JAMES M. MULLIGAN, JR.
ARTHUR G. CONNOLLY, JR.
RUDOLF E. HUTZ
HAROLD PEZZNER
JOHN D. FAIRCHILD IMI,BAR)
RICHARD M. BECK (D.C. BAR)
PAUL E. CRAWFORD
STANLEY C. MACEL, III
THOMAS M. MESHBESHER
HENRY E. GALLAGHER, JR.
GEORGE PAZUNIAK
N. RICHARD POWERS
RICHARD DAVID LEVIN
JOHN A. CLARK, III
JEFFREY B. BOVE
JAMES J. WOODS, JR.
COLLINS J. SEITZ, JR.
EDWARD F. EATON
CHARLES J. DURANTE
PATRICIA SMINK ROGOWSKI
MARY W. BOURKE
ROBERT G. McMORROW, JR. (PA.BAR)
R. ERIC HUTZ
ARTHUR G. CONNOLLY, III

LAW OFFICES

CONNOLLY, BOVE, LODGE & HUTZ
1220 Market Street
P.O. Box 2207
WILMINGTON, DELAWARE 19899

TELEPHONE (302) 658-9141
FACSIMILE (302) 658-5614

ARTHUR G. CONNOLLY
PARTNER EMERITUS

WERNER H. HUTZ
1944-1970
JANUAR O. BOVE, JR.
1949-1991
COUNSEL

F.L. PETER STONE
WILLIAM E. LAMBERT III (PA.BAR)
M. EDWARD DANBERG

JOHN C. KAIRIS
JAMES D. HEISMAN
ASHLEY I. PEZZNER
WILLIAM E. McSHANE (PA.BAR)
ANNE L. BARNETT
GERARD M. O'ROURKE
KAREN C. BIFFERATO
OLEH V. BILYNSKY (PA.BAR)
JULIE S. DVORAK
ALLAN N. KUTZENCO (N.J.BAR)

Jun 5 4 07 PM '97

June 5, 1997

VIA HAND DELIVERED
Honorable Roderick R. McKelvie
United States District Court
U.S. Courthouse, Boggs Federal Bldg.
844 King Street
Wilmington, DE 19801

Re: ***The Johns Hopkins University, et al. v. CellPro, Inc.,***
U.S.D.C., District of Delaware, Case No. 94-105 RRM

Dear Judge McKelvie:

On May 15, 1997, Plaintiffs filed a second revised form of proposed injunction and a letter arguing its merits, suggesting that inhibiting the further dissemination of the CellPro device would not deny patients access to treatment in view of the "large number of U.S. transplant centers" that already had a stem-cell immunoselection device. In fact, only about one-quarter of all transplant centers in the U.S. possess such devices. (See Supplemental Declaration of Edward Kenney, ¶ 4, attached.) We think there can be little doubt that patient access to treatment would be impaired if further distribution of the only immunoselection device that is commercially available in the U.S. were inhibited.

Moreover, the economic impact of Plaintiffs' current proposal would inhibit further distribution of CellPro's therapeutic device just as surely as if it barred such distribution explicitly, as CellPro would be forced to shut down operations while awaiting the outcome of the appeal. (See Declaration of CellPro's Chief Financial Officer, Larry Culver, recently filed with the National Institutes of Health, attached.) Corroborating Mr. Culver's view is the attached Declaration of James Mack Folsom, former Acting Director of the Bureau of Economics of the Federal Trade Commission, which reaches the same conclusion from an economic-theory approach.

Plaintiffs' position that their proposal would not deny patients access to treatment is untenable.

During the April 30 oral argument, Plaintiffs handed to the Court a letter from the FDA to Dr. Monica Krieger, CellPro's Director of Regulatory Compliance, concerning the text of CellPro's 1996 Christmas card (4/30/97 Tr. pp.76-77). CellPro objected for irrelevance and lack of notice. (Id., p. 76 L. 25 - 77 L. 2.)

Attached is a Supplemental Declaration of Dr. Krieger, which puts the FDA's letter in context and, in particular, rebuts Plaintiffs' argument that the letter is proof that the FDA disapproves "off-label use" apart from "an authorized IDE." (See 4/30/97 Tr. p. 77, L. 23 - p. 78, L. 1.) As Dr. Krieger explains, the treatment of the "Christmas Card" child was under an authorized IDE (Krieger Supp. Decl. ¶ 4). Hence, the letter could not have been addressing the question whether off-label uses apart from an IDE were approved or disapproved. Obviously, the FDA's focus in the letter could only have been on the question whether there was improper promotion – not improper use – of the CellPro device to treat the condition from which the child suffered.

Respectfully submitted,

Gerard M. O'Rourke
Bar I.D. #3265

cc: Clerk, U.S. District Court (Via Hand Delivery, with enclosures)
William J. Marsden, Esquire (Via Hand Delivery, with enclosures)
Coe Bloomberg, Esquire (All Via Federal Express, with enclosures)
Donald Ware, Esquire (All Via Federal Express, with enclosures)
Steven Lee, Esquire (All Via Federal Express, with enclosures)
Michael Sennett, Esquire (All Via Federal Express, with enclosures)

Attachments: Declarations of Edward Kenney, Larry Culver,
James Mack Folsom and Dr. Monica Kreiger

GMO/alb/4218

CAL

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,	:	Case No. 94-105 RRM
Plaintiffs.	:	
v.	:	
CELLPRO, INC., a Delaware corporation,	:	
Defendant.	:	

SUPPLEMENTAL DECLARATION OF DR. MONICA S. KRIEGER IN OPPOSITION TO PLAINTIFFS' MOTION FOR PERMANENT INJUNCTION AND IN SUPPORT OF ALTERNATIVE MOTION FOR STAY OF INJUNCTION

I, MONICA S. KRIEGER, Ph.D., hereby declare as follows:

1. I am the Director of Regulatory Affairs at CellPro, Inc., Bothell, Washington. I have personal knowledge of the matters set forth in this declaration and if called as a witness could competently testify thereto.

2. I am informed and believe that during oral argument on plaintiffs' permanent injunction motion held April 30, 1997, plaintiffs produced and handed to the court a copy of a letter which I received from the FDA in January 1997, a copy of which is attached hereto as **EXHIBIT A.** The handwritten notation at the top of the first page is mine, added after the letter was received at CellPro. I caused the letter, with my handwritten notation, to be circulated internally within CellPro but I gave no one permission (and to the best of my knowledge no one else at CellPro gave anyone permission) to disseminate the letter outside the company. The version of the letter containing my handwritten notation was not obtainable by the plaintiffs from any public-record source, and could only have come into plaintiffs' hands as a result of having been improperly divulged by someone from CellPro.

