Year of report: 2022	
Name of Working Group: ECFS-Diagnostic Network Working Group	Date of initial approval of working group: 2004 (M Sinaasappel)

Contact details of coordinator, vice coordinator and assistant (if applicable) including ECFS membership numbers:
Coordinator: Elke De Wachter
Vice coordinator name: Nick Simmonds
Assistant name: Marlies Destoop

Long term aims of the working group (maximum 100 words) including estimated achievement date:

For none of these topics a final achievement date can be determined. These are ongoing projects with the need to change/support whenever needed (depending on local regulations, new insights in disease liability of mutations, financial support)

1/ To achieve pan-European cooperation on definitions of CF and clinical entities of the CF-spectrum.
2/ Standardization of existing electrophysiological techniques. Development, validation and standardization of new diagnostic technologies.
3/ Interpretation of disease liability of CFTR-mutations and discussion of difficult cases within the group
4/ Improvement/support for sweat test facilities and diagnostic challenges in LMIC
5/ Cooperation with other networks:
- ECFS-CTN and CFF TDN, standardization committee
- ECFS NSWG: newborn screening and diagnosis are closely related
- European CF-Registry: Inclusion criteria remain: fulfilling the diagnostic criteria of CF
- ECFS educational platform

Outcomes already achieved (maximum 100 words):

1/ CFF-ECFS recommendations for CF Diagnosis - Farrell 2017: a close link between CFF experts in diagnosis and ECFS-DNWG is maintained and will be used in future projects
2/ Sweat test Project:
  - Sweat test survey (Cirilli 2017): highlighting deficiencies/barriers in sweat testing in real life in Europe.
  - Hands-on Training Workshops to improve sweat test performance in Europe. (Belgrade 2018, Liverpool 2019)
  - Publication: Standards of care guidance for sweat testing; phase two of the ECFS quality improvement programme (Cirilli 2022; https://doi.org/10.1016/j.jcf.2022.01.004). This paper is the result of a joint writing and discussion process with different members of the DNWG.

3/ CFTR biomarkers: standardization and diagnostic reference values
- NPD and ICM validation studies have been performed in HC and CF in different European centres. Summary of the results, further statistical analysis is needed.

1/ Short term goals for the year

- Despite the prolonged Covid pandemic we kept on organising our **meetings** in a virtual way (see further)
- S**weat test project** has achieved its next step in January 2022 with the publication of the new standards of care guidance for sweat testing in Europe. (Cirilli 2022). This work has been achieved thanks to the efforts of all co-authors, being all members of the DNWG: N. Cirilli, K.W. Southern, J. Barben, F. Vermeulen, A. Munck, M. Wilschanski, Thao Nguyen-Khoa, M. Aralica, N Simmonds, E. De Wachter. Different on-line meetings were held in order to finalize this work.
- Due to the change in Medical Device Regulation (MDR) in Europe, the sweat test project has certainly not come to an end. We are now facing challenges to supply European labs with sweat test consumables due to these changes in MDR. Currently, the DNWG is closely involved in trying to resolve this issue.
- Development of **new guidelines on CFTR-related disorders (CFTR-RD**):

The Bombieri paper (JCF 2011) is 10 years old and describes recommendations on how to establish the diagnosis of CFTR-RD. New insights in CFTR-disease liability led to the need of new recommendations on how to diagnose, treat and follow up people with a CFTR-RD. This project started in March 2020. CFTR-RD core group: Carlo Castellani, Kevin W Southern, Elke De Wachter, Nick Simmonds, Kris De Boeck, Isabelle Sermet-Gaudelus. Due to the COVID pandemic only virtual meetings were held. This work led to the submission of 2 papers (the first 2 in a series of 4) to the JCF, which is still under revision at this time.

The first paper focusses on the updated diagnostic criteria and general principles of management. The second paper gives clearer guidance on CFTR dysfunction and relevant CFTR variants. The next step in this process is to focus on each separate condition that can be designated as a CFTR-RD. Colleagues from different subdisciplines will be involved in this part of the project.

- During the brainstorm meeting in October 2 new projects have started:

a/ Beta-adrenergic sweat test: A core group (I Sermet, T Gonska, B Tümmler, P Melotti, T Leal) aims at a better harmonisation for the beta-adrenergic sweat test. The goal is to develop a standardized harmonized protocol, aiming to validate this diagnostic method and implement this at a later stage in other clinics to overcome some limitations of the sweat test.

b/ Widespread screening for CF in lower- and middle-income countries (LMIC): Leaders of this project are Samia Hamouda (Tunis, Tunesia) and Anne Munck (Paris, Fr). The objective is to determine the incidence of CF in these countries and to improve CF management. In addition we hope it will contribute to the introduction of CF neonatal screening programs especially for countries with a high CF incidence.

2/ Current number of members: 99 members. Despite repeated reminders to renew ECFS membership, not all members have responded. We should discuss with the board how to solve this issue and if members should be withdrawn after repeated reminders.

3/ Measures to encourage ECFS membership

- During each official meeting (symposia and annual meetings) this issue is stressed. "Being part of the European CF Society is mandatory to become/remain a member of the DNWG".
- e-mails (before each registration for a meeting) were sent to all DNWG members to remind them that ECFS-membership is mandatory to remain part of ECFS-DNWG.
- For future initiatives and annual meetings we will only fund CONFIRMED ECFS members for their accomodation/meals.

