



Project no: LSHM-CT-2005-018932

EuroCareCF

European Coordination Action for Research in Cystic Fibrosis

Coordination Action

Priority 1, Life Sciences, Genomics and Biotechnology for Health

Publishable Final Activity Report

Period covered: 01/01/06 to 30/06/09

Date of preparation: 26/02/10

Start date of project: 01/01/06

Duration: 42 months

David N. Sheppard, PhD
University of Bristol

Revision 1

SECTION 1 – PROJECT EXECUTION

1.1. Background:

Cystic fibrosis (CF) is a life-shortening, childhood-onset inherited disorder in Europe characterized by progressive lung disease leading to premature death. It is estimated that in the European Union there are about 30,000 CF patients, with one new case per 2,500-3,000 newborns. Mutations in a single gene encoding the cystic fibrosis transmembrane conductance regulator (CFTR) cause CF and a spectrum of related disorders. Despite impressive advances in relating the molecular basis of CF to organ-level disease, life expectancy and quality of life are still limited in CF. The median survival of CF patients in Europe is ~27 years.

Besides CF itself being a clinically heterogeneous disease, a number of CFTR-associated diseases have recently emerged. These include obstructive azoospermia, uni- or bilateral absence of vas deferens, disseminated bronchiectasis, idiopathic pancreatitis, sarcoidosis and asthma. These are clearly distinct from CF and have been termed 'CFTR-related diseases'. However, they share one or more pathogenetic / clinical features with the classical form of CF and usually are associated with one or both mutant alleles of the CF gene /CFTR/. Their prognosis *quoad vitam* is markedly better than in the case of classical CF. However, identification of CFTR-related diseases and distinction from atypical CF is not trivial and still poses difficulties to clinicians. CF, although a monogenic disease, thus exemplifies the complex challenges of genetic diseases in the post-genomic era (including those of multigenic diseases), and is by many considered as a paradigm to explain the mechanisms of disease and provides rationale for clinical management and therapy development.

It is also expected that the main respiratory diseases amongst the EU-population (e.g. asthma, chronic obstructive pulmonary disease, cryptogenic fibrosing alveolitis) might ultimately benefit from actions, developments and advancements in CF, the most common genetic form of chronic bronchitis.

In recent years, many advances have emerged both from clinical and fundamental research (e.g. better clinical programmes, more advanced technological developments with potential for refined diagnosis and lead compounds from high-throughput screening assays). However, these advances have not been fully translated to the clinical setting nor widely disseminated across Europe. Moreover, research efforts in the CF area are still fragmented in Europe.

1.2. Project Objectives:

EuroCareCF aimed to bring together the results of ongoing EU research in the CF field and translating them into better care, treatment and quality of life for CF patients. Towards this goal, **EuroCareCF** created a European forum for CF and CFTR-related diseases, in which all stakeholders had the opportunity to interact, exchange and collaborate to achieve common goals. **EuroCareCF** sought to involve actively CF professionals from all European countries, including clinicians, healthcare professionals and basic scientists. To achieve this goal, **EuroCareCF** worked closely with its principal stakeholder the European Cystic Fibrosis Society (ECFS).

The major goals of **EuroCareCF** were:

- To improve the survival and quality of life of CF patients
- To optimise clinical management and therapy development

To achieve these goals, **EuroCareCF** was organised into a series of workpackages each with its own programme of work. Through a variety of activities such as meetings, workshops and training visits, **EuroCareCF** developed consensus guidelines in specific areas of CF research and patient care, built networks of scientists and healthcare professionals and promoted the distribution of key resources to facilitate research and patient care.

Workpackage 1: Optimising Patient Care & CF Team Work

Leader: Carla Colombo (Milano, Italy)

Aims: To promote good standards of care for CF patients in all European countries

Expected end results:

- Recommendations on good standards of care for CF patients
- Specialist training in CF Team Work
- Establishment of a clinical network for each speciality in the team delivering CF patient care

Workpackage 2: European Cystic Fibrosis Patient Registry

Leader: Anil Mehta (Dundee, UK)

Aims: To create a uniform and highly secure Registry of CF patients in Europe

Expected end results:

- Secure, industry-standard software for a registry of CF patients in Europe
- Collection of consent-driven anonymised patient data
- Report on the demographics of European CF patients

Workpackage 3: Coordination of Clinical Research

Leader: Christiane De Boeck (Leuven, Belgium)

Aims: To optimise the screening and diagnosis of CF and related diseases, improve microorganism control and design clinical trials

Expected end results:

- New clinical diagnostic procedures for European CF patients
- Specialist training in CFTR bioassays for CF diagnosis
- Recommendations for the design, conduct and evaluation of clinical trials
- A European network of reference laboratories for molecular typing of microbiological specimens
- Consensus guidelines for the detection and identification of microbiological pathogens using molecular diagnostics
- Recommendations for neonatal screening in Europe
- Recommendations for the classification of diseases as CFTR-related

Workpackage 4: Small and Medium-Sized Enterprises (SMEs) Group

Leader: Andreas Reimann (Bonn, Germany)

Aims: To encourage cooperation between CF researchers and SMEs

Expected end results:

- Identification of the needs of SMEs and the obstacles they face to place 'orphan drugs' into clinical trials
- Consensus document on the medical needs of CF patients and policies for fair and mutually beneficial co-operation between SMEs and patient organisations
- Identification of new opportunities posed by emerging technologies to support the development of novel diagnostics/therapeutics through the co-operation of SMEs and academic centres

Workpackage 5: Novel Therapies

Leader: Massimo Conese (Milano, Italy)

Aims: To evaluate innovative therapies for CF patients

Expected end results:

- Consensus guidelines for the transfer of innovative CF therapies from research laboratories to clinical trials
- Specialist training in translation research

Workpackage 6: Animal Models

Leader: Bob J Scholte (Rotterdam, Netherlands)

Aims: To optimise the distribution of animal models for CF research

Expected end results:

- Colonies of mouse models of CF for their distribution to ordering laboratories for fundamental and translation research
- Consensus guidelines for standard laboratory techniques in fundamental and translation research using CF mouse models
- Specialist training in the use of animal models for CF research

Workpackage 7: Integration of Fundamental Research

Leader: Margarida D Amaral (Lisboa, Portugal)

Aims: To assess surrogate end-points for therapy evaluation and distribute resources for research

Expected end results:

- A physical repository of CF resources for fundamental and translation research (e.g. cell lines, cDNAs and antibodies) that will distribute resources to ordering laboratories
- Consensus guidelines for good laboratory techniques to support the evaluation of novel diagnostics / therapies
- Specialist training in laboratory techniques to assess therapeutic interventions

Workpackage 8: Ethical / Legal / Social Issues

Leader: Herman Nys / Kris Dierickx (Leuven, Belgium)

Aims: To examine the ethical, legal and social implications of the **EuroCareCF** Coordination Action

Expected end results:

- Guidelines for the introduction of informed consent to place personal / clinical data in the Registry of European CF patients
- Review of ethics and legislation on clinical trials involving CF minors

Another workpackage (**General Coordination**) managed the **EuroCareCF** project, promoting the close interaction of all participants and collaborators, ensuring the on-time delivery of a series of deliverables and disseminating widely information about the project.



1.3. Project Participants:

EuroCareCF was coordinated by Dr David N. Sheppard from the University of Bristol (UK), who can be contacted at:

University of Bristol
Department of Physiology and Pharmacology
School of Medical Sciences, University Walk, GB-BS8 1TD Bristol, United Kingdom
T: (+44) 117 331 2290; F: (+44) 117 331 2288
Email: D.N.Sheppard@bristol.ac.uk

The other project partners were:

Prof. Margarida D. Amaral
University of Lisboa
Department of Chemistry and Biochemistry
Faculty of Sciences, Campo Grande-C8, P-1749-016 Lisboa, Portugal
T: (+351) 21 750 0861; F: (+351) 21 750 0088
Email: mdamarl@fc.ul.pt

Prof. Carla Colombo
University of Milan

Department of Pediatrics - CF Center
School of Medicine, Via Commenda 9, I-20122 Milan, Italy
T: (+39) 02 5503 2456; F: (+39) 02 5503 2814
Email: carla.colombo@unimi.it

Dr. Anil Mehta
University of Dundee
Tayside Institute of Child Health
Ninewells Hospital & Medical School, GB-DD1 9SY Dundee, United Kingdom
T: (+44) 1382 63 2555; F: (+44) 1382 63 2597
Email: a.mehta@dundee.ac.uk

Prof. Dr. Kris De Boeck
University Hospital of Leuven
Department of Paediatrics
Faculty of Medicine, Herestraat 49, B-3000 Leuven, Belgium
T: (+32) 16 34 3820; F: (+32) 16 34 3842
Email: christiane.deboeck@uz.kuleuven.ac.be

Prof. Kris Dierickx
Catholic University of Leuven
Centre for Biomedical Ethics and Law
Faculty of Medicine, Kapucijnenvoer 35/3, B-3000 Leuven, Belgium
T: (+32) 16 33 6955; F: (+32) 16 33 6952
Email: Kris.Dierickx@med.kuleuven.be

Dr. Andreas Reimann
Mukoviszidose e.V.
In den Dauen 6, D-53117 Bonn, Germany
T: (+49) 228 987 8012; F: (+49) 228 987 8077
Email: areimann@muko.info

Dott. Massimo Conese
San Raffaele Scientific Institute
Institute for Experimental Treatment of Cystic Fibrosis
DiBiT, Via Olgettina n. 58, I-20132 Milano, Italy
T: (+39) 02 2643 4301; F: (+39) 02 2643 4153
Email: conese.massimo@hsr.it

Dr. Bob J. Scholte
Erasmus University Medical Centre Rotterdam
Department of Cell Biology
Dr. Molewaterplein 40-60, NL-3015 GE Rotterdam, The Netherlands
T: (+31) 10 408 7205; F: (+31) 10 408 9468
Email: b.scholte@erasmusmc.nl

Prof. Burkhard Tuemmler
Medizinische Hochschule Hannover
Klinische Forschergruppe, OE 6710
Carl Neuberg Str. 1, D-30625 Hannover, Germany
T: (+49) 511 532 2920; F: (+49) 511 532 6723
Email: tuemmler.burkhard@mh-hannover.de

Dr. Dorota Sands
Instytut Matki i Dziecka
Kasprzaka 17 a, PL-01-211 Warszawa, Polska
T: (+48) 60 222 0506; F: (+48) 22 327 7043
Email: dorotasands@rubikon.pl

Prof. Milan Macek Jr.

Charles University Prague
Department of Molecular Genetics and National Cystic Fibrosis Centre
Institute of Biology and Medical Genetics, University Hospital Motol and Second School of Medicine, V
Uvalu 84, CZ-150 06 Prague 5, Czech Republic
T: (+420) 224 43 9548; F: (+420) 224 43 3520
Email: milan.macek.jr@lfmotol.cuni.cz

Prof. Dr. Peter A.R. Vandamme
Universiteit Gent
Laboratorium voor Microbiologie
Faculteit Wetenschappen, Vakgroep Biochemie, Fysiologie en Microbiologie (WE10), Ledeganckstraat
35, B-9000 Gent, Belgium
T: (+32) 9 264 5113; F: (+32) 9 264 5092
Email: Peter.Vandamme@UGent.be

Prof. Pier Franco Pignatti
Università di Verona
Dipartimento Materno Infantile e di Biologia-Genetica
Sezione di Biologia e Genetica, Strada Le Grazie 8, I-37134 Verona, Italy
T: (+39) 045 58 4602; F: (+39) 045 80 27180
Email: pierfranco.pignatti@univr.it

Prof. Frédéric Becq
Université de Poitiers
Institut de Physiologie et Biologie Cellulaires, Pôle Biologie Santé
40 avenue du recteur Pineau, F-86022 Poitiers Cedex, France
T: (+33) 5 4945 3729; F: (+33) 5 4945 4014
Email: Frederic.becq@univ-poitiers.fr

PD Dr. Dr. Robert Bals
Philipps-Universität Marburg
Innere Medizin, Pneumologie
Baldinger Strasse 1, D-35033 Marburg, Germany
T: (+49) 6421 286 4994; F: (+49) 6421 286 8987
Email: bals@staff.uni-marburg.de

Prof. William H. Colledge
University of Cambridge
Department of Physiology, Development and Neuroscience
Downing Street, GB-CB2 3EG Cambridge, United Kingdom
T: (+44) 1223 33 3881; F: (+44) 1223 33 3840
Email: whc23@cus.cam.ac.uk

Prof. Marcus Mall
University of Heidelberg
Department of Pediatrics III
University Hospital, Im Neuenheimer Feld 153, D-69120 Heidelberg, Germany
T: (+49) 6221 56 8840; F: (+49) 6221 56 8806
Email: Marcus.Mall@med.uni-heidelberg.de

Dr. Martin J. Hug
Universitätsklinikums Freiburg
Hugstetter Str. 55, D-79106 Freiburg, Germany
T: (+49) 761 270 5455; F: (+49) 761 270 5490
Email: martin.hug@uniklinik-freiburg.de

1.4. Project Website:

For further details about EuroCareCF, see the project website: <http://www.eurocarecf.eu/>

1.5. Work Performed:

The work performed by the different workpackages was as follows:

Workpackage 1. Optimising Patient Care & CF Team Work:

Period 1:

- Activities of workpackage 1 promoted at international CF conferences
- Information about standards of patient care collected and analysed
- Teaching materials collected to produce a teaching tool about multidisciplinary CF patient care
- Development of networks of experts for each member of the multidisciplinary team

Period 2:

- Organised meetings of the different specialists within the multidisciplinary CF patient care team to develop further the networks of experts for each clinical speciality
- Held a patient care workshop
- Continued the collection and analysis of documents on standards of patient care from different European countries
- Continued the collection of documents to prepare a teaching package on the multidisciplinary approach to CF patient care
- With WP10, organised the specialist training of European clinicians and healthcare professionals in multidisciplinary CF patient care

Period 3:

- Continued to elaborate the networks of clinicians and healthcare professionals for each member of the multidisciplinary team responsible for the care of CF patients
- Organised workshops and meetings on multidisciplinary CF patient care at the following international scientific conferences:
 - 31st European CF Conference, Prague, Czech Republic, 11-14 June 2008
 - V4-CF Conference, Kraków, Poland, 20-22 November 2008
 - 4th Congress of the Italian Cystic Fibrosis Society, Torino, Italy, 27-29 November 2008
 - "What's New in the Diagnosis, Treatment and Prevention of Cystic Fibrosis?", First Eastern European CF Conference, Zagreb, Croatia, 28-30 November 2008
 - 32nd European CF Conference, Brest, France, 10-13 June 2009
- Organised the preparation of Deliverable 1a (Recommendations on good standards of care for CF patients) for WP1. This Deliverable includes an overview of the implementation in Europe of the ECFS standards of care for CF patients and consensus guidelines addressing the management of:
 - CF liver disease
 - Distal intestinal obstructive syndrome (DIOS)
 - CF bone disease
 - Psychological issues and
 - The performance of palliative care
- Continued the collection of documents to prepare a teaching package on the multidisciplinary approach to CF patient care
- With WP10, organised the specialist training of European clinicians and healthcare professionals in multidisciplinary CF patient care
- Organised or assisted with the organization of specific training courses in multidisciplinary CF patient care, including:
 - 2009 Balkans Regional CF conference, Skopje, Macedonia, 17-18 April 2009 (organised by CF Worldwide)
 - Workshop about CF Care in Slovakia, CF Center for Children, Children's Faculty Hospital, Košice, Slovakia, 25-28 May, 2009

- In collaboration with CF Worldwide developed a pocket guide to serve as a teaching tool for multidisciplinary CF patient care
- Undertook a variety of dissemination activities for **EuroCareCF**

Workpackage 2. European Cystic Fibrosis Patient Registry:

Period 1:

- Activities of workpackage 2 promoted at international CF conferences
- Identifying the contacts in Europe who will be able and willing to participate and ensuring widespread support for the registry
- Ensuring each participant complies with their local legal and ethical laws with respect to placing patient data in the European registry
- Providing the software for the registry
- Collecting the patient data

Period 2:

- Communicated with representatives of the 40 countries involved in the European CF Patient Registry
- Designed and circulated to all countries a pro-forma to confirm that the ethical and legal requirements of their countries had been met in full
- Made ready for implementation in Europe the registry software PortCF
- Reached agreement with **EuroCareCF**'s partner for the European CF Patient Registry, the European Cystic Fibrosis Society (ECFS) to host the European CF Patient Registry at the ECFS's preferred site to facilitate the long-term development of the Registry.
- In collaboration with the ECFS, begun to collect demographic data from all countries and where available clinical data also
- Explored future funding for the European CF Patient Registry
- Disseminated widely information about the European CF Patient Registry

Period 3:

- Communicated with representatives of the 40 countries involved in the European CF Patient Registry
- Checked and validated all data received from the 40 countries involved in the European Cystic Fibrosis Patient Registry
- When patient data appeared incorrect, prepared error reports for the patient(s) concerned. Communicated errors in patient data to the countries concerned, requesting feedback and comment
- Prepared summary graphs for key demographic variables for (i) each individual countries and (ii) Europe as a whole. Validated and error-checked the analyses for individual countries and Europe as a whole
- Contacted each country to inform them of the results of the analysis of their demographic data and obtain their agreement with the results. Where necessary, the methodology employed and the justification for its use was explained to countries with questions about their summary demographic data
- Confirmed that for the total number of CF patients in the European Cystic Fibrosis Patient Registry (29,095 patients), the inclusion or exclusion of data for deceased CF patients did not exert a statistically significant effect on demographic variables
- Assisted the ECFS with the tasks necessary to evaluate and host the registry software PortCF in Italy in a legally and ethically compliant manner

