



*Under the aegis of Fondation Transplantation*

# **European Drug Development Hub EDDH**

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## **1 Presentation of the EDDH network**

The aim of this initiative – a partnership between a public body and a foundation with recognised public interest status – is to create a **cluster of excellence in clinical research**, with the declared ambition of becoming a major national and international player.

Based in the Clinical Investigation Centre (CIC 9501) of Nancy Teaching Hospital, the EDDH started its activity at the end of 2007, taking over the initial activities of the academic Clinical Research Organization of the CIC. This structure, under the aegis of the Fondation Transplantation, is a consortium of various established entities (cardiovascular CICs, network of hospital and independent cardiologists in France, GICIPI, etc.). Its operational objective is to utilize their complementary features and increase their critical mass to develop a high-performance clinical research platform.

The EDDH is thus a national network with two departments, one for cardiology, the other for neuropsychopharmacology, which have operated separately for several years. The association of these two components will make it possible to pool individual expertise and skills and enhance recruitment potential.

## **2 Creation of the EDDH**

The cardiology department, which runs a network of national investigators and the network of cardiovascular CICs, has gradually developed around the CIC Nancy since 2002, in parallel to the neuropsychopharmacology department.

The association of the two departments, under the aegis of the Fondation Transplantation, has been operational since January 2008.

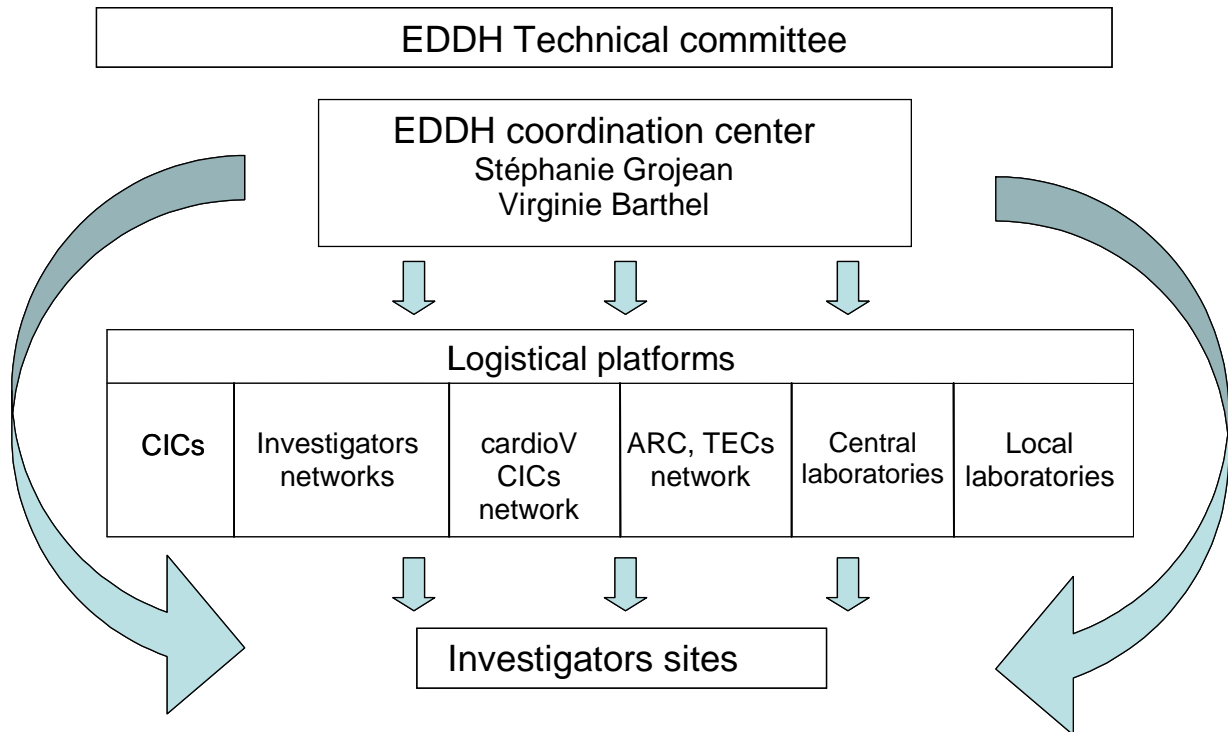
## **3 Objectives of the EDDH network**

The objectives of the EDDH network are to:

- develop and coordinate clinical and therapeutic research programmes for industrial and institutional promoters, both private and public, some jointly with public research bodies and academic research departments.
- produce work on drug efficacy and safety, and on public health issues, including impact on the quality of life of the population.
- provide education and training for personnel and investigators.

