UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

THE JOHNS HOPKINS UNIVERSITY, a Maryland corporation, BAXTER HEALTHCARE CORPORATION, a Delaware corporation, and BECTON DICKINSON AND COMPANY, a New Jersey corporation, Plaintiffs, v. CELLPRO, INC., a Delaware corporation, Defendants.	:	Case No. 94-105-RRM

CELLPRO'S BRIEF IN OPPOSITION TO PLAINTIFFS' MOTION FOR A PERMANENT INJUNCTION AND IN SUPPORT OF ALTERNATIVE MOTION FOR STAY OF INJUNCTION PENDING APPEAL

PREPARED BY:

CONNOLLY, BOVE, LODGE & HUTZ
GERARD M. O'ROURKE
Delaware Bar No. 3265
1220 Market Building
P.O. Box 2207
Wilmington, Delaware 19899
(302) 658-9141

Attorneys for Defendant
CELLPRO, INC.

OF COUNSEL:
COE A. BLOOMBERG
ROBERT C. WEISS
ALLAN W. JANSEN
JERROLD B. REILLY
LYON & LYON LLP
633 West Fifth Street, Suite 4700
Los Angeles, California 90071-2066

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases (cont'd) Page(s)

Cases (cont'd) Page(s)

Statutes

I. NATURE OF THE CASE AND STAGE OF PROCEEDINGS

The validity and infringement of U.S. Patent Nos. 4,714,680 and 4,965,204 were determined by summary judgment, and in March 1997 a jury reached a verdict finding willful infringement and the amount of compensatory damages. However, certain defenses, including patent misuse, remain to be adjudicated.

One necessary predicate to the issuance of a permanent injunction is a final judgment. Eli Lilly & Co. v. Medtronics, Inc., 915 F.2d 670, 674 (Fed. Cir. 1990). And entry of a final judgment (even a partial final judgment under Rule 54(b)) requires that plaintiffs' infringement claim be finally adjudicated. See W.L. Gore & Associates, Inc. v. International Medical Prosthetics Research Associates, Inc., 975 F.2d 858, 863 (Fed. Cir. 1992).

Here, since CellPro's outstanding, bifurcated patent misuse defense is still pending, there has been no final adjudication and the final injunction cannot be entered. The Court in Virginia Panel Corp. v. Mac Panel Co., 887 F. Supp. 880 (W.D.Va. 1995) faced precisely this situation. In Virginia Panel, the defendant was found to have willfully infringed two of the plaintiff's patents; however, the defendant's patent misuse defense and antitrust claims had been bifurcated. Id. at 883. The Court found that entry of partial final judgment under Rule 54(b) was improper (Id. at 883-884) and declined to enter a permanent injunction because final judgment was not proper (Id. at 887).

Until the patent misuse defense is adjudicated, final judgment cannot be entered, and any final injunction is premature.

II. SUMMARY OF ARGUMENT

1. The proposed injunction would violate the prohibition of 35 U.S.C. § 271(e)(3), as it would enjoin activities reasonably related to the FDA approval process. A large part of CellPro's activities have been, are now, and for the foreseeable future will continue to be related to the development of new devices and new therapeutic approaches under the § 271(e)(1) exemption from patent infringement liability.

2. Important public interests dictate that no injunction should be granted. CellPro has created and is creating unique lifesaving technologies and there is no reason to think that Baxter's device, even if the FDA some day approves it, will be technically and therapeutically equivalent for the needs of all patients.

3. If a final injunction is entered, it should be stayed in its entirety pending appeal, in view of the four-factor test of Hilton v. Braunskill, 481 U.S. 770, 776 (1987).

4. The proposed injunction would have extraterritorial effects that not only violate U.S. law but offend the free-competition policies of other countries, where plaintiffs lack patents rights. Upon principles of international comity, the Court should refuse to grant these parts of the injunction, even if they were not violative of domestic law.

5. The part of the injunction which calls for a repatriation of 12.8 hybridoma made before the patent issued but sent to Canada thereafter is legally insupportable. The shipment aboard was not an act of infringement, nor can any use of the hybridoma aboard be an act of infringement.

6. The proposed injunction is overly broad as regards the '680 patent, for its language implies that the mere sale of the device is an inducement of infringement or a contributory infringement, and it is neither.

III. FACTS

Litigation has been called a blizzard of words. In any blizzard, voices can be muffled or drowned out. Before the Court decides this most important motion, we believe that the Court needs to hear from those who have not been heard so far in this case – physicians who rely on the CellPro CEPRATE® SC Stem Cell Concentrator in their day-to-day work. Those clinicians and clinical researchers, better than anybody else, know what is at stake here.[1/]

With regard to Baxter's argument that the CellPro FDA-approved device can be withdrawn from the market without harm to patients, consider the following sworn statements by physicians involved in patient care:

> The device is the only FDA-approved device for this indication [autologous BMT for breast cancer], and removing the device from the market would withdraw from cancer patients in this country a safe and effective therapy against a widespread, and lethal, disease. – FRED LeMAISTRE, M.D. (Decl. ¶ 8(a))

[1/]The facts set forth here and elsewhere in the brief are taken from testimony and exhibits already of record, and/or from the following persons' declarations, which are being filed and served herewith: Dr. Claudio Anasetti; Dr. Kenneth Anderson; Dr. Edward Ball; Dr. Oscar Ballester; Dr. Michael Bishop; Dr. William Burns; Dr. Richard Burt; Dr. Stanley Calderwood; Dr. Richard Champlin; Dr. John DiPersio; Dr. Anthony Elias; Dr. Cesar O. Freytes; Dr. Dr. Jed B. Gorlin; Dr. Charles Hesdorfer; Dr. Helen Heslop; Dr. Kent Holland; Dr. Mary Horowitz; Dr. Cindy A. Jacobs; Mr. Edward Kenney; Dr. Monica S. Krieger; Dr. Fred LeMaistre; Mr. H. Colin Overbury; Dr. Robertson Parkman; Dr. Gordon L. Phillips; Dr. Oliver W. Press; Dr. Gary Schiller; Dr. Leonard Sender; Dr. Thomas Shea; Mr. William E. Simpson; Dr. Joseph Tarnowski; Mr. Robert Vandervelde; Mr. David F. Weeda; Dr. Andrew M. Yeager; Dr. John A. Zaia. These Declarations are hereinafter cited in the form, "Anderson Decl. ¶__," "Anasetti Decl. ¶__," etc. Of the clinicians-declarants who are quoted and/or cited herein, two (Drs. Parkman and Press) are persons who at other times have been compensated by CellPro as testifying and/or consulting experts in this litigation. No other clinician-declarant has had any prior relationship to this case; and no clinician-declarant, (including Drs. Parkman and Press) has been paid or offered any compensation in connection with these declarations. They all donated their time.

Until the CellPro device made possible these haploidentical transplants, such [pediatric cancer] patients simply had no therapeutic options; they all died. – DR. STANLEY CALDERWOOD (Decl. ¶ 7)

Prior to the advent of the CellPro device, these [leukemia] patients had no transplant option because no adequate and willing donor was known, and therefore no potentially curative therapy was available to them. – RICHARD BURT, M.D. (Decl. ¶ 7)

In a pilot study in children, we achieved survival rates in the range of 30 to 40% for these patients who underwent haploidentical transplantation using parental donor cells manipulated with the CEPRATE® device. Before, these patients had no treatment option at all; they were not transplant candidates and, without transplantation, they typically succumbed to leukemia within 3 to 6 months after diagnosis....–KENT HOLLAND, M.D. (Decl. ¶ 6)

Patients know this technology is available. In my practice, parents of young children facing these life threatening diseases, are increasingly educating themselves ..... It would be like holding up a carrot to these parents, to confirm that you now have such promising methods that could be used to reduce the number of tumor cells in their child's marrow, but it can't be used because of a legal dispute. – LEONARD SENDER, M.D. (Decl. ¶ 9)

I was asked what effect the inability to obtain the CellPro CEPRATE® device would have on our clinical research programs .... [O]ur in utero program would essentially be ended since I know of no other manufacturer that offers a system to stem cell select and T cell deplete. – ROBERTSON PARKMAN, M.D. (Decl. ¶ 8)

This past winter we initiated another clinical trial involving CellPro's second-generation ("TCD") immunoselection column.... [T]he donors are haploidentical parents and the patients are children with end-stage leukemia for whom there are no conventional treatment options available.... If for any reason the CellPro TCD device were to become unavailable, this study would need to be shut down. If that were to happen, children would die. – ANDREW M. YEAGER, M.D. (Decl. ¶ 6)

To those who would discount the miseries that patients suffer when deprived of treatment options they want, I would say that I wish they could experience what I have had to experience when explaining to a desperately sick patient why he does not meet the eligibility criteria for a limited-enrollment study which he believes might hold his best hope of a life-saving cure. I recently had to deliver such an explanation to a patient, only to be told a week later, by a relative of the patient, that his inability to enroll in the study had left him so despondent that he had tried to kill himself. – RICHARD BURT, M.D. (Decl. ¶ 10)

