ECFS Diagnostic Network Working Group
Meeting Report

22nd Annual Meeting, Brussels, Belgium - February 6th - 8th 2025

Thursday, 6th of February 2025

Part 1. Hands-on sessions on beta-adrenergic sweat test: evaporimetry

One of the highlights of the meeting was a hands-on session on the beta-adrenergic sweat test: evaporimetry. This is a diagnostic tool for cystic fibrosis under development. The session was presented and led by Sophie Gohy (Brussels, Belgium) and Isabelle Sermet-Gaudelus (Paris, France) and their team. After the introduction, participants got the chance to perform the beta-adrenergic sweat test themselves, gaining practical experience with this innovative diagnostic method.

Part 2. Scientific Program

At 14:30 the meeting started with welcome words from Elke De Wachter and Nick Simmonds to the 74 participants of the 22nd annual ECFS DNWG meeting in Brussels, Belgium.

Session 1: Let's start with the world's best beer and cheese

Chair: Elke De Wachter (Brussels, Belgium) - Caroline Raynal (Montpellier, France)

The session began with **Veerle Vloebergs** (Brussels, Belgium) and **Stefanie Vincken** (Brussels, Belgium) providing an overview of the pathophysiology of congenital absence of the vas deferens (CAVD) and its link with CF. They then outlined the journey of affected men as they visit the fertility clinic in UZ Brussel, detailing how they are counseled on their options in assisted reproductive technology (ART) and the clinical workup to exclude CF conducted afterwords. Additionally, they introduced the CFTR-RD registry at UZ Brussel, presenting an overview of the patients included so far. Following this, **Marlies Destoop** (Utrecht, Netherlands/Brussels, Belgium) provided an update on the current status of the HIT-CF project, with a particular focus on the CHOICES trial. Next, **Sophie Gohy** (Brussels, Belgium) introduced the beta-adrenergic sweat test using evaporimetry. She summarized the existing evidence on the beta-adrenergic sweat test and the various techniques available to perform it. Additionally, she presented the "Stracyfic Project," which aims to compare different beta-adrenergic sweat test techniques in collaboration with Isabelle Sermet-Gaudelus (Paris, France), Manuel Nietert (Hannover, Germany), and Andrea Gramegna (Milan, Italy).

Session 2: What else is happening in the Low Countries?

Chair: Nicholas Simmonds (London, UK) - Simon Gräber (Berlin, Germany)

The second session commenced with a presentation by **Senne Cuyx** (Leuven, Belgium) on the use of rectal organoids for diagnosis and personalized medicine in CF. He demonstrated how the ROMA CFTR bioassay can distinguish between CF and non-CF cases and discussed ongoing efforts to validate the assay as a biomarker. Next, **François Vermeulen** (Leuven, Belgium) and **Inez Bronsveld** (Utrecht, Netherlands) presented illustrative cases that explored the use of organoid morphology as a diagnostic tool. They examined the dynamic range of the assays and highlighted the missing data and information needed to further validate this approach. To conclude the session, **Nicholas Simmonds** (London, UK) provided a summary of the day's discussions, and **Elke De Wachter** (Brussels, Belgium) shared details about the evening's planned activities.

Friday, 7th of February 2025

Session 3: Neonatal screening session

Chairs: Jürg Barben (St Gallen, Switzerland) – Olaf Sommerburg (Heidelberg, Germany)

The second day began with **Jürg Barben** providing an overview of the NSWG activities and future plans. As the outgoing coordinator, he introduced Olaf Sommerburg as the next NSWG coordinator. Next, **Jane Davies** (London, UK) and **Idan Bokobza** (London, UK) discussed the diagnostic and management challenges associated with CFTR-modulator therapy in fetuses and infants. They presented findings from their survey on European follow-up practices for babies exposed to Kaftrio during pregnancy and lactation and shared responses. Additionally, they presented their Matriarch study (**MAT**e**R**nal, **I**nf**A**nt, **R**eproductive & **C**hild **H**ealth in CF), which aims to improve understanding of maternal and child health in CF. **Marijke Proesmans** (Leuven, Belgium) then provided an overview of CF newborn screening in Belgium, highlighting current challenges and plans to consolidate regional data into national data for better evaluation. **Anaïs Le** (Paris, France), a young investigator, presented findings from the MODUL-CF study, the first real-world study on fetal therapy in CF. Following this, **Andrea Párniczky** (Budapest, Hungary) presented a complex diagnostic case, "Can we rely on sweat chloride measurement?", emphasizing the limitations of newborn screening programs. **Andrea Kowalik** (Stockholm, Sweden) also shared a challenging diagnostic case on pseudo-Bartter syndrome. Both cases sparked a lively and insightful discussion among the audience.