- In May 2009, the ECFS decided to discontinue its use of PortCF as the registry software. Following this decision, Mrs Gita Mehta has helped to ensure that the design of the replacement software system for the European Cystic Fibrosis Registry complies in full with the legal and ethical constraints determined by **EuroCareCF** and continues to safeguard patient anonymity
- Prepared Deliverable D3c (Report on the demographics of European CF patients) for WP2. For two reasons, this report deserves special mention. First, it includes data for 35 European countries instead of the 22 specified in the technical annex of **EuroCareCF**. Second, demographic data for each country are compared with the data for Europe as a whole, providing a comprehensive overview of the European CF patient population
- Undertook a variety of dissemination activities for **EuroCareCF**

Workpackage 3. Coordination of Clinical Research:

Period 1:

- Activities of workpackage 3 promoted at international CF conferences
- Agree a CF diagnostic algorithm and begin its evaluation in the clinical setting
- Draft a document for discussion on outcome variables for clinical trials
- Initiate discussions with the ECFS about the development of a European clinical trials network for CF
- Plan and organise (i) the distribution of microbial reference material and (ii) a “Hands-On” training course for the molecular identification of microbial pathogens
- Discussion of common guidelines for neonatal screening
- Plan and organize a workshop on CF related diseases

Period 2:

- Evaluated a CF diagnostic algorithm through a pan-European study, which collected standardized anonymous patient data
- Organised a consensus meeting on the standardisation and use of outcome variables in CF clinical trials
- Worked with the European Cystic Fibrosis Society (ECFS) to establish a European Clinical Trials Network for CF
- Cooperated extensively with the ECFS Neonatal Screening Working Group to standardise the interpretation of test results
- Organised a “Hands-On” Training Workshop for Clinical Microbiologists to disseminate best practice in the diagnosis of the microbial pathogens, which cause CF lung disease
- Organised the First European Quality Assurance Trial in CF Microbiology
- In collaboration with BCCM/LMG Bacteria Collection staff (<http://bccm.belspo.be/>), designed, produced and distributed a parcel of microbiological reference cultures to clinical microbiological laboratories in Europe
- Provided support to European CF centres by identifying unusual infectious agents in CF patients
- With WP10, organised the specialist training of European researchers in clinical research
- Prepared outline consensus documents on (i) CF microbiological diagnostics and (ii) the molecular identification of unusual CF microbiological pathogens
- Organised a workshop to discuss the classification, diagnostic criteria and clinical management of CFTR-related diseases

Period 3:

- Organised four Joint Meetings between the Clinical Diagnosis Group of WP3 and the ECFS Diagnostic Network Group at:
 - Hannover Medical School, Hannover, Germany, 15-16 February 2008
 - 31st European CF Conference, Prague, Czech Republic, 11-14 June 2008
 - University of Liverpool, Liverpool, UK, 19-21 February 2009
 - 32nd European CF Conference, Brest, France, 10-13 June 2009
- Published an article in *Thorax* in March 2009 about the evaluation of the CF diagnostic algorithm developed by the Clinical Diagnosis Group using a population of patients with an intermediate clinical phenotype. These patients are identified by sweat Cl⁻ concentration values intermediate between those of CF patients and normal subjects
- Organised a half-day workshop to provide expert training in the use of the nasal potential difference assay to measure CFTR activity *in vivo* prior to the Joint Meeting between the Clinical Diagnosis Group of WP3 and the ECFS Diagnostic Network Group at the University of Liverpool, Liverpool, UK, 19-21 February 2009
- Organised the inaugural meeting of ECFS Clinical Trial Network at the University Hospital Gasthuisberg, Leuven, Belgium, 18-19 September 2008. The aim of this network is to promote efficient and high quality clinical research with the goal of developing new therapies for CF patients.
- Organised meetings of the ECFS Clinical Trial Network before and after the network was officially launched in September 2008. These meetings were held at:
 - 31st European CF Conference, Prague, Czech Republic, 11-14 June 2008
 - 32nd European CF Conference, Brest, France, 10-13 June 2009
- Organised two joint meetings with the the Neonatal Screening Group of WP3 and ECFS Neonatal Screening Working Group. These meetings were held at:
 - 31st European CF Conference, Prague, Czech Republic, 11-14 June 2008
 - 32nd European CF Conference, Brest, France, 10-13 June 2009
- Organised the Consensus Conference “*Cystic Fibrosis Neonatal Screening in Europe: Management, Development, Research*” at Lake Garda, Verona, Italy, 28-29 March 2008. This Consensus Conference gathered a wide spectrum of experts to discuss the implementation of neonatal screening in Europe and a strategy to achieve this goal
- Published Deliverable D7 (Recommendations for neonatal screening in Europe) in the *Journal of Cystic Fibrosis* in February 2009
- Organised a “Hands-On” Training Workshop for Clinical Microbiologists to disseminate best practice in the diagnosis of the microbial pathogens, which cause CF lung disease
- Organised the Second European Quality Assurance Trial in CF Microbiology
- Distributed reports to laboratories participating in the first and second European Quality Assurance Trials in CF Microbiology on their performance in two trials
- Published an article in the *Journal of Clinical Microbiology* about the quality assurance trials of CF microbiology performed in 2007 and 2008, which involved over 30 laboratories from 21 European countries
- In collaboration with BCCM/LMG Bacteria Collection staff (<http://bccm.belspo.be/>), designed, produced and distributed a parcel of microbiological reference cultures to clinical microbiological laboratories in Europe
- Provided support to European CF centres by identifying unusual infectious agents in CF patients
- With WP10, organised the specialist training of European researchers in clinical research
- Prepared consensus guidelines for:
 - Clinical diagnostic procedures in Europe
 - The design, conduct and evaluation of clinical trials
 - The detection and identification of microbiological pathogens using molecular diagnostic techniques

- Neonatal screening in Europe
- The classification of CFTR-related diseases
- Undertook a variety of dissemination activities for **EuroCareCF**

Workpackage 4. Small and Medium-Sized Enterprises (SMEs) Group:

Period 1:

- Activities of workpackage 4 promoted amongst SMEs, clinicians and scientists working in the area of CF and related diseases
- Election of deputy leaders of workpackage
- Production of an online database of European SMEs currently active in the area of CF and related diseases
- Plan and organize with workpackage 5 a partnering meeting for SMEs and academic centres

Period 2:

- Established a virtual network between SMEs and academic centres
- Co-organised with WP5 a partnering meeting between SMEs and academic centres
- Co-organised with WP10 a drug development workshop
- Contributed actively to the development of the European Clinical Trials network

Period 3:

- Co-organised with WP5 and WP10 the **EuroCareCF** Drug Development Workshop at the 31st European CF Conference, Prague, Czech Republic, 11-14 June 2008. This workshop reviewed drug development in Europe from the perspective of three groups: (i) academic researchers, (ii) the pharmaceutical industry and (iii) patient organisations and regulatory authorities
- Organised the **EuroCareCF** Consensus Workshop for SMEs and CF patient organisations at Bad Nauheim, Germany, 20-21 April 2009. This workshop discussed best practice guidelines to govern cooperation between SMEs and CF patient organisations
- Contributed actively to the development of the European Clinical Trials network
- Prepared (i) a report on the needs and obstacles for SMEs working in the area of CF and related diseases and (ii) consensus guidelines for fair and mutually beneficial cooperation between SMEs and CF patient organisations

Workpackage 5. Novel Therapies:

Period 1:

- Activities of WP5 promoted at international CF conferences
- Produce online databases of gene and pharmacological therapies for CF
- Plan and organize with workpackage 4 a partnering meeting for SMEs and academic centers
- Surveyed academic centers and SMEs in Europe willing to provide training in translation research

Period 2:

- Co-organised with WP4 a partnering meeting between SMEs and academic centres
- Co-organised with WP10 a pro-con debate about the treatment of CF lung disease
- Assisted WP4 and WP10 with the organisation of a drug development workshop
- With WP10, organised the specialist training of European researchers in translation research
- Co-authored reviews of gene and pharmacological therapies for CF

Period 3:

- With WP10, organised the specialist training of European researchers in translation research
- Co-organised with WP4 and WP10 the **EuroCareCF** Drug Development Workshop at the 31st European CF Conference, Prague, Czech Republic, 11-14 June 2008
- Organised the Joint **EuroCareCF**-ERS Research Seminar: "*Host-Pathogen Interactions in the Lung: Implications for Treatment of Respiratory Infections and Inflammatory Lung Diseases*" at Davos, Switzerland, 20-22 June 2008. This research seminar discussed actively respiratory infections and their roles in inflammatory lung diseases
- Held a pro-con debate and made symposium presentations to disseminate information about innovative therapies for CF based on a rational understanding of the disease
- Wrote a review on personalised drug therapies for CF patients
- Prepared consensus guidelines on the transfer of innovative therapies for CF from the laboratory to the clinic. These therapies include (i) gene therapy and stem cells, (ii) pharmacological therapy and (iii) antibiotic strategies

Workpackage 6. Animal Models:

Period 1:

- Activities of WP6 promoted at international CF conferences
- Established CF mouse colonies for distribution
- Initiated the updating of consensus guidelines for standard laboratory techniques
- Held meetings to disseminate information about CF mouse models and their role in studies of the pathogenesis of CF

Period 2:

- Maintained colonies of mouse models of CF
- Backcrossed mice onto common well-defined genetic backgrounds
- Provided breeding stock of or tissue samples from CF mice to ordering laboratories
- Established and validated a rapid and reliable PCR genotyping method using ear clips instead of tail tips
- Continued the cryopreservation of CF mouse strains
- With WP10, organized the specialist training of European researchers in the use of mouse models of CF in fundamental and translation research
- Held two workshops to disseminate information about CF mice and their role in studies of the pathogenesis of CF

Period 3:

- Maintained colonies of mouse models of CF
- Backcrossed mice onto common well-defined genetic backgrounds
- Provided breeding stock of or tissue samples from CF mice to ordering laboratories
- Cryopreserved CF mouse strains to ensure their continued availability to the scientific community
- With WP10, organized the specialist training of European researchers in the use of mouse models of CF in fundamental and translation research
- Held workshops, a pro-con debate and made symposium presentations to disseminate information about CF mice and their role in studies of the pathogenesis of CF and the evaluation of new therapies for the disease

- Organised the Joint **EuroCareCF**-ERS Research Seminar: “*Molecular and Cellular aspects of Chronic Lung Disease. Models of Lung Inflammation and Fibrosis, Experimental Therapy*” at Erasmus Medical Center, Rotterdam, The Netherlands, 18-20 June 2009. This research seminar discussed actively the role of animal models in the study of chronic lung disease.
- Co-authored reviews on the use of CF mice in fundamental and translation research
- Prepared consensus guidelines on the use of CF mice in fundamental and translation research
- Undertook a variety of dissemination activities for **EuroCareCF**

Workpackage 7. Integration of Fundamental Research:

Period 1:

- Activities of WP7 promoted at international CF conferences
- Established links with the “CFTR Folding Consortium”, a US group with similar aims and objectives as workpackage 7
- Initiated the development of a repository of CF resources by selecting antibodies for distribution and designing strategies to acquire normal and CF cell lines for CF research
- Implemented training of European researchers in the immortalisation of primary cultures of epithelial cells to produce novel cell lines

Period 2:

- Held a workshop on resources for CF research
- Developed a repository of CF resources (e.g. cell lines and antibodies) and distributed these resources to ordering laboratories
- Coordinated the activities of WP7 with the “CFTR Folding Consortium”, an initiative of the American Cystic Fibrosis Foundation with similar goals to WP7
- Organised a “Hands-On” Training Workshop in Epithelial Biology to disseminate expert tuition in the culture of epithelial cells and their functional evaluation
- With WP10, organized the specialist training of European researchers in fundamental research including the immortalisation of primary cultures of epithelial cells to produce novel cell lines

Period 3:

- Held workshops on “*Fundamental Research*” (Endpoints of CFTR Rescuing Therapies and Cellular Systems for CF Research) at the ECFS Basic Science Conferences in 2008 and 2009
- Coordinated the activities of WP7 with the “CFTR Folding Consortium”, an initiative of the American Cystic Fibrosis Foundation with similar goals to WP7
- With assistance from WP10, surveyed European lung transplant centres about their use of lung transplant tissue and the possibility of using this tissue to produce primary cultures of airway epithelial cells for the European CF community
- Organised the “Hands-On” Training Workshop: “*Epithelial Cells from the Lung: Production, Cultivation and Characterisation*” at the University of Lisboa, Lisboa, Portugal, 14-18 July 2008. This workshop disseminated expert tuition in the primary culture of epithelial cells from lung tissue and their use in fundamental and translation research
- Distributed CF resources (cell lines expressing recombinant CFTR) to ordering laboratories
- Established a collaboration to procure lung transplant tissue from normal subjects and CF patients undergoing lung transplantation. To date, lung has been received from three donors (two non-CF donors and one CF donor) and cells harvested from the two non-CF donors
- With WP10, organized the specialist training of European researchers in fundamental research including the immortalisation of primary cultures of epithelial cells to produce novel cell lines

- Prepared consensus guidelines on good laboratory techniques to be used for the assessment of therapeutic interventions
- Undertook a variety of dissemination activities for **EuroCareCF**

Workpackage 8. Ethical / Legal / Social Issues:

Period 1:

- Guidelines for informed consent to place personal / clinical data into the European CF patient registry completed
- Legislation and ethical literature on the position of minors in clinical research mapped

Period 2:

- Further documented and mapped the legislation on the position of minors in clinical research
- Identified the key ethical issues and principal patient concerns about the participation of minors in clinical research
- Analysed thoroughly the newly drafted EMEA guidelines on the implications of the clinical trials directive in paediatric practice

Period 3:

- Undertook further research on ethics and legislation in Europe relating to the position of minors in clinical research
- Based on the results of their research, elaborated recommendations for the involvement of minors in clinical trials of new therapies for CF
- Prepared a review of ethics and legislation in Europe on clinical trials involving CF minors
- Published articles and a commentary about the key ethical issues and principal patient concerns about the participation of minors in clinical research
- Undertook a variety of dissemination activities for **EuroCareCF**

Workpackage 10. General Coordination:

Period 1:

- Conducted a thorough risk assessment of **EuroCareCF** activities
- Organised Steering and Advisory Committee meetings for **EuroCareCF**
- Designed, produced and distributed **EuroCareCF** report forms
- Designed, produced and quarterly updated **EuroCareCF** website
- Design, production and wide dissemination of a **EuroCareCF** newsletter, published quarterly in English
- Produced a generic MTA for dissemination of **EuroCareCF** resources
- Drafted application and reporting forms for **EuroCareCF** training grants
- Arranged the change of **EuroCareCF** participant from P3 to P22
- Undertook a wide variety of dissemination activities for **EuroCareCF**

Period 2:

- Organised Steering and Advisory Committee meetings for **EuroCareCF**
- Research, tested and implemented an effective telenetworking service for **EuroCareCF** participants
- Distribution, collection and review of **EuroCareCF** reporting forms at 6 monthly intervals, including assessment and mitigation of project risk

- Quarterly updated **EuroCareCF** website (www.eurocarecf.eu)
- Design, production and wide dissemination of a **EuroCareCF** newsletter, published quarterly in English
- The organisation of **EuroCareCF** workshops and meetings
- Administered **EuroCareCF** Training Grants, including review, award, reimbursement and reports; disseminated widely information about these training grants
- Administered **EuroCareCF** Travel Grants to attend the “Hands-On” Training Course in Epithelial Biology, including drafting and distributing forms, reviewing applications, awarding grants, collection of reports and reimbursement of expenses. Negotiated further travel grants for course participants from national CF associations
- Researched, drafted and distributed Deliverable 18 to **EuroCareCF** participants
- Assisted WP2 with its negotiations with the ECFS to secure the long-term future of the European CF Patient Registry after the end of the **EuroCareCF** project
- Arranged changes to the **EuroCareCF** consortium
- Undertook a wide variety of dissemination activities for **EuroCareCF**

Period 3:

- Organised Steering and Advisory Committee meetings for **EuroCareCF**
- Provided telenetworking service for **EuroCareCF** participants; used service to host Steering Committee and individual workpackage meetings
- Distribution, collection and review of **EuroCareCF** reporting forms at 6 monthly intervals, including assessment and mitigation of project risk
- Quarterly updated **EuroCareCF** website (www.eurocarecf.eu)
- Design, production and wide dissemination of a **EuroCareCF** newsletter, published quarterly in English
- The organisation of **EuroCareCF** workshops and meetings
- Administered **EuroCareCF** Training Grants, including reviewing applications, awarding grants, collection of reports and reimbursement of expenses; disseminated widely information about these training grants
- Administered **EuroCareCF** Travel Grants to attend meetings and “Hand-On” training courses, including reviewing applications, awarding grants, collection of reports and reimbursement of expenses. Negotiated further travel grants for participants of “Hand-On” training courses from national CF associations
- Designed and distributed a questionnaire to European lung transplant centres about the production of primary cultures and novel cell lines from lung transplant tissue. Analysed the results of the survey
- Wrote a review on small molecule CFTR modulators, contributed towards a second review
- Organised the publication of consensus guidelines and reports for WP1, WP2, WP3, WP4, WP5, WP6 and WP8 in supplements to the *Journal of Cystic Fibrosis*
- Contributed to the preparation of consensus guidelines for WP3, WP5 and WP6
- Researched, drafted and distributed Deliverables 28 and 29
- Assisted WP2 with its negotiations with the ECFS to secure the long-term future of the European CF Patient Registry after the end of the **EuroCareCF** project
- Arranged changes to the **EuroCareCF** consortium
- Undertook a wide variety of dissemination activities for **EuroCareCF**