With regard to Baxter's argument that its Isolex 300 device is a reasonable substitute for the CellPro FDA-approved device, consider the following sworn statements by physicians involved in patient care:

> Baxter's Isolex device, according to what I have heard and read about it, lacks sufficient demonstrated T-cell depletion capability ... to be practical for my child and young-adult studies even if the device were FDA-approved. –KENT HOLLAND, M.D. (Decl. ¶ 11)

> I have personally evaluated the Baxter ISOLEX CD 34+ selection device, and found that it was not acceptable for my needs .... If the CEPRATE®SC device were not available, it would have a significantly negative effect on my ability to carry out the current and planned investigational protocols that I have described. Indeed, with regard to the Gaucher disease study, there would be no other options and the study would have to stop.– EDWARD BALL, M.D. (Decl. ¶¶ 5, 6)

> While at Johns Hopkins I saw both the CellPro and the Baxter therapeutic stem-cell selection columns in use, and based on my observations and discussions with knowledgeable persons there, I formed the impression that the CellPro device was far superior to the Baxter device. The latter was relatively slow and clumsy, requiring two persons to operate, and produced suspensions of inferior quality.... I do not regard the Baxter device as a fit or comparable substitute for the CellPro device and would not choose to use the Baxter device to treat my patients. – RICHARD BURT, M.D. (Decl. ¶ 8)

> If access by clinicians to the CellPro CEPRATE®SC stem cell concentrator were restricted in the United States, the practical availability of stem-cell-therapy options to clinicians and their patients would be diminished; and in my view it is not realistic to expect that Baxter's ISOLEX® device, or any other device that lacks FDA approval, could fully and adequately replace the CellPro device even if the therapeutic and technical equivalency of such device to the CellPro device were certain. – RICHARD CHAMPLIN, M.D. (Decl. ¶ 9)

> Even if Baxter had a device that could be used, because high-risk neuroblastoma is what is often called an "orphan disease," afflicting only about 200 children nationwide, any non-FDA-approved device may not be made available to me. It has been my experience that because these orphan diseases do not present a big enough market they are rarely approved by manufacturers for use in investigator sponsored trials. – LEONARD SENDER, M.D. (Decl. ¶ 7)

With regard to Baxter's argument that the proposed injunction would effect a "relatively seamless conversion" (Brief p. 12), consider the following sworn statements by

physicians involved in patient care as to the impact any switch would have on their ongoing clinical programs:

> Even if there are applications for which an alternate immunoselection device might be adequate, a switch over to such a device could not be accomplished without substantial delay.... [T]his delay would be fatal to the children involved in our haploidentical parent-to-child leukemia transplant studies, who are not candidates for non-immunoselected stem cell transplant and whose life expectancies (if untreated) are too short for any significant delay to be tolerable in their cases. – ANDREW M. YEAGER, M.D. (Decl. ¶ 9)

> Because the patients involved and to be involved in our autoimmune pilot studies are, by definition, persons with poor short-term prognoses, some of these patients would die, and others might become ineligible for the studies due to further deterioration in their conditions, during the period of delay that would be occasioned by a changeover (assuming that a changeover were otherwise possible) from the CellPro device to another stem-cell immunoseparation device. – MARY HOROWITZ, M.D. (Decl. ¶ 7)

> Without the CellPro device, our clinical work would be set back by up to two (2) years.... If the CellPro device is made unavailable, we would have to discard data of our clinical studies already in progress, and start over. We would further have to retrain staff to use a new device, and must reapply for FDA and institutional clearance to conduct our clinical studies with an unapproved device. Above all, I would not be certain that a substitute device would work as well for my purposes.– MICHAEL BISHOP, M.D. (Decl. ¶ 11)

> It is not clear that switching from one device to another in mid-trial would even be permitted by the FDA. Even if the FDA did not require that we discard data gathered using the CellPro device and begin anew, it would still be undesirable, from the standpoint of sound scientific methodology, to make a substitution of such an important piece of equipment in the midst of a trial. – ANDREW M. YEAGER, M.D. (Decl. ¶ 10)

> If the CellPro device were to become unavailable our clinical research and studies would be set back significantly. We would more than likely have to discard our already accumulated data, retrain staff with another device, and reapply for FDA and institutional clearances anew. I estimate that our efforts would be set back by up to two (2) years. Further, even if an alternative device were available, I would not be sure that it would work just as well for our purposes. – CHARLES HESDORFFER, M.D. (Decl. ¶ 10)

Even if the Baxter device were available, new and emerging treatments made possible by the CellPro FDA-approved device would be impacted, according to physicians involved in patient care:

> In my view, there is a compelling public interest in maintaining the availability of, and access to, the CEPRATE® SC device, because patients with advanced diseases would die without the benefit of the device which makes allogeneic transplantation feasible from HLA mismatched donor. Further, there is unquestionable benefit to be derived from keeping the device (as the only FDA-approved device) on the market as its removal would set back the development of new transplant technologies and treatment options. – CLAUDIO ANASETTI, M.D. (Decl. ¶ 9)

> Besides our own completed and planned clinical studies, I consider the availability of, and access to, the CellPro device as important to the development of other novel treatment procedures such as gene therapy. – OSCAR BALLESTER, M.D. (Decl. ¶ 6)

> My pilot study results to date suggest that the device affords a new, potentially lifesaving treatment option for multiple sclerosis patients for whom all conventional therapies have failed. – WILLIAM BURNS, M.D. (Decl. ¶ 8)

> If the CEPRATE® device were not available, the current trials regarding small cell lung cancer, as well as the future tumor purging studies, would be significantly disrupted, delaying what appear to be significant advances in the treatment of certain types of cancer. – ANTHONY ELIAS, M.D. (Decl. ¶ 8)

> I believe that FDA-approved status confers on the CellPro device what we may call a "halo effect," such that researchers are encouraged to explore new therapeutic frontiers through the use of the device because they believe that its already-FDA-approved status will facilitate expanded approval for new applications and because they believe that its widespread acceptance and wide distribution within the American medical community will help assure that any new therapies they develop, if successful, will quickly come into widespread use. – FRED LeMAISTRE (Decl. ¶ 8(b)

The CellPro FDA-approved device is an invaluable device for patient care as illustrated by the following comments of physicians involved in patient care:

> The time period between myeloablation...and engraftment...is a time period during which the patient...is at grave peril of death from opportunistic infections. The fact that use of the CellPro device reduces this period of extreme vulnerability to about 8 days, as compared to 18-21 days, is a patient-safety benefit which I expect will reduce transplant-related mortality significantly over the long run. – RICHARD BURT, M.D. (Decl. ¶ 5)

> The CellPro device in my experience results in superior stem cell product yields which quality is critical for small-donor-large-recipient allogeneic transplant settings in which large yields are needed. This is because if the yield is below that needed for engraftment count recovery, the graft could fail and the patient could die in the interim from infection or bleeding. – JOHN DiPIERSO, M.D. (Decl. ¶ 10)

> I consider the availability of, and access to, the CellPro's CEPRATE® SC device a compelling public interest. In fact, for patients afflicted with lymphoma, multiple myeloma, low grade lymphoma or breast cancer (where purging of tumor cells is potentially valuable), who are otherwise ineligible for treatment with an investigational device, the CellPro device offers the only available processing system. – GARY SCHILLER, M.D. (Decl. ¶ 9)

Any limitation on the quantity of CellPro devices would severely impact patient care as stated by the following physicians:

> If access by clinicians to the CellPro CEPRATE® SC stem cell concentrator were restricted in the United States, the practical availability of stem-cell-therapy options to clinicians and their patients would be diminished; and in my view it is not realistic to expect that Baxter's ISOLEX® device, or any other device that lacks FDA approval, could fully and adequately replace the CellPro device even if the therapeutic and technical equivalency of such device to the CellPro device were certain. – RICHARD CHAMPLIN, M.D. (Decl. ¶9)

> I understand that our supply of the CellPro device may be limited to the volume we were using as of March 1997. Such a restriction would adversely impact our ability to advance our pilot study in neuroblastoma to the randomized trial, thereby limiting the availability of this potentially life sustaining technology to these desperately ill children. – JED B. GORLIN, M.D. (Decl. ¶ 4)

> It is the only FDA-approved device which reliably prepares clinically useful volumes of concentrated stem cells. For some categories of patients, there were no practical therapeutic options available before the advent of the CEPRATE®SC concentrator and it still affords the only practical treatment option. I believe that <u>any</u> injunction, even if it contains significant exemptions and exceptions, would disserve compelling public interests. – CESAR O. FREYTES, M.D. (Decl. ¶ 3)