3. Attached hereto as **EXHIBIT B** is an original specimen of the Christmas card to which the FDA's letter pertains.

4. I understand that plaintiffs' counsel, at the April 30, 1997 hearing, argued that the FDA's letter is evidence of disapproval by the FDA of off-label uses of the CellPro

CEPRATE® SC stem cell concentration system apart from "an authorized IDE." In fact, the use reported in the Christmas card was made under, and not apart from, an authorized IDE. As the text of the Christmas card suggests, the child "guest artist" was enrolled for treatment of acute myelocytic leukemia (AML) in the course of an investigation under the direction of Dr. Andrew M. Yeager at Emory University, after his parents found out that physician-investigators at Emory were involved in a clinical trial evaluating stem cell transplants from half-matched (haploidentical) parents to children. The "Dr. Yeager" referenced in the Christmas card is, in fact, the same Dr. Yeager who submitted a declaration in this case on CellPro's behalf, and the clinical trial in which the "Christmas card" child was treated is in fact the same FDA-approved clinical trial which Dr. Yeager described at paragraph 3 of that declaration. In other words, the Christmas card, and the FDA's reaction to it, tell nothing whatsoever about what FDA's view, if any, might be toward off-label uses apart from authorized IDEs. The use in this situation was under, and not apart from, an authorized IDE, and the FDA's letter does not state that the use of the device to treat the child was in any way improper. Rather, the letter's expressed concern pertained to what the FDA termed "promotion" of the device via the Christmas card.

5. Attached hereto as **EXHIBIT C** is a true copy of my letter to the FDA in response to the FDA letter which is **EXHIBIT A**. Attached hereto as **EXHIBIT D** is a copy of a memo that I distributed to responsible personnel within CellPro. My purpose in doing so was to increase our company's vigilance in complying with the FDA's expectations as regards commercial statements concerning the CEPRATE® SC system.

6. The FDA's January 1997 letter to CellPro (**EXHIBIT A**) is what is known as an "untitled" letter. Although that letter was treated with due seriousness by CellPro, it should be noted that an "untitled" letter is the mildest form of written citation that the FDA issues. There is a recognized distinction between an "untitled letter" and a "warning letter," which is so titled and which denotes the FDA's view that a more serious infraction has taken place. Attached hereto as **EXHIBIT E** is a true copy of an excerpt from an FDA practice manual which explains the differences between an "untitled letter" and a "warning letter." Attached hereto as **EXHIBIT F** is an example of an FDA "warning letter," which was obtained under the Freedom of Information Act (FOIA). The letter, dated January 11, 1994 and addressed to the Chairman and CEO of Baxter Healthcare Corporation, reports the finding of an FDA investigation that Baxter's Bone Marrow Collection Kit was "misbranded" under the Federal Food, Drug and Cosmetic Act for failure to submit a Premarket Notification for significant changes made to the design of the device. As will be seen in the fourth paragraph of the letter, it threatens regulatory sanctions including seizure and/or injunction if prompt action is not taken to correct the violation. The January 1997 FDA letter **(EXHIBIT A)** received by CellPro, in contrast, is not entitled "warning letter" and does not contain a similar threat of regulatory sanctions. I have seen a number of additional FOIA-obtained titled FDA warning letters issued to Plaintiffs and related companies in the last five years.

7. I believe that CellPro's record of FDA regulatory compliance compares very favorably with those of Baxter, BD and related companies. In contrast to the titled warning letters mentioned above (and possibly others received by plaintiffs and related companies),

CellPro has never received a single warning letter, so titled, from the FDA.

8. As should be plain from **EXHIBIT F** and from the other warning letters mentioned above, infractions of FDA laws and rules, while regrettable, still occur with some frequency to health care firms larger, longer established, more experienced, more generously staffed and better financed than CellPro.

I declare under penalty of perjury that the foregoing is true and correct.

Executed at Bothell, Washington, this 23rd day of May 1997.

Monica S. Krieger

Monica S. Krieger, Ph.D.

DEPARTMENT OF HEALTH & HUMAN SERVICES

This is an untitled letter from FDA -

Food and Drug Administration
Rockville MD

RECEIVED
APR 1 0 1997
LAW DEPARTMENT

Monica Krieger, Ph.D.
CellPro, Incorporated
22215 26th Avenue SE
Bothell, Washington 98021

Rick suggested everyone have a copy so we understand the level of scrutiny we are under.)
Monica

Dear Dr. Krieger:

We are in receipt of a holiday greeting card that was disseminated by your company during the month of December, 1996. A copy is enclosed. Appearing on the back cover of the card is information about the artist which contains facts and efficacy claims related to a new indication for use of your CEPRATE® SC Stem Cell Concentration System for which a supplemental application has not been approved. As described in the conditions for approval of this device, no advertisement or other descriptive printed material issued by you or a distributor shall recommend or imply that the device may be utilized for uses that are not included in the FDA approved labeling.

The CEPRATE® SC Stem Cell Concentration System, manufactured by CellPro, Inc., is considered to be a device within the meaning of section 201(h) of the Federal Food Drug and Cosmetic Act (the Act). This device was approved for sale and distribution as a restricted device under the Premarket Approval (PMA) process described in section 515(d)(1)(B)(ii) of the Act for the following indication [Reference PMA Number BP940001]:

"...for the processing of autologous bone marrow to obtain a CD34+ cell enriched population which is intended for hematopoietic support after myeloablative chemotherapy."

The specific areas of concern related to the promotion of this device are noted below.

a. In your "about the artist" profile, a brief discussion regarding the use of the CEPRATE system in allogeneic stem cell transplants appears in the second paragraph.

> The evaluation of stem cell transplants from allogeneic donors (e.g. use of stem cells from parents who are half-matched at tissue type antigens) is still experimental. Thus far, the Center for Biologics Evaluation and Research (CBER) has not received data from you that would render conclusive evidence to base your claim for use of the device in allogeneic transplants thereby expanding the donor pool and providing many more children with curative treatment of high risk leukemia. The new indication for use of this device described above may not be promoted until a PMA Supplement has been submitted and approved.

b. In the third paragraph of the "about the artist" profile, the following claim is made: "Selecting stem cells reduces the chances of severe graft-versus-host disease that would otherwise occur if a child were to receive a half-matched bone marrow transplant from a parent"

> CBER has not received a supplement to your PMA providing the clinical data that would provide the evidence needed to support this claim. In the absence of this information, one cannot conclude that CEPRATE®-selected (T- cell depleted) allogeneic transplants will prevent graft-versus-host disease or otherwise confer a benefit to the patient.

The above mentioned misrepresentations or like misrepresentations about the CellPro CEPRATE® device misbrand your product under Section 502(o) in that you have failed to comply with Section 515 of the Act. Section 515 of the Act requires that you file a PMA Supplement in accordance with the provisions described in 21 CFR Part 814.39. This regulation requires that an applicant submit a PMA Supplement before making a change affecting the safety or effectiveness of the device for which the applicant has an approved PMA. We have determined the aforementioned claims regarding the CEPRATE® system affect both the safety and

efficacy of this device and, therefore, require the submission of a supplement that would provide the definitive evidence to support such claims.

In addition, as a restricted device, you are further misbranding your device under Section 502(q)(1) of the Act, by including uses and claims in your advertising for this device that are regarded to be false and misleading

It is your responsibility to ensure that the violations noted in this letter that may appear in other advertising or promotional materials are also corrected. You should take prompt action to correct the violations noted and assure compliance with the applicable regulations.