1.6. End Results:

The achievements of the different workpackages were as follows:

Workpackage 1. Optimising Patient Care & CF Team Work:

Deliverable 1a: Recommendations on good standards of care for CF patients

- Recommendations for the implementation of good standards of care for CF patients in Europe, based on an analysis of standards of care in 27 European countries
- Petitioned the governments of the Visegrad Group of countries (Czech Republic, Hungary, Poland and Slovakia) to implement the ECFS standards of care for CF patients
- New consensus guidelines to address specific aspects of CF patient care including CF-associated liver disease, distal intestinal obstructive syndrome (DIOS), CF bone disease, psychological issues and palliative care

Deliverable 1b: Specialist training in CF Team Work

- Specialist training of European clinicians and healthcare professionals in multidisciplinary CF patient care, including
 - Conferences and meetings (7 events)
 - Individual training visits (12 visits)
 - One-to-One training of all staff in team providing CF patient care (staff at Košice, Slovakia trained on-site in Košice by staff from Göteborg, Sweden)
- With CF Worldwide, the development of a pocket guide teaching tool for multidisciplinary CF patient care

Deliverable 2: Establishment of a clinical network for each speciality

- The development of European networks for clinicians and healthcare professionals involved in the care of CF patients, as follows:
 - Clinicians: 376 clinicians from 30 European countries
 - Specialist Nurses: 204 specialist nurses from 14 European countries
 - Physiotherapists: 60 physiotherapists with an average of 2 per country
 - Psychologists: 42 psychologists and psychiatrists from 6 European countries
 - Dieticians: 35 dieticians from 10 European countries
 - Patient Advocate: 25 national CF Associations are members of CF Europe (www.cfww.org/cfe/)

Workpackage 2. European Cystic Fibrosis Patient Registry:

Deliverable 3a: Secure, industry-standard software for a registry of CF patients in Europe

Deliverable 3b: Collection of consent-driven anonymised patient data for a registry of CF patients in Europe

- The development of a European CF Patient Registry with the European Cystic Fibrosis Society (ECFS) involving 40 countries (instead of the 22 specified in the Technical Annex of EuroCareCF)
- Collected demographic data on 29,095 CF patients from 35 European countries to populate the European CF Patient Registry
- Handed over the European CF Patient Registry to the ECFS at the end of the EuroCareCF project to ensure the long-term future of the invaluable patient database. The handover from EuroCareCF to the ECFS was fully compliant with all legal and ethical procedures

Deliverable 3c: Report on the demographics of European CF patients

- A report on the demographics of European CF patients. For two reasons, this comprehensive overview of the European CF patient population deserves special mention:
 - It summarises demographic data for 35 European countries
 - Data for each individual country are compared with the data for Europe as a whole

- The report includes demographic data for 29,095 patients from 35 European countries
- The countries contributing data were: Armenia, Austria, Belarus, Belgium, Bosnia, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, France, Georgia, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Latvia, Lithuania, Macedonia, Moldova, Netherlands, Portugal, Romania, Russia, Serbia, Slovakia, Slovenia, Sweden, Turkey, Ukraine and United Kingdom
- An article accepted for publication by the *Lancet* analysing the effect of EU membership on the demographics of the European CF patient population

Workpackage 3. Coordination of Clinical Research:

Deliverable 4a: Identification, development, improvement and validation of new clinical diagnostic procedures in Europe

- Validation of the European diagnostic algorithm for CF by comparison of the phenotype of patients with intermediate sweat Cl⁻ values and evidence of CFTR dysfunction (CFTR dysfunction group) with the phenotype of individuals with intermediate sweat Cl⁻ values and no further evidence of CFTR dysfunction (CF unlikely group).
- Consensus guidelines on New clinical diagnostic procedures for CF in Europe, which include a review of the steps taken to standardise the performance in Europe of the nasal potential difference assay and the intestinal current measurement technique

Deliverable 4b: Specialist Training in CFTR Bioassays for CF Diagnosis

- The specialist training of European researchers in clinical research, especially the nasal potential difference assay (2 workshops)

Deliverable 5: Recommendations for design, conduct and evaluation of clinical trials

- In collaboration with the ECFS, the establishment of a European Clinical Trial Network to perform high quality clinical research, which efficiently evaluates new therapies for CF patients. At the present time, the ECFS-CTN is composed of 18 centres from 8 European countries together with supporting structures including an Executive Committee, Coordinating Centre and different subcommittees. A code of conduct for interactions with pharmaceutical companies has been elaborated and standardized information provided to companies about the network. Protocol review will improve the quality and feasibility of clinical studies undertaken by the network. Moreover, standardization of outcome parameters will lead to uniform conduct and improved quality performance of clinical trials. A strong partnership with CF patient organisations will increase awareness of the need for efficient clinical research to identify better therapies faster and likely improve patient participation in clinical research
- The development of consensus statements on outcome variables in CF clinical trials, including:
 - Pulmonary exacerbations
 - Chronic *Pseudomonas aeruginosa* infection
 - Health-related quality of life (HRQoL)
 - Nasal potential difference (nasal PD) measurements

Deliverable 6a: Establishment of a European network of reference laboratories for molecular typing of microbiological specimens

- In collaboration with BCCM/LMG Bacteria Collection staff (<http://bccm.belspo.be/>), designed and produced microbiological reference strains (25 uncommon, difficult to identify bacteria that infect CF patients) to be distributed to ordering laboratories
- Distributed 50 parcels of microbiological reference strains to clinical microbiological laboratories in 21 European countries, Australia and the USA
- The specialist training of European Clinical Microbiologists in the diagnosis of microbial pathogens causing CF lung disease, including:
 - “Hands-On” training courses (2 event)
 - Individual training visits (4 visits)
- Organised the first European Quality Assurance Trials of CF Microbiology:

- Trial 1: 53 European clinical microbiological laboratories invited to participate. 33 laboratories from 19 European countries agreed to participate with 31 laboratories completing the trial
 - Trial 2: 61 European clinical microbiological laboratories invited to participate. 40 laboratories from 19 European countries agreed to participate with 37 laboratories completing the trial
 - The results of the trials suggest a continuum of quality for the clinical microbiological laboratories serving European CF centres. This gradient of quality is determined by the availability of resources and by domestic clinical microbiology quality control guidelines. It is not affected by CF microbiology research
 - The recommendations from the trials are further quality assurance trials, education in CF microbiology and possibly the setting up of CF microbiology reference laboratories
- Reference laboratory support for the molecular identification of unusual CF pathogens. Assisted CF centres from 12 European countries as well as centres in Canada, India, the United Arab Emirates and the USA

Deliverable 6b: Consensus guidelines for the detection and identification of microbiological pathogens using molecular diagnostics

- European consensus guidelines on the processing of respiratory specimens from cystic fibrosis patients for clinical microbiology

Deliverable 7: Recommendations for neonatal screening in Europe

- European best practice guidelines for cystic fibrosis neonatal screening

Deliverable 8: Recommendations for the classification of diseases as CFTR-related

- Recommendations for the classification of diseases as CFTR-related. These consensus guidelines propose a definition for CFTR-related diseases based on clinical and genetic data as well as the effects of disease-causing mutations on CFTR function

Workpackage 4. Small and Medium-Sized Enterprises (SMEs) Group:

Deliverable 9: Report on the needs and obstacles for SME activities (e.g. to place 'orphan drugs' into clinical trials)

- A virtual network of SMEs working in the CF area (14 SMEs from 8 countries)
- A report on the needs and obstacles for SMEs working in the area of CF and related diseases. This report highlights areas of action for the CF community and regulatory agencies and proposes ideas to stimulate collaboration between SMEs and the CF community. The conclusions reached in the report are likely to be highly relevant to SMEs developing new therapies for other rare diseases.

Deliverable 10: Consensus document on medical needs of CF patients and policies for fair and mutually beneficial co-operation between SMEs and patient organisations

- A report on the common interests of SMEs and patient organisations in mutually beneficial cooperation. This report identifies critical unmet medical needs of CF patients and analyzes potential areas for cooperation between SMEs and patient organisations.

Deliverable 11: Reports on three annual partnering meetings on opportunities for co-operation between SMEs and academic centres

- One partnering meeting organized, which was attended by representative of 13 academic centres and 11 SMEs. Because the needs of the SMEs did not match those of the academic centres, no partnerships between SMEs and academic centres were established
- The needs of SMEs (clinical research partners to set up clinical trials) were addressed by the developed of the European Cystic Fibrosis Society Clinical Trial Network (ECFS-CTN).
- The needs of academic centres (the development of novel therapeutics) are less easy to address. **EuroCareCF** recommend the development of funding programmes to enable academic researchers to conduct translation research.

Workpackage 5. Novel Therapies:

Deliverable 12a: Consensus guidelines for the transfer of innovative therapies (gene or drug) for CF from research laboratories to clinical trials

- Consensus guidelines on the transfer of novel therapies for CF from the laboratory to the clinic:
 - Gene therapy and stem cells
 - Pharmacological therapy
 - Antibiotic strategies for the treatment of CF lung disease

Deliverable 12b: Specialist training in translation research

- The specialist training of European researchers in translation research, including
 - Individual training visits (4 visits)

Workpackage 6. Animal Models:

Deliverable 13: Colonies of CF mice for their distribution to ordering laboratories for fundamental and translation research

- Maintained colonies of different mouse models of CF, including:
 - Strains bearing F508del-CFTR, the most common CF mutation (Cftr^{tm1eur} and Cftr^{tm2cam} mouse strains) on the FVB, C57Bl/6 and 129/Sv genetic backgrounds
 - CFTR knockout (Cftr^{tm1cam}) mice
 - The Tg(CMV-tetO-CFTR)TC35CH mouse, which carries a tetracycline-inducible human CFTR transgene
 - β ENaC overexpressing mice (Tg CCSPScnb1) on the C57Bl6xC3H genetic background
- Distributed CF mice to 16 ordering laboratories in Europe, North America and South America
- Distributed tissue samples to 13 ordering laboratories in Europe and North America
- Cryopreserved CF mice to ensure that this invaluable resource is preserved, including:
 - Strains bearing F508del-CFTR, the most common CF mutation (Cftr^{tm1eur} and Cftr^{tm2cam} mouse strains) on the FVB, C57Bl/6 and 129/Sv genetic backgrounds
 - CFTR knockout (Cftr^{tm1cam}) mice
 - The Tg(CMV-tetO-CFTR)TC35CH mouse, which carries a tetracycline-inducible human CFTR transgene

Deliverable 14a: Consensus guidelines for standard laboratory techniques using CF mouse models

- Consensus guidelines on the use of CF mice in fundamental and translation research:
 - The use of mice bearing CF mutations in studies of the disease pathogenesis and therapy evaluation
 - The β ENaC-overexpressing mouse as a model of cystic fibrosis lung disease

Deliverable 14b: Specialist training in the use of animal models for CF research

- The specialist training of European researchers in the use of mouse models of CF in fundamental and translation research, including:
 - Workshop on animal models of chronic lung disease (1 event)
 - Individual training visits (12 visits)

Workpackage 7. Integration of Fundamental Research:

Deliverable 15: A physical repository of CF resources for fundamental and translation research that will distribute resources to ordering laboratories

- Anti-CFTR antibodies and CFTR-expressing cell lines acquired to establish a repository of CF resources for fundamental and translation research
- Produced primary cultures of airway epithelial cells from 2 normal subjects
- Distributed anti-CFTR antibodies to 5 ordering laboratories in Europe and North America
- Distributed CFTR-expressing cells to 6 ordering laboratories in Europe and North America

- Surveyed European lung transplant centres about their performance of lung transplants for CF patients and the use of lung tissue removed from transplant recipients
- Organised two “Hands-On” training courses to disseminate best practice in the primary culture of epithelial cells from lung tissue and their use in fundamental and translation research

Deliverable 16a: Publication in a peer-reviewed journal of consensus guidelines for good laboratory techniques to be used for the assessment of therapeutic interventions

- Consensus guidelines for the measurement of epithelial ion transport in rectal biopsies from normal subjects and individuals with cystic fibrosis

Deliverable 16b: Specialist training in laboratory techniques to assess therapeutic interventions

- The specialist training of European researchers in fundamental research, including:
 - “Hands-On” training courses (9 grants to support student participation)
 - Individual training visits (4 visits)

Workpackage 8. Ethical / Legal / Social Issues:

Deliverable 19: Guidelines for the introduction of informed consent to place personal / clinical data in the Registry

- European CF Patient Registry designed to be fully compliant with all legal and ethical procedures
- Registry protocols designed to ensure that patient anonymity is guaranteed while retaining the research potential of the data

Deliverable 20: Review of ethics and legislation on clinical trials involving CF minors

- Published articles discussing the key ethical issues and principal patient concerns about the participation of minors in clinical research (3 articles and 1 commentary to date)
- A review of ethics and legislation in Europe on clinical trials involving CF minors including recommendations for harmonising legislation across Europe (1 review)
- Initiated an empirical study of informed consent for paediatric clinical research to:
 - Empirically document the actual course of informed consent discussions for participation in paediatric clinical research
 - Map the operational implementation of the ethical and regulatory frameworks governing paediatric research practice
 - Analyze decision making processes for the enrollment of minors in paediatric clinical practice

1.7. Degree to Which Objectives Achieved:

The project’s Deliverables relating to CF research and patient care were satisfied in full. Indeed, in several instances the achievements of different workpackages exceeded greatly their programme of work specified in Annex I. For example, Workpackage 2 developed a European CF Patient Registry for 40 European countries instead of the 22 countries specified in Annex I. Workpackage 3 established a European Clinical Trial Network and organised the first quality assurance trials of CF microbiology.

1.8. Methodologies and Approaches Employed:

The methodologies used were two-fold.

To discuss consensus guidelines, EuroCareCF organised workshops and meetings. By contrast specialist training in different areas of CF research and patient care involved dedicated training in either a laboratory or clinical setting.

1.9. Relationship of the Project Achievements to State-of-th-Art:

The project’s achievements are consistent with the current state-of-the-art in the CF field.

1.10. Impact of Project on Its Industry or Research Sector:

The activities of EuroCareCF will have a lasting effect on CF research and patient care.

SECTION 2 – DISSEMINATION AND USE

2.1. Published Results:

Over the course of the project, participants and collaborators of **EuroCareCF** have published outputs of the project in a variety of formats. These include consensus guidelines, original articles and reviews all published in international, peer-reviewed scientific journals. Other project publications include the handbooks of “Hands-On” training courses, the **EuroCareCF** Newsletter (11 issues) and the project website (<http://www.eurocarecf.eu/>).

Below, we list published outputs of the project during the project period:

Period 1:

EuroCareCF Newsletter:

Issue 1, June 2006.

Issue 2, September 2006.

Issue 3 (Workpackage 2), December 2006.

Period 2:

Reviews:

Scholte BJ, Colledge WH, Wilke M, de Jonge H (2006). Cellular and animal models of cystic fibrosis, tools for drug discovery. *Drug Discov Today Dis Models* **3**: 251-259.

Li H, Cai Z, Chen J-H, Ju M, Xu Z, Sheppard DN (2007). The cystic fibrosis transmembrane conductance regulator Cl⁻ channel: a versatile engine for transepithelial ion transport. *Sheng Li Xue Bao* **59**: 416-430.

Mall MA (2008). Role of Cilia, Mucus, and Airway Surface Liquid in Mucociliary Dysfunction: Lessons from Mouse Models. *J Aerosol Med* **21**: 1-12.

Course Handbooks:

A course handbook (Lectures and Laboratory Techniques) was produced for the “Hands-On” Training Course for Clinical Microbiologists: “*Diagnostic and Molecular Microbiology of Bacteria Retrieved from the CF Lung Habitat*” at Hannover Medical School, Hannover, Germany, 3-6 May 2007.

Two course handbooks (Lectures and Laboratory Techniques) were produced for the “Hands-On” Training Workshop: “*Epithelial Cells & Tissues: Production, Cultivation and Characterization*” at the University of Lisboa, Lisboa, Portugal, 2-6 July 2007. These handbooks are available on the **EuroCareCF** website (<http://www.eurocarecf.eu/wp7/WP7workshopsheld.htm>).

EuroCareCF Newsletter:

Issue 4, April 2007.

Issue 5, July 2007.

Issue 6 (Workpackage 3), October 2007.

Period 3:

Consensus Guidelines:

Workpackage 3. Coordination of Clinical Research:

Deliverable 7: Recommendations for neonatal screening in Europe

Castellani C, Southern KW, Brownlee K, Dankert Roelse J, Duff A, Farrell M, Mehta A, Munck A, Pollitt R, Sermet-Gaudelus I, Wilcken B, Ballmann M, Corbetta C, de Monestrol I, Farrell P, Feilcke M, Férec C, Gartner S, Gaskin K, Hammermann J, Kashirskaya N, Loeber G, Macek M Jr, Mehta G, Reiman A, Rizzotti P, Sammon A, Sands D, Smyth A, Sommerburg O, Torresani T, Travert G,

Vernooij A, Elborn S. (2009). European best practice guidelines for cystic fibrosis neonatal screening. *J Cyst Fibros*. **8**:153-173.