Baxter's argument that it would be a simple matter to initiate new IDEs with the non FDA-approved Baxter device in place of the FDA-approved CellPro device are contrary to the experience of the physicians involved in patient care:

> I find it important that the CellPro CEPRATE® SC device is the only FDA-approved stem cell concentration device, because I can use it for other clinical protocols as I deem appropriate without having to go through the cumbersome FDA approval process that would be the case with an unapproved device. Indeed, the fact that the CellPro device is FDA-approved makes it easier (in terms of cutting down the amount of red tape and institutional resistance) to get an experimental protocol approved by the FDA and/or the hospital's or university's approval committee if at least the stem-cell-enrichment and transplant step is done with an FDA-approved device. – MICHAEL BISHOP, M.D. (Decl. ¶ 8)

> In my experience it is very difficult, if not impossible, for an institution to obtain a non-FDA-approved device unless that institution is enrolled in an FDA-approved trial which involves the use of that device. Even if the institution is involved in such a trial, patient enrollment in FDA clinical and preclinical trials is restricted, so that not every patient who might benefit will meet the criteria for inclusion in the trial. – OLIVER W. PRESS, M.D., Ph.D. (Decl. ¶ 7)

To those physicians involved in patient care and to patients who are seeking treatment for their life-threatening afflictions, it makes a difference that the CellPro device is FDA-approved and the Baxter device is not FDA-approved:

> In my experience, the ability to obtain approval for an experimental protocol from the FDA and/or hospital's or university's approval committee, is made easier if at least the stem-cell-enrichment and transplant step of that experimental procedure is performed with an FDA-approved device such as CellPro's CEPRATE®SC device... – CHARLES HESDORFFER, M.D. (Decl. ¶ 7)

> [T]he CEPRATE®SC device makes it easier to obtain approval for investigational and experimental protocols incorporating that device. This is true not only scientifically, because at least one step of the process is already known to be safe and efficacious, but the availability of an approved product has the practical effect of making experimental treatments more available because of such reasons as the availability of medical insurance reimbursement. – KENNETH ANDERSON, M.D. (Decl. ¶ 7)

> Given a choice, I believe that any researcher whose goal is to see new therapeutic options become generally available would prefer to employ a device that is, or promises to be, FDA-approved and generally available. – WILLIAM BURNS, M.D. (Decl. ¶ 6)

Plaintiffs tell this Court that their proposed injunction will "allay any possible public health concerns" (Brief, p. 7); that it will "minimize] disruption to patients who currently are being treated using the CellPro therapeutic device and ensur[e] that hospitals in the United

States and abroad are able to make a smooth transition to Baxter's licensed Isolex® device" (Brief, p. 1); and that "it cannot be said that no substitute products are available to patients who need them" (Brief, p. 9). Plaintiffs suggest that their proposed injunction would leave CellPro able, until such time as another FDA-approved device may appear, to satisfy any public health need "on a non-profit basis" (Brief, p. 22) and that CellPro has no "basis for claiming hardship" (Brief, p. 7). Each of these positions is factually untenable.

The truth is that if an injunction were entered on the terms proposed by plaintiffs, there would be an immediate and dramatic chilling effect on stem-cell-therapy research in the United States, a general retardation of progress in the field, a serious disruption of clinical trials now in progress and of planned future clinical trials which, were they conducted, would be clearly within the "reasonably-related-to-FDA-approval" protection of 35 U.S.C. § 271(e)(1). The injunction would, moreover, erect geographic, economic and administrative roadblocks to patients seeking immunoselective stem-cell therapy, even if CellPro could afford to maintain supply at the rate of loss that would be imposed by plaintiffs' "incremental profits" formula.

Nor is it realistic to suppose that Baxter would be in a position any time soon (if ever) to fill the market void that would be created if the CellPro device were "frozen" at the number of U.S. installations that used it as of March 12, 1997, and if it were withdrawn for the rest of the world markets over the next twelve months. We will now examine each of these points in more detail.

Adverse Impact On Clinical Research

The granting of plaintiffs' proposed injunction, and even the threat of that injunction, would retard the pace of clinical research in numerous ways.

First, clinical researchers who undertake trials typically do so with the hope that if they discover new and better therapies, those therapies will quickly come into wide use. Obviously, if an investigator perceives that the medical device on which he contemplates building a new therapeutic approach is at risk of disappearing, that researcher will be reluctant to pursue clinical trials using that device.

Secondly, clinical researchers cannot be sure that any substitute device would be equivalent for their particular application. There is no guarantee that the Baxter device, even if it is someday FDA-approved, will prove to be as safe and efficacious as the CellPro device for every application to which it is put. In other words, there is simply no basis to assume – and even an FDA approval of the Baxter device would not afford any basis to assume – that the device can feasibly be substituted for the CellPro device in all clinical-research and patient treatment contexts.

Thirdly, if Baxter's device were to gain FDA approval, the proposed injunction would require CellPro to withdraw, rapidly, even from that limited position that it would (theoretically) be allowed to maintain pending FDA approval of the Baxter device. Clinical studies in progress at that point would need to be aborted unless they could convert over to use of the Baxter device, if feasible. But as the clinicians' quotations above (and other statements in their declarations) prove, conversion would cause delay which in some cases, would kill patients; and switching devices in mid-trial and attempting to "pool" the data pertaining to the first and the second devices is objectionable from the standpoint of sound scientific methodology, and is also frowned upon by the FDA. (Krieger Decl., ¶ 3(l).)

Yet another way in which the terms of the proposed injunction would set back clinical research involves cost. In CellPro-sponsored studies of its second generation

devices (i.e. those that combine a 12.8 antibody-based stem cell enrichment step with a T-cell depletion or tumor-purging step using another antibody), CellPro is barred by FDA regulations from charging subjects or investigators more than a cost-recovery price for the device and disposables. The injunction's prohibition against distributing goods free or at a discounted price would render it impossible to comply with the FDA regulation and would mean, presumably, that these would have to be aborted (Jacobs Decl. ¶¶ 8,9,12). Even for trials being conducted under investigator-sponsored IDEs, it is common for the manufacturer of the medical device involved in a trial to provide a measure of financial support. In a number of investigator-sponsored trials involving CellPro's stem-cell selection devices, CellPro has made commitments either to supply devices and/or disposables free of charge or to supply them at a lowered, "cost-recovery"price; and CellPro has typically undertaken to pay limited patient-care and/or administrative costs in support of the trials as well. (Jacobs Decl. ¶ 10.)

Finally, no fair consideration of adverse effects on clinical research could overlook the effects that the proposed injunction would have on the collection of scientists, medical professionals and engineers at CellPro, a group probably unrivaled in the world in terms of its focused expertise regarding stem-cells and therapies based thereon, and a group that has been a dynamic force behind the rapid expansion of the clinical utility of stem-cell therapies (Jacobs Decl. ¶ 3.) The practical barriers to conducting clinical trials under the terms of the injunction would probably force CellPro to dismantle the research, development and clinical teams it has assembled, to the great detriment of patient care and medical progress. (Jacobs Decl. ¶ 5.)

Hardships To Patients

Anything that hampers clinical research can, of course, mean hardship for patients who might benefit from the fruits of that research, but to the extent that the proposed injunction would cause interruption or abandonment of trials in progress for reasons like those discussed above, the effects on patients would be more direct, more personal, and more appalling. Only very seriously ill patients ever undergo stem cell transplantation; and in some of the studies, the CellPro device is being used where there simply is no known therapy for the target disease and no other hope for the patient.

Baxter's Inability to Fill the Void in the United States

Submitted herewith is a Declaration of David F. Weeda, Esq., former Associate Chief Counsel of the FDA, which rebuts the cardinal premise of the proposed injunction - namely, the premise that needy patients would not go without treatment if the CellPro device were enjoined because hospitals that wished to use Baxter's ISOLEX® device could do so simply by filing their own investigational device exemptions (IDEs) with the FDA. (Brief, p. 9.) For the reasons explained at length in the Weeda Declaration, the IDE procedure cannot render the still-experimental ISOLEX® 300 device a reasonable substitute for the availability of the FDA-approved CellPro device. (Weeda Decl. ¶14.)

An IDE is a

> "very narrow, controlled investigation-based exemption from the general rule that an unapproved device may not be shipped in interstate commerce for use on human subjects. It is not intended as a stop-gap for the commercialization of a device that is otherwise unapproved."

(Id. ¶3.) The IDE does not permit the investigational device to be promoted, test marketed, sold above cost, nor may the investigation be prolonged to promote the device. (Id. ¶10.)

Since the rationale of allowing an unapproved device to be used under an IDE is simply to gather data, in a carefully-controlled study, to support the device's safety and effectiveness,

> "it is quite common, for public health reasons, for FDA to limit the number of IDEs it will approve ... or the total number of clinical cites under one IDE .... It is not FDA's policy to carte blanche approve innumerable IDEs absent some unusual and urgent public health reason ...."