Please respond to this staff, in writing, within 15 days of the receipt of this letter. Your response should include the steps you plan on taking to remedy the above noted observations. Please send your response to the attention of:

Ms. Toni M. Stifano
Center for Biologics Evaluation and Research
Advertising and Promotional Labeling Staff, HFM-202
1401 Rockville Pike
Rockville, MD 20852-1448

Sincerely yours,

William V. Purvis
Director, Advertising and Promotional
Labeling Staff
Center for Biologics Evaluation
and Research

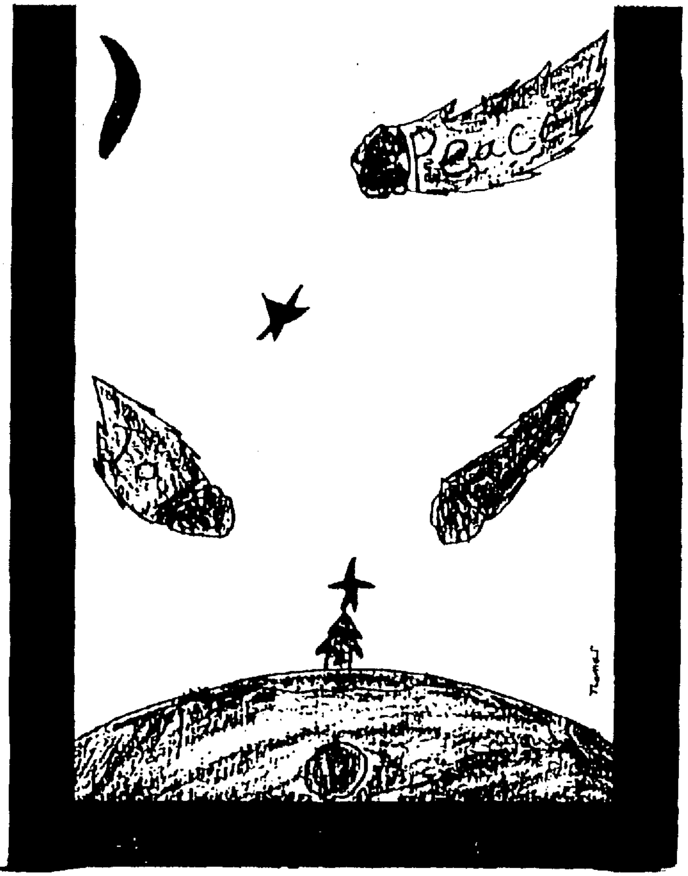
Enclosure

Thomas Green, our holiday poster artist, celebrated his ninth birthday in September 1996 and does pretty much all the things a healthy nine year old does. But when he was six years old, Thomas was diagnosed with acute myelocytic leukemia (AML). He received intensive chemotherapy [illegible] spent weeks in the hospital, and had problems with fevers and low blood counts. Although his AML initially responded to the chemotherapy, it relapsed just a few months later and required more intensive antileukemia drug treatments. Thomas was again in the hospital for treatment of complications like bloodstream infections [illegible] numerous bone marrow tests and spinal taps in the clinic and in the hospital.

After further chemotherapy, his leukemia went into a second remission. Thomas' doctors knew that the best chance to cure his AML was with a bone marrow transplant. But Thomas [illegible] not a tissue type (HLA) match, and there was not time to find a suitable matched [illegible] bone marrow donor. Faced with this dilemma, his family and doctors searched [illegible] options. They found out that physician investigators at the Pediatric Bone Marrow Transplant Program at Emory University and Egleston Children's Hospital in Atlanta were evaluating stem cell transplants from parents to children using the stem cell selection technology pioneered by CellPro, Incorporated. Using parents, who are half-matched at the tissue type antigens, as stem cell donors for their children greatly expands the donor pool and could provide many more children with curative treatment of high-risk leukemia.

A medical device developed by CellPro, called the CEPRATE® Stem Cell Concentration System, allowed the Emory physicians to select and purify the stem cells from Thomas's mother's bone marrow and peripheral blood cells. Selecting stem cells reduces the chances of severe graft-versus-host disease that would otherwise occur if a child were to receive a half-matched bone marrow transplant from a parent.

Under the direction of Andrew M. Yeager, M.D., Professor of Pediatrics and Medicine at Emory University, Thomas received a stem cell transplant from his mother, Nancy Green, in January 1995. Within two weeks after the stem cell transplant, Thomas's blood counts were returning to normal and there was no evidence of AML. Now almost two years after transplant, Thomas is off all medications, has normal blood counts, has no graft-versus-host disease and, most importantly, has no AML. He's back leading a busy, normal life, balancing school, little league, and an avid interest in outer space. He even found a bit of spare [illegible] to provide the artwork for this holiday greeting from CellPro!



APR 29 '97 12:58

About the Artist:

Thomas Green, our holiday guest artist, celebrated his ninth birthday in September 1996 and does just about all the things a healthy nine-year old does. But when he was six years old, Thomas was diagnosed with acute myelocytic leukemia (AML). He received intensive chemotherapy treatments, spent weeks in the hospital, and had problems with fevers and low blood counts. Although his AML initially responded to the chemotherapy, it relapsed just a few months later and required more intensive antileukemia drug treatments. Thomas was again *in the hospital for treatment of complications* like bloodstream infections, and he required numerous bone marrow tests and spinal taps in the clinic and in the hospital.

After further chemotherapy, his leukemia went into a second remission. Thomas's doctors knew that the best chance to cure his AML was with a bone marrow transplant. But Thomas's sister was not a tissue type (HLA) match, and there was not time to find a suitable matched unrelated bone marrow donor. Faced with this dilemma, his family and doctors searched for other curative options. They found out that physician-investigators at the Pediatric Bone Marrow Transplant Program at Emory University and Egleston Children's Hospital in Atlanta were evaluating stem cell transplants from parents to children using the stem-cell selection technology pioneered by CellPro, Incorporated. Using parents, who are half-matched at the tissue type *antigens, as stem cell donors for their children greatly expands* the donor pool and could provide many more children with curative treatment of high-risk leukemia.

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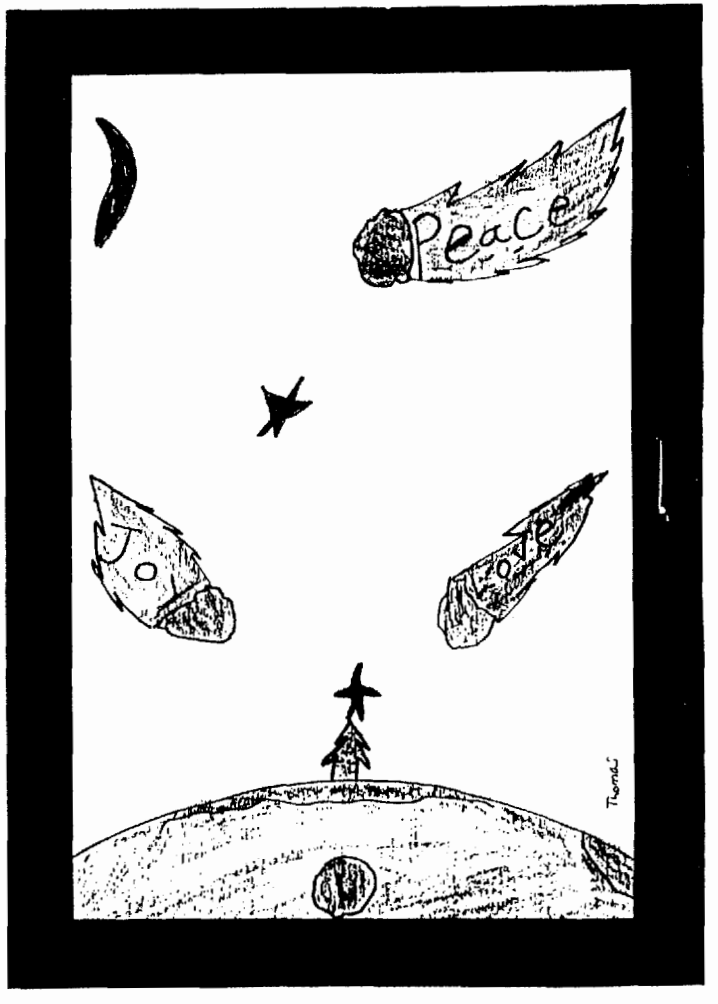


CellPro, Incorporated
22215 26th Avenue SE
Bothell, Washington 98021
(206) 485-7644
(206) 485-4787 Fax

February 10, 1997

Ms. Toni Stifano
Center for Biologics Evaluation and Research
Advertising and Promotional Labeling Staff, HFM-202
1401 Rockville Pike
Rockville, MD 20852-1448

Dear Ms Stifano:

We are in receipt of a letter from Mr. William Purvis dated January 30, 1997 regarding a holiday greeting card disseminated by CellPro during the month of December 1996.