Articles:

Goubau C, Wilschanski M, Skalická V, Lebecque P, Southern KW, Sermet I, Munck A, Derichs N, Middleton PG, Hjelte L, Padoan R, Vasar M, De Boeck K. (2009). Phenotypic characterisation of patients with intermediate sweat chloride values: towards validation of the European diagnostic algorithm for cystic fibrosis. *Thorax*. **64**:683-691.

Hogardt M, Ulrich J, Riehn-Kopp H, Tümmler B. (2009). EuroCareCF quality assessment of diagnostic microbiology of cystic fibrosis isolates. *J Clin Microbiol*. **47**:3435-3438.

Pinxten W, Dierickx K, Nys H. (2008). The implementation of Directive 2001/20/EC into Belgian law and the specific provisions on pediatric research. *Eur J Health Law*. **15**:153-161.

Pinxten W, Nys H, Dierickx K. (2008). Regulating trust in pediatric clinical trials. *Med Health Care and Philos* **11**:439-444.

Pinxten W, Nys H, Dierickx K. (2009). Ethical and regulatory issues in pediatric research supporting the non-clinical application of fMR imaging. *Am J Bioeth*. **9**:21-23.

Pinxten W, Dierickx K, Nys H. (2009). Ethical principles and legal requirements for pediatric research in the EU: an analysis of the European normative and legal framework surrounding pediatric clinical trials. *Eur J Pediatr*. **168**:1225-1234.

McCormick J, Mehta G, Olesen HV, Viviani L, Macek M Jr, Mehta A, on behalf of the European Cystic Fibrosis Registry (2009). Comparative demographics of the European cystic fibrosis population: Does EU membership confer an advantage? *Lancet* (**Accepted**).
(This publication will be the subject of a press release by the University of Dundee)

Reviews:

Carvalho-Oliveira I, Scholte BJ, Penque D. (2007). What have we learned from mouse models for cystic fibrosis? *Expert Rev Mol Diagn*. **7**:407-417.

Johannesson M, Olesen HV, Mehta G, Mehta A. (2007). Setting up a European registry for cystic fibrosis – lessons learned. *Eur Respir Dis* **2007**, 25-26.

Mall MA. (2009). Role of the amiloride-sensitive epithelial Na⁺ channel in the pathogenesis and as a therapeutic target for cystic fibrosis lung disease. *Exp Physiol*. **94**:171-174.

Li H, Sheppard DN. (2009). Therapeutic potential of cystic fibrosis transmembrane conductance regulator (CFTR) inhibitors in polycystic kidney disease. *BioDrugs*. **23**:203-216.

Becq F. (2010). Cystic fibrosis transmembrane conductance regulator modulators for personalized drug treatment of cystic fibrosis: progress to date. *Drugs* **70**:241-259.

Publications using resources produced by EuroCareCF:

Jouret F, Bernard A, Hermans C, Dom G, Terryn S, Leal T, Lebecque P, Cassiman JJ, Scholte BJ, de Jonge HR, Courtoy PJ, Devuyst O. (2007). Cystic fibrosis is associated with a defect in apical receptor-mediated endocytosis in mouse and human kidney. *J Am Soc Nephrol*. **18**:707-718.

Bonvin E, Le Rouzic P, Bernaudin JF, Cottart CH, Vandebrouck C, Crié A, Leal T, Clement A, Bonora M. (2008). Congenital tracheal malformation in cystic fibrosis transmembrane conductance regulator-deficient mice. *J Physiol*. **586**:3231-3243.

Noël S, Strale PO, Dannhoffer L, Wilke M, DeJonge H, Rogier C, Mettey Y, Becq F. (2008). Stimulation of salivary secretion *in vivo* by CFTR potentiators in *Cftr*^{+/+} and *Cftr*^{-/-} mice. *J Cyst Fibros*. **7**:128-133.

Noël S, Wilke M, Bot AG, De Jonge HR, Becq F. (2008). Parallel improvement of sodium and chloride transport defects by miglustat (*n*-butyldeoxyynojiramicin) in cystic fibrosis epithelial cells. *J Pharmacol Exp Ther.* **325**:1016-1023.

Ohlsson L, Hjelte L, Hühn M, Scholte BJ, Wilke M, Flodström-Tullberg M, Nilsson Å. (2008). Expression of intestinal and lung alkaline sphingomyelinase and neutral ceramidase in cystic fibrosis F508del transgenic mice. *J Pediatr Gastroenterol Nutr.* **47**:547-554.

Carvalho-Oliveira IM, Charro N, Aarbiou J, Buijs-Offerman RM, Wilke M, Schettgen T, Kraus T, Titulaer MK, Burgers P, Luider TM, Penque D, Scholte BJ. (2009). Proteomic analysis of naphthalene-induced airway epithelial injury and repair in a cystic fibrosis mouse model. *J Proteome Res.* **8**:3606-3616.

Gavilanes X, Huaux F, Meyer M, Lebecque P, Marbaix E, Lison D, Scholte B, Wallemacq P, Leal T. (2009). Azithromycin fails to reduce increased expression of neutrophil-related cytokines in primary-cultured epithelial cells from cystic fibrosis mice. *J Cyst Fibros.* **8**:203-210.

Meyer M, Huaux F, Gavilanes X, van den Brûle S, Lebecque P, Lo Re S, Lison D, Scholte B, Wallemacq P, Leal T. (2009). Azithromycin reduces exaggerated cytokine production by M1 alveolar macrophages in cystic fibrosis. *Am J Respir Cell Mol Biol.* **41**:590-602.

Course Handbooks:

A course handbook (Lectures and Laboratory Techniques) was produced for the "Hands-On" Training Course for Clinical Microbiologists: "On the Processing of Microbiological Specimens from Individuals with CF" at Hannover Medical School, Hannover, Germany, 10-13 April 2008.

Two course handbooks (Lectures and Laboratory Techniques) were produced for the "Hands-On" Training Workshop: "Epithelial Cells from the Lung: Production, Cultivation and Characterisation" at the University of Lisboa, Lisboa, Portugal, 14-18 July 2008.

EuroCareCF Newsletter:

Issue 7, January 2008.

Issue 8, May 2008.

Issue 9-10, December 2008.

Issue 11, May 2009.

2.2. Forthcoming Publications:

The majority of the consensus guidelines and reports produced by **EuroCareCF** will be published in two supplements to the *Journal of Cystic Fibrosis* following peer-review. Because of the size of Deliverable 3c (Report on the demographics of European CF patients), which compares demographic data for 35 European countries with demographic data for the whole of Europe, this Deliverable will be published as a single supplement. The other supplement will contain the consensus guidelines and reports of Workpackages 1, 3, 4, 5, 6 and 8. The supplements have been edited by Dr. David N. Sheppard, the Coordinator of **EuroCareCF** and they will contain Perspectives to highlight the impact of the consensus guidelines and reports on CF research and patient care.

To ensure that the **EuroCareCF** consensus guidelines and reports are disseminated as widely as possible, electronic copies of these documents will be posted on the websites of **EuroCareCF** and the European Cystic Fibrosis Society (ECFS) immediately upon their publication, where they will be freely available. To draw attention to the **EuroCareCF** consensus guidelines and reports, Workpackage 10 of **EuroCareCF** plans a number of actions. These include (i) a final issue of the **EuroCareCF** Newsletter highlighting outputs of the project distributed electronically to all members of the ECFS; (ii) leaflets distributed to delegates of the 33rd European CF conference, Valencia, Spain, 16-19 June, 2010 and the 24th North American Cystic Fibrosis Conference, Baltimore, USA, 21-23 October 2010; (iii) an article about the consensus guidelines and reports for CFCenters.com, a social networking site for CF healthcare professionals.

Consensus Guidelines:

EuroCareCF Supplement 1 for Journal of Cystic Fibrosis:

Workpackage 2. European Cystic Fibrosis Patient Registry:

Deliverable 3c: Report on the demographics of European CF patients

Mehta G, Macek M, Mehta A. (2010). Demographics of cystic fibrosis in Europe: graphical analyses of data from 35 countries. *J Cyst Fibros.* (**Submitted**).

EuroCareCF Supplement 2 for Journal of Cystic Fibrosis:

Workpackage 1. Optimising Patient Care & CF Team Work:

Deliverable 1a: Recommendations on good standards of care for CF patients

Colombo C, Littlewood J. (2010). The implementation of standards of care in Europe: state of the art. *J Cyst Fibros.* (**Submitted**).

Debray D, Kelly D, Houwen RH, Strandvik B, Colombo C. (2010). Best practice guidance for the diagnosis and management of CF-associated liver disease. *J Cyst Fibros.* (**Submitted**).

Colombo C, Ellemunter H, Houwen RH, Munck A, Taylor CJ, Wilschanski M on behalf of the ECFS. (2010). Guidelines for the diagnosis and management of distal intestinal obstruction syndrome in cystic fibrosis patients. *J Cyst Fibros.* (**Submitted**).

Sermet I, Haworth CS. (2010). Prevention and management of bone disease in CF patients. *J Cyst Fibros.* (**Submitted**).

Nobili R, Smrekar U, Ullrich G, Havermans T, Bryon M. (2010). Guidelines for good psychological care of CF patients. *J Cyst Fibros.* (**Submitted**).

Sands D, Repetto T, Korzeniewska-Eksterowicz A, Madge S, Catastini P. (2010). Standards of palliative care for people with cystic fibrosis. *J Cyst Fibros.* (**Submitted**).

Workpackage 3. Coordination of Clinical Research:

Deliverable 4a: Identification, development, improvement and validation of new clinical diagnostic procedures in Europe

De Boeck K, Derichs N, Fajac I, de Jonge HR, Bronsveld I, Sermet I, Vermeulen F, Cuppens H, Hug M, Melotti P, Middleton PG, Wilschanski W on behalf of the ECFS Diagnostic Network Working Group and the EuroCareCF WP3 Group on CF diagnosis. (2010). New clinical diagnostic procedures for CF in Europe. *J Cyst Fibros.* (**Submitted**).

Deliverable 5: Recommendations for design, conduct and evaluation of clinical trials

De Boeck K, Bulteel V, Tiddens H, Wagner T, Fajac I, Conway S, Dufour F, Smyth A, Lee T, Sermet I, Kassai-Koupai B, Elborn S on behalf of all ECFS-CTN network partners. (2010). Guideline on the design and conduct of CF clinical trials: the European Cystic Fibrosis Society Clinical Trial Network (ECFS-CTN). *J Cyst Fibros.* (**Submitted**).

Bilton D, Canny G, Conway S, Dumcius S, Hjelte L, Proesmans M, Tümmler B, Vavrova V, De Boeck K. (2010). Pulmonary exacerbation: towards a definition for use in clinical trials. Report from the EuroCareCF Working Group on Outcome Parameters in Clinical Trials. *J Cyst Fibros.* (**Submitted**).

Pressler T, Bohmova C, Conway S, Dumcius S, Hjelte L, Høiby N, Kollberg H, Tümmler B, Vavrova V. (2010). Chronic *Pseudomonas aeruginosa* infection definition: EuroCareCF Working Group report. *J Cyst Fibros.* (**Submitted**).

Abbott J, Hart A, Havermans T, Matossian A, Goldbeck L, Staab D, Barreto C, Bergsten-Brucefors A, Besier T, Catastini P, Lupi F. (2010). Measuring health-related quality of life in clinical trials in Cystic Fibrosis. *J Cyst Fibros.* (**Submitted**).

Deliverable 8: Recommendations for the classification of diseases as CFTR-related

Ferec C, Bareil C, Bombieri C, Castellani C, Claustres M, Cuppens H, Cutting G, De Boeck K, Derichs N, Dodge J, Drevinek P, Durie P, Elborn S, Farrell P, Girodon E, Gonska T, Jarvi K, Kerem B, Kerem E, Knowles M, Macek M, Munck A, Radojkovic D, Sermet I, Schwarz M, Sheppard DN, Stuurman M, Southern K, Tullis E, Tzetzis M, Wilshanski M, Zielenski J, Pignatti PF. (2010). Recommendations for the classification of diseases as CFTR-related. *J Cyst Fibros.* (**Submitted**).

Workpackage 4. Small and Medium-Sized Enterprises (SMEs) Group:

Deliverable 9: Report on the needs and obstacles for SME activities (e.g. to place 'orphan drugs' into clinical trials)

Schlangen M, Reimann ALG. (2010). Developing new products for patients with cystic fibrosis: needs and obstacles for activities of small and middle-sized companies. *J Cyst Fibros.* (**Submitted**).

Deliverable 10: Consensus document on medical needs of CF patients and policies for fair and mutually beneficial co-operation between SMEs and patient organisations

Schlangen M, Reimann ALG. (2010). Medical needs of CF patients and policies for a fair and mutually beneficial co-operation between SMEs and patient organizations. *J Cyst Fibros.* (**Submitted**).

Workpackage 5. Novel Therapies:

Deliverable 12a: Consensus guidelines for the transfer of innovative therapies (gene or drug) for CF from research laboratories to clinical trials

Conese M, Ascenzioni F, Boyd AC, Coutelle C, De Fino I, de Smedt S, Rejman J, Rosenecker J, Schindelbauer D, Scholte BJ. (2010). Gene and cell therapy for cystic fibrosis: from bench to bedside. *J Cyst Fibros.* (**Submitted**).

Becq F, Mall MA, Sheppard DN, Conese M, Zegarra-Moran O. (2010). Pharmacological therapy for cystic fibrosis: from bench to bedside. *J Cyst Fibros.* (**Submitted**).

Bals R, Hubert D, Tümmler B. (2010). Antibiotic strategies for treatment of CF lung disease: from bench to bedside. *J Cyst Fibros.* (**Submitted**).

Workpackage 6. Animal Models:

Deliverable 14a: Consensus guidelines for standard laboratory techniques using CF mouse models

Wilke M, Buijs-Offerman R, Aarbiou J, Colledge WH, Sheppard DN, Touqui L, Bot A, Jorna H, de Jonge HR, Scholte BJ. (2010). Animal models of cystic fibrosis, phenotypic analysis and applications. *J Cyst Fibros.* (**Submitted**).

Zhou Z, Duerr J, Johannesson B, Schubert SC, Treis D, Harm M, Graeber SY, Dalpke A, Schultz C, Mall MA. (2010). The β ENaC-overexpressing mouse as a model of cystic fibrosis lung disease. *J Cyst Fibros.* (**Submitted**).

Workpackage 8. Ethical / Legal / Social Issues:

Deliverable 20: Review of ethics and legislation on clinical trials involving CF minors

Pinxten W, Dierickx K, Nys H. (2010). Diversified harmony: supranational and domestic regulation of pediatric clinical trials in the EU. *J Cyst Fibros.* (**Submitted**).

In the case of the consensus guidelines of Workpackage 7 (Integration of Fundamental Research), Prof. Margarida D. Amaral and Dr. Martin J. Hug arranged with Dr. David N. Sheppard for these guidelines to be published separately in the reference book "*Cystic Fibrosis Protocols and Diagnosis*", a volume in the "*Methods in Molecular Medicine*" series edited by Profs. Margarida D. Amaral (University of Lisboa; P2) and Karl Kunzelmann (University of Regensburg). *Cystic Fibrosis Protocols and Diagnosis* will be published in 2010 by Humana Press Inc., Totowa, New Jersey, USA. This reference book will contain good laboratory protocols for a wide-range of experimental methods used in CF research, including fundamental, translation and clinical research. The protocols will contain a level of technical detail rarely seen in published articles.

Workpackage 7. Integration of Fundamental Research:

Deliverable 16a: Publication in a peer-reviewed journal of consensus guidelines for good laboratory techniques to be used for the assessment of therapeutic interventions

Hug MJ, Derichs N, Bronsveld I, Clancy JP. (2010). Measurement of ion transport function in rectal biopsies. In *Cystic Fibrosis Protocols and Diagnosis, Methods in Molecular Medicine*, Volume Editors: Amaral MD, Kunzelmann K. Humana Press Inc., Totowa, New Jersey, USA. **(Submitted)**.

Besides the above consensus guidelines, “*Cystic Fibrosis Protocols and Diagnosis*” will contain a number of other chapters co-authored by participants and collaborators of **EuroCareCF**. These include:

Design of gene therapy trials in CF patients
Davies JC, Alton EFW

Nasal potential difference measurements to assess CFTR ion channel activity
Rowe SM, Clancy JP, Wilschanski M

Application of high-resolution single-channel recording to functional studies of cystic fibrosis mutants and small molecule CFTR modulators
Cai Z, Sohma Y, Bompadre SG, Sheppard DN, Hwang T-C

Cellular models for cystic fibrosis research
Randell SH, Fulcher ML, O’Neal W, Olsen JC

The completion of Deliverable 6b (Consensus guidelines for the detection and identification of microbiological pathogens using molecular diagnostics) has been delayed. As a result, these consensus guidelines will not be published in the special supplement to the *Journal of Cystic Fibrosis* containing the other consensus guidelines produced by Workpackage 3. Instead, these consensus guidelines will be published as an article in the *Journal of Cystic Fibrosis* in the same way that Deliverable 7 (Recommendations for neonatal screening in Europe) was published in this Journal in May 2009. **EuroCareCF** expects Deliverable 6b to be published at the end of 2010.

