

July 1, 2002

Preston W. Campbell, III, MD
Executive Vice President for Medical Affairs
Cystic Fibrosis Foundation
6931 Arlington Road, Suite 200
Bethesda, MD 20814

RE: Infant BALF Study

Dear Dr. Campbell:

A subcommittee of the Cystic Fibrosis Foundation Data Safety Monitoring Board met today to discuss Dr. Terry Noah's Infant BALF protocol. The members of the subcommittee were myself, Dr. Jim Cunningham, and Dr. Lynne Quittell.

After considerable discussion, we believe that we can support the study going forward with the appropriate informed consent and the fact that an anesthesiologist is there to minimize any risk. We have based this decision upon our interpretation of how this study fits into CFR 46.405, 406, and 407.

We believe that BAL does represent a minor increase in risk over minimal risk. Thus, the study clearly does not meet 46.404.

We do not believe that the study represents more than minor risk. The risk of moderate to severe complications is very low in otherwise stable children; especially when done with the help of an anesthesiologist. Death is virtually unheard of in this setting in children.

We discussed four groups of children that would be participating in this study. They are: 1) Symptomatic with positive culture, 2) Asymptomatic with positive culture, 3) Symptomatic with negative culture, and 4) Asymptomatic with negative culture.

In the first three groups, the child clearly would benefit from this study. We believe that the early treatment of Pseudomonas is a wise step. Early treatment is frequently employed and most likely will be the standard of care in the next few years. For the symptomatic child who is negative, the benefit of the study is that the work up will be focused on other non-PA related issues such as nutrition, GERD, asthma, etc. Another

potential benefit would be that the use of antibiotics where they may be of no use would be prevented. We were convinced by Dr. Noah's arguments for the above.

It is not likely that there would be any benefit, at the time of the BAL, for children who are asymptomatic with negative culture. However, in this group and all other groups there definitely is the prospect of direct benefit. These children all have a genetic disease that, in virtually all cases, leads to lung disease that kills 85-90% of those involved. Half of all who have this disease will die before their fourth decade. Thus, even though the child is asymptomatic at the time of the BAL, it is highly likely that the knowledge gained from this very important research may benefit him or her later in life, potentially even before they reach their teenage years.

Finally, it is relatively clear that lung disease begins in infancy in most children with CF. Understanding the basic pathogenesis of this process will be key to the well-being not only of the subjects, but potentially of all other children with CF. This type of research is key to this understanding. (46.407)

Thus, although BAL such as this is not the standard of care currently, it is growing in its use for the guidance of therapy. Many centers are using BAL on a regular basis and this study is only moderately outside the standard of care at UNC. We believe Dr. Noah should continue to pursue IRB or DHHS/OHPR approval.

Sincerely yours,

Wayne J. Morgan, MD
Chair, Cystic Fibrosis Foundation DSMB
Professor, Pediatrics and Physiology