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.	:	

DECLARATION OF DR. CESAR O. FREYTES

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I, Cesar O. Freytes, M.D., do hereby declare:

1. I am the Director the Bone Marrow Transplant Program of the University of Texas Health Science Center, San Antonio, Texas. A copy of my curriculum vitae is attached hereto as **EXHIBIT A.**

2. I am well acquainted with the capabilities of CellPro's CEPRATE® SC stem cell concentrator, based on: (a) having been trained in its operation; (b) having read widely in the scientific and technical literature about its capabilities; (c) having regularly worked with the device in the course of clinical trials and studies over the last four or five years; (d) having performed stem cell transplant procedures on at least 30 human patients using suspensions prepared with the device; and (e) being currently involved in clinical trials of new therapies that utilize the CEPRATE® SC stem cell concentrator.

3. The CEPRATE® SC stem cell concentrator represents a great improvement over prior technology for preparing stem-cell-enriched suspensions for transplantation. 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. Even for those categories of patients for whom there were other treatment options available prior to the CEPRATE® SC concentrator, the device affords a superior treatment option, in that it prepares suspensions that pose

significantly lower risks of side effects in patients than did the prior technology for preparing stem-cell-enriched suspensions for transplantation.

4. Before the CEPRATE® SC stem cell concentrator became available, the standard method for preparing stem-cell-enriched suspensions was unpurified buffy coat progenitor cell transplantation ("buffy coat PCT"). That technology, which involved separation of marrow into components by centrifuge and recovering the "buffy coat layer" for injection into the patient after further processing, typically required a relatively large volume of suspension for transplantation. This was so because the buffy coat layer contained not only true hematopoietic stem cells but also a variety of other cells that there was no practical way to eliminate fully. The buffy coat PCT procedure required treatment of the suspension with a reagent known as DMSO, which, although necessary to protect the suspension from damage during freezing and thawing, was also toxic to the patient, and posed risks of potentially serious cardiopulmonary complications. In the autologous setting, there was also concern that malignant cells which had not been eliminated from the buffy coat layer would be reinfused into the patient along with the stem cells. There was, and still is, some question whether reinfusion of malignant cells substantially raises the risk of relapse and/or significantly shortens the period of remission; but the lack of a fully practical means of tumor cell purging with buffy coat PCT was a concern.

5. Because the CellPro device does a more efficient job than buffy coat PCT of concentrating stem cells and excluding other cell populations which are useless or harmful in a transplant setting, the CellPro device makes it possible to obtain a

therapeutically effective dose of stem cells in a much smaller volume than was possible with buffy coat PCT. Even if DMSO is still used as a cryoprotectant with a CellPro-prepared suspension, the volume of DMSO required is much less than is needed to cryoprotect the larger volume that is needed when buffy coat PCT therapy is used. Hence, DMSO's side effects are reduced.

6. Another advantage of having a smaller volume of transplant suspension, as is possible with the CellPro device, is that further manipulations of the suspension (following stem cell enrichment) are easier and more practical to carry out. Such further manipulations as T-cell depletion and tumor purging require the treatment of the suspension with secondary reagents, which can include an antibody, an antibody-with-complement reagent, and/or a chemotherapeutic drug to target and eliminate undesired cells. The smaller the volume being worked with, the less of these secondary reagents is typically required--an advantage that can improve efficiency and further lower toxic risk to the patient.

7. I was an investigator in the pivotal breast carcinoma trials that led to FDA approval of the CellPro device for autologous bone marrow transplantation. The results of those trials formed the basis of the FDA's conclusion that the use of the CellPro device afforded a reduction of toxicity compared to standard stem-cell-concentration methods without compromise to therapeutic efficacy. I am presently involved in two clinical trials using the CellPro device. One is a Phase II clinical trial aimed at reduction of the numbers of malignant cells in autologous peripheral blood transplant suspensions in patients with

multiple myeloma. The other is a Phase III clinical trial to determine if the use of the CEPRATE® device will prolong disease-free survival and survival in patients with multiple myeloma that undergo autologous peripheral blood stem-cell transplantation.

