrating the added value of using ECRIN, adapting the positioning of ECRIN and ECRIN services, and developing appropriate partnerships with user communities.
- 3 EXPANDING** ECRIN to new Member or Observer Countries with the ability to effectively provide services for ECRIN-supported trials.

The strategy plan outlines the key deliverables to effectively address these challenges.



ADMINISTRATION AND COMMON SERVICES

2016 was the third year that ECRIN operated with the status of a European Research Infrastructure Consortium (ERIC), which was awarded by the European Commission in December 2013.

This section provides an overview of the developments of ECRIN's legal, administrative and financial organisation, as well as other core support services (communications, human resources), throughout 2016.

GENERAL ADMINISTRATION AND FINANCE

The development of general administration and financial tasks was led by the Administrative Manager.

Financial contributions were received from Member Countries in 2016. Observer Countries, which make in-kind contributions only, paid for the cost of their respective local European Correspondents.

In 2016, an appendix to the rules of internal procedures on how to report and validate in-kind contributions was applied.

COMMUNICATIONS

The optimisation of internal and external communications activities was a continued focus in 2016. For this purpose, the Communications Officer supported the development of new tools and resources including an external newsletter.

Scientific communications remained a central activity, with ECRIN organising various scientific meetings and/or participating in European and international scientific conferences. ECRIN held its annual meeting in honour of International Clinical Trials Day in Prague, Czech Republic in May; the topic for 2016 was 'Clinical trials in the era of personalised medicine'. The aim was to increase awareness of ECRIN and its Czech national scientific partner – Czech Clinical Research Infrastructure Network (CZECRIN) – among Czech policymakers and the scientific community, as well as to address issues related to personalised medicine and multinational clinical trials. In 2016, the Director General made around 30 presentations at various conferences.

In terms of project communications, ECRIN continued to support the communications work package of the CORBEL project. Led by the German biological resource centre DSMZ³, the work package supports effective documentation, communication and outreach to internal and external stakeholders including the participating BMS RIs, infrastructure users, funding networks, and more.

Another activity related to communications continued to be the submission of articles to peer-reviewed scientific journals. In 2016, six articles to which ECRIN contributed were published (see 'ECRIN Publications in 2016'). These articles are related to the trials that ECRIN supports, the projects it participates in or leads (e.g. ECRIN-IA), its quality initiatives, and activities of its national networks (e.g. PtCRIN).

³ Stands for The Leibniz-Institut DSMZ (Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH), or German Collection of Microorganisms and Cell Cultures GmbH. It is coordinated by the Microbial Resource Research Infrastructure (MIRRI). ESFRI is a strategic instrument developed by the European Commission to focus on optimal use and development of research infrastructures through strategic policymaking and multilateral initiatives.



STAFF TRAINING

ECRIN held its annual Summer School in Seville, Spain from 26 to 28 October. The meeting was primarily targeted at ECRIN's European Correspondents (EuCos), with the Core Team participating as well. The 2016 Summer School focused on regulatory aspects and in particular the transition between Directive 2001/20/EC and Regulation EU No 536/2014; pharmacovigilance and safety monitoring; and the type of intervention in clinical studies. Several sessions were dedicated to funding applications and legal and financial aspects. One workshop focused on communications and communication tools.

Throughout the year, several internal training sessions were also conducted on topics such as clinical trials (e.g. design methodology), ERA-Net programmes, and H2020 projects (e.g. grant lifecycle, ECRIN involvement).

LEGAL

2016 was another busy year for contracting, especially as the number of ECRIN-supported multinational clinical trials increased.

A priority in 2016 continued to be the signing of framework agreements with ECRIN's national scientific partners in each Member and Observer Country. For this purpose, ECRIN's template agreement – developed in 2014 by a special task force chaired by the Capacity Director and supported by the Legal Officer – was used. The framework agreement is essential as it sets out the terms for collaboration between ECRIN and its national scientific partners for the provision of joint support to clinical studies. It also establishes the roles and responsibilities of the EuCos (typically seconded by the national partner to ECRIN) and helps to define the status of the national partner in H2020, IMI or other European projects.