## 4. Organization

### 4.1 General organization



### 4.2 Technical committee

#### *CARDIOLOGY*

**Coordinators :** Pr Faiez ZANNAD

**Scientific Leaders :** Pr A. LEIZOROVICZ  
Pr G. MONTALESCOT  
Pr G. STEG

#### *NEUROPSYCHOPHARMACOLOGY*

**Pr Raymund SCHWAN**

Pr PM. LORCA  
Pr P. COURTET  
Dr J GAILLEDREAU

## 5 Services offered by the EDDH

### 5.1 Academic Clinical Research Organization (CRO)

The EDDH acts as a service provider, drawing on the experience and skills of the CIC Nancy. Over the past five years, this entity has deployed an academic CRO activity and coordinated several national and European-scale multicentric protocols.

The CIC has the capacity to offer the same services, both nationally and Europe-wide, as private-sector CROs, namely:

- Assistance or submission to competent authorities on behalf of the promoter.
- Creation of trial documents (*CRFs, project management plan, clinical monitoring plan, etc.*).
- Sourcing investigator centres and carrying out feasibility studies.
- Managing investigator centres in both administration (*setting up centres, management and payment of extra costs and investigator fees*) and trial follow-up (*monitoring, research technician to assist the investigator*).
- Implementing a patient recruitment strategy (*proactive recruitment, poster campaigns, press announcements*).
- Managing subcontractors (*central laboratory, local laboratories, patient transport services, etc.*)

### 5.2 Logistic platforms

As part of its activity as an academic CRO, CIC Nancy can draw on logistic platforms.

#### 5.2.1 The Clinical Investigation Centre, Nancy

The CIC Nancy was created in February 1995. It is an investigation facility, with a team of scientists and professionals specifically dedicated to clinical research. Its main areas of expertise are pathophysiology, pharmacology and clinical therapeutics, proof of concept and Phase I-III clinical trials. The CIC is plurithematic, but the cardiovascular domain, metabolism and nutrition are among its core competencies.

In its own structure, the CIC Nancy has facilities for cardiovascular investigations (cardiac and vascular echography, echodoppler, ANAPRES, FINAPRES, measurement of compliance, distensibility and arterial diameter, measurement of intima-media thickness, etc.), respiratory investigations (FRE, NIOX nitric oxide test system), and investigations of sleep disorders (polysomnography, measurement of ventilation parameters, thoracic and abdominal movements, thermocouple (nasal air flow), oesophageal probe for measurement of intrathoracic pressure, etc.) together with a biological resource centre. In addition to its own facilities, the CIC Nancy has privileged access to the clinical research platforms at the Nancy University Hospital.

## **5.2.2 The Clinical Investigation Centre, Clermont-Ferrand**

The CIC Clermont-Ferrand is a platform of particular interest for phase I protocols, which can be entrusted to the EDDH network.

The CIC 501 at Clermont-Ferrand was set up in January 2005.

This CIC is supported by two clinical research structures: the Clinical Pharmacology Centre of the University Hospital and the Clinical Cancer Research Unit at the Jean Perrin Cancer Research Centre.

This Centre has the monitoring and emergency facilities required to study the action of new chemical entities in humans right at the start of their clinical development (Phase I trials). Its capacity (700 m<sup>2</sup>, 18 research beds and five functional exploration stations), makes the CIC well-equipped for carrying out pharmacokinetic and (or) pharmacodynamic studies on several dozens of subjects on a short time scale.

## **5.2.3 The network of cardiovascular Clinical Investigation Centres**

In April 2003, INSERM set up a national network of CICs. The CIC Nancy is the coordinator of the network of cardiovascular CICs.

Given the experience of the CICs and their professional outlook, this network offers a national logistic platform that the EDDH can call upon for its multicentric industrial trials.

Coordination is headed by Prof. F Zannad.

## **5.2.4 The network of Clinical Research Assistants and Clinical Trial Technicians**

In the last three years the department of cardiology of the EDDH has been working jointly with a national network of independent Clinical Research Assistants and Clinical Trial Technicians. These service providers work in compliance with the standard operating procedures developed by the CIC Nancy, and are trained and experienced in its proactive methods of patient recruitment.

A network of about 30 Clinical Research Assistants and Clinical Trial Technicians has thus been set in place throughout France and its overseas territories. All these informations are included in a database declared to the CNIL "*Commission National de l'informatique et des libertés*".

## **5.2.5 Access to investigators trained in clinical research**

### **5.2.5.1 Network of psychiatrists**

The GICIPI is an association, created at the end of 2001 and officially registered on 30 January 2002, that groups a total of 53 independent and hospital investigators among the most active and experienced in Phase II and III industrial trials. The association also provides training for investigators.