By way of background, it is important to point out that the card was not intended to be a promotional piece. We have procedures in place to assure that all promotional materials meet regulatory requirements. Simply put, this card slipped through the cracks. We are taking steps to assure that this type of problem does not occur again.

The company will take the following action to remedy the observations noted in Mr. Purvis's letter.

1. A copy of the letter will be distributed to employees responsible for preparation and distribution of advertising and promotional materials.

2. In the future, we will assure that all materials distributed by the company are properly reviewed and are in accord with the labeling reviewed and approved by the FDA.

We are confident that our present procedures, coupled with the training of our staff, will assure that only appropriate materials meeting all regulatory requirements are distributed by CellPro. If you have any further questions in this regard, please do not hesitate to call me.

Sincerely,

Monica S. Krieger, Ph.D.
Director, Regulatory Affairs

signed copy sent to FDA

FROM: MONICA KRIEGER
TO: EXECUTIVE STAFF, MARKETING, CLINICAL
SUBJECT: FDA LETTER/CORRECTIVE ACTION -FEBRUARY 13, 1997

ATTACHED PLEASE FIND A COPY OF THE LETTER THAT WE SENT TO THE FDA REGARDING OUR CHRISTMAS CARD. PLEASE NOTE THAT WE SHOULD ASSURE THAT ALL MATERIALS THAT MAY BE SENT TO CUSTOMERS (CLINICAL SITES) THAT COULD BE CONSTRUED AS PROMOTIONAL LITERATURE SHOULD BE REVIEWED THROUGH THE PROCESS ESTABLISHED IN THE MARKETING DEPARTMENT. IF YOU HAVE ANY QUESTIONS, PLEASE DON'T HESITATE TO CALL ME.

Sent via E-mail
2/13/97

CHAPTER 4
ADVISORY ACTIONS

CONTENTS

SUBCHAPTER
WARNING LETTERS

PURPOSE

The purpose of this chapter is to specify the agency's enforcement procedures governing the use of Warning Letters.

BACKGROUND

Various forms of letters containing warnings of violations have been used throughout the history of FDA. However, such letters were sparingly used until 1967, when District Directors were authorized to issue such correspondence. A proposed regulation was published in 1978 that would have formally defined the agency's procedures and prescribed the use of two forms of Warning Letters (Notice of Adverse Findings Letters and Regulatory Letters).

The proposal was withdrawn in 1980; however, the criteria for such letters were placed in the RPM and used by the agency until May 1991. On May 23, 1991, the agency implemented the single Warning Letter system to replace the two letter warning system. The Warning Letter system placed more authority, responsibility, and flexibility at the district level concerning enforcement strategy decisions than previous procedures.

Warning Letter - A written communication from FDA notifying an individual or firm that the agency considers one or more products, practices, processes, or other activities to be in violation of the Federal FD&C Act, or other acts, and that failure of the responsible party to take appropriate and prompt action to correct and prevent any future repeat of the violation, may result in administrative and/or regulatory enforcement action without further notice.

PROCEDURES

When it is consistent with the public protection responsibilities of the agency and depending on the nature of the violation, it is FDA's practice to afford individuals and firms an opportunity to voluntarily take appropriate and prompt corrective action prior to the initiation of enforcement action. Warning Letters are issued for the purposes of achieving this voluntary compliance and establishing prior notice (see definitions in RPM Chapter 10 and the RPM section on "Prior Notice". The use of the Warning Letter and the prior notice policy are based on the expectation that a majority of individuals and firms will voluntarily comply with the law. The agency position is that Warning Letters should only issue for violations of regulatory significance; i.e., those violations that may actually lead to enforcement

action if not promptly and adequately corrected.

The Warning Letter was developed and initiated to correct violations of the statutes or regulations. Also available to the agency are enforcement strategies which are based on the particular set of circumstances at hand and may include sequential or concurrent FDA enforcement actions such as recall, seizure, injunction, administrative detention, and/or prosecution to achieve correction. Despite the significance of the violations, there are a number of circumstances which may preclude the agency from pursuing any further enforcement action following the issuance of a Warning Letter. For example, the violation may be serious enough to warrant the issuance of a Warning Letter and subsequent seizure; however, if the seizable quantity fails to meet the agency's threshold value, the agency may choose not to pursue a seizure. In this instance, the Warning Letter would appropriately document prior warning if adequate corrections are not made and enforcement action is warranted at a later time.

Responsible officials in positions of authority in regulated firms have a legal duty to implement whatever measures are necessary to ensure that their products, practices, processes, or other activities are in compliance with the law. Under the law such individuals are presumed to be fully aware of their responsibilities. Consequently, responsible individuals should not assume that they will receive a Warning Letter, or other prior notice, before FDA initiates enforcement action.

FDA is under no legal obligation to warn individuals or firms that they or their products are in violation of the law prior to taking enforcement action, except in a few specifically defined areas. When acting under the authority of the Radiation Control for Health and Safety Act (RCHSA), FDA is required by law to provide a written notification to manufacturers when the agency discovers products that fail to comply with a performance standard or that contain a radiation safety defect. Due to the legal requirements of the RCHSA, minor variations on the procedures specified below may occur.

A Warning Letter is informal and advisory. It communicates the agency's position on a matter, but it does not commit FDA to taking enforcement action. For these reasons, the agency does not consider Warning Letters to be final agency action on which FDA can be sued.

There are instances when issuance of a Warning Letter is not appropriate, and, as previously stated, issuance of such a letter is not a prerequisite to taking enforcement action. Examples of situations where the agency will take enforcement action without necessarily issuing a Warning Letter include:

1. The violation reflects a history of repeated or continuous conduct of a similar or substantially similar nature during which time the individual and/or firm have been notified of a similar or substantially similar violation.
2. The violation is intentional or flagrant.
3. The violation presents a reasonable possibility of injury or death.
4. The violations, under Title 18 U.S.C. 1001, are intentional and willful acts that once having occurred, cannot be retracted: also such a felony violation does not require prior notice. Therefore, Title 18 U.S.C. 1001 violations are not suitable for inclusion in Warning Letters.

In certain situations, the agency may also take other actions as an alternative to, or concurrently with, the issuance of a Warning Letter. Additional instructions concerning the issuance of Warning Letters in specific product areas are located in various agency compliance programs and compliance policy guides.