LOOKING FORWARD: A COMMITMENT TO SCIENCE AND SOCIETY

Moving forward, ECRIN plans to continue to develop and expand projects across its various domains of activity. In 2017 and beyond, we can expect to see additional multinational clinical trials in diverse disease areas, stronger partnerships with investigation networks, international collaboration on clinical research issues, and more. We are particularly excited about the prospect of enhancing our capacity, through PedCRIN, to provide trial management services to multinational paediatric clinical trials, while minimising risk and protecting the child participants.

In general, ECRIN will strive to make a greater scientific and socio-economic impact on health and the economy. This will be mainly achieved by providing support to large, multinational comparative effectiveness trials testing various authorised preventive, diagnostic or therapeutic solutions for a disease condition, leading to evidence-based medical decisions. This benefits patients and healthcare systems, by comparing the safety, efficacy and effectiveness of each option in real life, thus optimising medical decisions and healthcare strategies while containing the cost of treatments.



GEOGRAPHIC DISTRIBUTION

36
COUNTRIES

ECRIN MEMBER COUNTRIES (as of 31 December 2016)

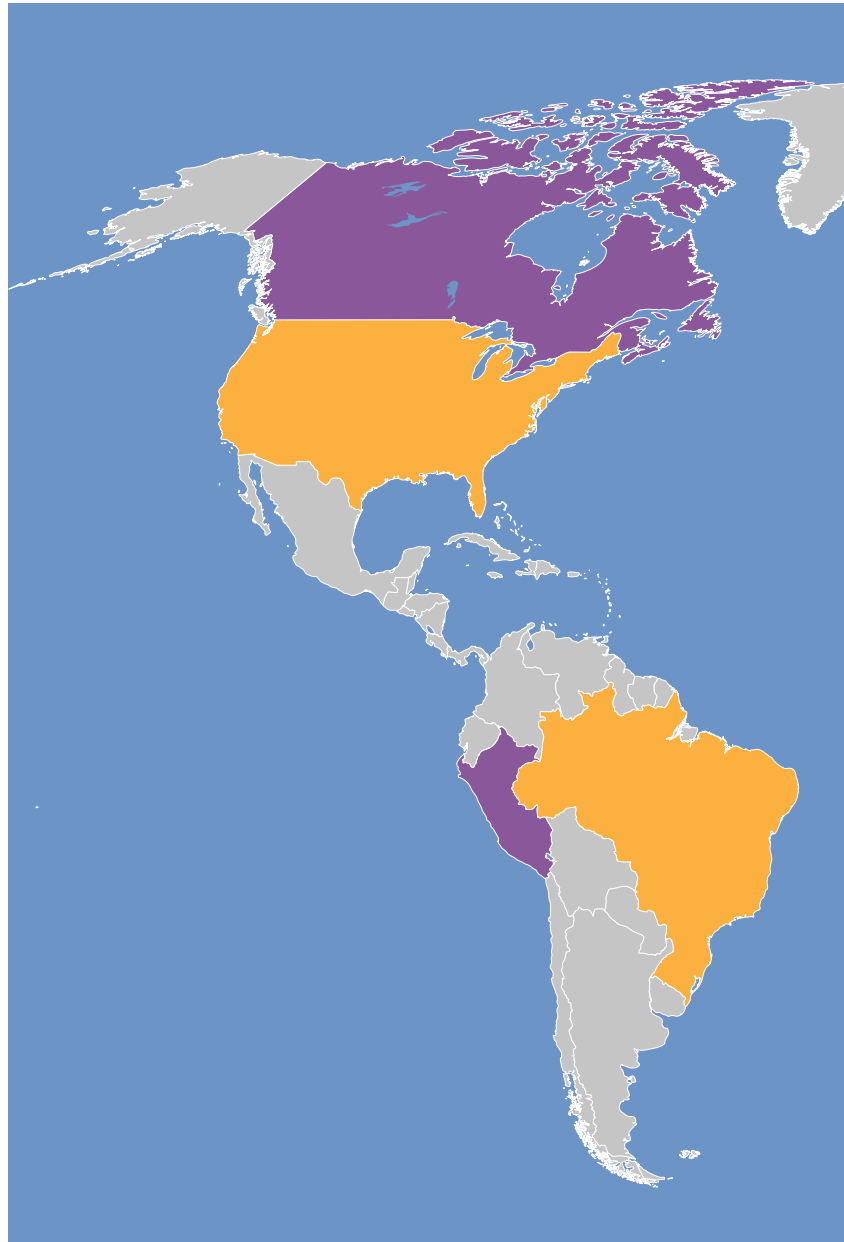
France
Germany
Hungary
Italy
Norway
Portugal
Spain