Session 4: CFTR biomarkers - Does age matter?

Chair: Kevin Southern (Liverpool, UK) – Natalia Cirilli (Ancona, Italy)

This session focused on the impact of age on CFTR biomarkers. **Nicholas Simmonds** opened with an overview of the relationship between sweat chloride concentration (SCC) and age, summarizing current knowledge. He then discussed recent findings from the national Difficult Cystic Fibrosis Diagnosis Service, which aimed to describe SCC distribution in adult patients and assess its ability to differentiate diagnostic outcomes. **Michael Wilschanski** (Jerusalem, Israel) followed with insights on the performance of nasal potential difference (NPD) testing in young children, focusing on reducing the time required for the test. He concluded that the shortened NPD protocol shows promise as a diagnostic tool for young children, particularly in cases with an indeterminate CF diagnosis. However, he emphasized the need for further validation studies to confirm its efficacy and reliability. Next, **Simon Gräber** (Berlin, Germany) presented findings on the age dependency of CFTR function in rectal tissue. He demonstrated that chloride secretion in non-CF rectal epithelium declines with age, as does ion transport in CFTR rectal epithelium and the number of secretory colonocytes at the crypt base. Additionally, he highlighted an age-dependent response to CFTR modulator therapy, underscoring the importance of age-specific reference values for diagnosing CF and CFTR-related disorders. **Chris Smith** (Brighton, UK), Director of the ECFS-Education Committee, then provided an overview of the collaborative efforts between the Diagnostic Network Working

Group (DNWG) and ECFS Education. He outlined current projects and presented upcoming initiatives and opportunities. The session concluded with the introduction of a new DNWG project on sweat testing. **Kevin Southern** highlighted existing current challenges in sweat testing, while **Natalia Cirilli** proposed potential solutions. A discussion followed, during which the audience deliberated on the content and goals of the project. The consensus was that new reference values for SCC are needed, necessitating a large collaborative study within the DNWG group to examine SCC variations across different age groups and populations.

Session 5: CFTR-genetic session part 1

Chair: Karen Raraigh (Baltimore, US) – Emmanuelle Girodon (Paris, FR)

Milan Macek (Prague, Czech Republic) provided insights from his exploratory population genetic study, concluding that the shifting demography and epidemiology of CF worldwide necessitate robust and reliable CFTR sequencing using MPS (NGS). **Elke De Wachter** outlined the progress in establishing the ECFS-DNWG diagnostic forum. She proposed utilizing the existing secure web-based IT platform from the Clinical Patient Management System (CPMS) by ERN to facilitate its setup. **Caroline Raynal** (Montpellier, France) introduced a complex diagnostic case involving an unusual scenario of a false-negative NBS and normal sweat test. She emphasized the importance of minimal CFTR testing as a first-line assessment for patients with pulmonary symptoms who will undergo whole-genome sequencing (WGS). **Emmanuelle Girodon** (Paris, France) followed with another case, "Positive sweat test: it may not be CF." The case involved hyponatremic hyperkalemic dehydration, with an extremely high sweat test result leading to the diagnosis of CA XII deficiency. **Peter Middleton** (Sydney, Australia) provided an update on a case previously discussed at a past meeting, titled "CFTR-RD is not always a mild disease." He described a young man experiencing progressively worsening bronchiectasis, repeated hemoptysis despite embolization and surgery, alongside a paratracheal mass. The case sparked a compelling discussion about the true nature of the patient's condition—whether it aligns with CF, CFTR-related disorder (CFTR-RD), or IgG4 disease.

Session 6: Key Note Lecture (CFTR-genetic session part 2)

Chair: **Milan Macek (Prague, Czech Republic) – Caroline Raynal (Montpellier, France)**

Karen Ragaigh (Baltimore, USA), the keynote speaker of this year's meeting, shared ongoing work on the expansion of CFTR2. She outlined the project's primary goal of providing detailed variant interpretation to the CF community by integrating clinical data, functional test results, and expert analysis. She explained the methodology behind this process, highlighted its significance in improving CF diagnostics, and discussed current challenges and future directions for the initiative. Wrap-up of the second day and plans for the evening were shared by Elke De Wachter.

