ECFS Patient Registry
Business Plan 2018-2020

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Introduction

This Business Plan outlines the ECFSPR strategy for 2018-2020 and the actions required to pursue it.

Many of the objectives that were set in the 2015-2018 Business Plan have been fulfilled, and for the others we are confident that we are on the right track (see page 9 of this document for a report). In the last few years the Registry has grown considerably and it is now the largest CF database in the world, largely thanks to the essential support received from the contributing centres and national registries in Europe and surrounding countries. Valuable collaboration with several groups, such as CF Europe and the ECFS Data Quality Management Group, have led to the implementation of a number of important projects, and we will continue this work in the coming years.

A strategic plan should be dynamic and easily adaptable, if necessary, in response to internal or external factors. The time has come to shift our focus, and for the coming years our main projects will concern improving and monitoring data quality, and increasing the use of the data in the scientific domain and in published manuscripts; complete longitudinal data-sets of high quality data and coverage in each participating country of 80% or more are essential if the data is to be employed for research and in clinical trials and pharmacovigilance studies. The objectives mentioned in our previous Strategic Plan remain valid.

in order to fulfil these objectives and to secure the sustainability of the Registry in the long-term, adequate funding is needed.

In this document we redefine and prioritise our objectives for the next three years.

Mission Statement

The aim of the European Cystic Fibrosis Society Patient Registry (ECFSPR) is to provide a comprehensive view of CF care in Europe by measuring and comparing aspects of CF and its treatment across participating countries. The ECFSPR will be used to improve the health and wellbeing of people with CF: anonymised data will be used to better understand the disease, encourage new standards of CF care, provide data for epidemiological research and post-marketing studies, and inform European public health-planning.

Achievements & Progress Report 2015-2017

From 2015 to 2017 the following objectives have been successfully accomplished:

Number of Countries

The ECFSPR has further expanded in the years 2015 to 2017.

The number of countries contributing data to the ECFSPR as of 31 December 2017 has increased to 32, from 27 in 2015; 18 countries have a national registry and 85 centres input data directly to the online data-collection software.

Number of Patients

The number of patients with CF who consented to the inclusion of their data in the ECFSPR database has increased considerably in the past years and is still rising.

Data of the year	Number of patients	Number of countries	Year of publication annual report
2007	20,204	16	2009-2010
2008	18,537	19	2011
2009	17,978	19	
2010	32,248	22	2014
2013	38,985	27	2015
2014	35,582	26	2016
2011	36,340	27	2017
2012	37,404	27	2017
2015	42,054	29	2017

Coverage and Participation

The estimated coverage per country is the estimated percentage of CF patients living in that country who are included in the national registry or national data collection. Countries with a national registry have a broad coverage of CF patients nationwide; it can also be the case in some countries that an individual centre treats almost all of patients in the country, e.g. Latvia and Serbia.

We have been working continuously with the countries that had a coverage of <80% to increase this to above the threshold of 80%. The 2015 Annual Report includes the most recent overview of the estimated coverage per country; now only 7 countries remain below the threshold.

In 2015-2017 we were in contact with Bulgaria, Lithuania, Romania, Spain and Ukraine to motivate more centres to participate in the ECFSPR and thereby increase coverage.

The following countries joined the ECFSPR in 2015-2017: Albania, Bosnia, Cyprus, Georgia, Luxembourg and Norway. Poland is currently organising the approval of the data-protection authorities.

In 2017 we contacted many of the remaining countries not yet in the ECFSPR and discussions are ongoing with Iceland, Finland, Estonia, Belarus and Malta.

Coverage as presented in the ECFSPR Annual Report 2015:

Country	Patients registered, not lost to follow-up	Patients seen	Estimated coverage 2015
Austria	733	704	90%
Bulgaria	134	134	66%
Czech Republic*	590	571	>95%
Denmark*	496	467	>95%
France*	6553	6553	90%
Germany*	5363	5363	>90%
Greece**	590	561	>95%
Hungary*	558	558	>90%
Ireland*	1263	1060	>90%
Israel**	665	550	95%
Italy*	5222	5206	95%
Latvia	38	37	>90%
Lithuania[1]	14	14	20%[1]
Luxembourg	26	26	>80%
Rep of Macedonia	114	105	>90%
Rep of Moldova*	54	45	68-76%
The Netherlands*	1401	1367	98%
Portugal**	338	300	>95%
Romania[2]	46	44	10%[2]
Russian Federation*	2883	2875	83%
Serbia	180	180	>90%
Slovak Republic**	256	213	>90%
Slovenia	96	94	>95%
Spain	1854	1772	62-66%
Sweden*	645	645	>95%
Switzerland**	878	852	>95%
Turkey	95	93	3%
Ukraine	159	122	15-18%
United Kingdom*	10810	9587	99%
Total	42054	40098	

* Countries with an established national CF registry.

** Countries that have established a national registry, since all centres participate in the ECFSPR and use the direct data-entry function of ECFSTracker.

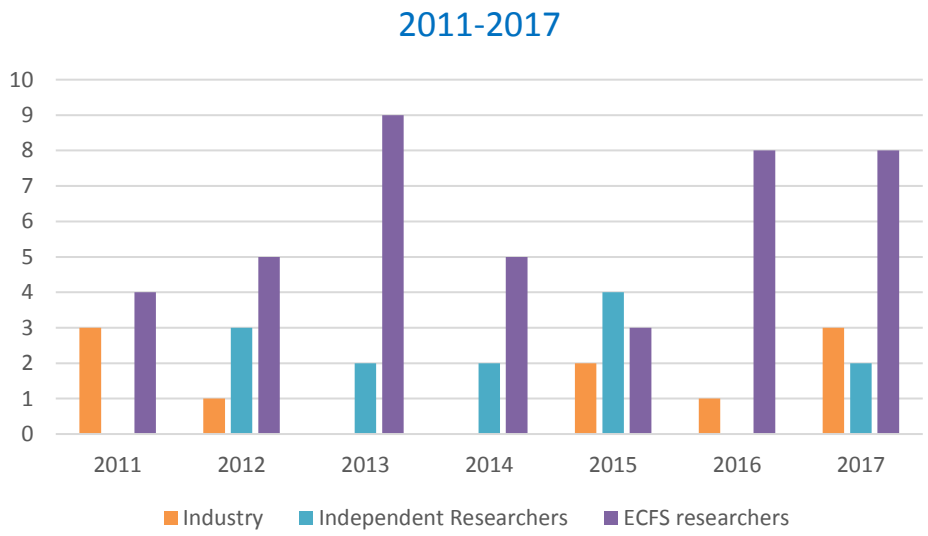
Data Requests

The ECFSPR database is an important source of key demographic and clinical data of patients with CF and since longitudinal data from 2010 to 2015 is available, as of 31 December 2017, it is a unique basis for epidemiological analyses. The ECFSPR has promoted the use and significance for research of this important data at conferences, meetings and on the website.

The number of applications to use the data from researchers, from both inside and outside the ECFS, including pharmaceutical companies, i.e. the Industry, has continued to rise in recent years. Data requests are handled in accordance with a standard operating procedure that takes into account current, applicable data protection regulations and a formal, internal decision-making process.

The application form to be completed by the data-requester has been updated and contains complete information on procedure and fee-structure. Standard operating procedures for data-requests on genetic information and mutation prevalence have been defined. These documents were approved by the ECFSPR Steering Group in February 2017.

Overview of data requests handled 2010 – 2017:



Publications

From 2015-2017 the following manuscripts were published:

Effect of Allergic Bronchopulmonary Aspergillosis on FEV1 in Children and Adolescents with Cystic Fibrosis: A European Cystic Fibrosis Society Patient Registry Analysis. Kaditis AG, Miligkos M, Bossi A, Colombo C, Hatziagorou E, Kashirskaya N, Monestrol de I, Thomas M, Mei-Zahav M, Chrousos G, Zolin A.
Arch Dis Child 2017; 102: 742-747

Year to year change in FEV1 in patients with cystic fibrosis and different mutation classes. De Boeck K, Zolin A. J Cyst Fibros. 2017; 16: 239-245.