Workpackage 3. Coordination of Clinical Research:

Deliverable 6b: Consensus guidelines for the detection and identification of microbiological pathogens using molecular diagnostics

Tümmler B, Besier T, Chabanon G, Cimon B, Cocchi P, Cunha MV, Foweraker J, Gaillard JL, Govan JR, Häußler S, Hirschl AM, Kahl B, Kalka-Moll WM, Haase B, Hart CA, Krogh-Johansen H, McCaughan J, Meis JF, Oliver A, Petterson A, Plesiat P, Segonds C, Wiehlmann L, Winstanley C, Vandamme P. (2010). European consensus guidelines on the processing of respiratory specimens from cystic fibrosis patients for clinical microbiology. *J Cyst Fibros.* **(In Preparation)**.

Finally, **EuroCareCF** expects further articles and reviews to be produced by project participants and collaborators. These include a further article on the demographics of CF in Europe, a review of rational new therapies for CF and publications using resources produced by **EuroCareCF**.

ANNEX – PLAN FOR USING AND DISSEMINATING THE KNOWLEDGE

Section 1 - Exploitable knowledge and its use:

EuroCareCF co-ordinates fundamental and clinical research in the area of cystic fibrosis and related diseases. As such, **EuroCareCF** is not directly involved in research activities, which might potentially lead to exploitable knowledge. Nevertheless, activities of the different workpackages of **EuroCareCF** have significant implications for the optimisation of the clinical care of CF patients and the development of new therapies to treat the disorder. These include:

Workpackage 1. Optimising Patient Care & CF Team Work:

- Recommendations on good standards of care for CF patients in Europe, including consensus guidelines on different aspects of the care of CF patients
- Specialist training of European clinicians and healthcare professionals in multidisciplinary CF patient care, including
 - Training courses
 - Individual training visits
 - One-to-One training of all staff in teams providing multidisciplinary CF patient care
- Development of a pocket guide teaching tool for multidisciplinary CF patient care

Workpackage 2. European Cystic Fibrosis Patient Registry:

- In collaboration with the European Cystic Fibrosis Society (ECFS), the development of a European CF Patient Registry involving 40 countries
- A report on the demographics of European CF patients. For two reasons, this comprehensive overview of the European CF patient population deserves special mention:
 - It summarises demographic data for 35 European countries
 - Data for each individual country are compared with the data for Europe as a whole

Workpackage 3. Coordination of Clinical Research:

- In collaboration with the ECFS, the establishment of a European Clinical Trials Network to perform high quality clinical research, which efficiently evaluates new therapies for CF patients
- A Clinical Microbiology “Hands-On” training course to disseminate best practice in the diagnosis of microbial pathogens causing CF lung disease
- The specialist training of European researchers in clinical research, especially the nasal potential difference assay and clinical microbiology
- Quality assurance trials of CF Microbiology in Europe involving more than 30 laboratories from 21 countries
- In collaboration with BCCM/LMG Bacteria Collection staff (<http://bccm.belspo.be/>), the design, production and distribution of a parcel of microbiological reference cultures to 50 clinical microbiological laboratories in Europe
- Consensus guidelines for:
 - Clinical diagnostic procedures in Europe
 - The design, conduct and evaluation of clinical trials
 - The detection and identification of microbiological pathogens using molecular diagnostic techniques
 - Neonatal screening in Europe
 - The classification of CFTR-related diseases

Workpackage 4. Small and Medium-Sized Enterprises (SMEs) Group:

- A report on the needs and obstacles for SMEs working in the area of CF and related diseases
- Consensus guidelines for fair and mutually beneficial cooperation between SMEs and CF patient organisations

Workpackage 5. Novel Therapies:

- Specialist training of European researchers in translation research
- Consensus guidelines on the transfer of novel therapies for CF from the laboratory to the clinic

Workpackage 6. Animal Models:

- Distribution of CF mice or tissue samples to ordering laboratories
- Specialist training of European researchers in the use of mouse models of CF in fundamental and translation research
- Consensus guidelines on the use of CF mice in fundamental and translation research

Workpackage 7. Integration of Fundamental Research:

- A “Hands-On” training course to disseminate best practice in the primary culture of epithelial cells from lung tissue and their use in fundamental and translation research
- Specialist training of European researchers in fundamental research
- Consensus guidelines on good laboratory techniques to be used for the assessment of therapeutic interventions

Workpackage 8. Ethical / Legal / Social Issues:

- Publication of articles discussing the key ethical issues and principal patient concerns about the participation of minors in clinical research
- A review of ethics and legislation in Europe on clinical trials involving CF minors including recommendations for harmonising legislation across Europe

Section 2 – Dissemination of knowledge:

EuroCareCF employed a variety of strategies to disseminate widely information about its activities. These include (i) an electronic newsletter, published quarterly in English, (ii) a website with online databases, (iii) leaflets and flyers distributed at international scientific conferences and (iv) the organisation of meetings and workshops. EuroCareCF has also used the media including press, radio and TV to communicate its work to the general public and enhance public awareness about CF.

Period 1:

Overview Table:

Completed Activities

Planned/ actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
04/2006	Meeting: ECFS Basic Science Conference ¹	Basic researchers	Europe and North America	100	Partners 2, 7 & 8a and 1, 16, 18, 19 & 20
04/2006	Meeting: IBCWG 2006 ²	Clinicians and microbiologists	Europe	65	Partners 5b & 14
04/2006	Meeting: Joint Meeting of EuroCareCF WP3 & The CFDN Working Group of the ECFS ³	Clinicians, basic researchers	Europe	35	Partner 8b and 5a & 20
05/2006	Meeting: ECFS registry board meeting	Clinicians and healthcare professionals	Europe	15	Partner 4
05/2006	Meeting: Meeting between P4	Clinicians and healthcare	Central and Eastern	10	Partner 4 & 12

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
	and P12 of EuroCareCF to plan implementation of registry	professionals	Europe		
05/2006	Publications: ECFS Newsletter	Clinicians, healthcare professionals, basic researchers	Europe	>500	Partners 1 & 4
06/2006	Meeting: Meeting between EuroCareCF and CF Foundation	Leaders of US CF patient registry	USA	4	Partner 4
06/2006	Meeting: 29 th ECFS Conference ⁴	Clinicians, healthcare professionals, basic researchers	Europe and North America	1,500	Partners 1, 2, 3, 4, 5b, 9, 10, 11, 12, 14, 15 & 22
06/2006	Film/video: Interview with Spanish journalist	CF patients, families and supporters	Spain	Not known	Partners 1 & 4
06/2006	Leaflets: Delegates of 29 th ECFS Conference	Clinicians, healthcare professionals, basic researchers	Europe and North America	1,500	Partners 1 & 4
07/2006	Project web-site: EuroCareCF website ⁵	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters, general public	All	Global	Partners 1 & 4
07/2006	Project web-site: Web-site links to/from ECFS, CF Europe, Orphanet... ⁶	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters	All	Global	Partners 1 & 4
07/2006	Publications: EuroCareCF Newsletter ⁷	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters	All	Global	Partners 1 & 4
07/2006	Direct e-mailing	Members of ECFS and CFE	Europe	>500	Partner 1
07/2006	Media (TV, radio, press)	General public	All	Global	Partner 4
09/2006	Publications: The House Magazine ⁸	Member of Parliament	UK	>1,000	Partner 1
09/2006	Publications: The Parliamentary Monitor ⁸	Members of political parties	UK	>1,000	Partner 1
09/2006	Project web-site: EuroCareCF website ⁵	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters,	All	Global	Partners 1 & 4

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
		general public			
09/2006	Publications: EuroCareCF Newsletter ⁷	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters	All	Global	Partners 1 & 4
10/2006	Meeting: 40 th anniversary of the Belgium CF Parent Association	Parents of children with CF, healthcare professionals	Belgium	300+	Partner 5b
10/2006	CF Europe website: EuroCareCF presentation and newsletter	CF Europe members	Europe	Global	Partners 1 & 4
11/2006	Meeting: 20 th North American CF Conference ⁹	Clinicians, healthcare professionals, basic researchers	North America, Europe and Australia	2,500	Partners 5b, 8a, 22 and 1, 2, 4, 7, 10, 11, 12, 14, 16, 17 & 19
11/2006	Leaflets: Delegates of 20 th North American CF Conference	Clinicians, healthcare professionals, basic researchers	North America, Europe and Australia	2,500	Partner 1
11/2006	Meeting: Meeting between EuroCareCF and Canadian Studies Network	Leaders of Canadian Studies Network	Canada	2	Partner 1
11/2006	Meeting: CF symposium in honour of Prof. M. Sinaasappel	Clinicians, healthcare professionals	The Netherlands	100	Partner 5b
11/2006	Meeting: EURORDIS	Clinicians, basic scientists and pharmaceutical company representatives	France	70	Partner 4
11/2006	Meeting: 1 st European CF Awareness Day	Press, politicians, CF Europe members	Europe	>100	Partners 1 & 4
12/2006	Letter: Joint letter from ECFS and EuroCareCF to the Rt. Hon. Gordon Brown, MP Chancellor of the Exchequer	Politician	UK	2	Partners 1 & 4
12/2006	Publications: Quote in Grazia magazine	General public	UK	Not known	Partners 1 & 4
12/2006	Interview for press	Serbian press readers	Serbia	Not known	Partner 4
12/2006	Meeting: EuroCareCF / ECFS registry meeting ¹⁰	National registry leaders	Europe	30	Partners 4 & 12

Planned/ actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
12/2006	Project web-site: EuroCareCF website ⁵	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters, general public	All	Global	Partners 1 & 4
12/2006	Publications: EuroCareCF Newsletter ⁷	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters	All	Global	Partners 1 & 4

Short descriptions of major activities:

1. **EuroCareCF** organised a symposium on “Steps on the Pathway to Therapy Development” and workshops on novel therapies, animal models and fundamental research at the 2006 ECFS & UK Physiological Society Joint Conference “*New Frontiers in Basic Science of Cystic Fibrosis*”, Carvoeiro, Portugal, 19-23 April 2006. These workshops served to highlight the activities of **EuroCareCF** to researchers in Europe and forge links with scientists in North America with similar goals.
2. Professors Christiane De Boeck (P5b) and Peter Vandamme (P14) organised the International *Burkholderia cepacia* Working Group 2006 meeting, Gent, Belgium, 20-23 April 2006. This conference provided a multidisciplinary forum for microbiologists and clinicians to exchange knowledge about an important pathogen in CF patients. During the meeting all participants were informed about **EuroCareCF** with special emphasis on the activities of WP3.
3. Professor Maarten Sinaasappel (P8b) organised the joint meeting between the Clinical Diagnosis sub-group of WP3 and the European CF Diagnostic Network that was held at Erasmus University, Rotterdam, 28-29 April 2006. This meeting considered CF diagnostic terminology and algorithms.
4. A range of activities were organised at the 29th European CF Conference, Copenhagen, Denmark, 15-18 June 2006 to introduce the **EuroCareCF** project to clinicians and healthcare professionals. These activities included a plenary lecture by Dr. David N. Sheppard (P1), a satellite symposium to inform conference delegates about **EuroCareCF** activities and workshops on patient care, clinical research and SMEs.
5. The **EuroCareCF** website is <http://www.eurocarecf.eu/>. This site provides an overview of the project, its members and the activities of different workpackages. It provides information of meetings and future events and serves as a gateway to the online databases of **EuroCareCF**. The site is updated as further information becomes available (at least quarterly).
6. **EuroCareCF** has agreed to establish a bi-directional links with several other web sites with interests in cystic fibrosis. These sites include the ECFS site, CF Europe, Orphanet and the US CFTR Folding Consortium. Links with other national bodies are being developed.
7. The **EuroCareCF** newsletter is published quarterly in English. It includes (i) an editorial, (ii) articles summarising the activities of different workpackages, (iii) reports on recent meetings, (iv) discussion of controversies, (v) updates of the online databases and (vi) information about forthcoming events. On publication, this electronic newsletter is automatically distributed to members of the ECFS and CF Europe. It is also freely available from the website of **EuroCareCF**.
8. To raise awareness about cystic fibrosis and the activities of **EuroCareCF** with UK politicians, P1 prepared dissemination articles in the *House Magazine* and the *Parliamentary Monitor*. All attendees of the annual party conferences of the three main UK political parties received copies of this dissemination article.

9. **EuroCareCF** organised three workshops at the 20th North American CF Conference, Denver, 2-5 November 2006, the largest annual worldwide gathering of clinicians, healthcare professional and scientists working in the area of cystic fibrosis and related diseases. These satellite meetings focused on patient care, clinical trials and mouse models of the disease. They served to highlight the activities of the project to North American colleagues
10. **EuroCareCF** and the ECFS jointly organised a meeting in Amsterdam on 15th December to inform representatives of 35 countries from across Europe about the European CF patient registry.

Future Activities

Planned/ actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
01/2007	ECFS newsletter – published on ECFS website	ECFS membership	All		Partner 4
02/2007	Meeting: Joint Meeting of EuroCareCF WP3 & The CFDN Working Group of the ECFS ¹	Clinicians, basic researchers, legal and ethical experts	Europe	100	Partners 5b and 2, 5a & 20
03/2007	Meeting: Workshop on CF-Related Diseases ²	Clinicians, basic researchers	Europe and North America	25	Partners 15 and 12
04/2007	Meeting: ECFS Basic Science Conference ³	Basic researchers	Europe and North America	100	Partners 2 & 8a and 1, 4 & 20
05/2007	Training course: Hands-on training workshop for clinical microbiologists ⁴	Clinicians, healthcare professionals	Europe	25	Partner 9 and 14
05/2007	Meeting: EuroCareCF - Partnering Meeting ⁵	SMEs, basic and clinical researchers	Europe	50	Partner 6 and 7, 16 & 17
06/2007	Meeting: 30 th ECFS Conference ⁶	Clinicians, healthcare professionals, basic researchers	Europe and North America	1,500	Partners 4, 5b & 22 and 1, 2, 6, 10, 11 & 12
07/2007	Training course: Epithelial Cells & Tissues: Production, Cultivation and Characterization ⁷	Basic researchers	Europe	20	Partner 2 and 1 & 20

Short descriptions of major activities:

1. Professors Christiane De Boeck (P5b) and Michael Wilschanski (P11) will organise a Joint Meeting between WP3 of **EuroCareCF** & the European CF Diagnostic Network at the University Hospital Gasthuisberg, Leuven, Belgium on 9-10 February 2007. This meeting will review the evaluation of CF diagnostic terminology and algorithms and further consider outcome variables for clinical trials. It will be followed by a meeting on newborn screening organised with the European Respiratory Society.
2. Professor Pier Franco Pignatti (P15) will organise a workshop on CF-Related Diseases at Lake Garda, Verona, Italy, 22-23 March 2007. This workshop will precede the meeting “*Use and Interpretation of Cystic Fibrosis Mutation Analysis in the Clinical Setting*” organised jointly by the ECFS, the European Society for Human Genetics (ESHG), and the FP6-funded Network of Excellence EuroGenTest (FP6-512148), which will be held at the same location and benefit greatly from the experts gathered for this meeting. The workshop on CF-Related diseases aims to develop

a widely accepted consensus on the definitions of CF related diseases, diagnostic criteria and clinical management.

3. **EuroCareCF** will organise workshops on animal models and fundamental research at the ECFS Basic Science Conference, Tavira, Portugal, 25-29 April 2007. These workshops will benefit from the participation of researchers from the USA, who will be funded by the American CF Foundation to attend the ECFS Basic Science Conference.
4. Professor Burkhard Tuemmler (P9) will organise the “*Hands-on Training Workshop for Clinical Microbiologists: Diagnostic and Molecular Microbiology of Bacteria Retrieved from the CF Lung Habitat*” at Hannover Medical School, Hannover, Germany, 3-6 May 2007. This training workshop will disseminate best practice in the diagnosis of the microbial pathogens, which cause CF lung disease.
5. Dr. Andreas Reimann (P6) and Professor Massimo Conese (P7) will organise the **EuroCareCF** Partnering Meeting: “*From Bench to Bedside - How Academic Science and Companies Can Make It Work*” at Frankfurt Airport on 15 May 2007. This partnering meeting aims to establish contacts between SMEs and academic centres with the goal of promoting co-operation between SMEs and academic centres.
6. **EuroCareCF** will organise workshops on patient care and clinical research and meetings for the European CF patient registry and SMEs at the 30th ECFS Conference, Belek, Turkey 13-16 June 2007. These workshops and meetings will serve two purposes: first, to assess progress towards consensus guidelines and second, to provide expert teaching to Turkish clinicians and healthcare professionals.
7. Professor Margarida Amaral (P2) will organise the training workshop: “*Epithelial Cells & Tissues: Production, Cultivation and Characterization*” at the University of Lisboa, Lisboa, Portugal, 2-7 July 2007. This workshop aims to provide expert tuition in the culture of epithelial cells from normal subjects and CF patients and their use in fundamental and translation research.

