ECFS Diagnostic Network Working Group
Meeting Report

DNWG meeting during 45th ECFS Conference 2022
Rotterdam, The Netherlands,
June 10th, 2022

Chair: Elke De Wachter *(Brussels, Belgium)* ***– Nick Simmonds*** *(London, UK)*

The welcome words, given by the coordinator Elke De Wachter, summarized the work that has been done in the previous months by the working group.

A first part of the meeting was dedicated to **Hugo de Jonge**, who unexpectedly passed away on the 6th of June. Inez Bronsveld (Utrecht, The Netherlands) gave an overview on his extraordinary career in the field of CF and expressed her condolences to friends and family of Hugo. We will always remember him as an intelligent, kind and honest active member of our working group.

The second part of the meeting stressed our concerns regarding sweat testing in the EU. The newest implemented MDR (Medical Device Regulation) and IVDR (In Vitro Diagnostic Medical Device Regulations) allow only EU-certified medical devices and in vitro testing in all European labs. A new recertification process for sweat test equipment is needed in order to be in line with the most recently updated regulations. This has huge implications for sweat test services in Europe. Currently, the most commercially provided sweat test equipment is provided by Elitech, which is a US company. Sweat testing is categorized as 'highest risk' in the new EU-MDR/IVDR, due to the application of pilocarpine to the skin. This is a new position and has not been an issue for FDA, nor for previous certification processes. Due to different factors the recertification process has been extremely delayed. Summarized, this means that from June 2022 Elitech does not have the permission anymore to export "Macroduct kits" (as the pilogel discs and the collectors) to the European market, until they receive 'green light'. No start date has been communicated yet. As this certification process was at a high cost, Elitech decided to only move on with the "Macroduct Advance System" (the newest sweat test equipment for stimulation and collection of sweat) and the

Macroduct 'supply kits'. They will not support other devices anymore, nor will other Elitech products (Nanoduct and Sweat Check device) be available on the European market. This decision may have huge implications for sweat testing in European countries. Especially, countries that have a newborn screening program running may face important restrictions, as the consumables may run out of stock.

In the session dedicated to this topic speakers from different countries will explain the implications of the new MDR and IVDR in their country.

First, **Isabelle Sermet** *(Paris, France)*, explained the situation regarding sweat testing in France. Next, **Jürg Barben** *(St Gallen, Switzerland)* gave an overview on the situation for Switzerland. **Bülent Karadag** *(Istanbul, Turkey*) highlighted the situation in Turkey, where a Turkish sweat test device is used (Utsat). However, also this device will face the same problems and restriction for its use in Europe. To conclude, **Bryce McEuen** *(USA*), the Elitech Vice president, explained the problem the company is facing. He shared the steps the company is currently undertaking to resolve the problem as soon as possible. . Hopefully by September, each lab will be provided by new stock of disposables.

Unfortunately, the planned talk by **Inez Bronsveld** *(Utrecht, The Netherlands)* and **Peter Van Mourik** *(Utrecht, The Netherlands)* on the use of intestinal organoids in diagnostic challenges had to be postponed to our February meeting in Montpellier (2023), due to time matters

Anne Munck (*Paris, France*) gave an overview of the recent work on widespread screening for CF in LMIC in collaboration with **Samia Hamouda** *(Tunis, Tunesia)*. This study aims to determine a representative sample of children (<15 years) in each developing country and wants to find out how many children within this group have chronic obstructive pulmonary disease and/or chronic diarrhea. The goal of this project is to perform “Mass Screening” for CF in children with chronic obstructive pulmonary disease and/or chronic diarrhea in LMIC using sweat test as the diagnostic tool. In case of intermediate or abnormal values, further CFTR analysis will follow. This approach could finally determine an estimate of CF incidence in each investigated country. These data would be helpful to underline the need for governmental investment in CF diagnostic tools (sweat test, genetic tests…) in LMIC. It could encourage the improvement of CF care and the introduction of CF neonatal screening strategies in countries with a high incidence of CF.

Marco Zampoli *(Cape Town, South Africa)*, talked about the beta-adrenergic sweat test. As access to reliable sweat testing (QPIT) and extensive CFTR sequencing is limited in South-Africa, this alternative sweat test could offer advantages and perspective in suspected individuals. Besides, NPD and ICM are not available. In order to be able to apply beta-adrenergic sweat test as the first choice diagnostic test for CF in his country a pilot study was set up. Healthy adults, adults with CF, parents of children with CF and children in which CF is suspected, were recruited. All CF suspects underwent CFTR next generation sequencing. In all subjects, beta-adrenergic sweat (BAST) test and QPIT sweat test was performed. The overall results showed improved diagnostic accuracy of BAST in comparison to QPIT. Remarkably, sweat secretion after beta-adrenergic stimulation is lower in children compared to adults, favouring the use of 'ratio's, compared to peak values of beta-adrenergic secretion. In conclusion, BAST is feasible and safe in children, avoiding more complicating physiological diagnostic tests as ICM or NPD.

