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NIH Legal Advisor
Office of General Counsel
Public Health Division
Room 2B-50, NIH Building 31
31 Center Drive MSC2111
Bethesda, MD 20892-2111

Re: Petition of CellPro, Inc.

Dear Mr. Lanman:

This letter responds to the questions raised in your letter dated June 13, 1997 concerning Baxter's commitment to install its device, for free, at any clinical site abandoned by CellPro that does not already have a Baxter system. It also responds to your questions concerning the recent announcement by Baxter of a proposed alliance with VIMRX Pharmaceuticals.

1. *The Baxter Commitment.*

Before responding to your questions concerning the implementation of Baxter's commitment, it is important to emphasize that the Baxter commitment is merely a back-up contingency plan. The principal step we have taken to ensure that there will be no gap in patient access to stem cell selection technology is our request to the federal court that CellPro be permitted to continue its commercial sales of the Ceprate® SC system throughout the United States, and to continue its provision of the system for use in clinical trials in U.S. transplant centers, until after FDA approval of Baxter's system or another licensed alternative.

If CellPro acts reasonably and responsibly in response to the court's order, we have no reason to expect that the contingency plan will ever come into play. As discussed in our letter to the NIH dated June 17, 1997 and the declaration of MIT economics professor Dr. Jerry Hausman, it would make no economic sense for CellPro to abandon its customers while at the same time it is appealing the court's order and assuring its stockholders that it has a good faith basis to do so.

Under these circumstances, and where CellPro has a $54 million cash position available to provide continuing customer support, CellPro's threats to pull its product off the market are purely tactical.

Nevertheless, to protect against even a remote contingency, Baxter made the commitment that it will support any CellPro clinical site that CellPro abandons on the same contract terms to which CellPro had previously agreed. This commitment is described in Hopkins' letter to NIH dated June 2, 1997 and confirmed in the letter of Vernon R. Loucks Jr., Baxter's Chairman and Chief Executive Officer, to Secretary Shalala dated June 12, 1997. In the extremely unlikely event that CellPro carries out its threats, this commitment will minimize and hopefully eliminate any disruption caused by CellPro's maneuver.

As noted, Baxter is prepared to provide any clinical site abandoned by CellPro with a Baxter device free of charge. Past experience has shown that, assuming the necessary training of technicians can be promptly scheduled, it is possible to have a new Baxter system installed and in operation in as little as two weeks.

The paperwork for implementing Baxter's commitment at a site conducting an active clinical trial would vary somewhat depending on whether the trial is company-sponsored or investigator-sponsored. In either case, the first step would be to modify the protocol to identify use of the Baxter device instead of the CellPro device in the stem cell selection step. If it is a company-sponsored trial, Baxter's regulatory group would file the protocol and some additional documentation from the principal investigator to the appropriate IDE file in the FDA. If it is an investigator-sponsored trial, the investigator would make the filing to his or her own IDE/IND file, and Baxter would provide a letter of cross reference to the Baxter IDE.

Baxter has no reason to believe that the FDA would object to substitution of Baxter's device for CellPro's device in an approved protocol. Currently, Baxter has approved, active IDE's in the same areas as CellPro's, including autologous peripheral blood stem cell ("PBSC") transplants, allogeneic PBSC transplants, and allogeneic bone marrow transplants. (Clinical trials in other areas such as gene therapy are generally done under an investigator-sponsored IDE or IND). In addition, as you are aware, the FDA is actively reviewing Baxter's premarket approval application for autologous PBSC transplants and thus is familiar with Baxter's clinical data.[1] In these circumstances, notification to the FDA of a clinician's intent to substitute Baxter's device for CellPro's device would not appear to raise any significant regulatory issues. Also, our discussions with clinicians who have been through the process have indicated that the FDA has procedures in place that permit prompt implementation of a modified protocol such as this.

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[1] The FDA has scheduled an Advisory Committee meeting to consider Baxter's PMA for July 24, 1997.