4/ Meetings (between May 2021-May 2022)

- DNWG session at the 44th ECFC-virtual platform: 11th June 2021: 12.30-14.30
- 1st DNWG-brainstorm meeting: 1 October 2021. This meeting was held during the initial timeframe of NACFC. The aim was to brainstorm about the development of new projects and the short presentation of ongoing projects. Despite its virtual format, lively discussion was possible, which led to a successful initiatives.

- 19th Annual DNWG-meeting. Despite our hope to have an in-person meeting in Montpellier we were forced to have a virtual meeting again, due to the COVID pandemic. The meeting was held on 3 consecutive days (3x1/2 day) 9th-11th February 2022.

Programs and reports of each meeting are posted on the ECFS website.

5/ Website development

News regarding DNWG activities was posted on the website. Webinar, filmed during the September meeting is available on the website.

A new logo was developed in 2021 to increase visibility AND to stress the link with ECFS

6/ Publications from the DNWG as a group:

- Cirilli N, Southern KW, Barben J, Vermeulen F, Munck A, Wilschanski M, Nguyen-Khoa T, Aralica M, Simmonds NJ, De Wachter E; ECFS Diagnostic Network Working Group. Standards of care guidance for sweat testing; phase two of the ECFS quality improvement programme. J Cyst Fibros. 2022 Jan 19:S1569-1993(22)00025-X. doi: 10.1016/j.jcf.2022.01.004. Epub ahead of print. PMID: 35063396.

Under review:

- Castellani C, De Boeck K, De Wachter E, Sermet-Gaudelus I, Simmonds NJ, Southern KW, on behalf of the ECFS Diagnostic Network Working Group. ECFS standards of care on CFTR-related disorders: updated diagnostic criteria. Submitted to JCF March 2022

- I Sermet-Gaudelus, E Girodon, F Vermeulen, GM Solomon, P Melotti,, S Graber, I Bronsveld, S Rowe, M Wilschanski, B Tuemmler, G Cutting, T Gonska. ECFS standards of care on CFTR-related disorders: diagnostic criteria of CFTR dysfunction. Submitted to JCF April 2022.

- Samia Hamouda, Sondess Hadj Fredj, Taieb Messaoud, Virginie Scotet, Khadija Boussetta, Anne Munck. Up-to-date incidence and initial characteristics of cystic fibrosis in Tunisia. Submitted as a letter to the editor to JCF May 2022.

7/ additional issue: extension of the 3 year mandate.

Due to the Covid pandemic, the coordinator and co-coordinator of the mandate June 2019-June 2022 have not been able to achieve their goals in full; for example in person meetings during the year.

Therefore, we request the prolongation of this mandate for another 3 years with the following structure:

Elke De Wachter: Coordinator
Nick Simmonds: Vice-coordinator (becoming the coordinator in June 2025)
Marlies Destoop: DNWG-assistant

This suggestion was brought up at the annual (virtual) DNWG meeting in February. No objection was received from the members to neither Elke nor Nick after this communication.

Aims for the coming year (please state year) (max 50 words):
Period June 2022-2022

1/ planned meetings for the upcoming year:
- 1.1 DNWG meeting at ECFC Rotterdam (Friday 10th June, 12.30-14.30)
- 1.2 Closed DNWG-brainstorming meeting during NACFC 2022
- 1.3 Symposium at NACFC 2022 regarding CFTR-RD. Preliminary scheduled on November 3rd in Philadelphia
- 1.4 Annual ECFS-DNWG meeting in Montpellier (Fr) 9-11th February 2023

2/ Supporting the process of sweat test device delivery to European labs, as we face difficulties due to changes in the European MDR
3/ Continue the work on the CFTR RD project (paper 3 and 4)
4/ Implementing beta-adrenergic sweat tests as an additional diagnostic tool in European centres.
5/ Continue the link with LMIC at improving diagnosis in CF
6/ Improve link with ECFS education committee to create an online sweat test educational tool, in line with the manuscript

Summary (maximum 100 words):

DNWG is an active, heterogeneous group of enthusiastic CF specialists with a special interest in diagnostic issues. It consists of CF physicians (adult and paediatric), geneticists, clinical biochemists, basic scientists, and other MDT members, making a very complementary group. This enables us not to focus only on one topic of diagnosis, but to have in depth expertise. We are strongly convinced that our work has not finished yet. The interpretation of CFTR mutations, their disease liability, the CF spectrum and the interpretation of biomarkers that measure CFTR activity and its translation to the individual patient are topics that need further investigations and a platform supporting this.

Breakdown of expenses (please include total amount received as well as expenditure and, if applicable, the outstanding balance (Euros)):
Due to the inability to have in-person meetings, we had no expenses in the last year.
We did have support from the ECFS to organize virtual meetings, with help from an assistant. No expenses were declared for this support

Budget amount requested for next year (please give the amount in Euros and the year):

- We would like to receive the annual 10.000 euro to support the annual DNWG-meeting in 2023 - Montpellier.
- We plan to set up an educational tool for sweat testing, in line with the recommendations published. A link with the educational platform will be made. We assume that ECFS has provided funding to the education committee to make this happen.