Epidemiology of nontuberculous mycobacteria (NTM) amongst individuals with cystic fibrosis (CF). Vivani L, Harrison MJ, Zolin , Haworth CS, Floto RA. J Cyst Fibros. 2016; 15: 619-23.

Future trends in Cystic Fibrosis demography in 34 countries. Burgel P-R, Bellis G, Olesen HV, Viviani L, Blasi F, Elborn JS on behalf of the ERS/ECFS Task Force on The Provision of Care for Adults with Cystic Fibrosis in Europe 2015; Eur Respir J. 2015; 46: 133-41.

www.ecfs.eu/projects/ecfs-patient-registry/articles

As of 31 December 2017, there are 10 manuscripts in the pipeline.

Six posters were presented at conferences:

Cystic Fibrosis Survival and Socio-economic status across Europe, McKone EF, Ariti C, Jackson A , Zolin A, Carr S, van Rens J, Keogh R, Naehrlich L. ECFS conference June 2017, Seville. J Cyst Fibros, 2017; 16 (Suppl 2): S20.

Genetic epidemiology of CFTR nonsense mutations across Europe. E.F. McKone, A. Jackson, A. Zolin, K. De Boeck, J. van Rens, C. Ariti, R. Keogh, L. Naehrlich. J Cyst Fibros, 2017; 16 (Suppl 2): S47.

The effect of CFTR nonsense mutations on phenotype and mortality in patients with cystic fibrosis. McKone EF. ECFS conference June 2016, Basel.

The European Cystic Fibrosis Patient Registry, a useful tool for patients with CF. Van Rens J, McKone E. 8th European Conference on Rare Diseases & Orphan Products, 26-28 May 2016, Edinburgh, UK.

Demographic and clinical aspects of cystic fibrosis-related diabetes (CFRD) – a registry comparison between the European CF Society Patient Registry (ECFSPR) and the German/Austrian/Luxembourg diabetes patient follow-up registry DPV. N. Prinz, A. Zolin, K. Konrad, L. Nährlich, K. Laubner, H.V. Olesen, M. Bauer, A. Jung, and others. J Cyst Fibros, 2017; 16 (Suppl 2): S168.

Patients with cystic fibrosis and the R117H mutation: The European experience. L. Naehrlich, A. Zolin, C. Colombo, K. De Boeck, N. Kashirskaya, H.V. Olesen. J Cyst Fibros, 2015; 14 (Suppl): S32.

Software

In order to accommodate the large number of participating countries and centres with varied IT and other requirements, the universal data-collection platform, ECFSTracker, was developed. It is an open source, multipurpose and multinational web-based software, custom-designed for the collection of CF patient data.

Data is submitted to the ECFSPR once a year, either by direct data-input or by the uploading of an Excel-file. The Encounters module of ECFSTracker can be used to collect longitudinal data from each patient visit in a follow-up year and to individual patients with CF over the long term. www.ecfs.eu/ecfspr-software

In 2017 development work began on an updated version of ECFSTracker, based on recent technology, and in response to important changes in clinical, and other, aspects of CF. The adaptable format of the new software will allow us to easily add modules to collect additional data, for example for pharmacovigilance (i.e. post-marketing) purposes and clinical trials etc. The software will be compliant with the new European General Data Protection Regulations, and will be launched in participating countries at the beginning of 2019.

Projects

From 2015-2017 the ECFSPR conducted the following projects:

- Data Quality project:
  Aims to advise and develop data quality standards and procedures to ensure accuracy of national and European CF data, by working together with countries with an established national registry. Members are Steering Group representatives from national registries and single centre countries. The members meet twice a year, during the January and June ECFS meetings.

- Definitions project:
  Aims to align the definitions used in the European national CF registries with those of the ECFSPR. In 2017 the group was re-activated to participate in the discussions on the introduction of new variables to the core data and annual data-set, which will be integrated into the new ECFSTracker (2.0).
  Members are Steering Group representatives, i.e. national registries and single centre representatives. The group meets when necessary during one of the ECFS meetings in January or June.

- Harmonisation project:
  Aims to bring registry capability into step with the globalisation that has been occurring in CF research and care, and to enhance the ability of registries to contribute to advances in care and improved CF outcomes. A plan for harmonised data will provide a blueprint for emerging CF registries and for the periodic redevelopment of existing registries.
  Members are representatives from the global CF registries in Australia, Canada, Europe and the USA. This group meets twice a year, during the ECFS conference in June and the NACFC in October/November.

- Pharmacovigilance project:
  Was established in October 2016 when the European Medicine Agency (EMA) set up a Registry Initiative to discuss using existing patient registries for pharmaco-epidemiological studies, and expressed their interest to use the ECFSPR as a model to draft a procedure to conduct these kind of studies, as well as set clear guidelines for the type of data collected and how it should be shared with EMA and Industry. The aim of this project is to develop a standard operating procedure for how the ECFSPR and national CF registries can be used for pharmacovigilance purposes. For more detailed information on this project please refer to objective 7 on page 22.
  Members are representatives from national registries of DE, FR, IE, NL, SE, UK, data-controller and Clinical Trial Network (CTN). The group meets twice a year during the January and June ECFS conferences, and in between teleconferences are organized upon request.

- Patient project:
  Was established in 2015 in collaboration with CF Europe, the federation of patient associations of people with CF throughout Europe, to ensure that people with CF and their families directly benefit from the information collected and analysed by the ECFSPR, and that patient involvement in the registry remains central to its future development. By combining efforts, the ECFSPR and CFE have defined and implemented projects to raise awareness of the relevance of the ECFSPR and how people with CF and their families can benefit from the data.

All project groups involve members of the Steering Group and at least one member of the Executive Committee. The groups report twice a year, during the ECFS meeting in January and June, to the Steering Group.

Progress Report

Annual Reports		Annual Data Reports: The ambition to decrease the gap between the close of a calendar year and publication of the report to 18 months, which should give the national registries sufficient time to publish their country report before the European report, has almost been realised. Data of 5 years have been collected with ECFSTracker. In our first data-collection round, 3 years of data were collected: 2011-2012-2013. We decided to publish and print the Annual Data Reports 2013 and 2014 first as these reports would be more relevant, since they contained more up-to-date data, and publish the 2011 and 2012 reports at a later stage online.	
	a	Annual Data Report 2013: published February 2016. www.ecfs.eu/sites/default/files/general-content-files/working-groups/ecfs-patient-registry/ECFSPR_Report2013_02.2016.pdf	February 2016
	b	Annual Data Report 2014: published November 2016. www.ecfs.eu/sites/default/files/general-content-files/working-groups/ecfs-patient-registry/ECFSPR_Annual%20Report%202014_Nov2016.pdf	November 2016
	c	Annual Data Report 2011: published August 2017. www.ecfs.eu/sites/default/files/general-content-files/working-groups/ecfs-patient-registry/ECFSPR_Annual_Report_2011_Aug2017.pdf	August 2017
	d	Annual Data Report 2012: published August 2017. www.ecfs.eu/sites/default/files/general-content-files/working-groups/ecfs-patient-registry/ECFSPR_Annual_Report_2012_Aug_2017.pdf	August 2017
	e	Annual Data Report 2015: publication in November 2017. www.ecfs.eu/sites/default/files/general-content-images/working-groups/ecfs-patient-registry/ECFSPR_Report2015_Nov2017.pdf	Nov 2017
Research	a	The research goals were presented to and approved by the ECFSPR Steering Group at the ECFS conference in Brussels.	June 2015
	b	The Scientific Committee identified the research projects for the next years, defined the management of the projects and initiated each project. The proposal was presented to the ECFSPR Steering Group at the winter meeting in Prague.	January 2016
		Scientific projects: - Changes in demography and clinical outcomes in CF in Europe. - International and pan-European comparison of survival in CF. - Mortality during pediatric age in patients with CF in Europe.	2015-2017
	c	Publications: 4 manuscripts were published and 6 posters presented. www.ecfs.eu/projects/ecfs-patient-registry/articles	2015-2017

