Reviewer’s report

Title: Large Genomic Rearrangements in the CFTR Gene Contribute to CBAVD

Version: 1 Date: 16 February 2007

Reviewer: Charles M Strom

Reviewer’s report:

General:
The paper is the second comprehensive study for CFTR rearrangements in CBAVD patients and the study
is well designed and the conclusions are well supported. The paper adds more evidence to occurrence of
deletions in the CFTR gene in CBAVD patients and supports prior conclusions by Hantash et al of
importance of screening for large rearrangements in the CFTR gene in CBAVD patients. The exon phasing
tool is a very good visual tool for easy determination of in-frame or out-of frame deletions-duplications in the
gene.
However, the methods utilized by the authors are similar to those described previously (Audrezet et al,
Hantash et al, Niel et al). Furthermore, the deletions identified are not novel, as they have been described
before (see Ferec et al 2006 and other papers above) to warrant two full figures of breakpoint junction and
DNA sequence traces. One figure of the agarose gels confirming the deletions might be sufficient.

Minor Essential:
1. While the paper by Hantash et al was the first major comprehensive study for rearrangements in the
CFTR gene in CBAVD patients, Niel et al, in the paper describing a method for detecting deletions in the
CFTR gene, also described a deletion in one patient suffering from CBAVD but without pulmonary or
pancreatic insufficiency.
2. The significance of the R170H mutation in the patient harboring a deletion of exons 22-24 is not
discussed. The authors should comment that it might be a "benign mutation". The R170H is listed in the
CFTR database. The authors should consult some predicting algorithms such as PolyPhen or SIFT.
3. Did the deletion of exon 22-24 occur on the same allele as that reported by Hantash et al? i.e. do the
authors believe it occurred on a 7T Allele?

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author
can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
The reviewer (Dr. Feras M. Hantash, for Dr. Charles M. Strom) is an employee of Quest Diagnostics, where
he holds stock options.