### **5.2.5.2 Network of cardiologists**

The CIC Nancy has succeeded in creating its national network of investigators grouping 300 independent and teaching hospital cardiologists posted all over France and its overseas territories. All these informations are included in a database declared to the CNIL "*Commission National de l'informatique et des libertés*".

These investigators are all conversant with clinical research and have all worked with the CIC. They therefore know the site and its administrative practices, which is essential for the operation of a centre.

Generally, whenever possible and with the promoter's assent, the CIC Nancy endeavours to encourage a partnership with the network of Clinical Research Supervisors and Clinical Trial Technicians described above.

### **5.2.5.3 Network of general medical practitioners**

This network, set up in 1985 and headed by Prof. Zannad, initially grouped general medical practitioners to respond to the numerous research protocols based on health disorders encountered in general medicine rather than in hospitals. Later it was reshaped around the CIC Nancy, under the guidance of Dr Boivin, a general practitioner attached to the CIC, and extended to independent specialists. It currently groups 600 general practitioners and specialists in the Lorraine region.

This network works in partnership with other similar networks of independent GPs grouped around CICs and SMOs in France.

### **5.2.6 CeNGEPS support**

The EDDH responded to the CeNGEPS call for projects on "Support for investigation networks in industrial clinical research".

The presentation of our expertise, results and ambitions earned CeNGEPS support through a specific allocation for "investigation networks".

## **5.3 Quality assurance at the EDDH**

### **5.3.1 The EDDH quality management system**

The EDDH quality management system is based on that developed by CIC Nancy, which has just been reviewed and validated by external audit and has been adapted to the specificities of the project coordination

### **5.3.2 Training**

The quality of the work performed by the EDDH network depends on the training of the personnel of the centres who are involved in the trials, including the investigators.

For each protocol, the EDDH sets specific training schemes. In addition, the EDDH undertakes to draft a detailed operating manual for every protocol when this is not supplied by the promoter.

## **5.4 Recruitment strategies developed by the EDDH**

### **5.4.1 Feasibility study**

For greater efficiency, the EDDH systematically carries out a feasibility study on its investigators for every protocol.

This study is necessarily based on a verification of the patient potential of the centre through a proactive inspection of the investigator's patient files. This study means that a centre can be set up only if the centre has the patient potential. A tested, operational POS is specifically dedicated to this aspect.

The GICIPI network, affiliated to the EDDH, has also developed a shared software tool that meets HAS standards for psychiatric patient files and FDA CFR Part 11 for computer files. This software can be used by the two EDDH networks.

### **5.4.2 Recruitment strategy**

The EDDH offers all its investigators active assistance in finding patients.

They can be sourced through patient files, consultation reports, discharge notes and examination results, via either electronic or paper-based media. In the case of a paper media, the search can be done manually by the Clinical Trial Technician under the responsibility of the investigator and in their own patient files. If the media is electronic, it can be done using a search engine, which the investigator can install and use directly on any computer.

The search can if necessary be facilitated by accessing the Department of Medical Information for hospital investigators. The search is based on PMSI codes. After a request by the investigator made to the hospital's Department of Medical Information, a shortlist of eligible patients is drawn up. One or more research technicians are then instructed to search for patient files that meet the trial selection criteria.

## **5.5 The partners of the EDDH**

As part of its academic CRO activity the CIC Nancy has had the opportunity of working jointly with structures identical to its own, including Duke University ([www.duke.edu](http://www.duke.edu)), STICARES ([www.sticaresinteract.com](http://www.sticaresinteract.com)) and others.

## 6 Dissemination of Knowledge and training

EDDH participates to the teaching of "DIU FARC, formation des attachés de recherches cliniques", located this year in Nancy and Strasbourg.

EDDH is implicated also in the teaching of Master Ingénierie de la santé at Montpellier.

## 7 Commitments of the EDDH – performance evaluation

The EDDH network undertakes to evaluate its performance for each protocol on the following criteria:

### Network development

- Number of new investigators
- Number of approaches by promoters

### Protocol administration

- Time between first contact with promoter and first EEDGH budget estimate.
- Time elapsed before signature of the agreement.
- Time to mobilize the centre: *(from the day the contract is signed to the day the centre is set up)*.

### Protocol feasibility

- Time between the first contact with the promoter and the estimate of the capacity of the EDDH (number of investigators participating, number of patients who can be included, time needed for inclusion of these patients).
- Number of EDDH refusals due to insufficient patient potential.

### Protocol recruitment

- Time between set-up and the first patient inclusion for each centre.
- Number of patients included relative to the number planned.

### Quality

- Number of wrong inclusions.
- Number of queries per patient.
- Survey of promoter satisfaction.

A performance report will be drafted yearly and sent to the investigators participating in the various protocols, together with any actions that need to be taken to improve items with low performance. This report will also be made available on-line on the EDDH website so that promoters can consult it.