AGENCY POLICY ON THE ISSUANCE OF WARNING LETTERS

Warning Letters should be issued only for violations of "regulatory significance." The threshold for determination of what constitutes "regulatory significance" is that failure to adequately and promptly achieve correction to the Warning Letter may be expected to result in enforcement action. It is recognized that despite the seriousness of the violations there are a number of circumstances which may mitigate against the Agency pursuing further regulatory action following the issuance of a Warning Letter. For example, the violation may be serious enough to warrant the Warning Letter and subsequent seizure. If, however, the seizable quantity fails to meet the Agency's threshold value, the Warning Letter would be appropriate to document prior warning if adequate corrections aren't made and subsequent enforcement action is warranted, i.e., injunction or prosecution.

WARNING LETTERS TO OTHER GOVERNMENT AGENCIES

All government establishments should be held to the same standards as non-governmental establishments. However, although the public health standards are identical, the process utilized to ensure compliance with these standards may vary. The Agency believes that government establishments will achieve and maintain a higher rate of voluntary compliance with FDA regulations compared to non-government establishments. Therefore, the most efficient use of our limited enforcement resources is

Division of Compliance Policy has developed 17 criteria points.

The audit form, see Exhibit 21, can assist in insuring uniformity in the issuance of warning letters. Through use of an audit, strengths and weakness can be addressed and plans for correction implemented.

EXHIBITS

Imports
4-1 Sample Warning Letter (WL) - Violative Shipments
4-2 Sample WL Language (WLL) - Failure to Hold Entry Misrepresentation
Sample WLL - Distribution Prior to Release
Sample WLL - Misrepresentation
Sample WLL - Standard of Identity/Foreign Language

Biologics
4-3 *Sample WL - Blood or Plasma*
4-4 Sample WLL - Computer Software
Sample WLL - Source Plasma

Drugs
4-5 Sample WL - Misbranded
4-6 Sample WL - Tamper-Resistant Packaging
4-7 *Sample WLL - Sterile drugs/CGMP*
Sample WLL - DESI Drug/NDAs and ANDAs
Sample WLL - Homeopathic Drugs

Devices
4-8 Sample WL #1 - GMPs and MDR
4-9 Sample WL #2 - GMPs and MDR
4-10 *Sample WL #3 - GMPs and MDR*
4-11 Sample WL #4 - GMPs and MDR
4-12 Sample WL #5 - GMPs and MDR
4-13 Sample WL #6 - GMPs and MDR
4-14 Sample WL #7 - GMPs and MDR
4-15 Sample WL #8 - GMPs and MDR
4-16 *Sample WL #9 - X-Ray Assemblers*

Foods
4-17 Sample WLL - Standard of Identity
Sample WLL - Undeclared Additive
Sample WLL - Seafood Misbranding
Sample WLL - Labeling
Sample WLL - Sulfites in Potatoes
Sample WLL - Infant Formula
Sample WLL - Interstate Sanitation
Sample WLL - Insanitary Conditions
Sample WLL - NLEA

Cosmetics
4-18 Sample WLL - Color Additives

Veterinary Medicine
4-19 Sample WL --Medicated Feed Mill
4-20 Sample WLL - GMP Veterinary Drug
Sample WLL - Producer Warning Letter
Sample WLL - Misbranding
Sample WLL - Dealer Warning Letter

Other
4-21 WL Audit Report Form

SUBCHAPTER
UNTITLED LETTERS

AGENCY POLICY ON ISSUANCE

There are some specific circumstances in which the agency has a need to communicate with regulated industry about documented violations that do not meet the threshold of regulatory significance. *Therefore, when circumstances warrant the issuance* of an untitled letter to a member of an FDA-regulated industry, the letter should be in a format that clearly distinguishes it from a Warning Letter. The essential elements of this untitled letter are:

1. Not titled;
2. May be issued by *any appropriate agency* compliance official;
3. No statement that FDA will advise other federal agencies of the issuance of the letter so that they may take this information into account when considering the awarding of contracts;
4. No warning statement that failure to take prompt correction may result in enforcement action;
5. No mandated district follow-up;
6. Time frames for correction are not specified; and
7. A written response may be an option, but is not necessary.

The following types of correspondence should be issued as untitled letters and not as warning letters:

1. Letters sent to an entire industry, such as the letter on excessive glazing of seafood. Letters issued to put an entire industry "on notice" should be untitled letters.
2. The district may issue a brief untitled letter with the FDA-483 attached to assure that top management of a firm (i.e. president, CEO, etc.) has a copy of the FDA-483 when the original FDA-483 was not issued to top management during the inspection. Since this correspondence is only a brief transmittal letter it is not considered a warning letter. If

significant deviations are found, a warning letter should be sent and not an untitled letter.

UNTITLED LETTERS ISSUED TO INDUSTRY ON ILLEGAL PROMOTIONAL ACTIVITIES

If a center is willing to support further Agency regulatory action if the violative practice doesn't cease, a warning letter and not an untitled letter should be issued for illegal promotional activities such as the promotion of a device or drug which has not been approved by FDA for commercial distribution and making representations that the device or drug is safe or effective for such purposes. If the center is not prepared to support regulatory action should a firm ignore a letter issued for illegal promotional activities, neither a warning letter nor an untitled letter should be used. An alternate approach would be to alert the district office of the violation and request that they bring the promotional activity to the attention of the firm on the next scheduled visit. This way if the district inspection reveals additional problems, this violation may be included as part of their regulatory action plan, should the firm fail to make appropriate corrections. If the problem is deemed to be more urgent the district could also request a meeting with the firm to discuss the violations.

192199 HFI-3

January 11, 1994

WARNING LETTER
CHI-857-94

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Vernon R. Loucks, Jr.
Chairman and CEO
Baxter Healthcare Corporation
One Baxter Parkway
Deerfield, IL 60015

Dear Mr. Loucks:

An inspection of the corporate headquarters of the Fenwal Division of Baxter Healthcare was conducted on November 2, 1993, by Investigator Nalini Patel. The inspection covered the Baxter Bone Marrow Collection Kit. The Bone Marrow Kit is a medical device as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (Act).

The inspection revealed that the Baxter Bone Marrow Collection Kit is misbranded under Section 502(o) of the Act for failure to submit to FDA a 510(k) Premarket Notification for significant changes made to the design of the device. The size and composition of the filters were changed and a pre-filter was added to the collection container of the kit in May 1993. Under Title 21, Code of Federal Regulations, 807.81(a)(3)(i), a premarket notification submission is required when a change or modification is made to a device that could significantly affect the safety or effectiveness of the device.

This is not intended to be an all inclusive list of violations which may exist at your firm. It is your responsibility as a manufacturer of medical devices to ensure that your operations are in full compliance with all requirements of the Act and regulations promulgated thereunder.

We request that you take prompt action to correct this violation. If such action is not taken, we are prepared to invoke regulatory sanctions provided for by law including seizure and/or injunction. No pending application for premarket approval (PMA) or quality assurance evaluation requests for procurement by government agencies will be approved until adequate corrective actions have been taken with respect to the above violation.

Please advise this office in writing within 15 working days of receipt of this letter as to the specific actions your firm has taken or intends to take to correct this violation. If corrective action cannot be taken within 15 days, state the reason for the delay and time within which the corrections will be completed.

Your reply should be sent to Jerome Bressler, Director, Compliance Branch, 300 S. Riverside Plaza, Suite 550 South, Chicago, Illinois 60606.