8. In addition to its usefulness in the present clinical trials, I believe that the CellPro device, which provides the only FDA-approved means to immunoselect a stem-cell-enriched population for transplant, is of great value in opening new therapeutic horizons in gene therapy, treatment of autoimmune diseases, treatment of solid tumors, and the like. Attached hereto as **EXHIBIT B** is a copy of a letter dated July 12, 1995 which I prepared for submission to the FDA which outlines and explains my view that the availability of the CellPro device will play an important role in bringing new therapies into use. I continue to believe the views stated in this letter; and subsequent experience has fortified my belief that the CellPro device has an important role to play in the development of new therapies.

9. From the standpoint of an investigator designing and planning a clinical study, the fact that CellPro's CEPRATE® SC stem cell concentrator is the only FDA-approved device is a matter of considerable significance. The FDA-approved status of the device not only reassures patients faced with the decision whether to participate in experimental studies but also streamlines the process of obtaining the necessary protocol approvals from the FDA and from protocol-approval bodies within hospitals and universities.

10. It is my strong opinion that compelling public interests demand the continued, and legally unfettered, availability of the CellPro device for both experimental and fully-approved therapeutic applications. If the CellPro device were removed from the U.S.

market by injunction, physicians who used or wished to use that device for experimental or established therapies would be put to substantial hardship. Even if it is assumed that other, non-FDA-approved devices are available which could feasibly be substituted, substantial delay, expense and inconvenience would be occasioned by the need to discard already-gathered data and start from scratch, the need to put new user agreements in place and obtain new protocol approvals, and the need to train staffs up to the same level of experience and competence they now have in using the CellPro device. Moreover, even an ill-founded belief that the CellPro device might be enjoined has, in my opinion, a chilling effect on important medical research. Any real (or imagined) doubt that a device will continue to be available will tend to discourage patients from willingness to submit to experimental therapies involving that device; and no investigator wants to spend time, effort and money to develop a therapy using a device that is at risk of disappearing from the market. For these reasons I believe that <u>any</u> injunction, even if it contains significant exemptions and exceptions, would disserve compelling public interests.

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

Executed at San Antonio, Texas, this 24 day of March, 1997.

Cesar O. Freytes, M.D.

CURRICULUM VITAE

CESAR O. FREYTES, MD, FACP

Date of Preparation: 3/10/97

I. GENERAL INFORMATION

A: Personal Data:

1. **Current Position:** Director, Bone Marrow Transplant Program
   Associate Professor of Medicine/Hematology

2. **Address:** 7703 Floyd Curl Drive,
   San Antonio, TX 78284-7880

3. **Phone, FAX, E-mail:** (210) 617-5268, FAX (210) 617-5271,
   E-mail FREYTES@uthscsa.edu

4. **Citizenship Status:** USA

5. **SSN:** 584-80-4368

6. **DOB:** 09/04/54

B. Education

(Year)	(Degree)	(Major)	Institution/Location)
1979	MD	N/A	University of Puerto Rico School of Medicine
1976	BS	Biology	Univ. of Puerto Rico, San Juan

C. Postgraduate Training (e.g. Internship, Residency, Postdoctoral Fellowship):

(Year)	(Degree)	(Major)	Institution/Location)
1982-85	Fellowship	Hematology/Oncology	Washington University St. Louis, MO
1980-81	Residency	Medicine	San Juan VAMC, PR
1979	Internship	Medicine	San Juan VAMC, PR

D. Academic Appointments:

(Month/Year)	(Position)	(Institution/Location)
9/96-Pres.	Associate Professor of Mecine	UTHSCSA
11/91-8/96	Ass't Professor of Medicine	UTHSCSA
1990-1991	Chief, Hematology Training Program	San Juan City Hospital
1990/1991	Chief, Hematology Section	San Juan City Hospital
8/87-10/91	Ass't Professor of Medicine	Univ. of Puerto Rico School of Medicine
7/85-6/87	Instructor in Medicine	Univ. of TN Center for the Health Sciences