Period 2:

Overview Table:

Completed Activities

Planned/ actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
01/2007	Meeting: EuroWilson Oversight Committee	Clinicians	Europe	15	Partner 4
02/2007	Meeting: Irish Cystic Fibrosis Society	Clinicians, healthcare professionals and basic researchers	Ireland	100	Partner 5b
02/2007	Meeting: Gordon Conference on Cilia, Mucus and Mucociliary Interactions	Basic and clinical researchers	North America and Europe	100	Partner 19
02/2007	Meeting: Joint EuroCareCF - ECFS Diagnostic Network Group Meeting ¹	Clinicians and basic researchers	Europe	100	Partner 5b / Partners 2, 5a, 6, 8a, 11 and 20
02/2007	Meeting: 3 rd Workshop of Gulf Society for Pediatric Respirology ²	Clinicians	Middle East	250	Partner 12
03/2007	Meeting: CFTR-Related	Clinicians and basic researchers	Europe and North	25	Partner 15 / Partners 5b

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
	Diseases Workshop ³		America		and 12
03/2007	Meeting: ECFS-ESGH- EuroGentest Meeting	Clinicians and basic researchers	Europe and North America	100	Partners 5b, 12 and 15
04/2007	Publications: EuroCareCF Newsletter ⁴	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters	All	Global	Partner 1
04/2007	Project web-site: EuroCareCF website ⁵	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters, general public	All	Global	Partner 1
04/2007	Meeting: ECFS Basic Science Conference ⁶	Basic researchers	Europe and North America	100	Partners 2 and 8a / Partners 1 and 4
04/2007	Leaflets: Delegates of ECFS Basic Science Conference	Basic researchers	Europe and North America	100	Partners 1 & 2
04/2007	Meeting: CFF Therapeutics Development Network Meeting	Clinicians, healthcare professionals, basic researchers	North America	200	Partner 5b
04/2007	Meeting: Medical Science for School Teachers	Secondary school teachers	UK	20	Partner 18
05/2007	Training Course: "Hands-On" Training Course for Clinical Microbiologists ⁷	Clinical Microbiologists	Europe	20	Partner 9 / Partner 14
05/2007	Meeting: Partnering Meeting ⁸	SMEs, basic and clinical researchers	Europe and North America	50	Partners 6 and 7 / Partners 1, 8, 16 and 17
06/2007	Meeting: 30 th European CF Conference ⁹	Clinicians, healthcare professionals, basic researchers	Europe and North America	1,500	Partners 1, 2, 4, 5b, 6, 7, 8, 10, 11, 12, 14 and 22
06/2007	Meeting: International Society of Aerosols in Medicine Conference	Clinicians, healthcare professionals, basic researchers	Europe and North America	1,000	Partner 19
07/2007	Training Course: "Hands-On" Training Course in Epithelial Biology ¹⁰	Basic researchers	Europe and South America	20	Partner 2 / Partners 1 and 20
07/2007	Publications: EuroCareCF Newsletter ⁴	Clinicians, healthcare professionals, basic researchers, CF	All	Global	Partner 1

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
		patients, families and supporters			
07/2007	Project web-site: EuroCareCF website ⁵	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters, general public	All	Global	Partner 1
08/2007	Meeting: 25 th International Congress of Pediatrics	Clinicians	Europe and North America	1,000	Partner 12
09/2007	Meeting: Pro-Con Debate on Treatments for CF Lung Disease ¹¹	Basic and clinical researchers	Europe and North America	100	Partners 1, 4 and 7 / Partners 2, 8a, 16 and 19
09/2007	Meeting: EuroCareCF-Novartis Meeting	Basic researchers	Europe	7	Partner 1 / Partners 4, 7, 8a and 16
09/2007	Meeting: EC Conference on Rare Diseases ¹²	Basic and clinical researchers, healthcare professionals, patient supporters and media	Europe	250	Prof. Marie Johannesson (ex-Advisory Committee) / Partner 1
10/2007	Meeting: 20 th North American CF Conference ¹³	Clinicians, healthcare professionals, basic researchers	North America, Europe and Australia	2,500	Partners 1, 6 and 8a / Partners 2, 4, 10, 12, 16, 19 and 22
10/2007	Meeting: CFW Workshop ¹⁴	Clinicians and healthcare professionals	Armenia	50	Partner 12
10/2007	Meeting: South West CF Network Meeting	Clinicians and healthcare professionals	UK	50	Partner 1
10/2007	Meeting: 15 th Annual congress of European Society of Gene and Cell Therapy	Basic and clinical researchers	Europe and North America	1,000	Partner 8a
11/2007	Publications: EuroCareCF Newsletter ⁴	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters	All	Global	Partners 5b and 1 / Partners 14 and 15
11/2007	Project web-site: EuroCareCF website ⁵	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters, general public	All	Global	Partner 1
11/2007	Meeting: European Clinical Trials Network Meeting	Clinicians and healthcare professionals	Europe	50	Partner 5a / Partner 6
11/2007	Meeting:	Basic researchers	Europe and	50	Partner 1

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
	Joint EuroCareCF -The Physiological Society Meeting ¹⁵	and healthcare professionals	North America		
11/2007	Leaflets: Delegates of Joint EuroCareCF -The Physiological Society Meeting	Basic researchers and healthcare professionals	Europe and North America	50	Partners 1
11/2007	Meeting: 3 rd Congress of Italian CF Society ¹⁶	Clinicians and healthcare professionals	Europe	200	Partner 22 / Partners 1, 4, 5b, 7, and 10

Short descriptions of major activities:

1. Profs. Christiane De Boeck (P5b) and Michael Wilschanski (Hadassah University Hospital) organised a Joint Meeting between the Clinical Diagnosis Group of WP3 and the ECFS Diagnostic Network Group at the University Hospital Gasthuisberg, Leuven, Belgium, 9-10 February 2007. This meeting reviewed the evaluation of CF diagnostic terminology and algorithms and further considered outcome variables for clinical trials. The Meeting was followed by the European Respiratory Society (ERS) research symposium "*Preventing Respiratory Sequelae in Children Diagnosed with Cystic Fibrosis by Newborn Screening*".
2. Prof. Milan Macek (P12) presented an overview of the work of **EuroCareCF** especially the development of a European Cystic Fibrosis Patient Registry at the 3rd Workshop of the Gulf Society for Pediatric Respiratory, Muscat, Oman, 28 February-1 March 2007. Prof. Macek was part of a delegation from CF Worldwide (CFW) visiting Oman to provide expert advice in the care of CF patients. This visit served to strengthen ties between clinicians in Europe and the Gulf States.
3. Prof. Pier Franco Pignatti (P15) organised a workshop on CFTR-Related Diseases at Lake Garda, Verona, Italy, 22-23 March 2007. This workshop preceded the meeting "*Use and Interpretation of Cystic Fibrosis Mutation Analysis in the Clinical Setting*" organised jointly by the ECFS, the European Society for Human Genetics (ESHG), and the FP6-funded Network of Excellence EuroGenTest (FP6-512148), which was held at the same location and benefited greatly from the experts gathered for the ECFS-ESHG-EuroGentest meeting. The workshop on CFTR-Related Diseases aimed to develop a widely accepted consensus on the definitions of CFTR-related diseases, diagnostic criteria and clinical management.
4. The **EuroCareCF** newsletter is published quarterly in English. It includes (i) an editorial, (ii) articles summarising the activities of different workpackages, (iii) reports on recent meetings, (iv) discussion of controversies, (v) updates of the online databases and (vi) information about forthcoming events. On publication, this electronic newsletter is automatically distributed to members of the ECFS and CF Europe. It is also freely available from the website of **EuroCareCF**.
5. The **EuroCareCF** website is <http://www.eurocarecf.eu/>. This site provides an overview of the project, its members and the activities of different workpackages. It provides information of meetings and future events and serves as a gateway to the online databases of **EuroCareCF**. The site is updated as further information becomes available (at least quarterly).
6. **EuroCareCF** organised workshops on Animal Models and Fundamental research at the ECFS Basic Science Conference, "*New Frontiers in Basic Science of Cystic Fibrosis*", Tavira, Portugal, 25-29 April 2007. These workshops benefited significantly from the active participation of researchers from the USA, including members of the *The CFTR Folding Consortium*. (The CF Foundation supported the travel costs of American investigators attending the ECFS Basic Science Conference).
7. Professor Burkhard Tümmler (P9) organised the "*Hands-on Training Workshop for Clinical Microbiologists: Diagnostic and Molecular Microbiology of Bacteria Retrieved from the CF Lung*".

- Habita*” at Hannover Medical School, Hannover, Germany, 3-6 May 2007. This training workshop disseminated best practice in the diagnosis of the microbial pathogens, which cause CF lung disease.
8. Dr. Andreas Reimann (P6) and Prof. Massimo Conese (P7) organised the **EuroCareCF** Partnering Meeting: “*From Bench to Bedside - How Academic Science and Companies Can Make It Work*” at Frankfurt Airport on 15 May 2007. The goal of this partnering meeting was to establish contacts between SMEs and academic centres to promote co-operation between SMEs and academic centres.
 9. **EuroCareCF** organised workshops on Patient Care and Clinical Research and meetings for the **EuroCareCF** / ECFS Registry Working Group and SMEs at the 30th European CF Conference, Belek, Antalya, Turkey, 13-16 June 2007. These workshops and meetings served two purposes: first, to assess progress towards consensus guidelines and second, to provide expert teaching to Turkish clinicians and healthcare professionals. **EuroCareCF** also held an Advisory Committee meeting and a Steering Committee / Advisory Committee Dinner at the Conference.
 10. Professor Margarida Amaral (P2) organised the “Hands-On” Training Workshop: “*Epithelial Cells & Tissues: Production, Cultivation and Characterization*” at the University of Lisboa, Lisboa, Portugal, 2-6 July 2007. This workshop disseminated expert tuition in the culture of epithelial cells and their use in fundamental and translation research.
 11. As part on the Lung Development Symposium to honour the career of Prof. RE Olver (Dundee, UK, 5-6 September 2007), **EuroCareCF** organised a Pro-Con Debate, “*Will Therapeutic Strategies that Target Sodium Hyperabsorption in CF Airways be of Value in the Treatment of CF Patients?*”, Dundee, UK, September 2007. The debate considered two motions: (i) *Inhibition of sodium hyperabsorption in CF airways has therapeutic potential for the treatment of CF lung disease* and (ii) *Restoration of function to CF mutants will correct sodium hyperabsorption in CF airways*.
 12. Prof. Marie Johannesson, a former participant of **EuroCareCF** and ex-President of the ECFS used the European Cystic Fibrosis Patient Registry to discuss rare disease research in a global context at the European Commission conference “*Rare Disease Research: Building on Success*”, Brussels, Belgium, 13 September 2007. Dr. David N. Sheppard (P1) served on the Conference’s scientific committee.
 13. **EuroCareCF** organised workshops at the 21st North American CF Conference, Anaheim, USA, 3-6 October 2007, the largest annual worldwide gathering of clinicians, healthcare professionals and scientists working in the area of cystic fibrosis and related diseases. These satellite meetings focused on (i) Animal Models and (ii) Drug Development, especially lessons that European researchers and SMEs might learn from the experiences of US companies. Of note, Prof. Margarida D. Amaral (P2) delivered the plenary lecture “*From Basic Science to the Clinic: Where are We & What Is Still Missing*”.
 14. Prof. Milan Macek (P12) made a series of presentations about cystic fibrosis and the **EuroCareCF** project as part of Cystic Fibrosis Worldwide (CFW) visit to Yerevan, Armenia, 25-27 October 2007. The aim of this CFW visit was to provide essential training in multidisciplinary care for CF patients.
 15. **EuroCareCF** co-organised with The Physiological Society the educational seminar “*Cystic Fibrosis: Latest Advances in Medical Research and Implications for Patients and Their Families*”, London, UK, 19 November 2007. This event explained what CF is, its basic pathophysiology, treatment issues from a clinician’s point of view, some exciting recent developments in research, and what it is like to live with CF. It was intended to be of interest to researchers and students in the area, clinicians, policy makers, the media, schools and the general public.
 16. Representatives of **EuroCareCF** played an active role in the 3rd Congress of the Italian Cystic Fibrosis Society, Milano, Italy, 30 November-2 December 2007. Prof. Carla Colombo (P22) organised the Patient Care workshop “*from Evidence Based Medicine to Evidence Based Practice*”, while Christiane De Boeck (P5b) and Dr. Anil Mehta (P4) delivered invited lectures about the development of a European Cystic Fibrosis Clinical Trials Network and the European Cystic Fibrosis Patient Registry, respectively.

Future Activities

Planned/ actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
02/2008	Joint EuroCareCF - ECFS Diagnostic Network Group Meeting ¹	Clinicians and basic researchers	Europe	100	Partner 5b / Partners 9 and 20
03/2008	Meeting: Joint EuroCareCF - ECFS Neonatal Screening Working Group Meeting ²	Clinicians and basic researchers	Europe and North America	100	Prof. Carlo Castellani / Partners 1, 4, 5b, 12 and 15
04/2008	Publications: EuroCareCF Newsletter	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters	All	Global	Partner 1
04/2008	Project web-site: EuroCareCF website	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters, general public	All	Global	Partner 1
04/2008	Meeting: ECFS Basic Science Conference ³	Basic researchers	Europe and North America	100	Partners 2 and 8a / Partners 1, 4, 19 and 20
04/2008	Training Course: "Hands-On" Training Course for Clinical Microbiologists ⁴	Clinical Microbiologists	Europe	20	Partner 9 / Partner 14
06/2008	Meeting: 31 st European CF Conference ⁵	Clinicians, healthcare professionals, basic researchers	Europe and North America	1,500	Partners 5b, 6, 7, 16 and 22 / Partners 1, 2, 8a, 10, 14 and 15
06/2008	Meeting: CFTR-Related Diseases Workshop ⁶	Clinicians and basic researchers	Europe and North America	50	Partners 12 and 15 / Partners 1, 4, 5b and 9
06/2008	Meeting: Anti-Microbial Therapies Workshop ⁷	Clinicians and basic researchers	Europe and North America	50	Partner 17
07/2008	Training Course: "Hands-On" Training Course in Epithelial Biology ⁸	Basic researchers	Europe	20	Partner 2 / Partners 1 and 20

Short descriptions of major activities:

1. Professors Christiane De Boeck (P5b) and Michael Wilschanski (Hadassah University Hospital) will organise a Joint Meeting between the Clinical Diagnosis Group of WP3 and the ECFS Diagnostic Network Group at Hannover Medical School, Hannover, Germany, 15-16 February 2008. This meeting will compare and contrast different bioassays to evaluate CFTR function. It will also feature a number of communications from junior scientists supported by **EuroCareCF** Travel Grants.

2. Professor Carlo Castellani (Cystic Fibrosis Center, Verona) leader of the Neonatal Screening Group of WP3 will organise the Consensus Conference "*Cystic Fibrosis Neonatal Screening in Europe: Management, Development, Research*" at Lake Garda, Verona, Italy, 28-29 March 2008. This Consensus Conference will gather a wide spectrum of experts to discuss the implementation of neonatal screening in Europe and plan a strategy to achieve this goal.
3. **EuroCareCF** will organise workshops on Animal Models and Fundamental Research (Endpoints of CFTR Rescuing Therapies and Cellular Systems for CF Research) at the 2008 ECFS Basic Science Conference, "*New Frontiers in Basic Science of Cystic Fibrosis*", Régua-Douro, Portugal, 9-13 April 2007. These workshops will benefit from the active participation of researchers from the USA, who will be funded by the American CF Foundation to attend the ECFS Basic Science Conference.
4. Professor Burkhard Tümmler (P9) will organise the "*Hands-on Training Workshop for Clinical Microbiologists: Diagnostic and Molecular Microbiology of Bacteria Retrieved from the CF Lung Habitat*" at Hannover Medical School, Hannover, Germany, 10-13 April 2008. This training workshop will disseminate best practice in the diagnosis of the microbial pathogens, which cause CF lung disease.
5. **EuroCareCF** will organise workshops on Patient Care, Clinical Research and Drug Development and host a Pro-Con Debate on Gene Therapy for Cystic Fibrosis at the 31st European CF Conference, Prague, Czech Republic 11-14 June 2008. These workshops and meetings will serve three purposes: first, to review draft consensus guidelines, second, to provide expert teaching to clinicians and healthcare professionals from Eastern Europe and third, to disseminate information about **EuroCareCF** activities.
6. Prof. Claude Férec (INSERM U613, Brest, France), Prof. Pier Franco Pignatti (P15) and Prof. Milan Macek (P12), will organise the Second Workshop for the CFTR-Related Diseases Group of WP3, Prague, Czech Republic, 15-16 June 2008. This workshop, which will immediately follow the 31st European CF Conference, will provide a valuable opportunity for a broad range of experts to assemble and discuss the classification, diagnostic criteria and clinical management of CFTR-related diseases.
7. Prof. Pieter S. Hiemstra (Leiden University Medical Center, Leiden, The Netherlands) and Prof. Robert Bals (P17) will organise the Joint **EuroCareCF**-ERS Research Seminar: "*Host-Pathogen Interactions in the Lung: Implications for Treatment of Respiratory Infections and Inflammatory Lung Diseases*" at Davos, Switzerland, 20-22 June 2008. This workshop will bring together established and young scientists from different research areas to discuss actively respiratory infections and their roles in inflammatory lung diseases. A special focus of the seminar will be translation to encourage interactions between basic and clinical disciplines.
8. Funding permitting, Prof. Margarida Amaral (P2) will organise the training workshop: "*Production of Epithelial Cells & Immortalization From Transplanted Lungs*" at the University of Lisboa, Lisboa, Portugal in July 2008. This workshop aims to provide expert tuition in the culture of epithelial cells from normal subjects and CF patients and their use in fundamental and translation research.