Benchmarking	a	Meeting with the ECFS Quality Management group to define the list of comparators for benchmarking and key indicators to assess Quality of Care, and draft of a proposal of requirements for a benchmarking module in ECFSTracker.	Sept-Dec 2015
	b	Meeting with the software company to discuss the requirements as in proposal.	Dec 2015
	c	Refining proposal and development module.	Jan-Dec 2016
	d	Demonstration module to ECFSPR Steering Group during winter meeting in Lisbon and the ECFS conference in Seville.	Jan & June 2017
Patient benefits	a	Meeting with patient representatives and ECFSPR representatives during the ECFS conference in Brussels to define projects to ensure that patients with CF and their families directly benefit from the information collected and analysed by the ECFSPR and that patient involvement is central to its development.	June 2015
	b	Project groups worked on the development of Infographics, an At-a-glance report and poster. The proposal of the Infographics and At-a-glance report was presented at the ECFSPR Steering Group meeting in January 2016 in Prague and the final proposal of the poster in June 2016 in Basel.	Jan & June 2016
	c	The At-a-glance Report 2013 was published in March 2016 following the publication of the Annual Data Report. www.ecfs.eu/sites/default/files/general-content-files/working-groups/ecfs-patient-registry/CF_At_A_Glance_Guide_Final_online_2016.pdf	Mar 2016
		The At-a-glance report 2014 was published after the publication of the Annual Data Report. www.ecfs.eu/sites/default/files/general-content-files/working-groups/ecfs-patient-registry/CF_At_A_Glance_Guide_2014.pdf	Nov 2016
	d	Development of a poster template to promote the value of the ECFSPR to patients and which will include infographics and country specific information compared to European information. The posters are translated in the local languages and distributed in the CF clinics and patient organisations across Europe. Every 3 years an update of the poster will be released.	Jan-May 2016
		Presentation poster template to and approval from the ECFSPR Steering Group in Basel.	June 2016
		Translation of the poster into the local languages.	Sept-Dec 2016
		Publication and distribution of posters, during 2017. Ongoing.	Jan-Dec 2017
	e	Kick-off meeting and definition proposal for social media, to increase visibility and promote the value of the ECFSPR.	June 2016
	f	Use of Facebook and Twitter.	2017

Coverage& Participation	a	In a joint effort with the country coordinators coverage in several countries has been increased. Data protection papers have been completed and centres have been trained how to use the data-collection software.	
		New countries: Albania, Bosnia, Cyprus, Georgia, Luxembourg, Norway.	2015-2017
		New centres: Cordoba, Zaragoza (Spain), Istanbul (Turkey). A centre in Bulgaria was re-activated.	2015-2017
	b	Meetings:	
		The ECFSPR was invited to the national CF meeting in Skopje (Macedonia), Dnipro (Ukraine) and Madrid (Spain) to increase coverage in these countries. New centres in Macedonia and Ukraine expressed their interest to join the ECFSPR and are completing the necessary paperwork.	Sept-Dec 2016
		The ECFSPR went to national CF meetings in Romania, Poland and Ukraine. Poland will join in 2018. For Romania and Ukraine it is important to recruit more centres in order to increase the coverage percentage.	Oct-Dec 2017
		Meeting for Interested Parties is organised during the ECFS conferences and is attended by many countries and centres interested in participating in the ECFSPR.	June 2015, 2016, 2017
ECFSTracker	a	A Service Level Agreement was agreed with the software company for 2016.	June-Dec 2016
	b	Upgrade of the software to ensure that ECFSTracker will become the main portal for the collection of CF data for all purposes, including collection of data for pharmacovigilance. The software is based on the technology used in VoiceTracker. Additional variables will be included.	From Nov 2017
	c	Expansion of variables: additional variables have been included in the Core data and Annual Summary data. Also the Encounter variables will be expanded.	June-Dec 2017
Harmonisation of data	a	Meeting of the worldwide Harmonisation Group (CF registries of Europe, Canada, USA, South America) at the ECFS conference in Basel.	June 2016
		Meeting of the worldwide Harmonisation Group at the NACFF conference in USA.	Oct 2016 & 2017
	b	As a result of the global CF Harmonisation project the Global Lung Function Initiative equations, described by Quanjer PH et al, will be used as the global reference for spirometry. In the ECFSPR Annual Data Report 2014 these equations to describe lung function were used for the first time.	From Nov 2016

Objectives 2018 – 2020

A distinction should be made between our core business and additional projects we undertake.

Core business is the production of annual reports, collection of data with an up-to-date software, ensuring data-quality, and increasing the use of data in research.

The following are considered additional projects: initiatives to promote involvement with patients; the development of additional software modules for pharma-epidemiology, clinical trials and the collection of other specific data.

The following objectives will be pursued in the next years:

1. Publish the ECFSPR Annual Report, with epidemiological European data, within 18 months of the close of a calendar year.
2. Ensure high quality data in the ECFSPR database and at source level.
3. Increase the use of ECFSPR data for CF related research.
4. Ensure the continued relevance of the ECFSTracker software to users; develop additional modules to collect data for specific studies, e.g. pharmacovigilance/pharma-economic, and expanded registry data collection.
5. Continue to work in close relationship with CF patient organisations to ensure that people with CF and their families directly benefit from the ECFSPR data.
6. Achieve realistic reflection of CF throughout Europe by supporting participating countries with a low coverage rate to increase coverage to 80% or higher.
7. Develop a standard operating procedure to handle and perform pharmacovigilance requests.

Strategy and Actions 2018 – 2020

1. Publish the ECFSPR Annual Report with epidemiological European data within 18 months of the close of a calendar year.

It is the ECFSPR's aim to decrease to 18 months the time between the end of a calendar year and the publication of the Annual Report with data for that year. Whilst allowing countries with a national registry to publish their own national report before the European report, this will ensure that the information is up to date, relevant and useful and has an impact in the public domain.

The availability and development of ECFSTracker has streamlined and simplified data-collection and provides added value incentives for timely and complete data-entry, alongside country specific initiatives.

Actions:

- Timely communication to contributors of the planning of the preparation of the Annual Report and the deadlines for data-collection.
- Continue to co-design, with patient representatives, At-a-glance reports that including key-information from the Annual Report, designed for patients and their families.
- Establish a working group to review the structure, content and design of the current reports and define a proposal for a new template, to use for future reports (2018 and onwards);
- Set-up a Memorandum of Understanding (MoU) with the individual countries, to consent on deliverables, roles and responsibilities of all parties involved (Steering Group representative i.e. Country Coordinator role in ECFSTracker, Centre Director, ECFSPR);
- Deadlines will be respected within reason. If a country/centre is not able to meet the deadline, the ECFSPR will liaise with the country/centre to explore possible solutions.
  When a country/centre is not able to deliver the data in time and no solutions are possible, and delay in data-delivery might interfere with the publication of the Annual Report, it is at the Executive Committee's discretion to decide – in agreement with the Country Coordinator/ Steering Group representative and the Centre Director – to not include the data in the report. In such case the demographic data of the year previous to the data-year collected in the Annual Report in question may be included.

2. Ensure high quality data.

Improving the quality of data is a continuous process. During the past years important work has been done: the Data Quality project has worked with national registries on controls to apply before uploading the data in the software, aligning definitions etc.; data-quality checks and controls have been incorporated in ECFSTracker; the statisticians continue to apply further rigorous checks after submission of data by the countries.

At the beginning of 2018 the ECFSPR contained data of more than 42,000 patients, with six years of longitudinal data (2010-2016). It is increasingly important to have a consolidated data-set that is relevant for epidemiological research and post-marketing studies. Our current and future focus is to ensure the quality of the data, decrease the amount of missing data, and increase coverage in participating countries to above the threshold of 80%.

An initial program was drawn up in the Data Quality Working group. The aims and outcomes will be discussed with all countries, and together, the ECFSPR and the national registries, will develop a harmonised strategy for the implementation of a strong data quality control and accreditation programme.

In 2018 a Data Quality programme will concentrate on developing a set of standard operating procedures (SOPs) to be shared with all participating countries, and defining an accreditation programme, which will include on-site monitoring visits, in a phased approach.

Guidelines for the Data Quality programme are the recommendations defined by EMA in the workshop report, and the requirements stated in the Context of Use document.

In June 2017 the European Medicine Agency (EMA) organized a workshop, the "Cystic Fibrosis workshop – Registries Initiative", and published recommendations for improvements in a report, www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2017/10/event_detail_001522.jsp&mid=WC0b01ac058004d5c3.

