ECFS-Diagnostic Network Working Group (DNWG)

Year of report: 2023	Date of initial approval of working group: 2004 (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 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:

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*-variants and discussion of challenging cases within the group
4/ Improvement/support for sweat test facilities in Europe and in LMIC
5/ Cooperation with other networks:
- ECFS-CTN and CFF TDN, standardization committee
- ECFS NSWG: neonatal screening and diagnosis are closely related
- European CF-Registry: expanding to CFSPID and CFTR-RD registries - supporting sweat test facilities in LMIC
- ECFS education committee

Outcomes already achieved:

1/ CFF-ECFS recommendations for CF Diagnosis - Farrell 2017: link between ECFS-DNWG and CFF experts in diagnosis is maintained (CFTR-RD for example)
2/ Sweat test Project:
  - Sweat test survey (Cirilli 2017)
  - Hands-on Training Workshops at ECFC: Belgrade 2018, Liverpool 2019
  - 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).

3/ CFTR biomarkers: standardization and validation for NPD, ICM: statistical analysis is ongoing. Organoids as diagnostic tool
4/ CFTR-Related Disorders-Project: Leader: Carlo Castellani
- Publication of 2 papers in a series of four:
  - Castellani C, et al. ECFS standards of care on CFTR-related disorders: Updated diagnostic criteria. J Cyst Fibros. 2022 Nov;21(6):908-921. doi: 10.1016/j.jcf.2022.09.011. Epub 2022 Oct 8. PMID: 36220763
  - Sermet-Gaudelus I et al. ECFS standards of care on CFTR-related disorders: Diagnostic criteria of CFTR dysfunction. J Cyst Fibros. 2022 Nov;21(6):922-936. doi: 10.1016/j.jcf.2022.09.005. Epub 2022 Oct 5. PMID: 36207272.

Report for this year

- short term goals for the year
- current number of members
- measures taken to encourage ECFS membership
- outcomes/achievements (e.g. meetings, activities, website development, awards, publications etc).

1/ Short term goals for the year

- S**weat test project.**

The third phase in the "Sweat test project" is to organize another **hands-on session**, taking into account the latest published ECFS-recommendations. The aim is to support centres and help in problem-solving to achieve acceptable standards for good sweat testing practice as a diagnostic tool in their CF centre. We plan to organize the first in a series of other sessions (depending on its success) at the ECFC in Vienna.

This session is planned in cooperation with the ECFS-PR and the ECFS education committee. This joint effort will further develop sweat testing standards in CF centres in LMIC that have already received initial support by an ECFS-PR program. In addition, the ECFS education committee will assist with the next step: working on an e-learning tool for the different sweat test techniques that are currently available in different clinics.

- **Adaptations in the European Medical Device Regulation (MDR)** and certification led to an important lack of sweat test devices and disposables in different European countries since the beginning of 2022. The DNWG has worked to find solutions for this issue, including by working with national regulators to **obtain a temporary authorization** of import and the use of sweat test consumables during the review process until they are recertified under the new EU-MDR.

- Development of **new guidelines/recommendations on CFTR-related disorders (CFTR-RD**):

The Bombieri paper (JCF 2011) is over 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. The plan is to develop a series of 4 papers, highlighting different sub-sections.

The first paper focusses on the updated diagnostic criteria and general principles of management. The second gives clearer guidance on CFTR dysfunction and relevant CFTR variants. Both papers were published in 2022. The third paper will focus on each separate condition that can be designated as a CFTR-RD. Colleagues from different sub disciplines will be involved in this part. The last section in this topic will focus on remaining questions including: the need for a CFTR-RD registry, the link with CFSPID, barriers to implementation and dissemination, clinical trials and therapy, and genetic counselling.

- **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.

- **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 increase awareness about CF by policy makers in LMIC, in order to improve financial support for the implementation of standards of care in countries with a high CF incidence.

2/ Current number of members: 117 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 DNWG members without ECFS membership 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 accommodation/meals
- A new logo was developed in 2021 to increase visibility AND to emphasise the link with the ECFS

4/ Meetings (between May 2022-May 2023)
- DNWG session at the 45th ECFS Conference (Rotterdam): 10th June 2022: 12.30-14.30
- 2st DNWG-brainstorm meeting at NACFC (Philadelphia): 4th October 2022.
- 20th Annual DNWG-meeting (Montpellier): 9th-11th February 2023.

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

5/ Website development
News regarding DNWG activities was posted on the website.

6/ Publications from the DNWG as a group:

- Castellani C, De Boeck K, De Wachter E, Sermet-Gaudelus I, Simmonds NJ, Southern KW; ECFS Diagnostic Network Working Group. ECFS standards of care on CFTR-related disorders: Updated diagnostic criteria. J Cyst Fibros. 2022 Nov;21(6):908-921. doi: 10.1016/j.jcf.2022.09.011. Epub 2022 Oct 8. PMID: 36220763.

- Sermet-Gaudelus I, Girodon E, Vermeulen F, Solomon GM, Melotti P, Graeber SY, Bronsveld I, Rowe SM, Wilschanski M, Tümmler B, Cutting GR, Gonska T. ECFS standards of care on CFTR-related disorders: Diagnostic criteria of CFTR dysfunction. J Cyst Fibros. 2022 Nov;21(6):922-936. doi: 10.1016/j.jcf.2022.09.005. Epub 2022 Oct 5. PMID: 36207272.

Aims for the coming year : (June 2023-May 2024)
1/ Planned meetings:
    1.1 Sweat test hands-on session, Vienna (Tue 6th June 2023: 15:00-18:00)
    1.2 DNWG meeting, Vienna (Fri 9th June, 12.30-14.30)
    1.3 Closed DNWG-brainstorming meeting - NACFC 2023
    1.4 Annual ECFS-DNWG meeting 8-10th Feb 2024 - *location will be announced on Tue 6th June 2023*
2/ Continue the work on CFTR RD project
3/ Develop an e-learning tool for sweat testing, plan other hands-on sessions and visits on site
4/ Implementation of beta-adrenergic sweat tests in European centres.
5/ Continue the link with LMIC at improving diagnosis in CF
6/ Develop organoid diagnostics capability

Summary:

DNWG is an active group of enthusiastic CF specialists with special interest in diagnostic issues. It consists of CF physicians, geneticists, clinical biochemists, basic scientists, and other MDT members, making a very complementary group. This enables us to have diverse and strong expertise. We have made significant progress but there are many scientific and clinical issues still to be resolved, which DNWG has the capability and expertise to address.. These include: the interpretation of *CFTR* mutations and their disease liability; the CF spectrum and the interpretation of biomarkers for CFTR activity; and CFTR activity and its translation to the individual patient. These 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)). Please refer to the WG TOR for examples of budget expenses:

Annual DNWG meeting in Montpellier:
54 attendees
Sponsorship for ECFS-DNWG: total amount 22723,0 euro
(ECFS, Network Muco/CFTR, Elitech, Vertex pharmaceutricals, Yourgene, CHU Montpellier)
Expenses: 22765,0 euro
(hotel 2 nights, meeting rooms, catering, dinner, social event, YI-award)
Total balance of the Annual meeting: -42 euro

Attached an overview of the DNWG-budget (

Budget amount requested for next year

- We would like to receive the annual 10.000 euro to support the annual DNWG-meeting 2024 and to set-up future hands-on sweat test sessions (covering partly the rent of the room)
- 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 for this.

Appendix

Please provide us with a list of all current members (name, professional title, email address and ECFS membership number): Please see attached file

For ECFS board use only:

Report received in Office on:

Number of years of working group

Report accepted / rejected
Follow-up action to be taken by ECFS