(Id.) If the Agency sees that the IDE procedure is being abused as a guise for commercialization of an unapproved device, it "has broad authority to withdraw approval of an IDE." (Id. ¶11.)

Moreover, the IDE application process is complex and burdensome (Weeda Decl. ¶5) and the record keeping, reporting and monitoring requirements on an investigator and sponsor under an IDE are substantial (Id. ¶6). These burdens mean, as a practical matter, that Baxter under an IDE could not supply its device to all clinicians who might wish to use it (Jacobs Decl. ¶15); that not all patients who might benefit will be eligible for the protocol (Id. ¶15 C); and that some transplant programs, especially smaller ones, will lack the wherewithal to handle the administrative burdens of obtaining and using a Baxter device under an IDE (Id. ¶15 A).

Baxter's argument that "CellPro's FDA approval ... is limited in significant ways [bone marrow but not peripheral blood; autologous but not allogeneic]" (Brief, pp. 8-9) misses the point entirely. As the Weeda Declaration explains:

> "FDA does not regulate the practice of medicine, which includes a physician's decision to use an approved medical device in a manner, or for a medical indication, that is not specifically approved for inclusion in the labeling of the device. Thus, a physician may, within his or her sound medical judgment and the bounds of state law, employ an approved device for an 'off-label' use in the treatment of a patient. Such off-label uses are quite common in many areas of medicine and the areas of cell therapy and transplantation are no exception." (Weeda Decl. ¶7.)

With an unapproved device, the physician has no such latitude. As Mr. Weeda explains:

> "[A]n investigational use of a device presents major restrictions in a physician's ability to treat a patient. .... [A] major limitation on the investigator under an IDE for the ISOLEX® 300 product would be the need to closely follow the investigational protocol submitted as part of the IDE. In the absence of a very limited, emergency use, ... if a change or deviation from the protocol may affect the scientific soundness of the investigation plan or the safety of the subjects, the sponsor of the IDE is required to submit to FDA a supplemental application for approval and to notify the IRB. Thus, if the use of the ISOLEX® 300 under an IDE were the only available option for a physician, his or her ability to use sound medical judgment in treating patients would be significantly constrained. Moreover, if Baxter shipped the ISOLEX® 300 device with knowledge that it was actually for use in a manner inconsistent with the IDE, that shipment would be in violation of the Federal Food, Drug, and Cosmetic Act. See also, 21 CFR §801.4." (Weeda Decl. ¶7)

Thus, because the CellPro device is FDA-approved, it is a comparatively simple matter for a physician to obtain it commercially and use it for an off-label indication where, in the physician's medical judgment, the treatment is appropriate for a particular specific patient (Jacobs Decl. ¶15).

As for the "very limited" emergency use policy to which Mr. Weeda refers,

> "[It] is not intended to be used to facilitate the nationwide, stop-gap use of an unapproved device by physicians, and unapproved devices cannot be shipped in anticipation of an emergency." (Weeda Decl. ¶12).

Strict criteria govern when an "emergency" exists, and if the emergency policy is abused, "FDA can take regulatory action against the device manufacturer or the physician/investigator." (Weeda Decl. ¶12)[2/] From the foregoing it should be clear that the major premise of plaintiffs' injunction rationale, the premise that

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[2/]There is a "compassionate use" procedure, but it is "enormously burdensome to the physician" and is "a rare and exceptional step, and one that it is quite impractical to take on a routine or even frequent basis." (Press Decl. ¶8)

"it cannot be said that no substitute products are available to patients who need them"

(Brief, p. 9), is, as a matter of practical reality, a false premise.

The Improbability of Baxter's Winning FDA Approval Without Long Delay

The average time from PMA-filing to approval is some 26 months (Krieger Decl., ¶ 2), and a complex device for a radical and potentially dangerous application can naturally be expected to take longer than a relatively simple device for a relatively non-dangerous use (Krieger Decl., ¶¶ 2,3.) CellPro's own PMA application took over 3 years to ripen into an FDA approval (id., ¶2), even though CellPro, as a startup enterprise, was far better motivated than the lumbering giants of the industry typically are to minimize delay. There are, moreover, many reasons to suspect that Baxter's PMA filing is of less than average quality and that it can expect to succeed only after a lengthy struggle, if it succeeds at all.

First there is the timing: after the plaintiffs' collective decade and a half of relative slumber, the PMA was suddenly filed one week before the damages trial in this case – and at a time when Baxter is rumored to be trying to sell the division that makes its still-experimental device. It is hard to believe that this timing is just coincidental. It seems obvious that the principal reason, if not the only reason, why the PMA was filed at that time was to allow Baxter to posture itself, before the jury and the Court, as offering needy patients a credible alternative to the CellPro device.

Moreover, the information that can be gleaned from public-record sources strongly suggests that Baxter's application improperly "pools" clinical data gathered using the

problem-plagued[2/] ISOLEX® 300SA device by putting it together with data gathered using the newer, ISOLEX® 300*i* device. Moreover, from what we know of the nature of Baxter's 300*i* device, it seems highly probable that the FDA will see significant safety issues, including toxicity from magnetic beads that are infused into the patient and possible allergic risks of the antibody used. (Krieger Decl., ¶ 3(iii)).

Additional Adverse Public Health Impacts on Patients in the Rest of the World

In the rest of the world, Baxter's proposed injunction would inflict a different sort of injury on the public health and a different kind of hardship on patients and clinicians. At a minimum, the harm would be that healthcare providers outside of the U.S. and their patients would be forced, because of what amounts to extraterritorial enforcement of the U.S. patent laws, to pay the same monopoly price as if Baxter's device were patented worldwide – even though it has not been and cannot be. Another harm, at a minimum, would be that European clinicians would be forced to conduct their clinical research and treat their patients with a device that they would, by a vast plurality, avoid if they had a choice. Although Baxter obtained regulatory approval in Europe earlier than CellPro did, still the CellPro device enjoys an 80% share of the market (Vandervelde Decl., ¶¶ 4-6) – a fact which seems a fair indicator of how clinicians would judge the relative merits of CellPro's and Baxter's devices in other markets if both were commercially available.

There is, moreover, reason to suspect that Baxter's proposed injunction would inflict greater harms than just thrusting an inferior product into the hands of unwilling Europeans

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[2/] We say "problem-plagued" because Baxters' own literature admits some of the shortcomings of its now-apparently-abandoned chymopapain-based release enzyme. (See Krieger Decl. ¶ 3(ii) and associated exhibits.)

at a monopoly price and disrupting their medical research and patient care preferences. There is the prospect that if the CellPro device were "phased out" of the rest of the world in 12 months, and CellPro banished from the world market for 2 years thereafter, there would be such a shortage of stem-cell immunoselection devices in Europe – and perhaps elsewhere – that needy patients would be unable to get any such treatment at all. It is reported that the CellPro's 300*i* device, although approved in Europe a year ago (Vandervelde Decl., ¶ 4) is in such short supply that Baxter has developed a reputation for unreliable delivery (id., ¶ 7). Baxter's evidence fails to show – and there is strong reason to doubt – that Baxter would have the capacity to supply enough units to meet the stem-cell immunoselective-therapy needs of Europe, even if it were to persuade this Court to sentence Europeans to monopoly pricing, as plaintiffs' proposed injunction so brazenly bids this Court to do.

Special Hardships to Patients in Canada and Australia

In Canada and Australia, where the Baxter device also has not been approved under local medical-device-regulatory laws, a phaseout of the CellPro device on Baxter's proposed one-year schedule (without regard, apparently, to whether Baxter gets approval in those countries or not) would mean that no alternative device was commercially available to clinicians and patients there. (Jacobs Decl., ¶ 13.)

IV. ARGUMENT

A. The Injunction Would Unlawfully Prohibit CellPro's FDA-Clinical Trial-Related Activities That Are Exempt From Infringement Liability Under 35 U.S.C. § 271(e)

Title 35 U.S.C. § 283 gives courts power to grant injunctions to prevent violation of "rights secured by patent." Nevertheless, despite the Court's infringement finding, the making, using, offering to sell, or selling of the 12.8 antibody, the 12.8 hybridoma or the CEPRATE® device does not violate "any rights secured by patent" when that activity is reasonably related to development and submission of information required for FDA approval. See 35 U.S.C. § 271(e)(1); Eli Lilly & Co. v. Medtronic, Inc., 496 U.S. 661 671 (1990) ("§ 271(e)(1) permits competitors, prior to the expiration of a patent, to engage in otherwise infringing activities in order to prepare for obtaining regulatory approval.")

Indeed, Congress has forbidden the courts from enjoining such exempt, FDA related activities. 35 U.S.C. § 271(e)(3) provides:

> **No injunctive or other relief may be granted which would prohibit the making, using, offering to sell, or selling within the United States or importing into the United States of a patented invention [exempt under § 271(e)(1)].**

Yet plaintiffs request an injunction that would plainly violate § 271(e)(3).