As a result of successful collaboration with national CF registries and extensive interaction with the EMA, the ECFSPR has received a qualification opinion from the EMA. This provides a detailed road map for the eventual use of the ECFSPR as an appropriate platform for the collection of CF data for Post Authorisation Safety Studies (PASS) and Post Authorisation Efficacy (PAES) studies.

A Context of Use document is available on the EMA website for public consultation. The document presents a model that can be used by other disease registries when applying for EMA qualification to carry out PASS and PAES studies.

www.ema.europa.eu/ema/index.jsp?curl=pages/includes/document/document_detail.jsp?webContentId=WC500243542&mid=WC0b01ac058009a3dc.

Actions:

- Develop a data-quality programme and accreditation process for countries, including planning, milestones and budget;
- Share European and national data-quality programmes;
- Increase the use of standard operating procedures in all registries to ≥ 90%;
- Increase the use of coding documents with the variables that are collected to 100%;

- Improve a check at data-entry level to 100%;
- Execute on-site monitoring visits, including source verification, at approx. 75% of the participating centres that input data directly in ECFSTracker (10-20% annually), limited to 10% of the data that has been provided. Key factors from the annual report and pharmacovigilance study, as well as new variables, will be monitored. As an example, the UK guideline will be followed: audits on 20-30 items, and issues arising from data-cleaning;
- Improve quality of current data collection by referring to existing data quality checks and controls.

3. Intensify research to increase data-output resulting in:

a) 2 manuscripts in submission with epidemiological and/or prognostic analyses by the end of 2020;
b) citation by at least 5 peer reviewed papers per annum.

The ECFSPR database contains longitudinal data from 2008 to 2016, and it is a unique resource for large-scale epidemiological analyses including prognostic analyses. To ensure the relevance of the ECFSPR for the CF community the number of publications using the data should increase in coming years.

The Scientific Committee has been active during the past years to initiate scientific projects, and most of these are currently publications in the pipeline (please refer to page 36). The number of applications to use ECFSPR data for research is increasing year by year (an overview of data-applications is available in appendix H, page 37).

The bottleneck to increase production of the research manuscripts is often the extra time needed to physically write the manuscript, therefore, external support and more involvement from the Steering Group and other ECFS groups is recommended.

Actions

- Increase epidemiological research on optimized longitudinal data to forecast trends in CF. The research will be initiated by the ECFSPR and working groups will be established, composed of members of the ECFSPR Steering Group, Scientific committee in potential conjunction with other researchers from CTN, ECFS working groups, CF Europe, and CFF (please refer to proposal Scientific Committee in Appendix C, page 31).
- Apply for research grants for pan-European research, such as Horizon 2020 and other resources such as foundations and fellowships.
- Recruit, on a project basis, external epidemiologists or healthcare researchers to work on specific epidemiological research projects, provided sufficient financial resources are available.
- Organise research mentorships to assist in the writing of manuscripts;
- Conduct statistical analyses to be ready for publication (statisticians co-author);
- Continue to promote the ECFSPR data for research to ECFS- and independent researchers or research groups, which should lead to 5 – 10 peer reviewed papers per annum.
- Ensure that a link to the names of the SG members is included in publications and presentations.
- Use the ECFSPR software as a web-based tool for data collection as part of Investigator-Initiated Studies.
- Promote and use the ECFSPR software as a tool for population-based Translational CF Research, e.g. CFTR2, modifier gene studies.

4. Continue to develop and expand ECFSTracker for specific data-collection, in order for it to continue being a relevant data-collection instrument.

The software ECFSTracker has been developed to provide a universal data-collection platform to collect information on consenting CF patients. Once a year, demographic and clinical data is collected on a concise set of variables. The software contains also an Encounters module to collect patient clinical data in real-time, useful for longitudinal monitoring.

In 2017 development started on an updated version of ECFSTracker, based on more advanced technology used for Vertex VoiceTracker, which will allow modules for specific data-collection, such as for pharmacovigilance, to be added.

At the same time the list of variables for the ECFSPR data-set, i.e. core data and Annual Summary data, as well as for the Encounter data, has been expanded. We hope to make the ECFSPR data and the Encounters module more relevant to users with these additions.

Actions

- Develop ECFSTracker 2.0 and launch in participating countries.
- Develop dedicated modules for pharmacovigilance and clinical trials, upon specific request.
- Promote the collection of Encounter data.
- Include Benchmarking tools in ECFSTracker 2.0, and provide benchmarking and quality improvement tools for participating countries. This is important to assess the quality of care and the impact of quality improvement initiatives.
- Motivate participating centres, in collaboration with the ECFS Quality Management Group, using the Benchmarking tool by providing guidance, structure and advice.
- Explore the possibility of generating Benchmarking annual centre reports, for the countries with individual centres submitting data to the ECFSPR, which will focus specifically on a limited number of quality metrics, report changes over time and include relevant comparisons.

5. Continue to work in close relationship with CF patient organisations to ensure that people with CF and their families directly benefit from the ECFSPR data.

The ECFSPR collects patient data that is valuable to CF clinical caregivers and researchers, yet the value to patients is often not as clear. The ECFSPR aims to continue to work closely with CF patient organisations to ensure that patients and their families directly benefit from the information collected and analysed by the ECFSPR and that patient involvement in the registry is central to its development.

Actions

- Present the value of the ECFSPR to CF Europe every 2 years at the ECFS conference in June.
- Engage with patients to co-design registry output to meet their evolving needs, and in particular further improve the patient friendliness of the ECFSPR Annual Report.
- Continue to develop posters for distribution in CF clinics presenting the value of the ECFSPR. Every 3 years the data in these posters will be updated.
- Continue to use social media resources, such as Twitter and Facebook, to inform about the value of the ECFSPR.
- Evaluate on a regular basis the At-a-glance reports, posters, and information on social media, to stay in tune with the specific needs of patients and their families.

6. Achieve realistic reflection of CF throughout Europe by increasing CF coverage in the participating countries to ≥ 80%.

As of January 2018, more than 42,000 CF patients were in the ECFSPR database, and 35 countries were participating in the ECFSPR.

In order to achieve a database that reflects the reality of CF throughout all countries in Europe the ECFSPR will continue to support the participating countries with less than 80% coverage of CF patients nationwide to increase its coverage to 80% or more. We will support requests from non-participating countries to join the ECFSPR. We refer you to appendix D for the list of member countries and potential members countries in Europe.

Factors that might prevent centres and countries from joining might be poor resources, data protection and data security issues, concerns about misuse of the centre summary data, perceived lack of value of CF registries, and local socio-political issues.

Actions

- In collaboration with the country representative of the participating country in the ECFSPR, develop improved strategies for recruitment of additional centres within that country.
- Contact key persons from the non-participating target countries, including representatives of patient organisations, to discuss barriers of enrolment.
- Work with CF Europe to involve patient organisations in motivating the centres/countries to join, and present the ECFSPR at the Eastern European meetings organised by CFE.
- Present the value of the ECFSPR at national CF meetings to support recruitment of additional centres in the countries.
- Arrange meetings at the ECFS conferences for non-participating centres and countries in Europe focused on the potential benefits of participation in the ECFSPR, in conjunction with the ECFS Standards of Care group.
- Continue to organise a dedicated ECFSPR information meeting during the ECFS conference on potential values of registry data, security and data protection, and software demonstrations and training for people with and interest in CF and registries.
- Develop and publicly publish a data security policy, which clearly documents how technical and process compliance is achieved, monitored and maintained.

7. Develop a standard operating procedure to handle and perform pharmacovigilance requests.

Multiple new medicines for CF are in the pipeline to come onto the market. For these new drugs post-authorisation safety surveillance (PASS) and efficacy (PAES) studies need to be conducted to support regulatory decision making.

In October 2016 the European Medicine Agency (EMA) set up a Registry Initiative to discuss using existing patient registries for pharmaco-epidemiological studies, and expressed their interest to use the ECFSPR as a model to draft a procedure to conduct these kind of studies and set clear guidelines of the type of data collected and how it is shared with EMA and Industry.