In addition to notification to the FDA, the investigator would submit the modified protocol to his or her local Institutional Review Board ("IRB"). Since the IRB will typically consist of a panel of physicians within the hospital that is conducting the trial, the time required to obtain IRB approval is within the control of the hospital itself. IRBs have emergency mechanisms to deal with situations like this, and the clinicians with whom we spoke were confident that, if necessary, IRB approval for a particular patient could be obtained within a day; the need for IRB approval should not hold up any individual patient's treatment.

Your letter also inquired about patients who are not enrolled in clinical trials. If there were no approved, active clinical trial in which to substitute the Baxter system, it would be necessary for the clinician to submit a protocol for a trial using the Baxter system. Since there are many approved IDEs specifying the Baxter system already in place that can serve as models, this task would not be burdensome, and Baxter's regulatory/clinical group is prepared to provide active assistance. Although CellPro has argued that the eligibility standards for a clinical trial could limit availability of the device, in fact eligibility standards need not pose an obstacle. There are already institutional eligibility standards imposed for the selection of patients to undergo autologous or allogeneic transplants, and a protocol for a transplant procedure that includes a stem cell selection step can be broad enough to cover all patients who are eligible for a transplant under the institution's existing eligibility standards. Once again, IRB approval will be required, but expedited IRB approval can be obtained if it is necessary to assure treatment for an individual patient.

The time periods required in order to substitute Baxter's device for CellPro's device should not deprive any patient of needed care, even if CellPro carries out its threats. Any institution currently using CellPro's device in all likelihood has an inventory of disposable kits available for treatment of some number of additional patients even if CellPro immediately ceased further supplies. Furthermore, we would expect CellPro to act responsibly to provide advance notice and a smooth transition in any site it decides to abandon. Finally, as noted above, the FDA and local IRBs have procedures to expedite review and approval of a new or modified protocol if the normal time for processing the paperwork would adversely affect an individual patient.

Your letter asks what institutions currently have Baxter's system in place. A list of those institutions is contained in the declaration of Kristen Houser, a copy of which was included in the Appendix accompanying Hopkins' May 7, 1997 submission. (Information concerning the number of patients treated at a particular site would have to be obtained from the institution itself).

As indicated in Hopkins' June 2, 1997 submission, we believe that at least twenty of CellPro's forty U.S. sites already have a Baxter system in place. We have asked repeatedly that CellPro provide specific information identifying its sites, but it has refused to do so. It would be helpful, in further refining Baxter's contingency plan, if CellPro were required to identify each clinical trial site that, as of today, is actively accruing patients. That number may be much smaller than forty, and many of those sites may in fact be sites that are also conducting Baxter clinical

trials.

Before turning to the proposed transaction with VIMRX, we offer some further observations. First, we believe that any responsible health care company in CellPro's position would continue to supply its clinical sites on whatever terms the federal court determines are fair and reasonable. Assuming, as plaintiffs proposed to the federal court, that CellPro recovers at least its incremental cost of each additional disposable unit, we cannot imagine why CellPro would refuse to supply additional disposables to clinicians who want to use them in treating patients. Moreover, where CellPro provides the disposables for free under the terms of a clinical trial, plaintiffs have not requested that any payment be made to them. Why, then, would CellPro threaten to abandon that trial, other than as an exercise of scare tactics?

Second, to put the issue in context, it is important to remember that the FDA has not determined that CellPro's system is safe and effective for anything other than reducing infusional toxicities in autologous bone marrow transplants. The FDA has described CellPro's public statements about its system's effectiveness for other indications to be "false and misleading."