Although CellPro has already received FDA approval to market its device for autologous bone marrow transplantation, CellPro is still engaged in on-going clinical trials designed to obtain further FDA approvals not only by way of label expansions for its CEPRATE® SC Stem Cell Concentrator but also for second-generation devices that combine the use of the 12.8 antibody for stem-cell concentration with other antibodies for other manipulations of the suspension (Jacobs Decl., ¶¶ 5,6,7,11,16). CellPro even plans trials in

Europe and Australia which are aimed at gathering data that are FDA-related (Id. ¶¶ 17,19). Under § 271(e) this is non-infringing activity which the Court cannot lawfully enjoin.

Despite the clear law to the contrary, plaintiffs seek to enjoin this exempt activity. See, e.g., the following portions of Plaintiffs' proposed permanent injunction:

> 1. CellPro, Inc. ... [is] permanently enjoined and restrained from any and all of the following:
>
> (a) From making, having made, selling, supplying, testing, evaluating or using for any purpose whatever within the United States, and from importing to or exporting from the United States, any CD34 antibody, including but not limited to the 12.8 antibody.[4/]
>
> 3. CellPro shall promptly destroy, in the presence of a United States Marshall, all [12.8] antibodies and hybridomas ....

As should be clear from the proposed language – "for any purpose whatever" – plaintiffs are requesting that CellPro be enjoined from doing exactly what Congress, through § 271(e), permits it to do. Indeed, by seeking the destruction of the 12.8 hybridoma, plaintiffs seek to preclude CellPro from conducting clinical trials now or at any time in the future, – after the expiration of the Civin patents. Without the unique 12.8 hybridoma to produce the unique 12.8 antibody, there will be no clinical trials. Plaintiffs' proposed injunction is, on its face, broader than allowed by law.

But more fundamental than this problem of overbreadth is that . . .

B. In View Of The Public Interest, No Injunctive Relief Should Be Awarded

Plaintiffs concede, as they must, that findings of patent validity and infringement do not confer on the patentee any absolute right to permanent injunctive relief (Brief, p. 4) and

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[4/] Similar language to this paragraph appears in subparagraphs (b), (e) and (f).

that such relief may and should be denied where there is a "sound reason" for denying it (id.).

Courts can, and do, deny permanent injunctive relief to prevailing patentees when public interests–including especially public health concerns–make that course appropriate. See e.g., Vitamin Technologists, Inc. v. Wisconsin Alumni Research Found., 146 F.2d 941, 956 (9th Cir. 1944); City of Milwaukee v. Activated Sludge, 69 F.2d 577 (7th Cir. 1934), cert. denied 293 U.S. 576 (1934).

In a similar vein are decisions which deny, or stay, injunctive relief even in situations where significant public hardship, or detriment to public health, are not evident. In Foster v. American Mach. & Foundry Co., 492 F2d 1317, 1324 (2d Cir. 1974), the court affirmed what amounted to a compulsory license–a reasonable royalty damage award without an injunction. The Court wrote:

> We do not find any difficulty in agreeing that an injunction would be an inappropriate remedy in this case. An injunction to protect a patent against infringement, like any other injunction, is an equitable remedy to be determined by the circumstances. .... Here, as the District court noted, the appellee manufactures a product; the appellant does not. In the assessment of relative equities, the court could properly conclude that to impose irreparable hardship on the infringer by injunction, without any concomitant benefit to the patentee, would be inequitable.
>
> . . . .
>
> Instead, the District Court avoided ordering a cessation of business to the benefit of neither party by compensating appellant in the form of a compulsory license with royalties. This Court has approved such a 'flexible approach' in patent litigation. Here the compulsory license is a benefit to the patentee who has been unable to prevail in his quest for injunctive relief. To grant him a compulsory royalty is to give him half a loaf. In the circumstance of his utter failure to exploit the patent on his own, that seems fair.

Similarly, in E.I. duPont de Nemours and Co. v. Phillips Petroleum Co., 835 F.2d 277, 278 (Fed. Cir. 1987), the court upheld the grant of a stay of a preliminary injunction

where duPont, the patentee, had licensed all who desired entry into the patented polyethylene business and planned to exit the market. The court observed that "harm to duPont here is of a different nature than harm to a patentee who is practicing its invention and fully excluding others." (id.)

Here, as in duPont, others beside Baxter have been licensed (actually sublicensed by Baxter itself) in the therapeutic field–namely, Applied Immune Sciences ("AIS") and Systemix (PTX 421 and PTX 836)–and although Baxter has aspirations to sell a competing therapeutic device in the United States, it is, and for the indefinite future will remain, legally inhibited from doing so because the device is not FDA approved.

Hence, granting the proposed injunction and "freezing" the number of CellPro installations at March 12, 1997 would leave American clinicians, clinical researchers and patients in a kind of limbo until the day (if it ever comes) when the FDA approves Baxter's device:[5/] CellPro would be unable adequately to serve the market despite its FDA approval, and Baxter would be unable adequately to serve the market for lack of FDA approval.

Finally, while it cannot be said that the plaintiffs are guilty of "utter failure to exploit the patent on [their] own" (Foster, supra, 492 F2d at 1324), it must be said that they have

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5/ Nor is FDA approval the all-or-nothing proposition that Baxter's proposed injunction supposes it to be. It is entirely possible that Baxter's device could gain FDA approval for some indications, on the basis of some safety or efficacy parameter, while CellPro's device would be FDA approved for other indications, based on some other safety or efficacy parameter. For example, CellPro's device is presently FDA approved for allogeneic bone marrow transplantation, the efficacy parameter being a lowering of infusional toxicity compared to conventional transplantation. Even if Baxter's device someday achieves FDA approval, it could well be for a different labeled indication and the FDA could well make different findings as to safety and efficacy advantages (or disadvantages). (See Jacobs Decl. ¶ 2.) Even if it were not naive to think that Baxter will soon have an FDA approval of some kind, it may still be naive to think that the Baxter device will ever prove to be a medically (or legally) appropriate and equivalent substitute for the CellPro device for all researchers' and patients' needs.

been guilty of extraordinary, and still-ongoing, delay in bringing U.S.-taxpayer-funded technology to the U.S. therapeutic market.[6/]

We take issue with plaintiffs' assertion that even irreparable injury to CellPro is "legally irrelevant" to the question whether permanent injunctive relief should be awarded. Clearly it is relevant. Nerney v. New York, 83 F2d 409, 411 (2d Cir. 1936), injunctive relief denied where "it was not absolutely essential to the patentee and caused the infringing defendant irreparable damage"]; Foster, 492 F2d at 1324, supra ["the court could properly conclude that to impose irreparable hardship on the infringer by injunction, without any concomitant benefit to the patentee, would be inequitable"].

Even if irreparable harm to CellPro were not relevant to the propriety of permanent injunctive relief, still it would be relevant to the issue of whether the injunction should be stayed pending appeal, an issue briefed in the following point. Hence, we discuss the issue of irreparable harm to CellPro.

[6/] Plaintiffs have indeed been remarkably slow to convert the discovery of the MY-10 antibody into a clinically practical immunoselection device. From Dr. Civin's Blood Abstract (DTX15) we know that he had the MY-10 antibody at least as early as November 1982 – about a decade and a half ago. The patent applications were filed over 13 years ago on February 6, 1984. Although Hopkins licensed BD fairly promptly after the application was filed (August 1984; see DTX980), BD sat on the license for over 6 years (until August 24, 1990) before it licensed Baxter for therapeutic applications – in the meantime failing itself to create a practical immunoselection device. Although Baxter granted sublicenses in 1992 and 1993 (PTX 421and PTX 836), both of those sublicenses apparently also failed to produce a practical device. Baxter itself has now been licensed for more than 6-1/2 years, but neither Hopkins, Baxter, nor any licensee or sublicensee under the Civin patents has yet produced an FDA-approved therapeutic device.

Although plaintiffs are fond of repeating that CellPro is ahead of them because it got an unfair "head start," plaintiffs ignore the fact that CellPro was not yet even in operation during the first half of the extraordinarily lengthy period during which the plaintiffs, collectively, have delayed developing the fruits of taxpayer-funded medical research to the level of practical therapeutic usefulness.

Even if the Court declines to award plaintiffs the direct monetary sums they seek--including a trebling of damages and award of attorney fees, for a total of some $13.9 million, still the combination of injunctive provisions plaintiffs seek would, by itself, inflict irreparable harm on CellPro. Throughout all of its corporate existence, CellPro has focused most of its effort on stem-cell therapy. Its one and only FDA-approved device is in that field, providing the one significant income stream to a company that has never made a profit and has had to depend on venture-capital investors and public stock offerings to support its endeavors. The overhang of litigation is enough of a hardship to such a company even when the litigation is at a early stage and even when the news is good; but if it should come to pass that CellPro is under Court order to phase itself out of the rest-of-the-world market (including the European market, in which it has an 80% share (Vandervelde Decl., ¶ 6); to sell temporarily at money-losing prices into a U.S. market that the Court will not let grow; and then to disappear, quickly, from that market if any Baxter device should ever become FDA-approved, it is not hard to predict what this would do to CellPro's ability to hold together the world-class team of medical, scientific and engineering professionals it has assembled, and to survive as a company. (Jacobs Decl. ¶¶ 3,4.)