A scientific consortium was set-up consisting of ECFSPR, larger national registries, ECFS clinical trial network, and a data-protection officer. The consortium submitted a proposal to EMA to establish CF registries as a tool for EMA PASS and PAES studies, in which their position was stated on aspects of data-completeness, data-quality, data delivery (raw data versus summary data) and governance. A multi-disciplinary qualification team of regulators was constituted with representatives from EMA, the clinical trial facilitation group, health technology assessment bodies, and patients.

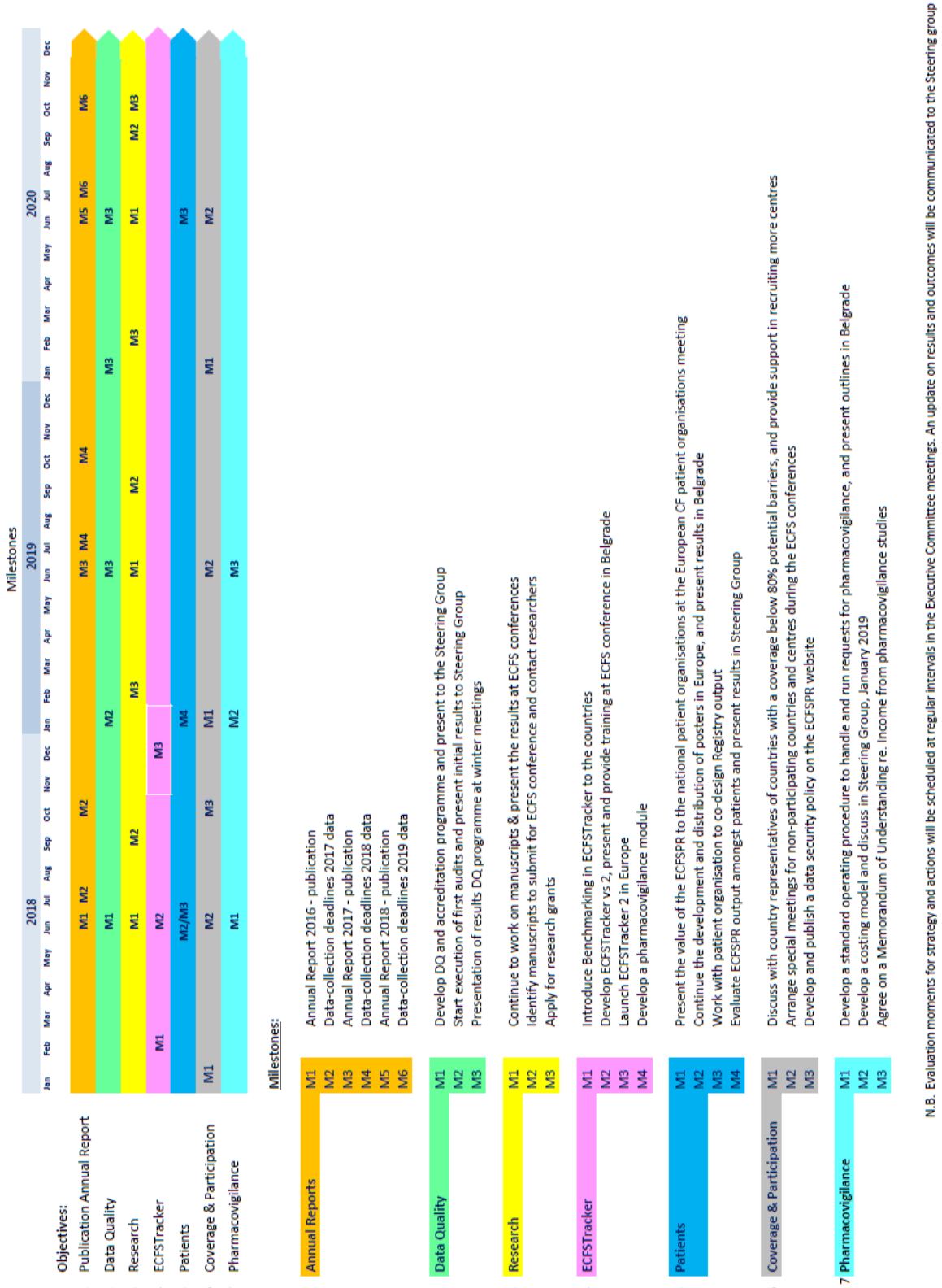
In two meetings at EMA's offices the proposal was discussed and reviewed by EMA. Recommendations and requirements were made (please refer to Data Quality, page 14). A draft Context of Use was produced, describing what CF registries can deliver and specific issues raised for discussion within the qualification procedure. The formal reply from the EMA qualification team is that ECFSPR is deemed by EMA as appropriate data source for post-authorisation studies to support regulatory decision making on medicines for the treatment of CF. The document is publicly available on the EMA website. It is a model that can be used by other disease registries when applying for EMA qualification to perform PASS and PAES studies.

Actions

- Define a standard operating procedure (SOP) on how to handle requests for PMV, including a central point of contact and information to patients about the use of their data.
- Set-up an implementation workgroup to outline and deploy the standard requirements.
- Ensure a robust governance structure is in place.
- Develop a transparent, fair cost model for pharmacovigilance studies.
- Agree on a memorandum of understanding with countries directly entering data in the data-collection software, regarding the income generated by pharmacovigilance studies that use ECFSPR data.
- Develop requirements for a software module for data-collection for PASS studies (please refer to Software page 16).
- Participate as ECFSPR in at least one PASS study.

To achieve the above mentioned goals collaboration with the Data Quality project group and the CTN is essential.

Planning and milestones

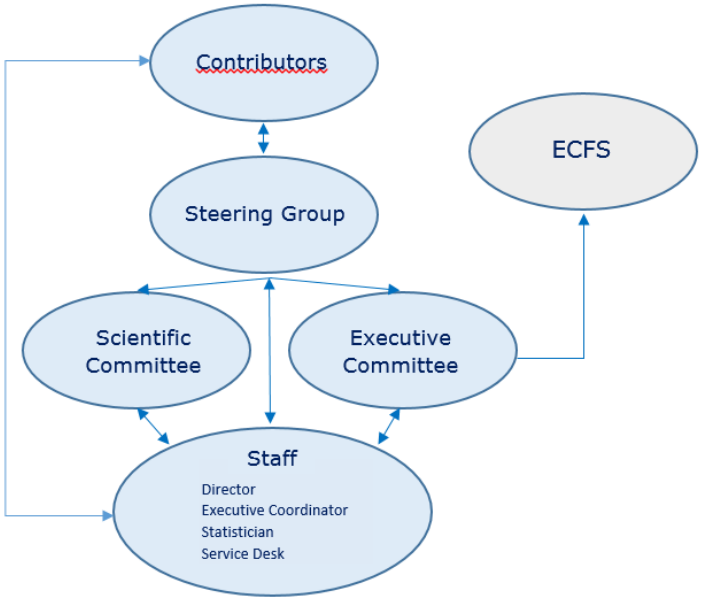


Organisation and Management

The ECFSPR has established an organisational structure that has worked successfully during the past years.

The purpose and structure of the ECFSPR are defined in the Terms of Reference and the Code of Conduct outlines the rules and responsibilities of all parties of the ECFSPR. The documents are published on the ECFSPR website www.ecfs.eu/projects/efcs-patient-registry/guidelines.

- Contributors: all centres and countries contributing data to the ECFSPR.
- Steering Group: consists of country representatives; sets out the strategic direction and is the overall governing body of the ECFSPR.
- Executive Committee: includes some Steering Group members, a patient representative, Executive Coordinator and ECFS Director; responsible for the management of the Registry.
- Scientific Committee: assembled of Steering Group members, a patient representative and Executive Coordinator; custodian of the scientific goals and reviewer of data applications.
- Staff: 4 FTE, consisting of Director (1 person: 0,1 FTE), Executive Coordinator (1 person; 1 FTE), Statistical Experts (2 persons; 2 FTE) and Service Desk (2 persons; 1,2 FTE).



In order to fulfil the objectives that refer to services, governance, research and output the ECFSPR staff will need to be enhanced with a data-quality manager, an epidemiologist, and administrative assistance.

To achieve the aim of further improvement in the quality of data, a data-quality project manager is required. Tasks will include development and execution of a data quality program, development of a SOP framework, etc.

