

# 1<sup>st</sup> EPICLUSTER event

## Consensus document on EPICLUSTER's mission and agenda

**OVERVIEW** EPICLUSTER was established in 2019 under EBRA as a **coordinating action for European epilepsy research**. The leadership of EPICLUSTER comprises the coordinators of multiple large-scale epilepsy research projects along with the Epi-CARE clinical network and professional and patient-representative organisations. The objective is to work collectively to agree and action key research challenges at scale.



### **Mission**

Establish a collaborative framework for the coordinated actions of epilepsy research in Europe

### **Strategic objectives**

- Promoting collaborations at both European and global level and contributing to European Policy
- Enhance European Epilepsy Training
- Increasing translation of project generated knowledge and innovative approaches into new health interventions
- Supporting internationalisation of participating industry partners
- Improve access to and optimise the use of research infrastructures and data sources
- Explore possibilities for broader scale cooperation at global level

### **R&I priority topics**

- Disease modifying and personalised medicines for epilepsy and their delivery systems
- Target led biomarker and diagnostics discovery and validation
- Innovative models for diagnostics and target development
- Digitalisation and personal monitoring for independent living in epilepsy
- Coordination of research infrastructures and the Epilepsy data ecosystem
- Funding initiatives and integration to society, industry, and regulatory space

### **Four activities are planned**

- EPICLUSTER consensus meeting
- EPICLUSTER general conference
- Sustainability policy forum
- Synthesis forum

The first of which was a meeting focused on reaching broad consensus for the cooperation among the different groups and the identification of the main objectives and actions.

**EPICLUSTER consensus meeting** On June 17<sup>th</sup>, 2020, the leadership of EPICLUSTER held the first meeting. The focus of the meeting was to bring together the leadership, hear from them on the organisations they represent, discuss the originally planned actions and priorities and assign people to responsibilities for delivery. The second part of the meeting was attended by a number of stakeholders from outside the EPICLUSTER leadership, facilitated by EBRA, including coordinators of other European epilepsy projects, experts in

big data, preclinical and clinical data sharing, the patient's perspective and industry. Each participant was enthusiastic to partner with EPICLUSTER and contribute to success.

### **Meeting attendees**

The following epilepsy stakeholder groups were represented during the meeting: Patients, caregivers and patient organizations, basic and clinical researchers, clinicians, industry, research infrastructures and data experts.

*EPICLUSTER leadership group:* David C. Henshall (Coordinator) RCSI/FutureNeuro (EpiRNA), Renzo Guerrini, Univ. Florence (DESIRE), Sergiusz Jozwiak, Medical Univ. Warsaw (EPI-STOP), Merab Kokaia, Lund University (EPI-TARGET), Asla Pitkanen, U. E. Finland (EPI-TARGET), Sanjay Sisodiya, University College London (EPI-PGX), Michele Simonato, U. Ferrara/U. San Raf. (EpiXchange, EPI-TARGET), Helen Cross, University College London/GOSH (EpiCARE), Philippe Ryvlin, U. Lausanne/CHUV (ILAE Exec, Lancet Comm), Martin Brodie, Univ. Glasgow (IBE/EAE).

*From EBRA:* Kristien Aarts, Elke De Witte, Frédéric Destrebecq.

*Stakeholders group:* Eugen Trinka, U. Salzburg (Chair of ILAE Europe, and member of the EAN Epilepsy panel management group), Roland Krause, U. Luxembourg (Research Infrastructures), Holger Lerche (Epi25, Solve-RD, EuroEPINOMICS), Matthew Walker, University College London (ECMED), Ana M. Sebastião, U. Lisbon (EpiEpiNet), Stefanie Dedeurwaerdere, UCB Pharma, Francesca Sofia, Italian Epilepsy Federation, Ulf Tölch, QUEST, Jan Bjaalie, Institute of basic medical sciences Oslo (Human Brain Project), Janet Mifsud, University of Malta.

**Toward consensus** The research and coordinating objectives and priorities of EPICLUSTER and the invited stakeholders were discussed before and during the meeting. These include (1) facilitating infrastructure, data and biosample sharing, (2) increasing translation of basic to clinical science, (3) joint funding initiatives of scale and (4) supporting the longer-term vision of a multi-stakeholder epilepsy research community.

EPICLUSTER will also input to the content of the planned European Forum on Epilepsy to be held in 2021. The actions will be achieved through expanding the membership of EPICLUSTER to include affiliated members and activities will be coordinated through EPICLUSTER's different working groups. The working groups are:

- (1) Synthesis
- (2) Policy & sustainability
- (3) Innovation & industry
- (4) Data and research infrastructure

EPICLUSTER will represent the entire epilepsy research community. Within this, several stakeholder categories can be identified, each of which has common as well as individual priorities. As part of the preparation for EPICLUSTER, these are acknowledged below and are written by the leadership and based on Pitkanen et al *Advancing research toward faster diagnosis, better treatment, and end of stigma in epilepsy*, *Epilepsia* 2019:

**Basic and translational science perspective** Major advances have been delivered by the various large-scale projects in terms of understanding mechanisms of genetic and acquired epilepsies. This has generated new targets, compounds and procedures for treatment and diagnosis and has increased the high quality science in the field. Challenges for the future

include accelerating the translation of novel therapies and biomarkers from the laboratory to the clinic, attracting and retaining talented researchers, increasing the pace of adoption of technologies such as iPSC, organoids and multi-omics and developing a comprehensive model of the epileptic brain.

***Clinical perspective*** Delivery of epilepsy care is changing, requiring transition to care outside of the hospital facilitated by eHealth platforms and digital healthcare. Creation of virtual epilepsy centres to optimize and deliver care across the community was the vision for European Reference Network (ERN) for Rare and Complex Epilepsies EpiCARE (<https://epi-care.eu>), to enhance cross border care, but also has relevance on a national level. Beyond better control of seizures, research is required into the various co-morbidities and their management. Artificial intelligence and machine learning offer ways to obtain deeper insights into clinical data that may generate findings on epileptogenesis, drug resistance mechanisms, comorbidities, prognosis and outcome. Advanced technologies are also enabling breakthrough progress in the fields of seizure detection and forecasting and on-demand therapies, which can lessen the impact of unpredictable seizures. Emerging biotechnologies such as gene therapy herald opportunities for discoveries by basic science on genetics of epilepsies to move into a therapy development pipeline. Investigator led clinical trials are badly needed in many epilepsy fields, including antiepileptogenic treatment, surgical therapies (including gene therapy) and prevention of premature mortality and additional outcome measures (secondary endpoints) are needed to assess meaningful efficacy in addition to seizure control.

***Infrastructures*** The different epilepsy projects have created unique biosample and data resources. These remain largely siloed, however, and are not yet community resources. There is now an opportunity to create a European Epilepsy Data Ecosystem to harmonize resources and establishing efficient mechanisms to share and exchange preclinical and clinical data between groups and projects and access expertise outside the epilepsy field. Further opportunities exist for data science analytics of multi-omics data to identify novel targets for therapy. Establishment of cooperating preclinical laboratories could provide a network for drug validation to de-risk new drug development pipelines. The recently established ERNs offer a unique opportunity of a high expertise network of hospitals, to perform academic trials with innovative therapies, and share data, which were acquired during routine clinical work for data analytic sciences. Now, EPI-CLUSTER should maximize opportunities to collaborate with infrastructures outside the field (e.g. Human Brain Project, ELIXIR, European Pediatric Translational Research Infrastructure, EpiCARE etc).

***Patient perspective*** Persons with epilepsy are major stakeholders and, with patient organisations, have a key role to play in advocacy and awareness around their disease, the process of research selection, drug-discovery, the development of new devices, the assessment of new neurosurgical techniques, and the design of clinical trials. New developments in rare and ultra-rare epilepsies is demonstrating the need for truly collaborative relationship with patients as partners to researchers, clinicians and industry, which is critical for conceiving, developing and establishing transformational treatment options. Experience from rare diseases can serve as a model for the more common epilepsies. Patients perform a vital role at the intersection of medicine and new digital technologies. For example, via education and empowerment to collect and report real-world data through digital diaries and wearable devices, which can drastically change the way we do epilepsy research and care for persons with epilepsy.

**Industry perspective** Epilepsy has to be seen as a more attractive field for investment by industry and new technology companies. This can be achieved through strengthening biology and target validation, more clinical trials with clear differentiation and stratification of patient populations that will benefit for both rare and common epilepsies. Industry is recognizing the need to focus more on disease-modifying therapies that target specific mechanisms of disease and the underlying pathophysiology. There is a need for more validated therapeutic targets and truly innovative approaches, for more SME and biotechnology companies to enter the field. This is starting to happen for some of the rare epilepsies. Industry would benefit from access to preclinical trial capabilities and expertise distributed throughout the EPICLUSTER network.

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