In other words, for all relevant indications, CellPro's product is still an investigational device undergoing clinical trials, which may or may not result in FDA approval. Baxter's product likewise is undergoing (or has completed) clinical trials. The difference between the two is that Baxter's product is licensed under Hopkins' patents, and CellPro's is not. Were NIH to treat this situation as justifying the initiation of a march-in proceeding on public health grounds, the implications would be far-reaching and most disturbing. It is no exaggeration to say that any time new medical technology is licensed out exclusively, an unlicensed competitor may decide to initiate its own clinical trials using the same technology, perhaps in the hope of obtaining a license ultimately, or perhaps in the hope that the patents will later be invalidated.

If, in order to avoid march-in, the exclusive licensee must now make the kind of commitment Baxter has made -- including an undertaking to incur the cost of substituting its product for the competitor's product in clinical trials should a court enjoin the competitor's continued infringement -- then the promise of exclusive licensing under the Bayh-Dole Act will have become illusory. We urge NIH to make clear in its decision in this case that where an exclusive licensee has actively conducted clinical trials to support regulatory approval of a licensed product, a competitor's infringing activities, including successful clinical trials, will not justify initiation of a march-in proceeding on "public health" grounds. Otherwise, the public health exception will have swallowed the Act whole, and companies that assumed they would be protected by the patent system will in the future decline to invest the tens of millions of dollars it takes to commercialize medical inventions. In the long run, it is this threat to public health that must be foremost in NIH's decision.

2. *Baxter's Proposed Alliance with VIMRX Pharmaceuticals.*

Your letter asks how Baxter would be able to fulfill its commitment if it enters into the proposed alliance with VIMRX Pharmaceuticals. We understand that your questions were formulated before you had an opportunity to see Mr. Loucks' letter dated June 12, 1997 to Secretary Shalala.

As explained in Mr. Loucks' letter, under the proposed transaction, Baxter will maintain ownership of its exclusive license to Hopkins' patented stem cell selection technology, will continue to manufacture the Isolex devices and associated disposables in the same facilities in which they are manufactured today, and will be the exclusive worldwide sales, marketing, and distribution company for cancer-related cell therapy products, including the Isolex® 300 system. Baxter employees will continue to take customer orders, provide customer service, and sell the products. These exclusive contractual agreements between Baxter and the newly formed company will form an integral part of the transaction.

Physicians and patients thus will experience no disruption in access to the Isolex® system or to Baxter's other cell therapy products. On the contrary, Baxter believes that the alliance with VIMRX will enhance its commitment to the support of patients needing stem cell selection as part of their cancer therapy.

* * *

For the reasons we have outlined here and elsewhere, we ask that NIH decline CellPro's request for initiation of a march-in proceeding. Merely initiating a formal proceeding, on the facts of this case, would have a devastating impact on private sector support of medical research in hospitals, universities and medical colleges. Initiation of a proceeding would lend a legitimacy to CellPro's petition and send a chilling message to biotechnology and pharmaceutical companies across the country that the threat of government march-in is real, even where an exclusive licensee has expended tens of millions of dollars to develop and commercialize a patented invention, and even where the petitioner has been found guilty of willful patent infringement. Moreover, the cost of an administrative trial would be huge (particularly on top of the cost of the recently completed patent infringement trial), and the continuing uncertainty as to NIH's position on march-in as the case proceeds through hearings and appeals would be likely to scare off many potential investors in new medical technology. For these reasons, it is especially important that CellPro's petition be denied at this stage, when it is still possible to repair the damage that CellPro's petition already has done.

Recently, Hopkins had an opportunity to meet with representatives of the American Cancer Society to review the information that has been presented to this agency. By letter dated June 19, 1997, ACS expressed its satisfaction that the steps Hopkins and its licensees have taken adequately assure "that patient access to stem cell purification technology will not be

compromised." ACS concluded that "CellPro's petition for "march-in" rights is not warranted at this time." We can see no reason why NIH would reach a contrary conclusion, and we urge it to deny CellPro's petition without further delay.

Sincerely yours,

Donald R. Ware

Donald R. Ware

DRW/kaw

cc. Barbara M. McGarey
Frederick G. Savage, Esq.
Gary D. Wilson, Esq.