Sincerely,

Raymond V. Mlecko
District Director

cc: EF
cc: SJ
cc: HFM-600
cc: HFR-230
cc: HFI-35
cc: HFR-MW150
cc: HFA-224
cc: SDE
cc: CHI-DO R/F (2)

RVM/JB/SDE/dag

CERTIFICATE OF SERVICE

I, Gerard M. O'Rourke, do hereby certify that on June 5, 1997, I caused to be served copies of the foregoing SUPPLEMENTAL DECLARATION OF DR. MONICA S. KRIEGER IN OPPOSITION TO PLAINTIFFS' MOTION FOR PERMANENT INJUNCTION AND IN SUPPORT OF ALTERNATIVE MOTION FOR STAY OF INJUNCTION upon the following counsel of record by the means indicated:

BY HAND:

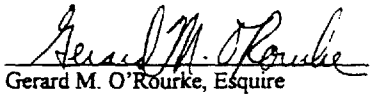
William Marsden, Esquire
POTTER, ANDERSON & CORROON
Hercules Building
Wilmington, DE 19801

BY FEDERAL EXPRESS:

Steven Lee, Esquire
KENYON & KENYON
One Broadway
New York, NY 10004

Michael Sennett, Esquire
BELL, BOYD & LLOYD
70 West Madison Street
Chicago, IL 60602

Donald R. Ware, Esquire
FOLEY, HOAG & ELIOT
One Post Office Square
Boston, MA 02109



Gerard M. O'Rourke, Esquire
Del. I.D. Number 3265

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

DECLARATION OF JAMES MACK FOLSOM

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
BRUCE G. CHAPMAN
LYON & LYON LLP
633 West Fifth Street, Suite 4700
Los Angeles, California 90071-2066

DECLARATION OF JAMES MACK FOLSOM

I, James Mack Folsom, declare as follows:

1. I am Senior Vice President of Glassman Oliver Economic Consultants, Inc. of Washington, D.C., having been employed by the firm for over 18 years. Prior to employment at Glassman Oliver, I worked for the Bureau of Economics at the Federal Trade Commission for over 14 years where my highest position was Acting Director of the Bureau. Prior to employment at the FTC's Bureau of Economics, I taught at Duke University for four years. A copy of my curriculum vitae is attached hereto. I have reviewed the financials of CellPro, including the material attached to Mr. Larry Culver's May 28, 1997 Declaration, and the declaration of Professor Hausman in this matter dated April 27, 1997.

2. The question examined in the Hausman declaration and in this declaration is when a firm like CellPro would cease production and sale of a good. Economic theory tells us that in <u>both</u> the short and long run, a firm will cease sales when its variable costs exceed its revenue. The difference between the short run case and the long run case is that some costs are fixed in the short run and no costs are fixed in the long run. Economic theory also tells us that a firm may sell below cost in the short run if it believes that in the long run it will make a profit that will more than offset the losses. That condition would not apply if the relief requested were granted, forcing CellPro to pay all of its "incremental profit" to the Plaintiffs until the Plaintiffs' product obtains FDA approval and to cease sales shortly thereafter.

3. Economic theory teaches us that a multi-product firm may continue to operate if it must continue to bear all other costs even if it ceases to produce a particular product. CellPro is, however, essentially a single product firm, with sales of the products in question amounting to more than 90 percent of the firm's total sales. This means that the remaining products of CellPro cannot support the overhead and research and development expenditures that are occurring.

4. I understand that it may well be two to three years before FDA approval could be obtained by the Plaintiffs in this matter. Accordingly, CellPro's decision making mode is a long run one. From a practical standpoint, an examination should be made of what CellPro's incentives would be if it could only recover, at a maximum, its short run variable costs when it is operating in a "long run" decision mode. It is obvious that virtually all of CellPro's costs would disappear if it shuts down operation. This would include its overhead costs and its research and development costs. It follows that CellPro should close its operations down if the overhead and research and development costs can be avoided by closing down but would have to be paid if CellPro continued to operate.

5. The argument that CellPro has a substantial sum of cash should not be a factor in the decision which must be made by CellPro as to whether it should continue to do research and development and to produce and sell the relevant products. CellPro has a responsibility to its stockholders not to throw that money

away. And, stockholders could well take the view that this is what CellPro would be doing if it were to operate while losing more funds than it would lose by closing down.

6. Mr. Larry Culver, Chief Financial Officer of CellPro, has examined what would happen to CellPro's cash under several scenarios in his declaration dated May 28, 1997. His models demonstrate that even if CellPro is required to pay only a 4 percent Bayh-Dole royalty during the time that the appeal of the matter is being heard, CellPro would be unable to operate for more than two years without going to the capital market to raise more funds. Mr. Culver believes that with the cash flow situation and certainty that would result from a 4 percent royalty, CellPro could raise capital to allow it to continue to operate. The models also confirm my expectation, as indicated above, that CellPro would have to go into a shutdown mode if it were required to pay the royalty urged by the Plaintiffs in this matter. The reason is that the approximately 50 percent royalty and other injunctive relief requested by Plaintiffs would make the cash flow situation and future prospects of CellPro so bad that it would eliminate reasonable access to the capital market to raise the funds that would allow CellPro to continue to operate. Such a shutdown decision by CellPro would, of course, result in a loss of any and all public health advantages that flow from continued availability of the CellPro product.

I declare under penalty of perjury that the foregoing is true and correct.

Executed at Washington, D.C., this 2nd Day of June, 1997.

J. M. Folsom

James Mack Folsom

CERTIFICATE OF SERVICE

I, Gerard M. O'Rourke, do hereby certify that on June 5, 1997, I caused to be served copies of the foregoing DECLARATION OF JAMES MACK FOLSOM upon the following counsel of record by the means indicated:

BY HAND:

William Marsden, Esquire
POTTER, ANDERSON & CORROON
Hercules Building
Wilmington, DE 19801

BY FEDERAL EXPRESS:

Steven Lee, Esquire
KENYON & KENYON
One Broadway
New York, NY 10004

Michael Sennett, Esquire
BELL, BOYD & LLOYD
70 West Madison Street
Chicago, IL 60602

Donald R. Ware, Esquire
FOLEY, HOAG & ELIOT
One Post Office Square
Boston, MA 02109

Gerard M. O'Rourke, Esquire
Del. I.D. Number 3265

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

JUN 5 4 03 PM '97

CLERK U.S. DIST. CT.

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

SUPPLEMENTAL DECLARATION OF EDWARD KENNEY IN OPPOSITION TO PLAINTIFFS' MOTION FOR PERMANENT INJUNCTION AND IN SUPPORT OF CELLPRO'S ALTERNATIVE MOTION FOR STAY

I, EDWARD KENNEY, do hereby declare:

1. I am the Vice-President of Marketing and Sales for CellPro, Inc. I have personal knowledge of the matters set forth in this declaration and if called as a witness could competently testify thereto.

2. I am informed and believe that, during an oral argument on April 30, 1997, plaintiffs' counsel suggested that the CellPro CEPRATE® SC stem cell concentrator may already be in place at most, or substantially all, of the transplant sites within the United States. Specifically, I am informed that plaintiffs' counsel remarked to the Court that it was "not clear" to him "that there are even a whole lot more transplant centers in the United States" than those that already had a CEPRATE® SC device.

