FRED HUTCHINSON CANCER RESEARCH CENTER
1124 Columbia Street
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September 28, 1983

E. Donnall Thomas, M.D.
Associate Director for Clinical Research
Fred Hutchinson Cancer Research Center

RE: H839-252R

Dear Don:

Dr. Fred Appelbaum's protocol entitled: "Autologous Marrow Transplantation for Treatment of Malignant Lymphoma, #159" was reviewed by members of the FHCRC Institutional Review Board, (formerly Human Subjects Review Committee) at the September 20th meeting. While there were a few minor questions which Dr. Appelbaum can address, there were some significant general questions raised relative to monoclonal antibody therapy. These questions affect a number of active or pending protocols and most appropriate require your attention.

Dr. Appelbaum's renewal application, like Dr. Martin's application H8211-171R (protocol 125), is seeking general IRB approval to use non-specified monoclonal antibodies as an element of therapy. Members do not feel comfortable with this approach, just as they would not feel comfortable about approving an application for chemotherapy without knowing the drug or drugs involved. In its present form, protocol 159 applies to monoclonal antibodies in general, and can cover a gambit of cellular specificity and imunoglobulin subtitles.

IRB members have asked that new applications, currently active applications and associated protocols be rewritten to specify the monoclonal antibody to be used. Just as currently done with drugs, each change in specific monoclonal antibody should be supported by separate or unique application. In order to assist IRB members in carrying out their review responsibilities, they ask that you and your staff provide the following information:

1. Define the decision-making process by which you and your staff decide which monoclonal antibody is suitable for clinical application.

2. What are the Division's established controls for monoclonal antibody production? If production standards have not been

drafted, IRB members ask that you and your staff please do draft them. Members would like to review standards for toxicity, both chemical and microbiological (e.g. screening for virus contamination). What preclinical (e.g. animal) screening is carried out to assure that final monoclonal antibody preparations are ready for clinical use?

3. Division guidelines for screening monoclonal activity in terms of biologic activity.

4. What checks and balances are utilized to deal with potential conflicts of interest between academic and financial considerations of the staff.

Division guidelines for clinical use of each monoclonal antibody, along with an investigator's committment to adhere to these guidelines, should be incorporated as a standard part of each protocol or application submitted to the I.R.B.

I.R.B. members voted to extend approval of Dr. Appelbaum's protocol for sixty days, pending his meeting some of the other Board requests. Dr. Martin's request to reactivate protocol 125 will not be acted upon, pending your response. Approval for currently active protocols using monoclonal antibody therapy will remain in effect to the end of this period. New application for use of monoclonal antibody therapy should be held by the Clinical Division pending resolution of the above.

Sincerely,

Henry Kaplan, M.D.
IRB Chairman

HK/ll
cc: Dr. John Hansen
Dr. Paul Martin
Dr. Rainer Storb
Dr. Fred Appelbaum
Dr. H.J. Deeg