The definition of "incremental profit" contained in the proposed injunction, together with the $2,000 "floor" on what CellPro would be required to pay per unit, would mean that CellPro could supply disposables only at a large loss. As appears from the Declaration of William E. Simpson, if CellPro were compelled to pay a royalty of $2,000 per unit and all appropriate costs were allocated, CellPro would loss some $1,510.81 per unit before considering fixed costs. It would, moreover, be unfair to prohibit CellPro from recovering such costs as research and development and administrative costs, as much of CellPro's

ongoing activity aims at developing new therapies and new products, which activities are § 271(e)(1) exempt. (Id. ¶¶ 17, 19).

C. If A Final Injunction Is To Be Entered, It Should Be Stayed In Its Entirety Pending Appeal

A district court "in its discretion may suspend ... an injunction during the pendency of the appeal." Fed. R. Civ. P. 62(c). Four factors are considered:

> "(1) Whether the stay applicant has made a strong showing that he is likely to succeed on the merits;
>
> (2) Whether the applicant will be irreparably injured absent a stay;
>
> (3) Whether issuance of a stay will substantially injure the other parties interested in the proceeding; and
>
> (4) Where the public interest lies."

Standard Havens Products v. Gencor Indus., 897 F.2d 511, 512 (Fed. Cir. 1990), quoting Hilton v. Braunskill, 481 U.S. 770, 776, 107 S. Ct. 2113, 2119, 95 L.Ed.2d 724 (1987). These factors do not constitute rigid, inflexible requirements; they are considered according to a sort of sliding-scale approach, such that if harm to the applicant is great enough, a court will not require a strong showing that the applicant is likely to succeed on the merits of the appeal. Standard Havens, 897 F.2d at 513; Hybritech, Inc. v. Abbott Laboratories, 849 F.2d 1446, 1451 (Fed. Cir. 1988) [the "factors, taken individually, are not dispositive; rather, the district court must weigh and measure each factor against the other factors and against the form and magnitude of the relief requested"].

Stays have been granted in cases where the applicant's showing as to one or more of the factors is wholly lacking or only weakly supportive of his position. For example, in In

re Hayes Microcomputer Products, Inc., 766 F. Supp. 818 (N.D. Cal. 1991), aff'd., 982 F.2d 1527 (Fed. Cir. 1992), the district court granted defendants' motion for a stay of the injunction although convinced that their chances on appeal were doubtful. The court reasoned that the defendants would have been put out of business or irreparably harmed pending appeal, even if ultimately not found to be willful infringers; that the plaintiff, having made a habit of licensing its technology, would not be substantially injured during pendency of the appeal; and that the public, though interested in seeing valid patents enforced, also had an interest in fostering legitimate competition by encouraging valid challenges to patents. The stay was granted on condition that the defendants deposit an amount equal to a reasonable royalty on infringing sales sold during appeal pendency.

We submit that the Hilton v. Braunskill factors all favor the granting of a stay pending appeal in this case, as follows:

1. Likelihood of Success on Merits

The principal liability and infringement issues have been thoroughly ventilated in prior briefing; we understand the Court's rulings; and we do not expect that rehashing our arguments at this late hour would change the Court's view of the merits. With respect, however, we would remind the Court that there were potentially dispositive issues that were close enough to withstand a first round of summary judgment motions, to prevail at trial, and thereafter to withstand JMOL motions.[2] This case, moreover, presents novel and

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[2] Baxter, in an issue of Blood dated four days after the jury's wilfulness finding, effectively admitted to the medical community that Baxter itself does not believe that CellPro achieves 90%-pure suspensions. Kenny Decl., ¶¶ 2-3 and Exhibit A.) The Court itself called CellPro's '204 nonenablement defense a "horse race"; and in the same

(continued...)

important policy issues as regards, for example, the appropriate scope of enablement and claim breadth which can fairly be supported by a 1-example patent, dealing with monoclonal antibody technology, a concededly unpredictable art. CellPro sincerely believes that its likelihood of appellate success is high; but even if this Court disagrees, at least it must be said that this record discloses fairly arguable and important issues for the appellate court. The likelihood-of-success factor is, in any event, not dispositive.

2. Irreparable Harm to CellPro

The lack of a stay pending appeal would irreparably harm CellPro, for the reasons mentioned above.

3. Whether Issuance of the Stay Will Substantially Injure the Other Parties Interested in the Proceeding

Because Baxter, for lack of FDA approval and possibly for other reasons, is incapable of fully supplying the needs of the U.S. market, and because Baxter's experimental device cannot lawfully command a commercial price under FDA standards, the extent to which Baxter can lose sales and revenues if CellPro continues distributing its products freely pending appeal is limited; and besides, there is ample precedent for requiring the stay applicant to deposit reasonable royalties into court pending appeal. In re Hayes Microcomputer, supra.

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[11](...continued)
statement the Court acknowledged its understanding why an accused infringer's trial strategy might reasonably differ from the defenses discussed in opinion letters--namely, that the enablement defense is typically one that does not develop until after discovery has been had (8/4/95 Tr. at 244).

Moreover, unless Baxter's patents are ultimately determined to be invalid, unenforceable or not infringed by CellPro, Baxter actually will be benefitted, not harmed, if CellPro is permitted during the appellate process to keep "growing the market" – to keep expanding the customer base, to keep sponsoring research that will broaden the range of the clinical utility of stem cell immunoselection.

Baxter's assertion that "the longer CellPro is permitted to remain in the market, and the greater its sales, the greater the obstacles its conduct will have created for Baxter by the time Baxter begins marketing its ISOLEX® device in the United States (Brief, p. 8), and its assertion that "CellPro's unlicensed sales of its competing therapeutic device has harmed Baxter and will continue Baxter by giving CellPro a market lead that will be difficult to overcome" (id.) are nonsensical in the circumstances of this case. Exactly the opposite is true: The more CellPro expands the market before Baxter wins FDA approval, the bigger Baxter's eventual windfall will be – if the Court of Appeals vindicates Baxter's position on the merits and a permanent injunction is found to be appropriate.

Baxter is helped more than it is hurt if CellPro continues to nurture and expand a market far broader than any that Baxter, without FDA approval, could efficiently develop and adequately serve, but which Baxter would "own" if CellPro were enjoined following the appeal.

4. The Public Interest

To what has already been said about the public interest, we would only add that it is clearly in the public interest that somebody, at least, continue to widen the availability, and expand the range of clinical utility, of stem-cell immunoselective therapy; and in this

country, Baxter cannot effectively do that if CellPro is enjoined pending appeal, given the FDA-related limitations on the use of Baxter's still- experimental device for human treatment.

D. The Final Injunction That Plaintiffs Seek is Too Broad and Violative of Legal and Public Policy Constraints

In addition to the overbreadth that comes of ignoring § 271(e)(l), the proposed injunction includes other features that are legally impermissible or inappropriate, as follows:

1. The Proposed Two Year Prohibition Upon CellPro Selling Foreign-Manufactured Products Abroad Would Not Only Prohibit Non-infringing Conduct But Would Also Intrude upon the Law and Policy of Other Sovereigns and Is Therefore Contrary to Applicable Principles of International Comity

In their proposed Permanent Injunction, plaintiffs seek a provision (para. 1(l)) that:

> "l. For a period of two (2) years from the date of this Order, from selling or otherwise supplying to customers outside the United States, any product which utilizes or is designed or intended for use with any CD34 antibody."

This provision would reach even products wholly made in Europe with an antibody made in Europe – a result that the Brief makes clear is intended. Such a provision would prohibit CellPro from competing with plaintiffs in the European Union, even though CellPro's competition in Europe is entirely free of any infringement of any intellectual property of plaintiff in Europe.

Plaintiffs do not cite a single authority in support of this daring provision. It is, in fact, contrary to basic principles of law and of international comity which has been endorsed by the United States Government.

a. A United States Patent Has No Force or Effect Outside the United States. An Attempt To Prohibit Conduct Outside the United States Improperly Extends the United States Patent Law beyond Its Inherent Reach.