An epidemiologist, on a project basis, is essential to intensify research and increase the output in manuscripts.

Part-time administrative support is required to assist in the increasing number of administrative tasks and projects, and to guarantee continuation of the daily business in case of absence of the Executive Coordinator.

To fulfill the needs of an increasing numbers of ECFSTracker users with a divergent language background the Service Desk will be re-organised. Countries will be divided in Eastern European countries and countries of West and Middle Europe between the two members of the Service Desk, based on their language background.

The countries with an established national registry that upload an Excel-file (e.g. Denmark, Czech Republic, France, Germany, Hungary, Netherlands, Norway, Russia, Sweden, Turkey and UK) will continue to upload the file, prepared according to the documents provided by the ECFSPR, into the system. Most countries are proficient in uploading the file in the software system, and for those that need it appropriate training will be provided. The Service Desk will remain at disposal for technical and other interventions.

Financial Plan

Running a registry comes with a cost, and ECFSPR will strive to establish independent and balanced financial resources to cover these costs and ensure ECFSPR's sustainability. The main consideration is whether ECFSPR income will be independent or funding-driven.

ECFSPR has been growing expansively during the past three years and costs have increased significantly. We anticipate that the total cost of running the ECFSPR will be in excess of € 406.000 per annum (please refer to Appendix A, Budget, page 29).

During the past years ECFSPR has been supported by the ECFS and patient organisations, occasional financial funding from the Industry, and a small amount from data-applications. Additional income was generated from the data-collection software ECFSTracker (based on our License Agreement with Open-App). Parties such as CF registries in non-European countries, other rare disease registries and pharmaceutical companies expressed their interest in ECFSTracker.

Patient organisations will continue to support ECFSPR in the next years. In 2017 ECFSPR renewed the applications for funding to Industry, thereby addressing the need for additional human resources in these grant applications. As a result Vertex Pharmaceuticals and Gilead will continue to support the ECFSPR with an unrestricted grant; Vertex for three years (2018-2020) and Gilead with an annual grant in 2018.

Other potential sources of revenue:
Pharmacovigilance data-collection, European grant applications, e.g. Horizon 2020, ECFSPR services (data protection administration, first line technical support, data management and statistical work) for CF registries in countries that are not part of the ECFS, other disease (non-CF) organisations, the pharmaceutical industry.

Actions

- Submit requests for financial support to pharmaceutical companies; preferably for a period of 3 years.
- Generate income from applications for data; fees have been increased for Industry in February 2018.
- Develop a cost-structure for pharmacovigilance data-collections requests.
- Promote ECFSTracker as a software platform for rare-diseases other than CF during rare disease meetings, and for pharmacovigilance purposes. Large pharmaceutical companies will be approached in conjunction with Openapp (EFSTracker developers).
- Promote ECFSTracker as a tool for multi-centered clinical trials and for use in Horizon 2020 projects.

Contingency Plan

In the case of significant deviation planned from the actions planned to achieve the goals, counter-measures will be defined. For each action, appropriate indicators will be identified and the outcome of the action will be monitored accordingly.

Since the software is essential for the working of the ECFSPR, the ECFSTracker source code is put into escrow and also any other Intellectual Property, confidential information and/or know-how of OpenApp related to ECFSTracker and/or improvements. The ECFS shall have access in the case of the software company being declared bankrupt or in case of a change of control over the software company by others. The appropriate measures are defined in the License Agreement with OpenApp, d.d. 15 December 2015.

Contact information

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www.ecfs.eu/projects/ecfspr

Appendices

A Budget

ECFSPR	Budget 2018		Expenses euro	Income euro
Personnel	Staff (Coordinator, statisticians, Service Desk)	188.000,00		
			188.000,00	
Software	Hosting, Support & Maintenance	22.151,00		
	Development costs (22 days x 550) + VAT	15.263,00		
	Escrow preparation fees	11.586,00		
			49.000,00	
Travel/Meeting	incl. presentations national CF meetings,	11.000,00		
	Travel staff	4.000,00		
			15.000,00	
External services	Legal advice	5.000,00		
	Statistical support	29.000,00		
	Epidemiological support	30.000,00		
			64.000,00	
Projects	PatientProject - posters & at-a-glance	4.000,00		
	Data Quality	80.000,00		
			84.000,00	
Overhead	Office supply / Printing / Telecommunication		6.000,00	
		Total	**406.000,00**	
ECFS Support				100.000,00
Patient Organisations				30.000,00
Industry Support	Vertex (3 yr), Gilead (1 yr)			250.000,00
HIT-CF	(over 3 yrs 43,672)			14.557,00
Data Requests	Roche (23,500-8,500 in 2017)			15.000,00
ECFSTracker	income on royalties & support to 3rd parties			unknown
		Total		**409.557,00**
Balance per 1 January 2018				7.806,00
Result			11.363,00	**417.363,00**

B Travel and meeting Policy

The ECFSPR has considerably expanded during the past years, and this has led to a significant increase in the financial demands on the registry. The ECFSPR Executive Committee has therefore defined a policy for meetings and travel, in accordance with the ECFS guidelines.

Travel:

All members of the ECFSPR Executive and Steering Group will cover their own travel expenses to the January ECFSPR Meeting. In rare cases where their own organisation has insufficient resources, Steering Group members can apply to the ECFSPR to assist with travel expenses to be able to attend the Steering group winter meeting in January. The ECFSPR will refund the travel expenses to a maximum of 200 euro per Steering Group member.

Applications for funding should be sent to the Executive Coordinator and need to be approved by the Director. The maximum total budget available to the ECFSPR per annum will be 2.000 euro for all travel expenses of the ECFSPR including Executive Committee and Steering Group members. No further funds will be available for travel.

Additional information on the ECFS Travel policy you will find on the website www.ecfs.eu/society-details/travel-policy.

Meeting:

The ECFSPR will cover one night of accommodation for one Steering Group member (or a nominated alternate) for each country as defined in the list on the ECFSPR website www.ecfs.eu/projects/ecfs-patient-registry/steering-committee. The ECFSPR will take no financial responsibility for any additional country representative attending the winter meeting.

Exceptions to this rule are only possible upon approval of the Director.

The ECFS will make hotel reservations according to the data submitted upon registration. Should there be changes in the hotel reservation, e.g. an extra night or less nights, after the communicated deadline the extra costs for these changes will be borne by the attendee.

C Research Objectives and Output

It is the ambition of the ECFSPR Scientific Committee to have 2 papers in submission with epidemiological and/or prognostic analyses by December 2020.

To define the research goals the following steps are involved:

1.1 Literature review

a. Undertake a systematic review of literature published by CF registries to:
   i. map out epidemiological and clinical issues already addressed by CF registries;
   ii. identify priority areas for novel (or further) investigation.

b. Produce a document for circulation to the Steering Group to initiate discussion. This could be prepared as a scientific article and submitted to a peer-reviewed journal.

Potential epidemiological and clinical issues might include:

- Prevalence/incidence
- Mortality and survival
- General epidemiology
- Genotypes
- Diagnostic aspects
- Screening
- Respiratory function
- Growth and nutrition
- Microbiology
- Complications
- Transplants
- Phase IV studies
- Translational research

Some specific studies identified by the scientific committee:

- Characterisation of meconium ileus cases;
- Characterisation of screening positive newborns;
- Mortality during infancy;
- Ursodeoxycholic acid and the progression of liver disease.

1.2 Stakeholder engagement

- Engage with ECFSPR Steering Group members, CTN and patient advocates (CF Europe) to identify what they consider to be areas of priority research.
- Seek input/comment on literature review document;
- Identify any *a priori* research questions;
- Identify extenuating circumstances which would require particular areas of research to be expedited;
- Engage with CFF (US), CF Canada, CF Patient Registry Australia, to seek their involvement in pursuing a programme of international comparative CF registry research.

1.3 Agree priority research objectives

1.3 Identify resource requirements

Develop working groups within the ECFSPR Steering Group (and involve other ECFS members with relevant expertise, as required) and identify candidates to lead these working groups.

Involve a research programme manager to oversee the various working groups (if possible), to ensure research objectives are met within the required time period.

1.5 Research outputs

Define minimum research output objectives:

- two papers in submission by December 2020;
- possibly a supplement to a scientific journal in 2019-2020.