Carlo Castellani (*Genova, Italy*), summarizedthe current status of the project: "ECFS standards of care on CFTR-related disorders". The aim of this project is to update the recommendations of CFTR-RD, which is a study on behalf of a core group of DNWG members (Carlo Castellani, Elke De Wachter, Christiane De Boeck, Nick Simmonds, Kevin Southern and Isabelle Sermet)

In the final part of the meeting, difficult cases were presented. The first case was presented by **Paola Melloti** *(Verona, Italy).* This case stressed the possible favorable clinical effect of Kaftrio in a 53-year-old patient with primary ciliary dyskinesia carrying F508del on one allele and a sweat chloride concentration of 23 mmol/L.
The second case was presented by **Marlies Destoop** *(Brussels, Belgium)* about a delayed diagnosis of CF despite NBS. The possible pitfalls regarding NBS were discussed.

Nicholas Simmonds and Elke De Wachter closed the DNWG session during the ECFS conference and invited all the participants to the next DNWG meeting (9 - 11th February 2023) which will take place in Montpellier, France.

We would like to thank ECFS for this successful meeting. We thank all speakers and

participants for their fantastic contribution and for making the meeting such a great success!

We are looking forward to seeing you at our brainstorm meeting in Philadelphia and our next annual DNWG Meeting in Montpellier.
More details on the evolution of the sweat test regulatory affairs will be separately sent in the upcoming weeks.

11th June 2022

Elke De Wachter – ECFS DNWG Coordinator

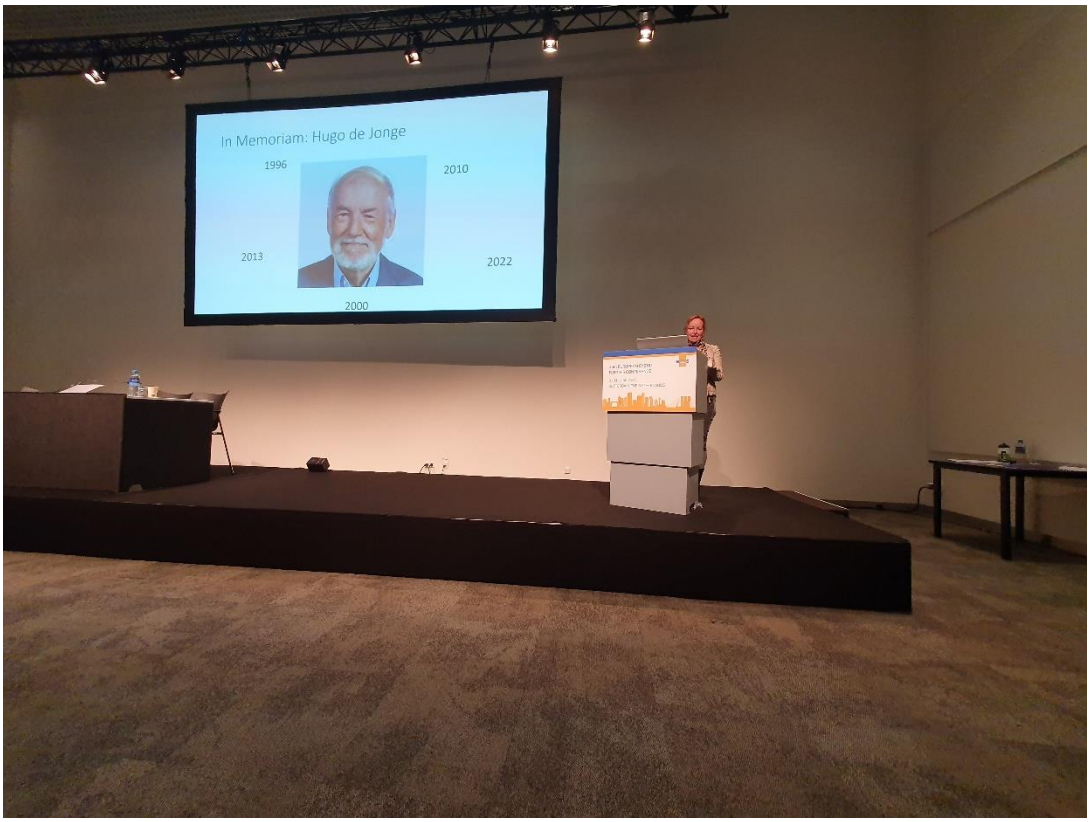
Nicholas Simmonds – ECFS DNWG Vice-coordinator