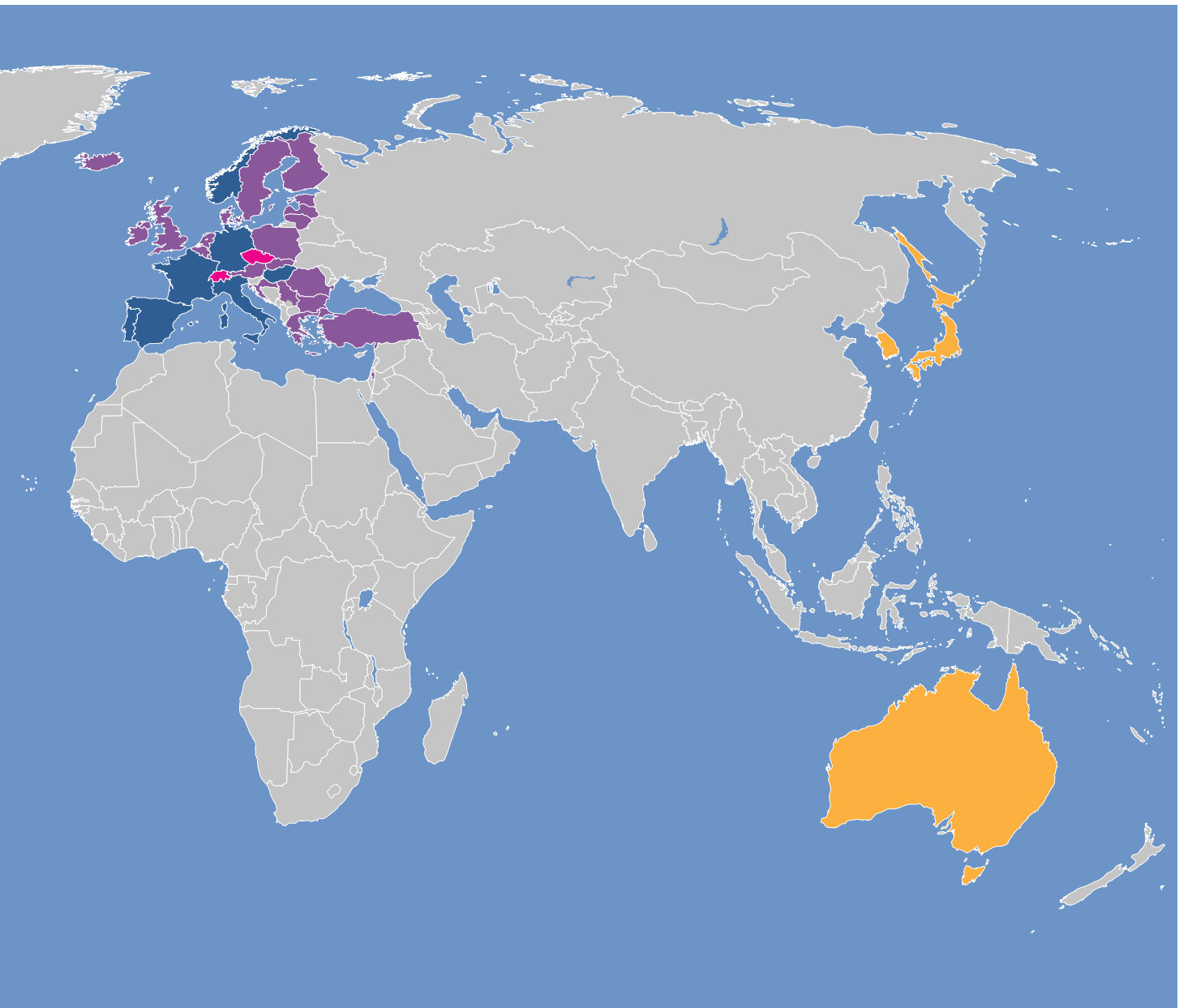
ECRIN OBSERVER COUNTRIES (as of 31 December 2016)

Czech Republic
Switzerland

OTHER COUNTRIES IN ECRIN-SUPPORTED TRIALS / COLLABORATIVE PROJECTS (CURRENT/PAST TRIALS AND PROJECTS)

Austria	Croatia	Greece	Latvia	Peru	Slovakia
Belgium	Denmark	Iceland	Lithuania	Poland	Sweden
Bulgaria	Estonia	Ireland	Luxembourg	Romania	Turkey
Canada	Finland	Israel	Netherlands	Serbia	United Kingdom





ECRIN INTERNATIONAL PARTNERS

(with whom we have collaboration agreements)



Australia (Therapeutic Innovation Australia, TIA)

Brazil (Oswaldo Cruz Foundation, FIOCRUZ)

Japan (Foundation for Biomedical Research and Innovation, FBRI)

Korea (Korea National Enterprise for Clinical Trials, KoNECT)

USA (National Center for Advancing Translational Sciences (NCATS) at the National Institutes of Health (NIH))

GOVERNANCE

ASSEMBLY OF MEMBERS

ECRIN is governed by an Assembly of Members (AoM), which is composed of a representative from the government of each Member or Observer Country. In 2016, the AoM was chaired by Rafael de Andrés Medina of Carlos III Health Institute (Instituto de Salud Carlos III, ISCIII), Spain. Members included Nina Ånensen (Norway), Daniel Carapau (Portugal), Maria Ferrantini (Italy), Rainer Girgenrath and Amke Hesse (Germany), Gabor Kovacs (Hungary) and Claire Levy Marchal (France). Observers included Jan Buriánek (Czech Republic) and Annette Magnin (Switzerland).

ADDITIONAL ORGANISATIONAL BODIES

NETWORK COMMITTEE

The Network Committee represents the national scientific partners and provides advice to the AoM and Director General. It is composed of one senior delegate from each national scientific partner of Member and Observer Countries. In 2016, the Network Committee was chaired by Christian Ohmann (Germany). The vice chair was Emilia Monteiro (Portugal) and members included Ola Dale (Norway), Regina Demlová (Czech Republic), Jacques Demotes (France), Gabor Kovacs (Hungary), Antonio Portoles (Spain), Flavia Pricci (Italy), Olivier Rascol (France), Fabian Tay (Switzerland) and Heiko Von Der Leyen (Germany).

STEERING COMMITTEE

ECRIN's Steering Committee oversees activities and provides advice on budget, work plan and scientific/technical matters. It is composed of the Chair and Vice Chair of the AoM, two members from the Network Committee, as well as the Director General.

GOVERNANCE MEETINGS IN 2016

ASSEMBLY OF MEMBERS

25/1/2016
18/5/2016
28/6/2016
13/9/2016
12/12/2016

NETWORK COMMITTEE

18/5/2016
5/12/2016

KEY DATES

- 2004** | Creation of ECRIN
| Began its first project, ECRIN Reciprocal Knowledge Programme or ECRIN-RKP (funded by European Union Framework Programme 6, FP6, Societal challenges health sub-programme), involving six countries; ECRIN-RKP aimed to determine bottlenecks to multinational collaboration in academic clinical studies
- 2006** | Started its second project, ECRIN Transnational Working Group or ECRIN-TWG (also funded by FP6), involving 10 countries, to develop procedures and guidelines for investigators and sponsors involved in multinational clinical research in Europe.
| Listed on the European Strategy Forum on Research Infrastructures (ESFRI)⁴ roadmap
- 2008** | ECRIN's third project, ECRIN Preparatory Phase for Infrastructure or ECRIN PPI (funded by European Union Framework Programme 7, FP7, for which ECRIN was now eligible given its ESFRI status) was launched in 2008 with 14 countries. The goal was to define the necessary organisational and legal structure for ECRIN to support the establishment and implementation of multinational clinical trials in Europe.
- 2009** | Began to provide services to multinational clinical studies
- 2012** | ECRIN embarked on its fourth project, ECRIN Integrating Activity or ECRIN-IA (also funded by FP7), involving 23 countries and covering three main areas of expertise: rare diseases, medical devices and nutrition
- 2013** | Awarded the status of European Research Infrastructure Consortium (ERIC) by the European Commission⁵
- 2016** | Designated a 'Landmark' in the health and food area on the 2016 ESFRI roadmap

⁴ ESFRI is a strategic instrument developed by the European Commission to focus on optimal use and development of research infrastructures through strategic policymaking and multilateral initiatives.

⁵ The ERIC legal status is recognised in all European Union member states, and is designed to facilitate the establishment and operation of research infrastructures of European interest.

ECRIN PUBLICATIONS IN 2016

- Garattini S, Jakobsen JC, Wetterslev J, Bertele' V, Banzi R, Rath A, Neugebauer EA, Laville M, Masson Y, Hivert V, Eikermann M, Aydin B, Ngwabyt S, Martinho C, Gerardi C, Szmigielski CA, Demotes-Mainard J, Gluud C. Evidence-based clinical practice: Overview of threats to the validity of evidence and how to minimize them. *Eur J Intern Med.* 2016 May 5. pii: S0953-6205(16)30040-1
- Madeira C, Pais A, Kubiak C, Demotes J, Monteiro EC: Investigator-initiated clinical trials conducted by the Portuguese Clinical Research Infrastructure Network (PtCRIN). *Contemp. Clin. Trials Comm.* 4 (2016) 141-148.
- Mosconi P, Antes G, Barbareschi G, Burls A, Demotes-Mainard J, Chalmers I, Colombo C, Garattini S, Gluud C, Gyte G, McIlwain C, Penfold M, Post N, Satolli R, Valetto MR, West B, Wolff S. *Trials.* 2016 Jan 12;17(1):19. doi: 10.1186/s13063-015-1146-7.
- Kuchinke W, Ohmann C, Stenzhorn H, Anguista A, Sfakianakis S, Graf N, Demotes J: Ensuring sustainability of software tools and services by cooperation with a research infrastructure. *Per. Med.* (2016) 13:43-55.
- Napp AE, Haase R, Laule M, Schuetz GM, Rief M, Dreger H, Feuchtner G, Friedrich G, Špaček M, Suchánek V, Kofoed KF. Computed tomography versus invasive coronary angiography: design and methods of the pragmatic randomised multicentre DISCHARGE trial. *European Radiology.* 2016 Nov 18:1-2.
- Neyt M, Christiaens T, Demotes J, Walley T, Hulstaert F: Publicly-funded practice-oriented clinical trials: of importance for the healthcare payers. *J Comp. Eff. Res.* (2016) 5:551-560.
Canham S. and Ohmann C. (2016) A metadata schema for data objects in clinical research. *Trials* 17(1):557

FINANCIAL REPORT FOR 2016

INCOME

Member Country contributions (France, Germany, Hungary, Italy, Norway, Portugal, Spain) and local contribution for France ⁶	€1,360,000
European Commission-funded projects	€582,978
Other income	€54,316
Financial income	€19,671
TOTAL INCOME FOR 2016	€2,016,965

EXPENDITURES

Salaries, social expenses and taxes	€749,738
Other operational costs	€935,974
Financial expenses	€1,148
TOTAL EXPENDITURE FOR 2016	€1,686,860

NET RESULT

NET RESULT FOR 2016	€330,105
----------------------------	-----------------

⁶ ECRIN is composed of a Core Team and European Correspondents. The budget covering the activities of the European Correspondents (except in France) is not considered in the ECRIN accounts as these collaborators are currently not direct employees of ECRIN (except in France). The contribution covering the European Correspondents' budget is €850.000, including €100.000 for France. For this reason the ECRIN income in 2016, including the budget of European Correspondents, is €2.766.965

**ECRIN
ANNUAL
REPORT
2016**