3. In fact, as of March 12, 1997, there were 54 transplant centers in the United States that possessed at least one CellPro CEPRATE® SC Stem Cell Concentrator. In contrast, the total number of medical institutions in the United States that perform stem cell transplants is estimated to be at least 300. This number is probably conservative, and it is derived from the number of transplant centers that report to the Bone Marrow Transplant Registry. There are known to be other centers that perform transplants but that do not report to the Registry, and that would cause this number to be an undercount. Even if this probably-conservative estimate of 300 as the total number of transplant centers in the U.S. is adopted, the percentage of such

centers which possessed a CellPro device as of March 12, 1997 was only 18% -- that is, 54 of 300. If the number of transplant centers that report to the Registry is indeed an undercount of the total number of centers in the United States, then even this 18% percent figure would of course be an overestimate.

4. From the list appearing in the April 28, 1997 Declaration of Kristin F. Houser purporting to show the North American "transplant centers and other facilities" at which a Baxter ISOLEX system was "currently installed," it appears that there were, at most, 37 U.S. transplant centers represented (I did not count three facilities listed by Ms. Houser which are obviously Canadian, nor did I count Systemix, which according to my understanding is a business corporation that has a research facility but not a transplant center). By comparing this list with CellPro's list, I counted an overlap of 21 transplant centers that had both CellPro's and Baxter's device. This would yield a total of (54 + 37 - 21 =) 70 U.S. transplant centers which have at least one (CellPro's or Baxter's, if not both) therapeutic stem cell immunoselection device. Based on the above estimate of 300 as the total number of transplant centers in the U.S., it can be calculated that only some 23% (= 70/300) of such sites possess a therapeutic stem cell immunoselection device. This estimate is approximate not only because the 300-centers estimate is probably conservative but also because CellPro's number is taken at March 12, 1997 and Baxter's at April 28, 1997. Nevertheless, I believe it is fair to conclude, based on the

above estimates and analyses, that the proportion of all transplant centers in the U.S. that possess stem cell immunoselection devices is a small proportion, probably in the neighborhood of one-fourth of all U.S. transplant centers.

I declare under penalty of perjury that the foregoing is true and correct.

Executed at Bothell, Washington, this 3rd day of June ~~May~~ 1997.

Edward Kenney

CERTIFICATE OF SERVICE

I, Gerard M. O'Rourke, do hereby certify that on June 5, 1997, I caused to be served copies of the foregoing SUPPLEMENTAL DECLARATION OF EDWARD KENNEY IN OPPOSITION TO PLAINTIFFS' MOTION FOR PERMANENT INJUNCTION AND IN SUPPORT OF CELLPRO'S ALTERNATIVE MOTION FOR STAY upon the following counsel of record by the means indicated:

BY HAND:

William Marsden, Esquire
POTTER, ANDERSON & CORROON
Hercules Building
Wilmington, DE 19801

BY FEDERAL EXPRESS:

Steven Lee, Esquire
KENYON & KENYON
One Broadway
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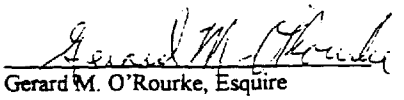

Gerard M. O'Rourke, Esquire
Del. I.D. Number 3265

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CENTER'S STAKES HIGH IN PATENT DISPUTE

SEE PAGES 3-4

HERE'S HOW TO MAKE THE MAXIMUM CONTRIBUTION TO YOUR RETIREMENT

SEE PAGES 8-9

CENTER NEWS

FRED HUTCHINSON CANCER RESEARCH CENTER
FACULTY/STAFF TWICE-MONTHLY NEWSLETTER

THURSDAY, JUNE 5, 1997

VOLUME 3, ISSUE 13

VISIT THE HUTCHINSON CENTER'S SITE ON THE WORLD WIDE WEB: *http://www.fhcrc.org*

OFF THE TOP

Don't miss party to honor retiring Dayon June 19

Dr. Robert Day

Hughes Institute taps Hahn, Roberts for prestigious 7-year appointments

Two researchers in the Center's Basic Sciences Division – Drs. Steve Hahn and James Roberts – joined 68 other scientists nationwide last month in being named to the faculty of the Howard Hughes Medical Institute.

The prestigious appointments last seven years.

The Hahn lab focuses on the complex series of molecular events that start the process of reading, or transcribing, genetic information into a protein blueprint. Roberts' laboratory studies the mechanisms involved in starting and stopping cell division.

Hahn says he is gratified to be named a Hughes investigator, as it offers an opportunity would otherwise be able to do," he says.

Billionaire industrialist Howard Hughes founded the institute in 1953. Instead of building its own research campus, the institute enters into long-term research agreements with universities and other academic research organizations, where

Dr. Steve Hahn

Dr. Jim Roberts

Patent dispute: Center's stakes high as rulings awaited on CellPro appeal, 'march in' request

It could be the bitterest patent dispute yet in the young biotechnology industry. And although the Center is not a party to the suit, the stakes for the Center – both for research and revenue – are high.

Since the beginnings of the nation's biotechnology industry in the early 1980s, patent lawsuits have become commonplace. But the dispute between Bothell-based CellPro, Inc., and Baxter International, of Deerfield, Ill., has been especially contentious, with more twists and turns than a daytime soap opera.

'It has implications beyond this case. Whole areas of research such as gene therapy, therapeutic cell expansion are also affected.

'There has to be a balance between allowing commercial development and granting such broadly interpreted rights as to restrict research.'

The Center's Dr. Bill Bensinger, co-inventor of the CellPro device

At stake in this dispute are patient access to a potentially life-saving technology and a market industry estimate of at least $60 million a year.

Founded in 1989 by former Center researcher Dr. Ron Berenson, CellPro, Inc. developed automated systems for purifying large quantities of specific cells for therapeutic and diagnostic applications.

The first cell type targeted by CellPro was the blood-making stem cell, a rare cell produced in bone marrow that gives rise to the body's blood and immune systems.

The Center granted the company an exclusive license to the patented core technology of the company's system, a column device that CellPro calls the Ceprate SC Cell Concentration System. At the same time, CellPro licensed an unpatented monoclonal antibody developed by the Center's Dr. Irwin Bernstein.

In 1991, Johns Hopkins School of Medicine was granted four patents, one of which claims all man-made monoclonal antibodies that bind to a molecule on the surface of stem cells identified as CD34. The other covers any means of isolating stem cells using the CD34 antigen that yields a cell collection substantially free of more mature lymph or marrow cells.

Dr. Bill Bensinger, a researcher in the Center's Clinical Research Division and co-inventor of the CellPro device, believes that such a broad patent is the root of the problem.

"It has implications beyond this case," he says. "Whole areas of research such as gene therapy, therapeutic cell expansion are also affected.

"There has to be a balance between allowing commercial development and granting such broadly interpreted rights as to restrict research."

Despite CellPro's contention that the Hopkins' patent was invalid, in January 1992 CellPro entered into negotiations with Baxter for a license to the Hopkins patents. Neither side could agree on terms for a license, however, and each sued the other.

In August 1995, CellPro thought it had won its patent dispute when a Delaware jury unanimously found that the patents held by Hopkins and licensed to Baxter were invalid.

In a surprising turnaround, however, the federal judge in the case refused to enter the jury's verdict. The judge determined that the jury's verdict was not supported by evidence and felt that he had erred in his instructions to the jury. He awarded damages to Baxter and ordered a retrial.