Marlies Destoop – ECFS DNWG Assistant

The meeting was kindly supported by:

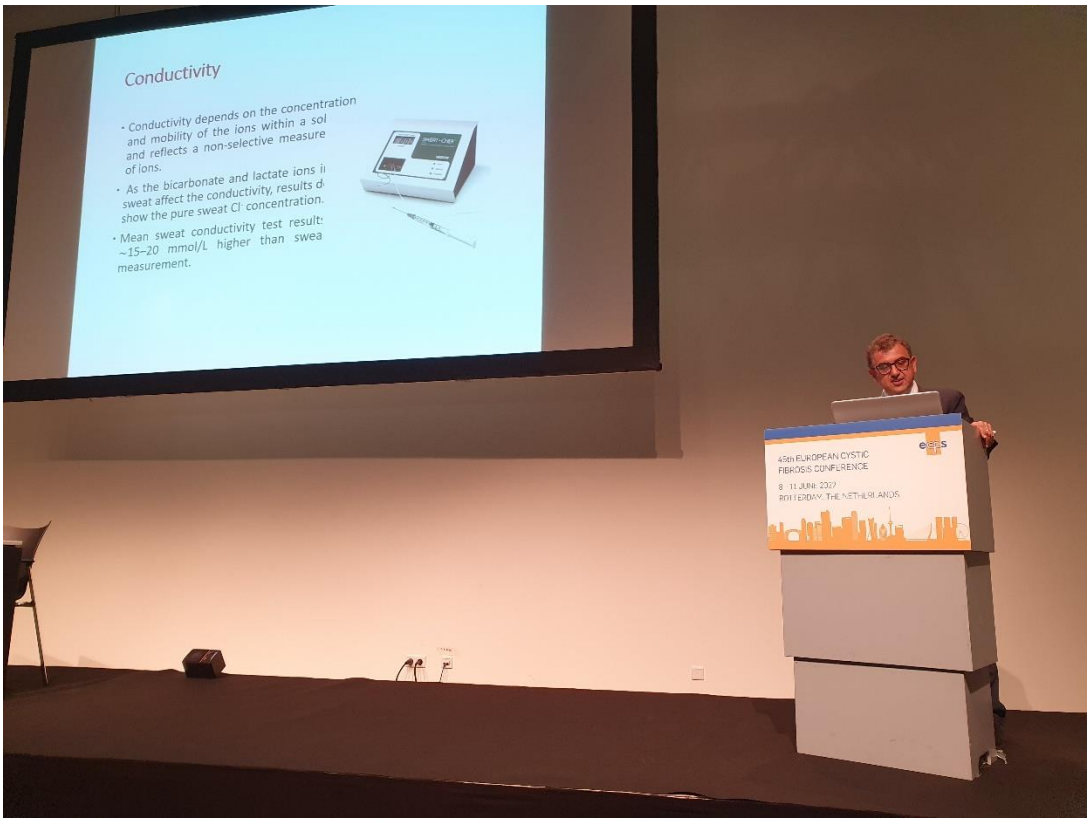
Photos taken during the meeting:

Elke De Wachter

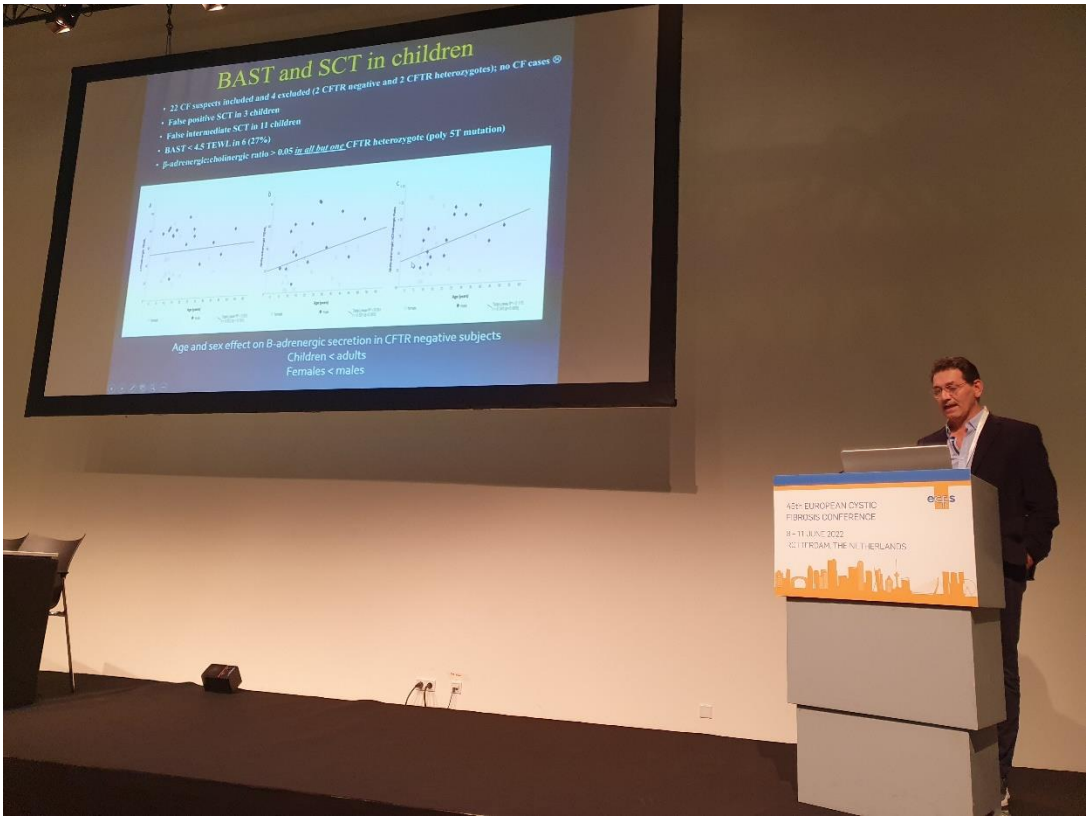


Inez Bronsveld
Picture on the screen: Hugo de Jonge

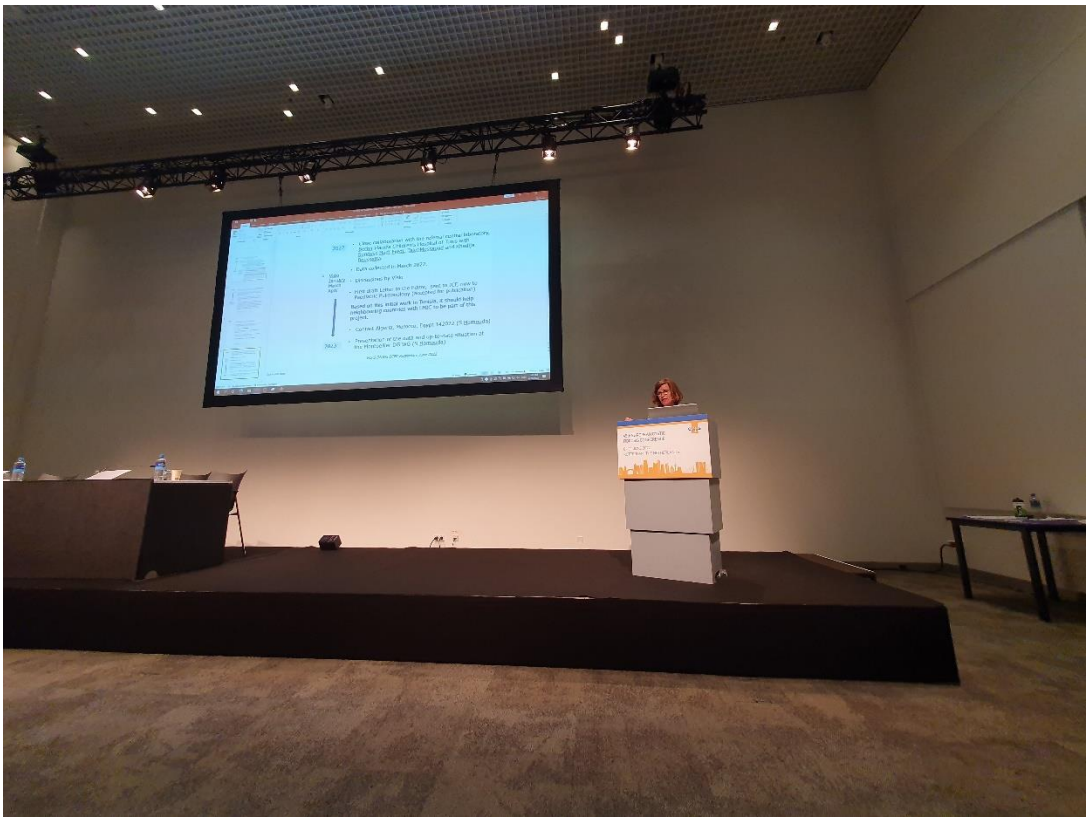
Jürg Barben



Bülent Karadag



Marco Zampoli



Anne Munck

Bryce McEuen