Clinical Trial Profile

CLINICAL INVESTIGATION

Developing an international network for clinical research in ophthalmology: the European Vision Institute Clinical Research Network (EVICR.net)

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There is a well-identified need for patient-oriented clinical research and this can only be achieved by creating active collaboration between academic centers with competence for clinical research, following GCP guidelines and supported by an infrastructure that provides appropriate management of clinical trials at a realistic cost. The European Vision Institute Clinical Research Network (EVICR.net) is a legal entity established as an independent European Economic Interest Grouping in accordance with the Council Regulation (EEC) #2137/85 and was built and developed to function as the necessary structure to perform clinical research in ophthalmology in the EU according to ICH GCP Guidelines and European Directives.

Keywords: clinical research • clinical trial • cornea • eye–anterior segment • glaucoma • ocular surface • ophthalmology • reading center • retina

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Medical research is the basis for optimal patient treatment in hospitals and health-care institutes throughout the world. Translational research brings the ideas from basic research into clinical patient-oriented research and vice-versa. Clinical patient-oriented research involves testing new discoveries in the clinic by carrying out carefully controlled investigations on patients – known as clinical trials. This includes testing not only new drugs, but also new methods, devices, imaging and surgical procedures.

For Europe, it is necessary to perform EU-wide patient-oriented research, with priorities set by patient needs. Such an approach would reduce fragmentation and duplication of research in Europe and provide a means for carrying out high-quality, multinational clinical studies. Efficient patient-oriented research requires both specialized competences and a supporting infrastructure. Such research is performed in academic medical centers and university hospitals and could also benefit from collaborations with the pharmaceutical industry. However, at present, there is a clear need for infrastructures that support patient investigations, database management, quality assurance, monitoring and regulatory affairs.

The process for discovering an innovation from biomedical research to implementing that innovation in the clinic depends on the development of strong and efficient links between academic clinical centers and networking centers that have the necessary competences to perform clinical research. It is, therefore, crucial to create an appropriate environment, such as networking, to perform multinational, large-scale, investigator-driven clinical trials (IDCTs), as these type of studies have a greater potential to change clinical management.

Clinical investigators often lack the expertise needed to plan all the necessary resources, requirements and agreements before starting a clinical trial. In addition, the costs of commercial US FDA- and EMA-compliant clinical data management

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systems are very high and the resources needed to develop in-house systems are often higher. Clinical investigators need to have access to robust data-collection methods at a realistic cost.

Networking and the development of excellent administrative support are required developments for patient-oriented clinical research. In ophthalmology, the example set by the Diabetic Retinopathy Clinical Research Network (DRCR.net) in the USA needs to be followed in Europe.

The European Vision Institute Clinical Research Network (EVICR.net) was created as a network of European ophthalmological clinical research sites (CS), dedicated to performing clinical research in ophthalmology with the highest standards of quality, following the European and International Directives for Clinical Research according to harmonized standard operating procedures (SOPs) compliant with ICH GCP guidelines.

The EVICR.net is a platform for clinical trial research in ophthalmology in Europe and aims to be a much-needed structure to support IDCTs as well as an industry resource in the development of new drugs and medical devices [1].

The Network was established in 2004, and since 2010 EVICR.net has been a legal entity established as an independent European Economic Interest Grouping (EEIG) in accordance with the Council Regulation (EEC) #2137/85.

The Network has a centralized infrastructure located at Association for Innovation and Biomedical Research on Light and Image (AIBILI), Coimbra, Portugal that functions as the coordinating center with contract research organization functions necessary for the management of multicenter clinical trials.

The main aims and objectives of EVICR.net are:

- To guarantee a high level of quality and excellence in the clinical research collaborative work performed by members according to ICH GCP guidelines;
- To promote multicenter clinical research trials within the EU;
- To coordinate training activities for its members;
- To serve as a resource for industry in performing clinical research in ophthalmology.