The Federal Circuit stated it starkly in Paper Converting Machine v. Magna Graphics, 745 F.2d 11, 17 (Fed. Cir. 1984), citing Deepsouth Packing Co. v. Laitram Corp., 406 U.S. 518 (1972), for the general proposition that there is a "horror of giving extraterritorial effect to United States patent protection." Deepsouth had made it clear (406 U.S. at 531) that:

> Our patent system makes no claim to extraterritorial effect; "these acts of Congress do not, and were not intended to, operate beyond the limits of the United States," [. . .] and we correspondingly reject the claims of others to such control over our markets. [. . .]. To the degree that the inventor needs protection in markets other than those of this country, the wording of 35 U.S.C. §§ 154 and 271 reveals a congressional intent to have him seek it abroad through patents secured in countries where his goods are being used.

The enactment of 35 U.S.C. § 271(f) with respect to manufacturing component parts in the United States for assembly abroad did not erode the fundamental proposition concerning extraterritoriality. See, e.g., Robotic Vision Systems v. View Engineering Inc, 39 U.S.P.Q.2d 1117, 1119 (C.D. Cal. 1995) (citing Deepsouth for proposition that it is not an infringement to make or use a patented product outside the United States, and denying an injunction of activities beyond the territorial reach of the statute.

Plaintiffs speak of an advantage supposed to have flowed to CellPro in respect of its foreign operations from CellPro's infringing conduct in the United States, saying (Brief, p. 11):

> "Rather than being the sole supplier to the ex-U.S. market for some period of time, Baxter has been forced to share that market with an illicit participant."

Plaintiffs conveniently overlook the fact that CellPro is not an "illicit participant" in competing with Baxter outside the United States. CellPro's infringement of Baxter's two United States patents concerns CellPro's conduct in the United States, which does not supply a scintilla of foundation for the assertion that CellPro's conduct in the "ex-U.S. market" constitutes the infringement of any patent right of Baxter in any such foreign jurisdiction. Plaintiffs have no patent rights in those jurisdictions, and Dr. Civin would be told that he was time-barred long ago if he sought them now.

b. The Proposed Extraterritorial Provision Would Be Contrary to the Law and Policy of the European Union.

We submit herewith the sworn statement of the Honorable H. Colin Overbury, CBE, an expert on European law and policy. Mr. Overbury was one of the highest officials in the European Commission, having served in numerous capacities in the portion of the Commission charged with competition (antitrust) responsibilities. Mr. Overbury's sworn statement sets out in detail the intrusion of the proposed extraterritorial prohibition upon the fundamental law and policy of the European Union.

For instance (Overbury para. 7),

- The terms of the proposed Permanent Injunction have the effect of preventing Cell Pro from competing with the plaintiffs in the European Union for a two year period. From the perspective of the European Union and its institutions, that would give to a United States patent an extraterritorial effect contrary to the competition law and policy of the European Union, directly impeding competition within the European Union and depriving the common market of the benefit of competition, and would be contrary to the basic tenet of the EC Treaty which renders void restrictions upon the free movement of goods within the common market.

- The only purportedly ameliorating effect of the proposed Partial Stay does not permit competition as it would be if European patent and competition law were given their normal reach, but would only have the effect of granting a license to CellPro which restricts CellPro's ability to fix its own prices, which limits the quantities CellPro can supply to its customers, and

which prevents CellPro from competing with the plaintiffs. Such restrictions are contrary to the EC Commission's Regulation on the Transfer of Technology.

- CellPro would also be prevented (subject to the terms of the Partial Stay) from reselling any of the products in question which had lawfully been placed on the market by the plaintiffs or with their consent, which contravenes the principles of the exhaustion of rights.

c. Such Intrusions Run Afoul of the Principles of International Comity.

Such intrusions upon the law and policy of another sovereign are contrary to the "longstanding principle of American law 'that legislation of Congress, unless a contrary intent appears, is meant to apply only within the territorial jurisdiction of the United States.'" EEOC v. Arabian American Oil Co., 499 U.S. 244, 248 (1991). If this Court were to accept plaintiffs' proposed extraterritorial provision, this Court would be compelling CellPro to refrain from competition that it would otherwise have provided in the European Union. CellPro could not voluntarily agree with Baxter not to compete and thereby to provide Baxter with the monopoly it so brazenly claims as its birthright; a court of the United States ought not compel conduct of a party that would violate foreign law and policy.

The authorities uniformly condemn such efforts and commend adherence to principles of international comity. E.g., Subafilms, Ltd. v MGM-Pathe Communications, 24 F.3d 1088 (9th Cir. 1994), expressing concern at the "international discord" that could arise if United States courts attempted to affect acts in other countries and to displace those countries' law "in circumstances in which previously it was assumed to govern." (24 F.3d at 1097.) Similarly, in Mannington Mills, Inc. v. Congoleum Corp., 595 F.2d 1287 (3d Cir. 1979), the court required careful attention to principles of international comity before

extending Walker Process antitrust liability to acts of fraudulent procurement of patents abroad. Cf., Nintendo of America, Inc. v. Aeropower Co., Ltd., 34 F.3d 246 (4th Cir. 1994) (in the context of trademark infringement); Timberlane Lumber Co. v. Bank of America, N.T. & S.A., 549 F.2d 597 (9th Cir. 1976)[8/].

Moreover, as Mr. Overbury explains, the United States Government has expressly agreed with the European Council to avoid enforcement actions which raise such issues. (Overbury para. 17.)

We respectfully submit that this Court ought not frame relief in such a way as to extend that statutory reach of the United States patent law, particularly where the proposed provision would so severely intrude upon important law and policy of a foreign sovereign, contrary to fundamental principles of international comity.

2. The 12.8 Hybridoma Outside the U.S. is Non-Infringing And Beyond The Court's Jurisdiction, and the Proposed Provision Requiring its Repatriation and Destruction is Legally Insupportable

a. The 12.8 Hybridoma is a non-infringing product

Plaintiffs have no patent coverage outside the U.S., and they lacked any patent claim to any hybridoma before October 23, 1991; yet they seek to expand the temporal and geographic scope of their patents by requesting that the Court order CellPro to bring 12.8

[8/] In Timberlane the Ninth Circuit held that, in order to allow extraterritorial application of the antitrust laws, (1) there must be some effect on American foreign commerce; (2) the effect must be sufficiently great to present a cognizable injury, and (3) the interests of and links to American foreign commerce must be sufficiently strong in relation to those of other nations to justify an assertion of extraterritorial authority. Star-Kist Foods, Inc. v. P.J. Rhodes & Co., 769 F.2d 1393, 1395 (9th Cir. 1985, Kennedy, J.), summarizing Timberlane, 549 F.2d at 613-615, and upholding district court's decision to exclude wholly foreign commerce from the scope of its injunction enforcing the Lanham Act.

hybridoma, made prior to the issuance of the '204 patent and located outside of the U.S., back to the United States to be destroyed. Plaintiffs' request is based on misstatement of the facts and misrepresentation of the law.

The 12.8 hybridoma was created in the early 1980's at the Fred Hutchinson Cancer Research Center. Under licence from the Hutchinson Center, 12.8 hybridoma was transferred to CellPro. In July 1990, CellPro created a "master cell bank" of 12.8 hybridoma by freezing about 100 vials. The '204 patent, with the first hybridoma claims, issued in October 1991. Thereafter, six of the frozen hybridoma vials were shipped to Canada. See generally D.I. 158 and 261; Tarnowski Declaration, filed herewith.

From these facts plaintiffs weave a series of convoluted and seriously erroneous arguments. First, plaintiffs argue that CellPro "used" 12.8 hybridoma master cell bank after the '204 patent issued in a way that infringed the patent. In arguing this, plaintiffs conveniently ignore the fact that that CellPro's "master cell bank" is not a single entity, but rather a collection of separate and distinct vials each containing hybridoma cells.[9/] As plaintiffs acknowledge, hybridoma that they say was "used" to make "working cell banks" and "extended cell banks" after issuance of the '204 patent was not the same hybridoma shipped to Canada:

> Mr. Bordonaro stopped recording withdrawals from the Master Cell Bank ... on December 9, 1991 [after the alleged extended and working cell banks were allegedly created], when there were only 82 vials left. However, after that date, cells from the master cell bank continued to be removed ...

9/ Indeed, plaintiffs have acknowledged and argued this very fact in an earlier brief. "The master cell bank originally contained approximately 100 vials of frozen hybridoma cells." D.I. 249 at pp. 4-10, Plaintiffs Opp. Mem. to CellPro's Motion for Partial Summary Judgment on Non-infringement (citing (Bordonaro Tr. 777-78, Appendix B, p. B117-118; Plaintiffs' Dep. Ex. 836, Appendix B, Ex. E).

> for shipment to Biomira in Canada... [and o]n or about July 19, 1993, CellPro sent six vials of cells from its master cell bank to Biomira in Canada.

D.I. 249 at p.8-9.

Plaintiff thus acknowledge that the hybridoma shipped to Canada was made before the '204 patent issued, stored separately from the hybridoma later used by CellPro in the U.S., and was never itself ever used in the U.S. The frozen hybridoma at issue was simply never tested or profiled or used in any way after the issuance of the '204 patent.