Period 3:

Overview Table:

Completed Activities

Planned/ actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
01/2008	Publications: EuroCareCF Newsletter ¹	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters	All	Global	Partner 1
01/2008	Project web-site:	Clinicians,	All	Global	Partner 1

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
	EuroCareCF website ²	healthcare professionals, basic researchers, CF patients, families and supporters, general public			
02/2008	Report: Outcome of Quality Assurance Trial in CF Microbiology ³	Clinical Microbiologists	Europe	35 labs	Partner 9
02/2008	Meeting: Joint EuroCareCF -ECFS Diagnostic Network Group Meeting ⁴	Clinicians, geneticists and basic researchers	Europe	50	Partner 5b / Partners 9 and 11 20
03/2008	Meeting: Joint EuroCareCF -ECFS Neonatal Screening Working Group Meeting ⁵	Clinicians and basic researchers	Europe and North America	100	Prof. Carlo Castellani / Partners 1, 4, 5b, 12 and 15
04/2008	Meeting: Research in Vulnerable Populations Meeting	Clinicians and ethicists	Europe	500	Partner 5a
04/2008	Meeting: Meeting of the German Society of Pediatric Pulmonology	Clinicians and basic researchers	Germany	250	Partner 19
04/2008	Meeting: ECFS Basic Science Conference ⁶	Basic researchers	Europe and North America	100	Partners 2 and 8a / Partners 1, 4, 19 and 20
04/2008	Training Course: "Hands-On" Training Course for Clinical Microbiologists ⁷	Clinical Microbiologists	Europe	20	Partner 9 / Partner 14
04/2008	Meeting: Hradec Days of Pediatrics, Molecular Genetics and Cytogenetics	Clinicians, geneticists and basic researchers	Central and Eastern Europe	100	Partner 12
05/2008	Publications: EuroCareCF Newsletter ¹	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters	All	Global	Partner 1
05/2008	Project web-site: EuroCareCF website ²	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters, general public	All	Global	Partner 1
05/2008	Training Course: Training day for Czech regional CF centres	Geneticists and database managers	Czech Republic	20	Partner 12
05/2008	Meeting:	Clinicians,	Europe and	150	Partner 12

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
	21 st Course in Medical Genetics organised by the European School of Genetic Medicine	geneticists and basic researchers	North Africa		
05/2008	Meeting: Italian CF Research Foundation	Clinicians, healthcare professionals and basic researchers	Italy	200	Partners 8a and 19
05/2008	Meeting: Translational Research in Paediatric Rheumatology (TRiPR) meeting	Clinicians, basic researchers and bioethicists	Europe	100	Partner 5a
05/2008	Meeting: Williamsburg Conference of the US CF Foundation	Clinicians and basic researchers	North America and Europe	100	Partners 1 and 2
06/2008	Meeting: Slovak Meeting of Pediatrics	Clinicians and geneticists	Central and Eastern Europe	120	Partner 12
06/2008	Meeting: 31 st European CF Conference ⁸	Clinicians, healthcare professionals and basic researchers	Europe and North America	2,000	Partners 1, 2, 4, 5b, 6, 7, 8a, 9, 10, 12, 16, 19 and 22
06/2008	Meeting: EuroCareCF CFTR-Related Diseases Workshop ⁹	Clinicians, geneticists and basic researchers	Europe and North America	50	Partners 12 and 15 / Partners 1 and 5b
06/2008	Meeting: Meeting of the Task-force in Europe for Drug Development for the Young (TEDDY) Network of Excellence	Clinicians, basic researchers and bioethicists	Europe	100	Partner 5a
06/2008	Meeting: EuroCareCF-European Respiratory Society Research Seminar ¹⁰	Clinicians and basic researchers	Europe and North America	50	Partner 17
06/2008	Leaflets: Delegates of EuroCareCF-European Respiratory Society Research Seminar	Clinicians and basic researchers	Europe and North America	50	Partners 17
07/2008	Meeting: Meeting of UK Physiological Society	Basic researchers	Global	2,500	Partner 19
07/2008	Training Course: "Hands-On" Training Course in Epithelial Biology ¹¹	Basic researchers	Europe and North America	17	Partner 2 / Partners 1 and 20
07/2008	Publications: Overview of requirements for involving minors in medical experiments regulated by Belgium law ¹²	Clinicians, healthcare professionals and bioethicists	Europe	Global	Partner 5a

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
07/2008	Publications: Analysis of how enrolment of minors in clinical trials is negotiated ¹²	Clinicians, healthcare professionals and bioethicists	Europe	Global	Partner 5a
09/2008	Meeting: The BA Festival of Science ¹³	The families and supporters of CF patients and the general public	UK	100	Partner 1
09/2008	Press Release: The BA Festival of Science ¹³	The families and supporters of CF patients and the general public	Global	Global	Partner 1
09/2008	Meeting: Slovak Medical Genetics Conference "Izakovicov Memorial"	Clinicians, geneticists and database managers	Central and Eastern Europe	100	Partner 12
09/2008	Meeting: ECFS Clinical Trial Network Meeting ¹⁴	Clinicians, healthcare professionals and basic researchers	Europe and North America	30	Partner 5b / Partner 6
10/2008	Meeting: South West CF Network Meeting	Clinicians and healthcare professionals	UK	50	Partner 1
10/2008	Meeting: Plymouth Meeting of CF Trust	The families and supporters of CF patients and the general public	UK	50	Partner 1
10/2008	Meeting: 20 th North American CF Conference ¹⁵	Clinicians, healthcare professionals, basic researchers	North America, Europe and Australia	2,500	Partners 8a / Partners 2, 4, 12, 16, 19 and 22
11/2008	Meeting: German CF conference	Clinicians, healthcare professionals, basic researchers	Germany	250	Partner 19
11/2008	Meeting: Czech DNA Diagnostics Conference	Clinicians, geneticists and database managers	Central and Eastern Europe	250	Partner 12
11/2008	Meeting: V4-CF Conference ¹⁶	Clinicians, healthcare professionals, CF families and their supporters	Central and Eastern Europe	100	Partners 10 and 22
11/2008	Meeting: 4 th Congress of Italian CF Society ¹⁷	Clinicians, healthcare professionals and basic researchers	Italy	200	Partner 22 / Partners 1, 7 and 8a
11/2008	Meeting: 1 st Eastern European CF Conference ¹⁸	Clinicians, healthcare professionals and basic researchers	Central and Eastern Europe	200	Partner 1 / Partners P10, P12, P16 and P19
12/2008	Meeting: Impact on Clinical Research of European Legislation (ICREL)	Clinicians, basic researchers and bioethicists	Europe	100	Partner 5a

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
	conference				
12/2008	Publications: EuroCareCF Newsletter ¹	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters	All	Global	Partner 1
12/2008	Project web-site: EuroCareCF website ²	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters, general public	All	Global	Partner 1
01/2009	Publications: Commentary on an article discussing the ethical issues of neuroimaging technology within and without the clinic ¹⁹	Clinicians, healthcare professionals and bioethicists	Europe and North America	Global	Partner 5a
01/2009	Publications: The European legal framework for pediatric clinical trials is analysed from the perspective of the major concerns of pediatric research ¹⁹	Clinicians, healthcare professionals and bioethicists	Europe	Global	Partner 5a
02/2009	Training Course: "Hands-On" Training Course for nasal PD measurement ²⁰	Clinicians and basic researchers	Europe and North America	30	Partner 5b
02/2009	Meeting: Joint EuroCareCF - ECFS Diagnostic Network Group Meeting ²⁰	Clinicians, geneticists and basic researchers	Europe and North America	50	Partner 5b / Partner 1
02/2009	Meeting: Gordon conference on mucus, cilia and mucociliary interactions	Clinicians and basic researchers	Europe and North America	200	Partner 19
02/2009	Report: Outcome of Quality Assurance Trial in CF Microbiology ³	Clinical Microbiologists	Europe	37 labs	Partner 9
02/2009	Publications: EuroCareCF consensus guidelines on neonatal screening for CF in Europe ²¹	Clinicians and healthcare professionals	Europe	Global	Prof. Carlo Castellani / Partners 4, 6, 10 and 12
03/2009	Meeting: Meeting of German Physiological Society	Basic researchers	Global	2,500	Partner 19
03/2009	Publications: Evaluation of CF diagnostic algorithm in	Clinicians and basic researchers	Europe	Global	Partner 5b

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
	individuals with intermediate clinical phenotype ²²				
04/2009	Meeting: ECFS Basic Science Conference ²³	Basic researchers	Europe and North America	100	Partner 2 / Partners 1, 4 and 8a
04/2009	Meeting: 2009 Balkans Regional CF Conference ²⁴	Clinicians and healthcare professionals	Central and Eastern Europe	200	Partner 22
04/2009	Meeting: EuroCareCF consensus workshop for SMEs and patient organisations ²⁵	Representatives of SMEs and patient organisations	Europe	25	Partner 6
04/2009	Meeting: Dutch Respiratory Society	Clinicians and basic researchers	The Netherlands	100	Partner 8a
05/2009	Publications: EuroCareCF Newsletter ¹	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters	All	Global	Partner 1
05/2009	Meeting: Italian CF Research Foundation	Clinicians, healthcare professionals and basic researchers	Italy	200	Partner 4 and 5b
05/2009	Meeting: Workshop about CF Care in Slovakia ²⁶	Clinicians and healthcare professionals	Slovakia	10	Partner 22
06/2009	Meeting: Meeting of Polish Pediatric and Medical genetic communities	Clinicians, geneticists and basic researchers	Central and Eastern Europe	200	Partner 12
06/2009	Meeting: Meeting to discuss interactions between patient organisations	Representatives of patient organisations	Europe	25	Partner 6
06/2009	Meeting: Workshop on Patients Partnering in Clinical Research	Clinicians, basic researchers and bioethicists	Europe	100	Partner 5a
06/2009	Meeting: 32 nd European CF Conference ²⁷	Clinicians, healthcare professionals and basic researchers	Europe and North America	2,000	Partners 1, 2, 4, 5b, 6, 9, 10, 12, 16, 19 and 22
06/2009	Web TV: 32 nd European CF Conference ²⁷	CF patients, their families and supporters and the general public	France	Global	Partner 1
06/2009	Meeting: EMEA meeting	Clinicians, healthcare professionals and basic researchers	Europe	75	Partner 5b
06/2009	Meeting: EuroCareCF-European Respiratory Society	Basic researchers	Europe and North America	40	Partner 8a / Partner 1

Planned/ actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
	Research Seminar ²⁸				

Short descriptions of major activities:

1. The **EuroCareCF** newsletter was published quarterly in English. It included (i) an editorial, (ii) articles summarising the activities of different workpackages, (iii) reports on recent meetings, (iv) discussion of controversies, (v) updates of the online databases and (vi) information about forthcoming events. On publication, this electronic newsletter was automatically distributed to members of the ECFS and CF Europe. It is also freely available from the website of **EuroCareCF**.
2. The **EuroCareCF** website is <http://www.eurocarecf.eu/>. This site provides an overview of the project, its members and the activities of different workpackages. It provides information of meetings and future events and serves as a gateway to the online databases of **EuroCareCF**. The site is updated as further information becomes available.
3. Prof. Burkhard Tümmler (P9) distributed reports to participating laboratories on their performance in the quality assurance trials of CF microbiology performed in 2007 and 2008. These trials involved over 30 laboratories from 21 European countries.
4. With assistance from Prof. Burkhard Tümmler (P9), the local organiser, Profs. Christiane De Boeck (P5b) and Michael Wilschanski (Hadassah University Hospital) organised a Joint Meeting between the Clinical Diagnosis Group of WP3 and the ECFS Diagnostic Network Group at Hannover Medical School, Hannover, Germany, 15-16 February 2008. This meeting compared and contrasted different bioassays to evaluate CFTR function. It also featured a number of communications from junior scientists supported by **EuroCareCF** Travel Grants.
5. Prof. Carlo Castellani (Cystic Fibrosis Center, Verona) leader of the Neonatal Screening Group of WP3 organised the Consensus Conference "*Cystic Fibrosis Neonatal Screening in Europe: Management, Development, Research*" at Lake Garda, Verona, Italy, 28-29 March 2008. This Consensus Conference gathered a wide spectrum of experts to discuss the implementation of neonatal screening in Europe and a strategy to achieve this goal. The output of this Consensus Conference was Deliverable D7 (Recommendations for neonatal screening in Europe), which was published in the *Journal of Cystic Fibrosis* in May 2009.
6. **EuroCareCF** organised workshops on Animal Models and Fundamental Research (Endpoints of CFTR Rescuing Therapies and Cellular Systems for CF Research) at the 2008 ECFS Basic Science Conference, "*New Frontiers in Basic Science of Cystic Fibrosis*", Régua-Douro, Portugal, 9-13 April 2008. The success of these workshops benefited greatly from the active participation of researchers from the USA, who were funded by the American CF Foundation to attend the Conference.
7. Prof. Burkhard Tümmler (P9) organised the "Hands-On" Training Course for Clinical Microbiologists: "*On the Processing of Microbiological Specimens from Individuals with CF*" at Hannover Medical School, Hannover, Germany, 10-13 April 2008. He was assisted in the delivery of this specialist course by Prof. Peter Vandamme (P14) and other members of the microbiology sub-group of Workpackage 3. This training workshop disseminated best practice in the diagnosis of the microbial pathogens, which cause CF lung disease.
8. **EuroCareCF** organised workshops and meetings on Patient Care, the European CF Patient Registry, Clinical Research, Drug Development and Gene Therapy at the 31st European CF Conference, Prague, Czech Republic, 11-14 June 2008. These workshops and meetings served two purposes: first, to assess progress towards consensus guidelines and second, to disseminate the latest information about CF and its treatment to clinicians, healthcare professionals and scientists from Central and Eastern Europe. **EuroCareCF** also held a joint meeting of its Steering and Advisory Committees at the Conference.
9. Prof. Claude Férec (INSERM U613, Brest, France), Prof. Pier Franco Pignatti (P15) and Prof. Milan Macek (P12), organised the Second Workshop for the CFTR-Related Diseases Group of WP3,

Prague, Czech Republic, 15-16 June 2008. This workshop, which immediately followed the 31st European CF Conference, provided a valuable opportunity for a broad range of experts to assemble and discuss the classification, diagnostic criteria and clinical management of CFTR-related diseases.

10. Prof. Pieter S. Hiemstra (Leiden University Medical Center, Leiden, The Netherlands) and Prof. Robert Bals (P17) organised the Joint **EuroCareCF**-ERS Research Seminar: "*Host-Pathogen Interactions in the Lung: Implications for Treatment of Respiratory Infections and Inflammatory Lung Diseases*" at Davos, Switzerland, 20-22 June 2008. This workshop brought together established and young scientists from different research areas to discuss actively respiratory infections and their roles in inflammatory lung diseases. To encourage interactions between basic scientists and clinicians, translation from bench to bedside was a special focus of the seminar.
11. Prof. Margarida Amaral (P2) organised the "Hands-On" Training Workshop: "*Epithelial Cells from the Lung: Production, Cultivation and Characterisation*" at the University of Lisboa, Lisboa, Portugal, 14-18 July 2008. This workshop provided expert tuition in the isolation and primary culture of epithelial cells from the lungs of normal subjects and CF patients and their use in fundamental and translation research.
12. With their research assistant Wim Pinxten, Profs. Kris Dierickx and Herman Nys (P5a) published two articles in July 2008. The first article, published in the *European Journal of Health Law*, is an overview of the requirements for involving minors in medical experiments specified by Belgium law in the context of the European Clinical Trial Directive (2001/20/EC). In the second article, published in *Medicine, Health Care and Philosophy*, the authors make policy recommendations to promote clearer, more ethically informed guidelines for enrolling minors in clinical research.
13. **EuroCareCF** co-organised with The Physiological Society the educational seminar "*Cystic Fibrosis: Better Understanding Better Lives*" at The BA Festival of Science, Liverpool, UK, 6-11 September 2008, the premier annual public understanding of science event in the UK. This educational seminar explained what CF is, its basic pathophysiology, treatment issues from a clinician's point of view, some exciting recent developments in research, and what it is like to live with CF. It was intended to be of interest to the general public and to inform families of CF patients and their supporters about the latest CF research. The presentation about drug therapies by Dr. David Sheppard (P1) attracted media coverage including newspapers and radio.
14. Prof. Christiane De Boeck (P5b) organised the inaugural meeting of ECFS Clinical Trial Network at the University Hospital Gasthuisberg, Leuven, Belgium, 18-19 September 2008. The aim of this network is to promote efficient and high quality clinical research with the goal of developing new therapies for CF patients. At the meeting, the organisation of the ECFS Clinical Trials Network was agreed and an executive committee elected.
15. **EuroCareCF** organised a workshop on Animal Models of CF at the 22nd North American CF Conference, Orlando, USA, 23-25 October 2008, the largest annual worldwide gathering of clinicians, healthcare professionals and scientists working in the area of cystic fibrosis and related diseases. This satellite meeting focused on the use of mouse models to study lung inflammation and remodelling.
16. Prof. Carla Colombo (P22) and Dr. Dorota Sands (P11) contributed actively to the V4-CF Conference, Kraków, Poland, 20-22 November 2008, which was co-funded by **EuroCareCF** together with CF Europe, the Polish CF Foundation MATIO, the Slovak CF Association, Klub nemocných cystickou fibrózou (Czech Republic) and the Hungarian Cystic Fibrosis Association. This conference provided an important opportunity to discuss standards of care for CF patients particularly in the Visegrad Group of countries (Czech Republic, Hungary, Poland and Slovakia).
17. Representatives of **EuroCareCF** played an active role in the 4th Congress of the Italian Cystic Fibrosis Society, Torino, Italy, 27-29 November 2008. Prof. Carla Colombo (P22) organised the Patient Care workshop "*Quality Management in CF Care and Accreditation Processes in CF Centres throughout the World*", while Drs. David Sheppard (P1) and Bob Scholte (P8a) delivered invited lectures about the molecular pharmacology of CFTR and mouse models of CF, respectively.