In order to become a member, a clinical site must apply to the Network and fulfil basic requirements such as having dedicated space to perform clinical trials, qualified and experienced personnel and experience of multicentric clinical trials, and agree to implement organizational SOPs according to ICH GCP Guidelines.

Each clinical site will be submitted to an on-site evaluation visit performed by independent auditors according to the Network procedures in order to become a certified member of EVICR.net.

At present, the EVICR.net has 73 center members from 16 European countries that are either certified or in the process of certification (Table 1).

EVICR.net also has a European Ophthalmic Reading Center Network (EORCN). In the performance of ophthalmology clinical trials, reading centers are often necessary for independent and standardized grading of ophthalmic procedures as well as for responding to the needs of a high-volume of images.

The EORCN, which connects different reading centers on a back-up basis, has 22 organizational SOPs that provide a common way of working and implementing a quality control system. In Europe, the EORCN has, therefore, created a structure able to perform centralized readings for high-volume studies. It is a useful resource in Europe as most of the high-volume reading centers in ophthalmology are located in the USA.

Organization of EVICR.net

The supreme organ of the Network is the General Assembly that consists of all EVICR.net members.

The EVICR.net has a Steering Committee that is responsible for the activities of the EVICR.net and acts as its decision-making body within the framework set by the General Assembly. The Steering Committee consists of up to seven representatives: the Chairman, the Coordinators of each Expert Committee and the CEO.

Presently, the Steering Committee is formed of:

- José Cunha-Vaz (CS 1), Chairman and Diabetic Retinopathy Expert Committee Coordinator;
- Jose Sahel (CS 6), Age-Related Macular Degeneration and Retinal Dystrophies Expert Committee Coordinator;
- Esther Hoffmann (CS 2), Glaucoma Expert Committee Coordinator;
- Jorge Alió (CS 7), Cornea, Cataract and Refractive Surgery Expert Committee Coordinator;
- Joaquim Murta (CS 70), Ocular Surface and Inflammation Expert Committee Coordinator;
- Tunde Peto (CS 10), Reading Centers Expert Committee Coordinator;
- Cecília Martinho, CEO.

The Steering Committee is supported by Expert Committees that have a fundamental role in the scientific organization of EVICR.net and cover the following main areas of research: age-related macular degeneration

Table 1. The European Vision Institute Clinical Research Network center members.

Clinical site	Institute
Austria	
19	Medical University of Vienna, Department of Ophthalmology, Vienna
Belgium	
8	Ghent University Hospital, Department of Ophthalmology, Ghent
12	Antwerp University Hospital, Department of Ophthalmology, Antwerp
18	University Hospital Leuven, Department of Ophthalmology, Leuven
Denmark	
30	Glostrup Hospital, Department of Ophthalmology, Copenhagen University, Glostrup
73	Department of Ophthalmology, Odense University Hospital, Odense
France	
3	Center Hospitalier Creteil, University Eye Clinic, Paris
6	Center National d'Ophthalmologie des Quinze-Vingts, Center d'Investigation Clinique, Paris
13	CHU Gabriel Montpied, Unité de Recherche Clinique, Service d'Ophthalmologie, Clermont-Ferrand
14	Hôpital Lariboisière, Department of Ophthalmology, Paris
42	University Hospital, CHU Dijon, Department of Ophthalmology, Dijon
45	Hôpital Purpan, Service d'Ophtalmologie, Toulouse
48	CLAIROP: Center loco-régional d'Amiens pour l'Innovation et la Recherché en Ophtalmologie Pédiatrique, Amiens
61	Groupe Hospitalier Pellegrin, Unité Medicale Segment Posterieur, Service Ophtalmologie, Bordeaux
Germany	
2	University Medical Center, Johannes Gutenberg University, Department of Ophthalmology, Mainz
5	Faculty of Medicine Mannheim of the Ruprecht-Karls–University Heidelberg, Department of Ophthalmology, Mannheim
9	University Hospital Tuebingen (UKT), STZ biomed & STZ eyetrial at the Center for Ophthalmology, Tuebingen
11	University Eye Hospital Munich, Munich
15	University of Bonn, Department of Ophthalmology, Bonn
21	University Medical Center Hamburg-Eppendorf, Department of Ophthalmology, Hamburg
24	University of Freiburg, Department of Ophthalmology, Freiburg
27	University Eye Hospital, Leipzig
43	RWTH Aachen University, Department of Ophthalmology, Aachen
44	University Eye Clinic Bochum, Center for Vision Science, Bochum
47	Staedtisches Klinikum Karlsruhe, Department of Ophthalmology, Karlsruhe
54	University of Düsseldorf, Department of Ophthalmology, Düsseldorf
55	Eye Center Spreebogen, Berlin
56	University of Heidelberg, International Vision Correction Research Center (IVCRC), Heidelberg
59	Johann Wolfgang Goethe University Frankfurt, Department of Ophthalmology, Frankfurt
65	Justus-Liebig University Giessen, Department of Ophthalmology, Giessen
Greece	
57	University of Crete, Institute of Vision and Optics (IVO), Crete
71	Laboratory of Research and Clinical Applications in Ophthalmology, Aristotle University of Thessaloniki, Department of Ophthalmology, AHEPA University Hospital, Thessaloniki
Ireland	
31	Mater Vision Institute (MVI), Dublin