Plaintiffs' argument that the act of shipping alone was a "use" has been rejected by the courts. See Amgen, Inc. v. Elanex Pharmaceuticals, Inc., 1996 WL 84590, *3-4 (W.D. Wash. 1996) (shipment of frozen cells outside U.S. is not infringement); Fausett v. Pansy Ellen, Inc., 19 U.S.P.Q.2d 1228, 1230 (N.D. Ga. 1990) (importation and exportation of alleged infringing product are not infringement).

Even the cases plaintiffs cite make it clear that shipment alone is not an infringing "use." The Supreme Court, in Bauer & Cie. v. O'Donnell, 229 U.S. 1 (1913), defined "use" as "put[ting] into service any given invention." Id. at 10-11. A hybridoma is "put into service" by making monoclonal antibody, and the 12.8 hybridoma shipped to Canada was never so "put into service" in the U.S.[10/]

The cases cited by plaintiffs to support their argument that shipment is use are clearly not on point. In Trans World Mfg. Corp. v. Al Nyman & Sons, Inc., 750 F.2d 1552,

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[10/] Olsson v. U.S., 25 F. Supp. 495 (Ct. Cl. 1938), Hughes Aircraft v. U.S., 215 U.S.P.Q. 787 (Ct. Cl. 1982), and Paper Converting Machine Co. v. Magna-Graphics Corp., 745 F.2d 11 (Fed. Cir. 1984) are not to the contrary. In Olsson the howitzers were "put into service" for deterrence; in Hughes the attitude control system was installed in an operational satellite; and in Paper Converting the machine was operated for testing. Nothing even remotely similar occurred with respect to the 12.8 hybridoma at issue here.

1564 (Fed. Cir. 1984), the "use" of the patented invention was aiding customers to sell eyeglasses in the U.S. by providing them with infringing racks. As such, the racks were "put into service" in the U.S. Similarly, in Thorn EMI North America v. Micron Technology, 821 F. Supp. 272, 275 (D. Del. 1993), the patented article was shipped into Delaware "in an attempt to solicit business." Again, the invention was "put into service" in the U.S. On the other hand, here, the shipped hybridoma was not "put into service" in the U.S. ,but rather in Canada, a country in which plaintiffs have no patent rights.

b. 35 U.S.C. § 271(f) Does Not Apply

Since the facts plainly reveal that the 12.8 hybridoma shipped to Canada was not infringing, plaintiffs resort to arguing that CellPro's shipment of hybridoma cells to Canada "appears to violate the intent of § 271(f)." Even under the broadest possible reading of § 271(f) this cannot be true. The plain language of § 271(f) is limited to "components" of patented inventions.

The 12.8 Hybridoma shipped to Canada is not "a component of a patented invention" and is furthermore not "uncombined in whole or in part." Rather, the 12.8 hybridoma is a complete and whole product with respect to the claims of the '204 patent. The legislative history of § 271(f) further supports its inapplicability here. Section 271(f) was enacted in 1984 to legislatively overrule Deepsouth Packing Co. v. The Laitram Corp., 406 U.S. 518 (1992), in which the Supreme Court held that the defendant, who had manufactured parts of a patented product within the United States during the patent term and then shipped them overseas for final assembly into the patented product, was not liable

for infringement because the defendant did not "make" the patented invention within the United States. Id. at 527.

> This proposal [§271(f)] responds to the United States Supreme Court decision in Deepsouth Packing Co. v. The Laitram Corp., 406 U.S. 518 (1972), concerning the need for a legislative solution to close a loophole in patent law.

U.S. Code Congressional and Administrative News, Vol. 5, p. 5828, 1984 98th Cong., 2nd Session. And the courts have also recognized this narrow purpose:

> This section [271(f)] of the patent law amendment was proposed in response to the [Deepsouth] decision... which corrected a loophole in prior patent law, allowing copiers to avoid liability for products patented in the United States, by shipping the... [un]patented components for combination in foreign countries.

T.D. Williamson, Inc. v. Laymon, 723 F. Supp. 587, 592 (N.D. Okl. 1989); aff'd, 18 U.S.P.Q.2d 1575 (Fed. Cir. 1990).

Plaintiffs argue that failing to apply §271(f) here would produce an "irrational" result, namely that unpatented components cannot be exported but patented articles can be. But this argument overlooks the temporal limitations on a patent: the 12.8 hybridoma is not "a patented article" because it was made prior to the issuance of the '204 patent. 35 U.S.C. § 271(a) unambiguously provides that only making, using and selling during the term of a patent is an infringing act, and 35 U.S.C. § 271(f) unambiguously provides that only exporting of components during the term of a patent is an infringing act. Neither section applies to CellPro's shipment of the 12.8 hybridoma. Thus, that shipment was not a "violation of a right secured by a patent" which can be subject to injunction under 35 U.S.C. § 283.

3. The Injunction is Overboard in Regard to the '680 Patent

Subparagraph 1(g) at page 3 of plaintiffs' proposed permanent injunction it could be read to imply that "making, using or selling any product designed to produce or capable of producing an infringing suspension" is an infringement, inducement of infringement, or contribution to infringement of the '680 patent. To the extent to which this provision is meant to apply to the CEPRATE® SC Stem Cell Concentrator, it is legally impermissible in its breadth. Even if a device is capable of producing an infringingly-purer suspension,[11/] that is not the legal test of inducement Joy Technologies, Inc. v. Flakt, Inc., 6 F.3d 770, 774 (Fed. Cir. 1993) ("Liability for either active inducement of infringement or for contributory infringement is dependent upon the existence of direct infringement"); and supplying the device cannot constitute contributory infringement if the device has a substantial noninfringing use. In re Certain Molded-In Sandwich Panel Inserts, 218 U.S.P.Q. 832, 836 (U.S. I.T.C. 1982).

As a result of the Court's June 28, 1996 decision which ruled that a suspension is within the '680 Patent claims if it is ninety percent free of mature cells, CellPro added a customer notice to its product literature (See Declaration of Ed Kenney, ¶ 4 and Exhibit B) which warns against operating the device in such a manner as to achieve ninety percent purity. Baxter, for its part, now advertises to the trade that CellPro's device cannot achieve ninety percent purity. In an advertisement for Baxter's ISOLEX® 300*i* device, appearing in the March 15, 1997 issue of Blood, Baxter asserts that CellPro's purity data are below ninety percent (See Declaration of Edward Kenney, ¶ 3 and Exhibit A.)

[11/] CellPro does not concede that the device is even capable of achieving ninety percent purity, if the calculation includes counting all cells in the suspension.

Given that CellPro's promotional literature recommends that customers not make suspensions over 90% pure – assuming they even could if they wanted to – and that Baxter's own promotional literature is broadcasting the idea that the CellPro product is incapable of making a ninety percent pure suspension, there is simply no basis to believe that CellPro's present sales of the device are made under conditions that could amount to inducement of infringement. See Manville Sales Corp. v. Paramount Systems, Inc., 917 F.2d 544, 553 (Fed. Cir. 1990) (Specific intent to induce infringement required.)

Particularly since Baxter itself is now conceding, in statements published to potential users of the CellPro device, that it cannot infringe the '680 Patent, no injunction against inducement is appropriate; and certainly would be inappropriate for the Court to sign any injunction that includes language which could imply that the mere act of selling the device constitutes an inducement to infringe the '680 Patent.

The same must be said of contributory infringement. Even if it were true – although Baxter itself now agrees that it is not – that the CellPro device is capable of infringing use, there is no doubt that it is at least capable of substantial non-infringing use. This being so, sale of the device by CellPro cannot, as a matter of law, be contributory infringement. Hence, any injunction stating or implying that sale of the CellPro device constitutes inducement of infringement or contributory infringement is impermissibly broad as it would prohibit non-infringing activity.[12/]

[12/] As to contributory infringement, CellPro notes a further objection: Plaintiffs, as the Court has found (June 28, 1996 Order (p.35), have abandoned any contributory infringement claim. They should not be permitted to seek injunctive relief on a claim they abandoned.

CONCLUSION

For the foregoing reasons, Plaintiffs' motion for permanent injunction should be denied. If any injunction is granted, it should be stayed pending appeal.

Dated: April 21, 1997 By: Gerard M. O'Rourke

Gerard M. O'Rourke
Delaware Bar No. 3265
CONNOLLY, BOVE, LODGE & HUTZ
1220 Market Building
P.O. Box 2207
Wilmington, DE 19899
(302) 658-9141

Attorneys for Defendant
CELLPRO, INC.

OF COUNSEL:

COE A. BLOOMBERG
ROBERT C. WEISS
Professional Corporations
ALLAN W. JANSEN
JERROLD B. REILLY
LYON & LYON LLP
633 West Fifth Street, Suite 4700
Los Angeles, California 90071-2006
(213) 489-1600
Attorneys for Defendant
CELLPRO, INC.

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