In an ironic twist of fate following that trial, Richard Murdock, the chief executive officer of CellPro was diagnosed with a form of non-Hodgkin's lymphoma. Given little more than two years to live, Murdock asked to be treated with an experimental procedure using his company's device.

Today Murdock is cancer-free, but his company, despite receiving FDA approval for the Ceprate SC system, has been given little more than two years to survive.

In March, the jury in the patent retrial found that CellPro had "willfully infringed" Baxter's patent and awarded it and its partners $2.3 million in damages. In a follow-up hearing April 30, Baxter asked the court to impose triple damages of $6.9 million, $7 million in legal costs and a two-year phase-out of sales of CellPro's product.

In response, CellPro is appealing the jury verdict. At the same time, it has asked U.S. Secretary of Health and Human Services Donna Shalala for permission to continue selling the product based on a compelling public interest and the fact that the technologies in question were developed through federally funded research.

Baxter says such government action is unnecessary because it is asking for the injunction to be phased in over two years. If such a staged injunction is granted, Deborah Spak, director of corporate communications for Baxter, says it will allow current clinical trials using the CellPro device to continue.

"Baxter has no intention of denying any patient or physician access to technology which can help treat cancer," Spak says. "Our intent is to assure a smooth transition to a licensed technology."

CellPro's Joann Reiter, director of corporate development, says that under the terms of the injunction, CellPro would lose money if it continues the clinical trials.

"We would only be able to treat a very narrowly defined patient population," Reiter says. "We would also have to pay Baxter for all the disposables at a cost of $2,000 per unit, which is more than our profit.

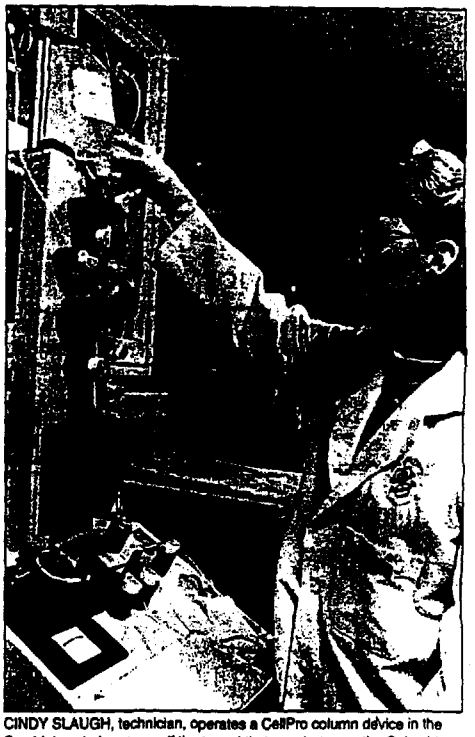
"In the end, the trial results will do us no good, since we won't be able to sell our product. So as a practical matter, CellPro could not continue operating under the terms of the injunction."

While the Center's interest in the case is not on the same scale as the two companies, Catherine Hennings, director of the Center's Technology Transfer Office, says the potential impact is significant.

"Should CellPro be forced out of business, thus leaving the product unsupported, it could disrupt some of our investigators' research," she says.

Dr. Scott Rowley, who heads the Cryobiology Laboratory, where both the CellPro system and Baxter's competing Isolex system are used for clinical trials, says the Center is conducting three clinical trials using the CellPro device, and another is planned.

If CellPro halted production suddenly, Rowley says the impact on those studies would vary depending on the level of support CellPro provides.



CINDY SLAUGH, technician, operates a CellPro column device in the Cryobiology Laboratory, off the tunnel that runs between the Columbia Building and Swedish Medical Center. The monoclonal antibody used in the device, which CellPro calls the Ceprate SC Cell Concentration System, is the subject of a bitter patent dispute.

Rowley, who serves as a scientific advisor to Baxter Biotechnology, explains that such trials typically are conducted in three ways.

In a study initiated by a Center investigator, a company will sell the necessary materials to the Center just as it would to any other customer.

In other cases, in which the study offers potentially useful data to the company, the manufacturer often provides materials for free.

The third scenario involves a company-sponsored study, in which the company not only provides all materials at no charge, but it also it pays the Center to conduct the study and collect data.

"We currently have studies using CellPro products under each of those scenarios," Rowley says. "In the case where CellPro is selling the column, it costs the Center $4,000 per use. If that study were to switch to Baxter's system, it would cost $3,000 because Baxter does not have FDA approval and therefore can only offer it on a cost recovery basis.

"In the other two cases, the cost impact could be significant. In the study where CellPro is providing the supplies at no charge, I don't know whether Baxter would support that study or not. For the CellPro-sponsored study, that research could be set back three to six months because Baxter is not quite there yet."

Rowley explains that the CellPro-sponsored study involves pediatric patients with mismatched related donors. The CellPro system removes the donor lymphocytes thought to produce graft-versus-host disease, and CellPro is ahead of Baxter in that area of research.

Dr. John Hansen, head of the Center's Clinical Immunogenetics Program, is collaborating with investigators at both the University of

Please see PATENT, page 4

Device was anticipated to be first 'home run' licensed by Center

PATENT
Continued from page 3

Washington and Swedish Medical Center on a kidney transplant study that uses the CellPro system.

"It would be very disruptive if CellPro could no longer provide the columns," Hansen says. "Theoretically, we could switch to the Baxter system, but that would take time and surely require additional negotiations."

In terms of financial impacts on the Center, Hennings says the CellPro device was anticipated to be the first "home run" licensed by the Center with the potential of generating millions of dollars in royalties.

"The Center has a significant interest in CellPro's ability to sell its device," she says.

In asking Shalala to step in, CellPro is seeking protection under a provision of the Bayh-Dole Act of 1980. That law is widely credited with launching the U.S. biotechnology industry by allowing academic institutions to own and patent technologies developed with federal funding.

To protect taxpayers' research investment, the bill's authors inserted a provision often referred to as "march in rights." Under this provision, the government retains the right to step in if a licensee is not commercializing a technology fast enough, or if there is a compelling public interest.

Hennings says that in the 17 years since the Bayh-Dole Act was passed, the government has never exercised its "march-in" rights.

Whether the government should intervene in this case is the subject of heated debate in the academic community. Technology transfer professionals differ sharply how such action would affect technology licensing.

Some vehemently denounce CellPro and predict that if the government does "march in," it will have a chilling effect on technology transfer. The argument goes that if CellPro succeeds, companies will be reluctant to license technologies developed at federally funded institutions.

Others say the CellPro case is just the type of situation the law's authors had in mind when they included the "march in" provision. Adding credence to that view is the fact that the 18-page letter from CellPro to Secretary Shalala was prepared and signed by former U.S. Sen. Birch Bayh, co-author of the law.

Without commenting on the merits of either party's case, the Center supports CellPro's request.

In a letter to Shalala, Drs. Robert Day, Center president and director, and Lee Hartwell, president and director-designate, express this support strongly.

"At a minimum," the letter states, "we believe it is incumbent upon the Department of Health and Human Services and the National Institutes of Health to ensure that a commercially reasonable license under the Johns Hopkins patents is offered to CellPro."

Rulings on Baxter's request for an injunction against CellPro, and on CellPro's request that the government exercise its "march in" rights, are expected this month.