Saturday, 8th of February 2025

Session 7: Exploring theratyping from different perspectives

Chair: Isabelle Sermet-Gaudelus (Paris, France) – François Vermeulen (Leuven, Belgium)

The final day of the meeting opened with **Nicoletta Pedemonte** (Genoa, Italy) presenting the Italian Theratyping program, which utilizes nasal epithelial cells to evaluate CFTR activity and modulator response. She highlighted nasal cells as a reliable model and demonstrated that CFTR function varies among healthy controls, with carriers of CFTR variants exhibiting subclinical dysfunction. **Mirjam Stahl** (Berlin, Germany) followed with an overview of the Berlin Theratyping program, which employs nasal epithelial cells for personalized medicine in CF patients ineligible for CFTR modulators. She introduced the PREMIUM-CF study, where participants undergo in vivo CFTR function assessments followed by clinical evaluations of modulator response. Her findings supported the effectiveness of nasal epithelial cells as a preclinical tool for predicting treatment responses in patients with rare variants. However, she cautioned that in vitro data may underestimate responses, reinforcing the importance of combining in vitro CFTR testing with in vivo biomarker validation. **Sacha Spelier** (Utrecht, Netherlands) provided insights into the use of intestinal organoids for theratyping in Utrecht. She outlined completed and ongoing work, including efforts to centralize the biobank, automate and standardize assays, and implement patient-derived intestinal organoids (PDIOs) as biomarkers. **Isabelle Sermet-Gaudelus** (Paris, France) concluded the session by discussing the French Theratyping program. She emphasized that measuring CFTR function in nasal epithelial cells offers a promising preclinical biomarker for predicting patient responses to treatments. However, she acknowledged ongoing challenges in inter-laboratory standardization and reproducibility that must be addressed.

Session 8: CFTR- biomarkers with/without CFTR-modulator therapy

Chair: **Jane Davies (London, UK) – Peter Middleton (Sydney, Australia)**

Natalia Cirilli (Ancona, Italy) provided an update on the ECFS Quality Improvement Program for sweat testing. This initiative focuses on enhancing the quality of sweat testing performance across both established and emerging CF services. Natalia proposed two distinct laboratory reports tailored to specific clinical needs: one optimized for the diagnosis of cystic fibrosis (CF) and another designed to monitor patients undergoing CFTR-modulator therapy. The latter report would include additional relevant information for treatment management. She also highlighted the need for future work on a separate report to address CFTR-related diseases (CFTR-RD) and CFSPID, with the goal of evaluating disease progression and evolution. **Jasmin Berger** (Berlin, Germany) presented her research on the effects of CFTR modulator therapy in young children aged 2-11 years, focusing on SCC, ICM, and NPD. She concluded that early initiation of ETI therapy in children with CF enhances CFTR function, providing long-term benefits and underlining the importance of early treatment.

Katharina Schütz (Hannover, Germany) shared two case studies illustrating the differences in NPD measurements in two children, both homozygous for p.Leu467Phe-p.Phe508del mutations, who exhibited a reduced response to ETI therapy. These cases highlighted the need for more comprehensive data on complex alleles. **Claudio Sorio** (Verona, Italy) introduced his work on enhancing the measurement of CFTR activity through the use of artificial intelligence (AI). His presentation set the stage for the next speaker, Bogdan Mihae Maris (Verona, Italy), who provided an overview of ongoing efforts to measure CFTR activity in intestinal organoids, utilizing AI techniques to advance this field of research.

Elke De Wachter (Brussels, Belgium) and **Nick Simmonds** (London, UK) brought the 22nd Annual Meeting to a close with a comprehensive summary of the meeting. Following this, Elke and Nick shared that their terms as coordinator and co-coordinator are ending in June. They introduced the next coordinator and co-coordinator, Caroline Raynal (Montpellier, France) and Simon Gräber (Berlin, Germany).