This should be tailored to the research goals and the resources available to execute the project.

D. ECFS countries

The list of ECFSPR members includes all countries participating in the European Cystic Fibrosis Society Patient Registry (ECFSPR) and the (potential) member countries of the European Union and the European Economic Area.

The participating countries in the ECFSPR are:

Albania, Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Cyprus, Czech Republic, Denmark, France, Georgia, Germany, Greece, Hungary, Ireland, Israel, Italy, Latvia, Lithuania, Luxembourg, Macedonia, Moldova, Netherlands, Norway, Poland, Portugal, Romania, Russian Federation, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, Ukraine, United Kingdom.

Potential member countries:
Armenia, Belarus, Croatia, Estonia, Finland, Iceland, Kosovo, Liechtenstein, Malta, Montenegro.

E. Stakeholders

- ECFS
- Patients and their families
- Patient organisations
- Cystic Fibrosis Europe
- Clinicians
- CF centres
- CF national registries
- Data managers
- Researchers
- Other healthcare providers
- Allied Health Professionals
- Industry
- National Health Services authorities
- European Commission
- European Medicine Agency
- Other global CF registries, such as Cystic Fibrosis Foundation USA, Cystic Fibrosis Federation Australia
- Other rare disease registries

F Publications

Effect of Allergic Bronchopulmonary Aspergillosis on FEV1 in Children and Adolescents with Cystic Fibrosis: A European Cystic Fibrosis Society Patient Registry Analysis. Kaditis AG, Miligkos M, Bossi A, Colombo C, Hatziagorou E, Kashirskaya N, Monestrol de I, Thomas M, Mei-Zahav M, Chrousos G, Zolin A. Arch Dis Child 2017; 102: 742-747.

Year to year change in FEV1 in patients with cystic fibrosis and different mutation classes. De Boeck K, Zolin A. J Cyst Fibros. 2017; 16: 239-245.

Epidemiology of nontuberculous mycobacteria (NTM) amongst individuals with cystic fibrosis(CF). Vivani L, Harrison MJ, Zolin A, Haworth CS, Floto RA. J Cyst Fibros. 2016; 15: 619-23.

Future trends in Cystic Fibrosis demography in 34 countries. Burgel P-R, Bellis G, Olesen HV, Viviani L, Blasi F, Elborn JS on behalf of the ERS/ECFS Task Force on The Provision of Care for Adults with Cystic Fibrosis in Europe 2015. Eur Respir J. 2015; 46: 133-41.

The European Cystic Fibrosis Society Patient Registry: valuable lessons learned on how to sustain a disease registry. Viviani L, Zolin A, Mehta A, Olesen HV. Orphanet Journal of Rare Diseases 2014: 9:81.

The relative frequency of CFTR mutation classes in European patients with cystic fibrosis. De Boeck K, Zolin A, Cuppens H, Olesen HV, Viviani L. Journal of Cystic Fibrosis 2014: 403-9.

Multi-Country Estimate of Different Manifestations of Aspergillosis in Cystic Fibrosis. Amstead J., Morris J., Denning D.W. PlosOne 2014, June 10; 9:e98502.

Factors associated with FEV1 decline in cystic fibrosis: analysis of the data of the ECFS Patient Registry. Kerem E, Viviani L, Zolin A, Macneill S, Hatziagorou E, Ellemunter H, Drevinek P, Gulmans V, Krivec U, Olesen H; on behalf of the ECFS Patient Registry Steering Group. Eur Respir J. 2014 43: 125-133.

Evidence of diminished FEV1 and FVC in 6-year-olds followed in the European cystic fibrosis patient registry, 2007-2009. VanDevanter DR, Pasta DJ. J Cyst Fibros. 2013; 12:786-9.

Reference percentiles for FEV(1) and BMI in European children and adults with cystic fibrosis. Boëlle PY, Viviani L, Busson PF, Olesen HV, Ravilly S, Stern M, Assael BM, Barreto C, Drevinek P, Thomas M, Krivec U, Mei-Zahav M, Vibert JF, Clement A, Mehta A, Corvol H; French CF Modifier Gene Study Investigators; European CF Registry Working Group. Orphanet J Rare Dis. 2012; 7:64.

Epidemiology of Cystic Fibrosis Lung Disease progression in adolescents. VanDevanter D. ECFS Book on Healthcare Issues and challenges in Adolescents in CF, December 2012.

Comparative demographics of the European cystic fibrosis population: a cross-sectional database analysis. McCormick J, Mehta G, Olesen HV, Viviani L, Macek M, Mehta A. Lancet 2010; 375: 1007-13.

Cystic fibrosis across Europe: EuroCareCF analysis of demographic data from 35 countries. Mehta G, Macek M Jr, Mehta A; European Registry Working Group. J Cyst Fibros. 2010; 9 Suppl 2: S5-S21.

G Manuscripts in the pipeline as of January 2018

- International and pan-European comparison of survival in CF.
  (McKone EF, Ariti C, Jackson A , Zolin A, Carr S, van Rens J, Keogh R, Naehrlich L)
- Changes in demography and clinical outcomes in CF in Europe. (Hatziagorou E, Zolin A)
- The effect of CFTR nonsense mutations on phenotype and mortality in patients with CF. (McKone EM)
- The effect of DNase on longitudinal lung function in patients with CF. (McKone EM)
- Clinical characteristics of CFRD: Lessons from the ECFSPR. (Olsesen HV, Zolin A)
- CF-specific reference equations for FEV1 and BMI: an updated analysis. (Corvol H)
- Risk Factors for the decline in FEV1 among Patients with CF in Europe. (Hatziagorou E, DeBoeck K, Orenti A)
- Changing Epidemiology of the Respiratory Bacteriology of Patients with CF in Europe. (Hatizagorou E, Orenti A)
- Life expectancy of cystic fibrosis patients with FEV1 < 40% predicted. (Jung A, Orenti A)
- Demographic and clinical aspects of cystic fibrosis-related diabetes – a registry; comparison between the ECFSPR and the German/Austrian diabetes patient follow-up registry. (Prinz N)

Manuscript in review for publication

- Cystic fibrosis mortality in childhood. Data from the ECFS Patient Registry.
  Padoan R, Zolin A, Cirilli N.

H. Data Requests 2015 – 2017

2015

No.	Requester		Research/ Industry	Aim/Title	Date of request	Approved/ Not	Data sent	Manuscript
290115	Eitan Kerem	Hadassah Medical University, Jerusalem, Israel	R	Genetic information: c.2421A>G; p.Ile807Met	7-1-2015	Approved	27-1-2015	NA
30115	Mieke Boon	University Hospital Leuven, Belgium	R	Information on the prevalence of c.1811-1.6kbA>G mutation in Spain	8-1-2015	Approved	19-3-2015	NA
310115	Hanne Vebert Olesen	CF Centre Skejby, Aarhus University Hospital, Aarhus, Denmark	R	Clinical characteristics of CFRD: Lessons from the ECFSPR	12-1-2015	Approved	18-3-2015	Manuscript in the pipeline.
320115	Batsheva Kerem	Department of Genetics, The Life Sciences Institute, the Hebrew University, Edmond J. Safra Campus, Givat Ram, Jerusalem, Israel	R	Number of patients homozygous for the W1282X in Europe	24-2-2015	Approved	Never replied to email with cost estimate	NA
330215	Silvia Bacci	University of Perugia, Department of Economics, Italy	R	A joint model for longitudinal and survival data based on an AR(1) latent process	19-2-2015	Reviewed by Sc. Co.	Seems only interested in UK data and requester has been bruoght into contact with UK	NA
340515	Raffaella Armiento	Royal Children's Hospital Melbourne, Australia Paediatric Registrar, 50 Flemington Rd, Parkville, VIC, Australia	R	Use of mucolytic agents in paediatric cystic fibrosis, a cross sectional study.	29-5-2015	Not approved by Sc. Co	NA	NA
350915	Simeon Piggott, International Medical Advisor	Vertex Pharmaceuticals	I	To gain a better understanding of the numbers of F508del homozygous and heterozygous patients potentially eligible for the VX-661/Ivacaftor program in Europe.	29-09-15	Not approved by Scientific Co.	NA	NA
361015	Aidan Gill, Senior Director Medical Affairs	PTC Therapeutics	I	Nonsense Mutation CF Prevalence in Europe. Provide regulatory and other government agencies in EU with estimated prevalence of CF patients eligible for ataluren.	28-10-15	Not approved by Scientific Co.	7-12-15 Informed PTC of conclusion SC and proposed co-authorship to a manuscript on stop codon mutations. 7-12-2015 PTC agreed. No follow-up; retreated from CF field.	Manuscript in the pipeline.
371115	Nicole Prinz, research fellow post doc	Ulm University, Institute of Epidemiology and Medical Biometry	R	Demographic and clinical aspects of cystic fibrosis-related diabetes – a registry; comparison between the ECFSPR and the German/Austrian diabetes patient follow-up registry DPV	26-11-15	Positive advice from Scientific Co.; Inform SG	15-4-2016	Manuscript in the pipeline.

2016

No.	Requester		Research/ Industry	Aim/Title	Date of request	Approved/ Not approved	Data sent	Manuscript
380116	Abi Jackson	ECFSPR Scientific Committee	R	International and pan-European comparison of survival in cystic fibrosis	20-01-16	Approved	7-4-2016.	Manuscript in the pipeline Jan 2017: Abstract for ECFS conference submitted. June 2017: Poster presented at ECFS conference in Seville.
390116	Abi Jackson	ECFSPR Scientific Committee	R	Changes in demography and clinical outcomes in cystic fibrosis in Europe	20-01-16	Approved	7-4-2016	Manuscript in the pipeline June 2017: Initial results presented at ECFS
400116	Rita Padoan, Natalia Cirilli	ECFSPR Scientific Committee	R	Mortality during paediatric age in European CF patients	18-01-16	Approved	Data provided. Manuscript submitted to JCF, declinded.	Manuscript submitted to JCF; declined.
410216	Harriet Corvol	Inserm U338 & 1136, Paris	R	CF-specific reference equations for FEV1 and BMI : updated analysis	6-01-16	Approved	13-4-2016	Manuscript in the pipeline.
420416 (ref. 371015)	Ed McKone/PTC	St. Vincent's Univerisity Hospital, on behalf of the ECFSPR	I	The effect of CFTR nonsense mutations on phenotype and mortality in patients with cystic fibrosis.	7-04-16	Approved	24-5-2016 .	Manuscript in the pipeline Jan 2017: abstract for ECFS conference submitted. June 2017: Results presented at ECFS conference in Seville.
430916	Meir Mei-Zahav	Country Coordinator IL	R	Survival of Cystic Fibrosis Patients in Israel	21-9-2016	Approved by SC	Wil use IL data in ECFSTracker	
451116	Amparo Escribano	Hospital Clínico Universitario de Valencia, Universidad de Valencia, Spain	R	Genetic Info on: clinical-epidemiological characteristics of CF patients with deletions of exons 17a 17b and 18 (according to traditional nomenclature) or of exons 19, 20 and 21 (according to the "new nomenclature").	22-11-2016	Approved by SC. UK: no such mutations, so no part of the data-set.	22-3-2017	NA
451116	Ed Mckone (collaboration with Roche)	ECFSPR, Cystic Fibrosis Registry of Ireland	R	The effect of DNase on longitudinal lung function in European patients with cystic fibrosis	9-12-2016	Approved	7-7-2017	Manuscript in the pipeline.
461216	Carmen del Luna	Paediatric CF unit, Hospital Doce (12) Octubre, Madrid, Spain	R	Clinical profile and response to Ivacaftor in paedictric patients homozygous to S549R	1-12-2016	Approved	21-3-2017	NA

2017

No.	Requester		Research/ Industry	Aim/Title	Date of request	Approved/ Not approved	Data sent	Manuscript
470117	dr Mark Higgins, senior medical director	Vertex Pharmaceuticals	I	Weight distriburion for 2-5 years old children	6-01-17	Approved by SC; Approved by CTN and SG. UK wants to be in contact directly with UK.	23-5-2017	NA
4801117	Batsheva Kerem	Department of Genetics, The Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem	R	The effect of combined CFTR therapies on splicing and stop mutations in the CFTR gene.	16-01-17	9/3 Approved by SC	23-3-2017 Requester was informed and invoice sent. No reply.	NA
490117	Concha Prados Sánchez	Pulmonology, Unit of Cystic Fibrosis, La Paz University Hospital, Madrid, Spain	R	Evaluation of the annual decline of the pulmonary function of patients with cystic fibrosis according to criteria of the Global Lung Initiative	14-01-17	Review SC, needs clarification	Will collaborate in Elpis' research project 540317.	NA
500117	Marianne Skov	CF centre, Copenhagen, Denmark	R	Genetic information on patients with mutation 508del heterozygous, and c638G>A, p.6213E or c.1399C>T	19-01-17	Approved by SC. UK no such mutations, so not to include in this request.	21-3-2017	NA
510217	Florian Gutzwiller	Novartis Pharma, ww Associate HEOR Director (health economics and outcomes research)	I	Baseline Patient Characteristics in Patients with CF carrying R33W and R117H mutations	27-2-2017	Review SC. CTN agrees.	Discussed in June in Seville. Requester has contacted France and Spain directly.	NA
520317	Elpis Hatziagorou	Aristotle University of Thessaloniki, Pediatric Pulmonology and CF Unit, Dept Pediatrics, Thessaloniki	R	Changing Epidemiology of the Respiratory Bacteriology of Patients With Cystic Fibrosis in Europe	6-3-2017	Approved	23-10-2017 analysis by ECFSPR	Manuscript in the pipeline.
530317	Kris De Boeck	ECFS	R	To anticipate on a Horizon 2020 project using organoids to test response to CFTR modulator drugs and to assess the feasibility of such a project .	9-3-2017	Review SC	6-4-2017	NA
540317	Elpis Hatziagorou	ECFSPR Scientific Committee	R	Risk Factors for the decline in FEV1 among Patients With Cystic Fibrosis in Europe	24-3-2017	Approved by SC	28-11-2017	Manuscript in the pipeline.
550417	Andreas Jung	ECFSPR Executive Committee / Children`s University Hospital Zurich, Switzerland	R	Life expectancy of cystic fibrosis patients with FEV1 < 40% predicted	12-4-2017	Approved by SC with some comments/additions	1-6-2017 Data provided. Presented at ECFS conference 2017 in Seville. Manuscript in the pipeline.	Manuscript in the pipeline.
560417	Concha Prados Sánchez	Pulmonology, Unit of Cystic Fibrosis, La Paz University Hospital, Madrid, Spain	R	Non tuberculous mycobacteria (NTM)) en Spain. Descriptive study	5-7-2017	Review by SC	Only ES data needed; no follow-up	Manuscript in the pipeline.
570817	Pinaki Chaudhuri	INC Research/inVentiv, UK	I	A Phase 2, multiple dose proof-of-concept, randomized, double blind, placebo controlled and dose-finding study to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary measures of efficacy of subcutaneously administered ELX-02 as monotherapy and in combination with XXX in cohorts of subjects with cystic fibrosis caused by nonsense mutations	4-9-2017	Reviewed by SC; CTN approves but with comments. Approved by SG, no rpely from FR	24-10-207 table with country info n nonsen mutations (excl FR); 1-12-2017: table with breakdown of non- sense mutations for BE-IT-ES; 9-1-2018: table with breakdown of nonsense mutations by country.	NA
581017	Kris De Boeck	University Hospital Leuven, CF Reference Centre, BE	R	Geographic distribution of patients with specific mutations: A561E, R334W, P2015S across EU, to assess feasibility and countries/sites to target for PI initiated trials in patients with these mutations. NB If feasible, the clinical trial will be submitted to Vertex as PI initiated trial.	28-9-2017	SG approved	7-11-2017	NA
591017	Kors van den Ent	Hit_-CF	R+I	HIT-CF: Personalised Treatment For Cystic Fibrosis Patients With Ultra-rare CFTR Mutations, To identify CF-centers and subjects with CF that are eligible for participation in our organoid study, and possibly for one of the subsequent clinical trial arms.	17-10-2017	Approved by SC & SG.	9-1-2018	