Table 1. The European Vision Institute Clinical Research Network center members (cont.).

Clinical site	Institute
Israel	
60	Tel Aviv Sourasky Medical Center, Department of Ophthalmology, Tel Aviv
Italy	
16	University of Milan, Center for Clinical Trials at San Paolo Hospital, Milan
20	GB Bietti Foundation – IRCCS, Rome
34	University of Milan, Luigi Sacco Hospital, Department of Ophthalmology, Milano
36	Catholic University, Institute of Ophthalmology, Rome
37	Sezione di Oftalmologia, Dipartimento di Scienze Otorino-Odonto-Oftalmologiche e Cervico Facciali, Parma
39	University of Padova, Department of Ophthalmology, Center for Clinical Trials, Padova
46	Policlinico di Monza, Clinica Oculistica, Monza
50	University of Udine, Department of Ophthalmology, Udine
63	University of Chieti-Pescara, Excellence Eye Research Center, Center for Excellence on Ageing, Chieti
64	University of Bari, Department of Ophthalmology and Otolaryngology, Bari
67	University Vita Salute - Scientific Institute of San Raffael, Department of Ophthalmology, Milan
Poland	
33	Poznan University of Medical Sciences, Department of Ophthalmology, Poznan
Portugal	
1	AIBILI, Center for Clinical Trials, Coimbra
28	Instituto de Oftalmologia Dr. Gama Pinto, Lisbon
32	Porto Medical School – Hospital S. João, Department of Ophthalmology, Porto
62	Centro Hospitalar de Lisboa Central, Centro de Investigação, Serviço de Oftalmologia, Lisbon
70	University Hospital of Coimbra, Ophthalmology Department, Coimbra
Slovenia	
23	University Medical Center of Ljubljana, University Eye Hospital, Ljubljana
Spain	
4	IOBA – Instituto Universitario Oftalmobiologia Aplicada, Valladolid
7	VISSUM – Instituto Oftalmologico de Alicante, Alicante
26	Centro de Oftalmología Barraquer, Barcelona
38	Institut Català de Retina (ICR), Clinical Trial Unit, Barcelona
41	Centro Médico Teknon, Institut de la Màcula i de la Retina, Barcelona
51	Fundación Oftalmológica del Mediterráneo, Valencia
52	Universitary Hospital Josep Trueta Of Girona, Department of Ophthalmology, Girona
Switzerland	
22	Inselspital, University of Bern, Department of Ophthalmology, Bern
49	Jules Gonin Eye Hospital, Lausanne
The Netherlands	
17	University Medical Center St Radboud, Ophthalmic Trial Center Nijmegen, Nijmegen
25	Academic Medical Center, Department of Ophthalmology, Amsterdam
40	Rotterdam Eye Hospital, Rotterdam
UK	
10	Moorfields Eye Hospital NHS Trust, Clinical Trials Unit and Reading Center, London
35	Queen's University, Institute of Clinical Science, Royal Victoria Hospital Ophthalmology and Vision Science Research Center, Belfast

Table 1. The European Vision Institute Clinical Research Network center members (cont.).