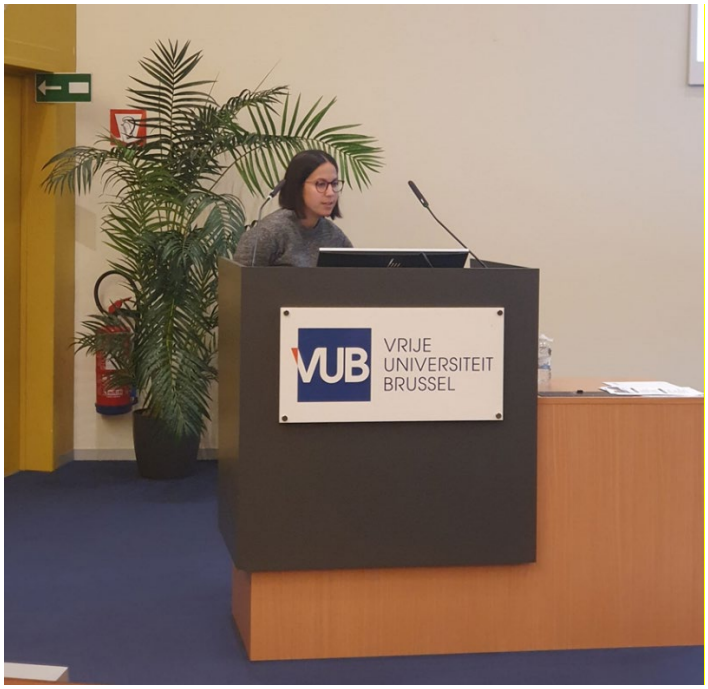
The sponsors, were warmly thanked for their support of this successful event.

We thank all speakers and participants for their fantastic contribution to making the n22nd Annual ECFS Diagnostic Network Working Group Meeting a great success! We are looking forward to meeting you at our next ECFS DNWG Meeting.

10th February 2025

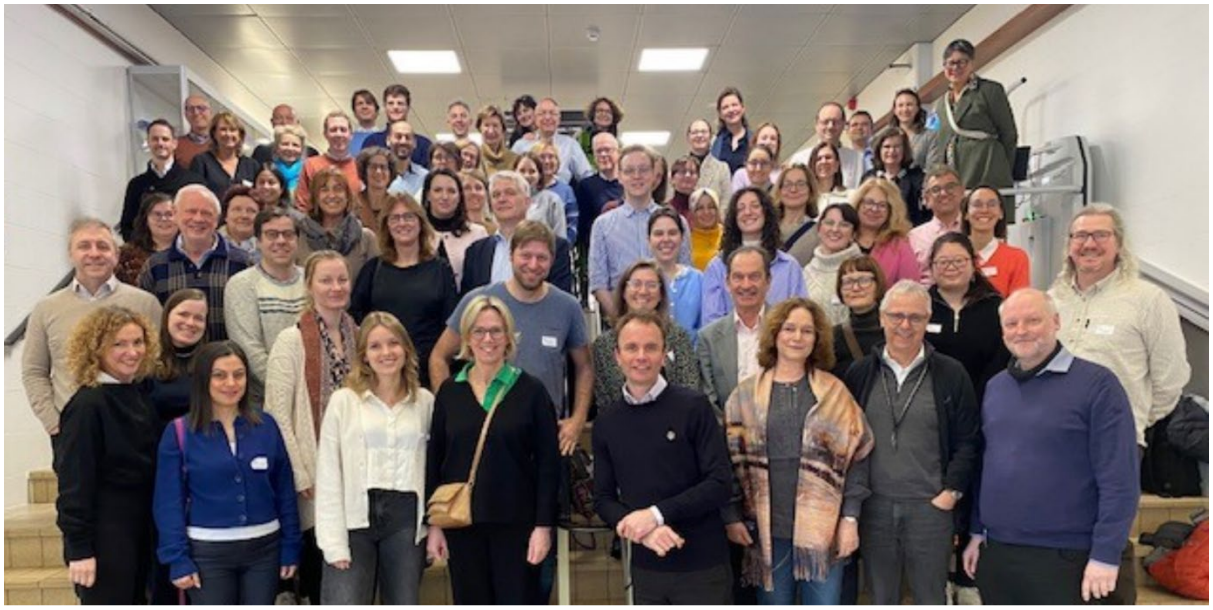
Elke De Wachter – ECFS DNWG Coordinator
Nicholas Simmonds – ECFS DNWG Vice-coordinator
Marlies Destoop – ECFS DNWG Assistant (author of the report)