18. **EuroCareCF** was the major sponsor of the conference “*What’s New in the Diagnosis, Treatment and Prevention of Cystic Fibrosis?*”, First Eastern European CF Conference, Zagreb, Croatia, 28-30 November 2008. The aims of this conference were two-fold: first, to inform clinicians and healthcare professionals working in Central and Eastern Europe, especially those in the Balkans, about the latest developments in the diagnosis and care of CF patients. Second, to promote closer ties between CF specialists in Eastern Europe with those in the West to spread widely in Europe best practice in the diagnosis and treatment of CF.
19. With their research assistant Wim Pinxten, Profs. Kris Dierickx and Herman Nys (P5a) published one article and a commentary in January 2009. The commentary, published in the *American Journal of Bioethics*, discusses an article (Fenton *et al. Am J Bioeth.* 2009; **9**:3-13) which considers the ethical issues of neuroimaging technology within and without the clinical setting. The article, published in the *European Journal of Pediatrics*, analyses the European legal framework for pediatric clinical trials from the perspective of the major concerns of pediatric research.
20. With assistance from Dr. Kevin Southern (University of Liverpool), Profs. Christiane De Boeck (P5b) and Michael Wilschanski (Hadassah University Hospital) organised a Joint Meeting between the Clinical Diagnosis Group of WP3 and the ECFS Diagnostic Network Group at the University of Liverpool, Liverpool, UK, 19-21 February 2009. This meeting discussed the standardisation of nasal potential difference (PD) and rectal current measurements between different centres for assaying CFTR function in clinical trials, while Dr. David Sheppard (P1) delivered an invited lecture about techniques to measure CFTR function *in vitro*. Prior to the meeting, there was a one-day workshop to provide expert training in the use of the nasal PD assay for measuring CFTR activity *in vivo*.
21. Led by Prof. Carlo Castellani (Cystic Fibrosis Center, Verona), the Neonatal Screening Group of WP3 published their consensus guidelines on neonatal screening for CF in Europe in the *Journal of Cystic Fibrosis* in February 2009.
22. Led by Prof. Christiane De Boeck (P5b), the Clinical Diagnosis sub-group of Workpackage 3 published an article in *Thorax* in March 2009 about the evaluation of their CF diagnostic algorithm using a population of patients with an intermediate clinical phenotype. These patients are identified by sweat Cl⁻ concentration values intermediate between those of CF patients and normal subjects.
23. **EuroCareCF** sponsored the special symposium “Translating Science into Clinical Practice” at the ECFS Basic Science Conference, “*New Frontiers in Basic Science of Cystic Fibrosis*”, Tavira, Portugal, 15-19 April 2009. This symposium benefited significantly from the active participation of researchers from the pharmaceutical industry actively engaged in drug design and development.
24. Representatives of **EuroCareCF** played an active role in the 2009 Balkans Regional CF conference, Skopje, Macedonia, 17-18 April 2009, which was organised by CF Worldwide. This conference provided an important opportunity to teach best practice in multidisciplinary patient care.
25. Dr. Andreas Reimann (P6) organised the **EuroCareCF** Consensus Workshop for SMEs and Patient Organisations at Bad Nauheim, Germany, 20-21 April 2009. The goals of this workshop were two-fold: first, to discuss how SMEs and CF patient organisations might collaborate to develop new therapies for CF. Second, to elaborate best practice guidelines to govern cooperation between SMEs and patient organisations.
26. Prof. Carla Colombo (P22) arranged with the Slovak CF Association for Prof. Birgitta Strandvik of the CF Centre, Göteborg, Sweden to take her multidisciplinary team of CF healthcare professionals to the CF Center for Children, Children’s Faculty Hospital, Košice, Slovakia, 25-28 May, 2009. In Košice, Prof. Strandvik and her team provided one-to-one training in multidisciplinary CF patient care. They also discussed how to implement the European recommendations about standards of CF patient care in Slovakia.
27. **EuroCareCF** organised workshops and meetings on Patient Care, the European CF Patient Registry, Clinical Research and CFTR-Related Diseases at the 32nd European CF Conference, Brest, France, 10-13 June 2009. These workshops and meetings served two purposes: first, to assess progress towards consensus guidelines and second, to disseminate, at a European level,

the latest information about CF and its diagnosis and treatment. After the conference, Dr. David Sheppard (P1) discussed the highlights of the conference, and the role of **EuroCareCF** in it, for the web-TV of Vaincre la Mucoviscidose, the French CF charity.

28. Dr. Bob J. Scholte (P8a) organised the Joint **EuroCareCF**-ERS Research Seminar: “*Molecular and Cellular aspects of Chronic Lung Disease. Models of Lung Inflammation and Fibrosis, Experimental Therapy*” at Erasmus Medical Center, Rotterdam, The Netherlands, 18-20 June 2009. This research seminar brought together leading experts from Europe and North America to discuss actively animal models of chronic lung disease (e.g. asthma, CF, chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF)) and the development of rational new therapies using these models.

Future Activities

Planned/ actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
07/2009	Meeting: The 41 st Meeting of the European Pancreatic Club	Clinicians and basic researchers	Europe and North America	500	Partners 1 and 12
09/2009	Meeting: ENCE CF-LAM-LTX project meeting	Clinicians and healthcare professionals	Europe	50	Partner 4
09/2009	Publications: Outcome of Quality Assurance trial in CF Microbiology ¹	Clinical Microbiologists	Global	Global	Partner 9
10/2009	Meeting: University of Miami CF Symposium 2009	Clinicians and healthcare professionals	USA		Partner 5a
11/2009	Meeting: European CF Week event at European Parliament	Members of the European Parliament, patient representatives	Europe	75	Partner 4
04/2010	Meeting: ECFS Basic Science Conference ²	Basic researchers	Europe and North America	100	Partner 1 / Partners 2, 4, 8a, 16, 19 and 20
06/2010	Publications: European CF Patient Registry report ³	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters	Europe	Global	Partner 4 / Partners 1 and 12
06/2010	Publications: EuroCareCF consensus guidelines ⁴	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters	Global	Global	Partner 1 / Partners 5a, 5b, 6, 7, 8a, 9, 10, 12, 15, 16, 17, 18, 19 and 22
06/2010	Publications: EuroCareCF Newsletter ⁵	Clinicians, healthcare professionals, basic researchers, CF patients, families and supporters	All	Global	Partner 1
06/2010	Project web-site: EuroCareCF website ⁶	Clinicians, healthcare professionals, basic researchers, CF	All	Global	Partner 1

Planned/actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner responsible /involved
		patients, families and supporters, general public			
06/2010	Meeting: 33 rd European CF Conference ⁷	Clinicians, healthcare professionals, basic researchers	Europe and North America	2,000	Partner 1 / Partners 2, 4, 5b, 6, 10, 12, 14, 15, 16 and 22

Short descriptions of major activities:

1. Prof. Burkhard Tümmler (P9)'s article on the quality assurance trials of CF microbiology performed in 2007 and 2008, which involved over 30 laboratories from 21 European countries was published in the *Journal of Clinical Microbiology* in September 2009.
2. The 2010 ECFS Basic Science Conference, "New Frontiers in Basic Science of Cystic Fibrosis", Carcavelos, Portugal, 7-10 April 2010 is an important gathering of the CFTR research community. It therefore represents an excellent forum to communicate to basic scientists from Europe and North America information about the outputs of workpackages 5 (Novel Therapies), 6 (Animal Models) and 7 (Integration of Fundamental Research).
3. Deliverable 3c (Report on the demographics of European CF patients) will be published as a special supplement to the *Journal of Cystic Fibrosis*. This report will compare the demographics of CF patient populations in individual European countries with data for Europe as a whole. The report will be available online as an open access report following its publication in the *Journal of Cystic Fibrosis*.
4. The majority of the consensus guidelines and reports produced by **EuroCareCF** will be published as a special supplement to the *Journal of Cystic Fibrosis*. These consensus guidelines will address patient care, clinical research, SMEs, novel therapies, animal models and ethical / legal / social issues. These consensus guidelines and reports will be available online as an open access documents following its publication in the *Journal of Cystic Fibrosis*.
5. To accompany the publication of the **EuroCareCF** consensus guidelines and reports in the *Journal of Cystic Fibrosis*, a final issue of the **EuroCareCF** newsletter will be published. On publication, this electronic newsletter will be automatically distributed to members of the ECFS and CF Europe. It will also freely available from the website of **EuroCareCF**.
6. To accompany the publication of the **EuroCareCF** consensus guidelines and reports in the *Journal of Cystic Fibrosis*, the **EuroCareCF** website (<http://www.eurocarecf.eu/>) will be updated to provide a permanent record of the project's activities.
7. The 33rd European CF Conference, Valencia, Spain, 16-19 June 2010 is an important gathering of clinicians and healthcare professionals treating CF patients. It therefore represents an excellent forum to communicate to clinicians and healthcare professionals from Europe and North America information about the outputs of workpackages 1 (Optimising Patient Care and CF Team Work), 2 (European CF Patient Registry) and 3 (Coordination of Clinical Research).

Section 3 - Publishable results:

Participants and collaborators of the **EuroCareCF** project have published work as follows:

Period 1:

EuroCareCF Newsletter:

Issue 1, June 2006.

Issue 2, September 2006.

Issue 3 (Workpackage 2), December 2006.

Period 2:

Reviews:

Scholte BJ, Colledge WH, Wilke M, de Jonge H (2006). Cellular and animal models of cystic fibrosis, tools for drug discovery. *Drug Discov Today Dis Models* **3**: 251-259.

Li H, Cai Z, Chen J-H, Ju M, Xu Z, Sheppard DN (2007). The cystic fibrosis transmembrane conductance regulator Cl⁻ channel: a versatile engine for transepithelial ion transport. *Sheng Li Xue Bao* **59**: 416-430.

Mall MA (2008). Role of Cilia, Mucus, and Airway Surface Liquid in Mucociliary Dysfunction: Lessons from Mouse Models. *J Aerosol Med* **21**: 1-12.

Course Handbooks:

A course handbook (Lectures and Laboratory Techniques) was produced for the "Hands-On" Training Course for Clinical Microbiologists: "*Diagnostic and Molecular Microbiology of Bacteria Retrieved from the CF Lung Habitat*" at Hannover Medical School, Hannover, Germany, 3-6 May 2007.

Two course handbooks (Lectures and Laboratory Techniques) were produced for the "Hands-On" Training Workshop: "*Epithelial Cells & Tissues: Production, Cultivation and Characterization*" at the University of Lisboa, Lisboa, Portugal, 2-6 July 2007. These handbooks are available on the EuroCareCF website (<http://www.eurocarecf.eu/wp7/WP7workshopsheld.htm>).

EuroCareCF Newsletter:

Issue 4, April 2007.

Issue 5, July 2007.

Issue 6 (Workpackage 3), October 2007.

Period 3:

Consensus Guidelines:

Castellani C, Southern KW, Brownlee K, Dankert Roelse J, Duff A, Farrell M, Mehta A, Munck A, Pollitt R, Sermet-Gaudelus I, Wilcken B, Ballmann M, Corbetta C, de Monestrol I, Farrell P, Feilcke M, Férec C, Gartner S, Gaskin K, Hammermann J, Kashirskaya N, Loeber G, Macek M Jr, Mehta G, Reiman A, Rizzotti P, Sammon A, Sands D, Smyth A, Sommerburg O, Torresani T, Travert G, Vernooij A, Elborn S. (2009). European best practice guidelines for cystic fibrosis neonatal screening. *J Cyst Fibros*. **8**:153-173.

Articles:

Goubau C, Wilschanski M, Skalická V, Lebecque P, Southern KW, Sermet I, Munck A, Derichs N, Middleton PG, Hjelte L, Padoan R, Vasar M, De Boeck K. (2009). Phenotypic characterisation of patients with intermediate sweat chloride values: towards validation of the European diagnostic algorithm for cystic fibrosis. *Thorax*. **64**:683-691.

Hogardt M, Ulrich J, Riehn-Kopp H, Tümmler B. (2009). EuroCareCF quality assessment of diagnostic microbiology of cystic fibrosis isolates. *J Clin Microbiol*. **47**:3435-3438.

Pinxten W, Dierickx K, Nys H. (2008). The implementation of Directive 2001/20/EC into Belgian law and the specific provisions on pediatric research. *Eur J Health Law*. **15**:153-161.

Pinxten W, Nys H, Dierickx K. (2008). Regulating trust in pediatric clinical trials. *Med Health Care and Philos* **11**:439-444.

Pinxten W, Nys H, Dierickx K. (2009). Ethical and regulatory issues in pediatric research supporting the non-clinical application of fMR imaging. *Am J Bioeth*. **9**:21-23.

Pinxten W, Dierickx K, Nys H. (2009). Ethical principles and legal requirements for pediatric research in the EU: an analysis of the European normative and legal framework surrounding pediatric clinical trials. *Eur J Pediatr*. **168**:1225-1234.

McCormick J, Mehta G, Olesen HV, Viviani L, Macek M Jr, Mehta A, on behalf of the European Cystic Fibrosis Registry (2009). Comparative demographics of the European cystic fibrosis population: Does EU membership confer an advantage? *Lancet* (**Accepted**).

Reviews:

Carvalho-Oliveira I, Scholte BJ, Penque D. (2007). What have we learned from mouse models for cystic fibrosis? *Expert Rev Mol Diagn*. **7**:407-417.

Johannesson M, Olesen HV, Mehta G, Mehta A. (2007). Setting up a European registry for cystic fibrosis – lessons learned. *Eur Respir Dis* **2007**, 25-26.

Mall MA. (2009). Role of the amiloride-sensitive epithelial Na⁺ channel in the pathogenesis and as a therapeutic target for cystic fibrosis lung disease. *Exp Physiol*. **94**:171-174.

Li H, Sheppard DN. (2009). Therapeutic potential of cystic fibrosis transmembrane conductance regulator (CFTR) inhibitors in polycystic kidney disease. *BioDrugs*. **23**:203-216.

Becq F. (2009). Cystic fibrosis transmembrane conductance regulator modulators for personalized drug treatment of cystic fibrosis: progress to date. *Drugs* **70**:241-259.

Publications using resources produced by EuroCareCF:

Jouret F, Bernard A, Hermans C, Dom G, Terryn S, Leal T, Lebecque P, Cassiman JJ, Scholte BJ, de Jonge HR, Courtoy PJ, Devuyst O. (2007). Cystic fibrosis is associated with a defect in apical receptor-mediated endocytosis in mouse and human kidney. *J Am Soc Nephrol*. **18**:707-718.

Bonvin E, Le Rouzic P, Bernaudin JF, Cottart CH, Vandebrouck C, Crié A, Leal T, Clement A, Bonora M. (2008). Congenital tracheal malformation in cystic fibrosis transmembrane conductance regulator-deficient mice. *J Physiol*. **586**:3231-3243.

Noël S, Strale PO, Dannhoffer L, Wilke M, DeJonge H, Rogier C, Mettey Y, Becq F. (2008). Stimulation of salivary secretion *in vivo* by CFTR potentiators in *Cftr*^{+/+} and *Cftr*^{-/-} mice. *J Cyst Fibros*. **7**:128-133.

Noël S, Wilke M, Bot AG, De Jonge HR, Becq F. (2008). Parallel improvement of sodium and chloride transport defects by miglustat (*n*-butyldeoxynojirimycin) in cystic fibrosis epithelial cells. *J Pharmacol Exp Ther*. **325**:1016-1023.

Ohlsson L, Hjelte L, Hühn M, Scholte BJ, Wilke M, Flodström-Tullberg M, Nilsson Å. (2008). Expression of intestinal and lung alkaline sphingomyelinase and neutral ceramidase in cystic fibrosis F508del transgenic mice. *J Pediatr Gastroenterol Nutr*. **47**:547-554.

Carvalho-Oliveira IM, Charro N, Aarbiou J, Buijs-Offerman RM, Wilke M, Schettgen T, Kraus T, Titulaer MK, Burgers P, Luider TM, Penque D, Scholte BJ. (2009). Proteomic analysis of naphthalene-induced airway epithelial injury and repair in a cystic fibrosis mouse model. *J Proteome Res*. **8**:3606-3616.

Gavilanes X, Huaux F, Meyer M, Lebecque P, Marbaix E, Lison D, Scholte B, Wallemacq P, Leal T. (2009). Azithromycin fails to reduce increased expression of neutrophil-related cytokines in primary-cultured epithelial cells from cystic fibrosis mice. *J Cyst Fibros*. **8**:203-210.

Meyer M, Huaux F, Gavilanes X, van den Brûle S, Lebecque P, Lo Re S, Lison D, Scholte B, Wallemacq P, Leal T. (2009). Azithromycin reduces exaggerated cytokine production by M1 alveolar macrophages in cystic fibrosis. *Am J Respir Cell Mol Biol*. **41**:590-602.

Course Handbooks:

A course handbook (Lectures and Laboratory Techniques) was produced for the “Hands-On” Training Course for Clinical Microbiologists: “*On the Processing of Microbiological Specimens from Individuals with CF*” at Hannover Medical School, Hannover, Germany, 10-13 April 2008.

Two course handbooks (Lectures and Laboratory Techniques) were produced for the “Hands-On” Training Workshop: “*Epithelial Cells from the Lung: Production, Cultivation and Characterisation*” at the University of Lisboa, Lisboa, Portugal, 14-18 July 2008.

EuroCareCF Newsletter:

Issue 7, January 2008.

Issue 8, May 2008.

Issue 9-10, December 2008.

Issue 11, May 2009.