Clinical site	Institute
UK (cont.)	
53	Gloucestershire Hospitals NHS Foundation Trust, Clinical Trials Unit, Department of Ophthalmology, Gloucestershire
58	Royal Liverpool University Hospital, Clinical Eye Research Center, Liverpool
66	Frimley Park Hospital NHS Foundation Trust, Clinical Trials Unit – Ophthalmology Treatment Center, Camberley
68	Heart of England NHS Trust, Ophthalmic Research Unit, Birmingham
69	King's College Hospital, University of London, Laser and Retinal Research Unit, London
72	Torbay Hospital Eye Department, Devon

and retinal dystrophies; diabetic retinopathy; glaucoma; cornea, cataract and refractive surgery; ocular surface and inflammation; and reading centers.

Each Expert Committee supervises a scientific section with the participation of the subspecialty representatives from each EVICR.net clinical site member. Each clinical site nominates one representative for each area of interest and expertise. This representative will be part of the chosen scientific section.

The Steering Committee is advised by the Industry Advisory Board in all matters of strategic relevance, particularly pertaining to collaborations with industry. The Industry Advisory Board is composed of individuals or representatives of entities who have supported the development of the Network.

The Coordinating Center of EVICR.net is located in Portugal, at AIBILI in the Coimbra Coordinating Center for Clinical Research (4C), a structure qualified to support investigator-driven and/or industry-sponsored clinical trials by providing the following services: protocol design and statistical planning; elaboration of the necessary documents for the submission of the clinical trial; coordination and implementation of the clinical trial; monitoring; quality control; data management; statistical analysis; periodical reports to the sponsor and/or regulatory authorities; final clinical trial report; and publication support.

The EVICR.net is prepared to provide Industry with a cohesive network of certified clinical centers in ophthalmology with harmonized procedures (SOPs), quality control and qualified personnel. This provides an environment that will help in achieving high recruitment rates. Furthermore, the network may also be used by industry for feasibility assessments, scientific advice on clinical trial design in ophthalmology and in training (Box 1).

Feasibility assessments have been provided for industry domain clinical trials to be performed in Europe within a 2-week period.

Recently, the EVICR.net provided for Allergan the certification of technicians for refraction and visual acuity procedures. The Coordinating Center identified and certified technicians in seven countries (France, Germany, Israel, Italy, Portugal, Spain and the UK) according to ETDRS Allergan procedures. These EVICR.net certified technicians are now able to certify technicians in clinical sites selected by Allergan to participate in their clinical trials. Allergan has recently started a clinical trial that needs ETDRS Technician Certification in Israel and Italy and will involve also France, Germany and the UK. Future Allergan studies in Europe that require certification of technicians for refraction and visual acuity will be performed by EVICR.net.

EVICR.net is also prepared to provide training courses and has organized the following courses:

- Refraction and Visual Acuity Testing Course, 18 November 2008 – Alicante, Spain;
- Visual Fields Training Course, 17 November 2009 – Mainz, Germany;
- Reading Center Course, 16 November 2010 – London, UK;

A GCP course for ophthalmology will be organized by EVICR.net in 2011.

Standard operating procedures

EVICR.net has developed a quality system for its members, which is based on the ICH-GCP guidelines. All the clinical sites members agree to adopt and implement these SOPs in their centers that will be checked before they are certified as EVICR.net sites of excellence.

The implementation of nine organizational SOPs will permit the clinical sites to have a standard way of working and in compliance with ICH-GCP Guidelines when performing clinical trials. Since they are common to all members, it is a platform to perform investigator- or industry-driven clinical trials within the network.

EVICR.net has also developed technical SOPs, which are a valuable tool for performing clinical trials. These are written SOPs for performing specific ophthalmic examinations or evaluations that can be used within the Network for investigator- or industry-driven clinical trials. Presently, the Network has six technical SOPS for retina, six for glaucoma, nine for cornea, cataract

Box 1. Services provided by the European Vision Institute Clinical Research Network.

- Certified Clinical Trial Centers with harmonized procedures, quality control and qualified personnel.
- Feasibility assessment for center participation and recruitment (performed at short notice).
- Help in achieving recruitment rates by contacting directly and regularly to the participating centers.
- Scientific advice including contributions to clinical trial design.
- Certification and training of technical personnel.
- Facilitation of administrative setup of contracts with clinical trial centers.
- Subspecialty clinical trial research networks.
- Access to the European Ophthalmic Reading Center Network.

and refractive surgery and nine for ocular surface and inflammation.

For the Reading Centers of EVICR.net, 22 organizational SOPs have been written. They establish a common way of organizing and working together within the EORCN.

IDCTs through the Network

The EVICR.net Coordinating Center at AIBILI, Coimbra, Portugal, offers the necessary infrastructure for management of IDCTs and epidemiological studies across Europe through the Network.

Presently, there are two observational IDCTs ongoing, one in retina and another in cornea, cataract and refractive surgery [2,3].

Future perspective

EVICR.net has gone through a process of consolidation and its membership has increased steadily. The initiation of its first two IDCTs is clearly an important step forward.

It is felt that funding from the EU Health Research Programs will create the appropriate basis for future growth and development of the Network. The same has happened with the DRCR.net in the USA, which increased markedly its activity and success when regular funding from the NIH became available.

The need for this type of Networking in Clinical Research has been well recognized in a recent report of the European Science Foundation on IDCTs.

The EVICR.net is considered by its members as a much-needed tool to address the goal of more innovative patient-oriented research with expected positive results of improved healthcare in the EU.

Financial & competing interests disclosure

José Cunha-Vaz is President of the Administration Board of AIBILI and Chairman of EVICR.net. He is a consultant for Novartis, Pfizer, Alcon, Bayer, Allergan and Astellas Pharma Europe. Cecilia Martinho is Director of AIBILI and Chief-Executive Officer of EVICR.net. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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Executive summary

- Clinical patient-oriented research involves testing new discoveries in the clinic by carrying out carefully controlled investigations on patients – known as clinical trials.
- Efficient patient-oriented research requires both specialized competences and a supporting infrastructure.
- Clinical investigators often lack the expertise needed to plan all the necessary resources, requirements and agreements before starting a clinical trial.
- Networking and the development of excellent administrative support are needed developments for patient-oriented clinical research.
- The European Vision Institute Clinical Research Network is a platform for clinical trial research in ophthalmology in Europe and aims to be a much needed structure to support investigator-driven clinical trials as well as an industry resource in the development of new drugs and medical devices.
- At present, the EVICR.net has 73 centers members from 16 European countries that are either certified or in the process of certification.

Websites

1 European Vision Institute Clinical Research Network (EVICR.net). www.evicr.net

2 Rozema J, Antwerp, Belgium (CS 12). Protocol number: ECR-CCRS-2010-01. Project Gullstrand – European project for the determination of average biometric values of human eyes. ClinicalTrials.gov identifier: NCT01173614. http://clinicaltrials.gov/ct2/show/NCT01173614

3 Cunha-Vaz J, Coimbra, Portugal (CS 1). Protocol number: ECR-RET-2010-02. Identifying progression of retinal disease in eyes with NPDR in diabetes Type 2 using non-invasive procedures. ClinicalTrials.gov identifier: NCT01145599. http://clinicaltrials.gov/ct2/show/NCT01145599