ECFS DNWG Young Investigators 2025

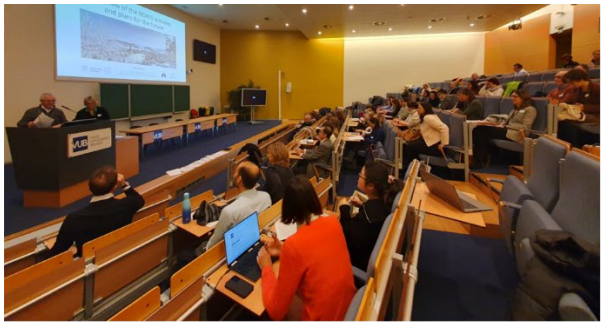


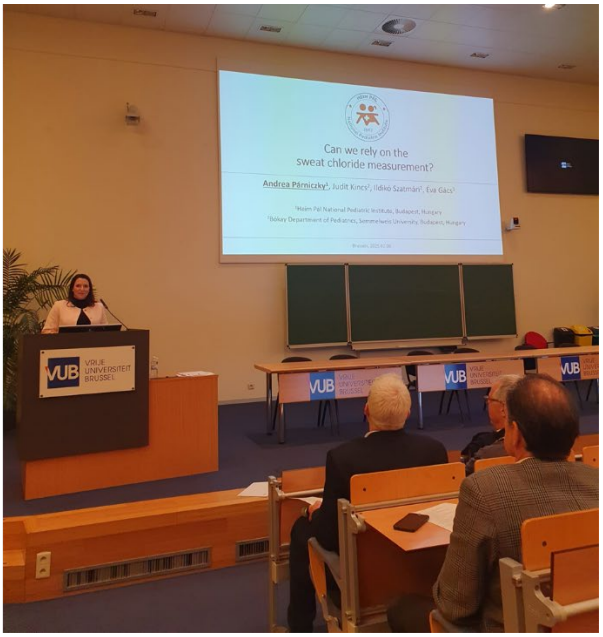
Anaïs Le (Paris, France)

ECFS Diagnostic Network Working Group 2025

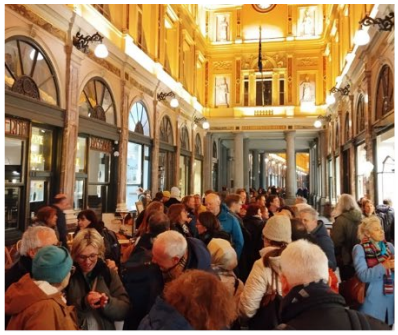


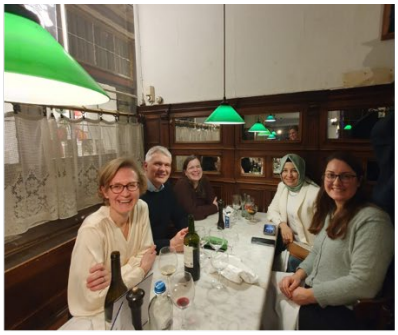
Scientific program:

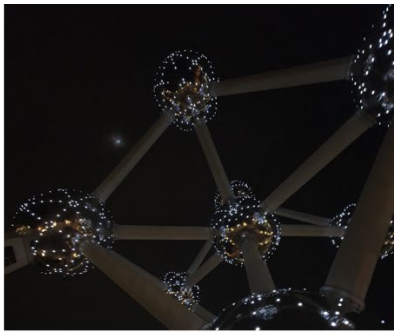


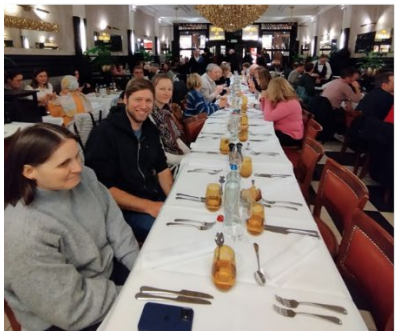


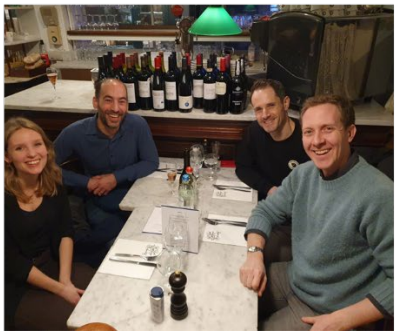
Social program:

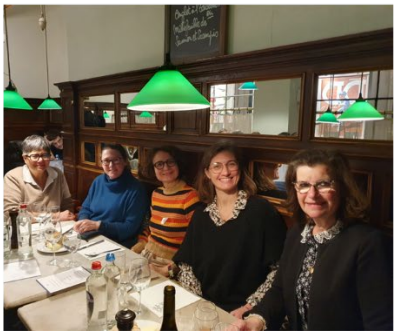












The meeting was kindly supported by: