IN THE 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,	)	Civil Action No. 94-105-RRM
v.	)	
CELLPRO, INC., a Delaware corporation,	)	
Defendant.	)	

DECLARATION OF DAVID F. WEEDA

I, David F. Weeda, being duly sworn, declare as follows:

1. I am an attorney, duly licensed to practice law in the District of Columbia and the State of Maryland. I am currently a senior partner of Olsson, Frank and Weeda, P.C., a law firm in Washington, D.C. which specializes in food, drug, and medical device regulatory and legal matters. From 1976-1981, I served as Associate Chief Counsel in the Food and Drug Administration's (FDA) Office of Chief Counsel. In 1981, I joined the firm, then known as Olsson and Frank, P.C. In my practice, I specialize in the regulatory and legal requirements for pharmaceuticals and medical devices as imposed by FDA under the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301, et seq., and FDA's implementing regulations and related policies. I assist our clients with, among other things, FDA's regulatory requirements applicable to the

investigational device exemptions (IDE). From 1984-1990, I was Adjunct Professor of Law, Catholic University of America, Columbus School of Law, where I taught the Food and Drug Law and Regulation Course. Part of that course included the regulation of medical devices under FDA's IDE system. Other than to the extent that I have been compensated by the Defendant for my time associate with this Declaration, I have no financial or professional relationship with any party to this litigation.

2. I have been asked by counsel to the Defendant, CellPro, Inc., to provide my opinion as to legality and practicality of Plaintiffs' contention, put forth by John Osth in his March 5, 1997 trial testimony, and Plaintiffs' April 7, 1997 *Brief in Support of Plaintiffs' Motion for a Permanent Injunction*, that, should a permanent injunction be issued, hospitals that wish to use the Baxter Isolex device may do so by simply filing their own investigational device exemptions (IDEs) with the Food and Drug Administration (FDA). It is my opinion that this contention vastly understates the issues associated with the shipment and use of the Baxter Isolex® 300 device in place of the approved CellPro device.

3. Fundamentally, the IDE must be understood for what it 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 in human subjects. It is not intended as a stop-gap for the commercialization of a device that is otherwise unapproved.

4. Section 520(g) of the Federal Food, Drug, and Cosmetic Act, as amended, authorizes FDA to grant an IDE to a researcher using a device in clinical studies undertaken to develop safety and effectiveness data. An approved IDE application permits the device, which would otherwise be subject to marketing clearance, to be shipped lawfully for the purpose of conducting

the specific clinical study described in the IDE. Some investigations for nonsignificant risk devices are not required to be the subject of an IDE application to FDA. A cell separation and concentration system, as involved in this case, is a significant risk device. In order to conduct a significant risk study, a sponsor must submit the investigational plan and reports of prior investigations to an instititutional review board (IRB) for review and approval *and* submit a complete IDE application to FDA for review. The investigation of the device cannot begin until both FDA and IRB approval are granted.

5. An IDE application is not an inconsequential submission. An IDE must include, in part:

- a complete report of prior investigations, including reports of all prior clinical, animal, and laboratory testing of the device; the report must be comprehensive and adequate to justify the proposed investigation;
- an investigational plan;
- a description of the methods, facilities, and controls used for the manufacture, processing, packing, storage, and installation of the device;
- an example of the agreements to be signed by the investigators and a list of the names and addresses of all investigators;
- certification that all investigators have signed the agreement, that the list of investigators includes all investigators participating in the study, and that new investigators will sign the agreement before being added to the study;
- a list of the names, addresses, and chairpersons of all IRBs that have or will be asked to review the investigation and a certification of IRB action concerning the investigation;

- the amount, if any, charged for the device and an explanation of why sale does not constitute commercialization;
- copies of all labeling for the device; and
- copies of all informed consent forms and all related information materials to be provided to subjects.

FDA may request additional information about an investigation. However, the core of any IDE is the investigational plan. The investigational plan must include:

- the objectives and duration of the investigation;
- a written protocol describing the methodology to be used and an analysis of the protocol demonstrating its scientific soundness;
- a description and analysis of all increased risks to the research subjects and how these risks will be minimized; a justification for the investigation; and a description of the patient population including the number, age, sex, and condition;
- a description of each important component, ingredient, property, and principle of operation of the device and any anticipated changes in the device during the investigation; and
- monitoring procedures.

6. The burdens on an investigator and sponsor under an IDE are substantial. Detailed records related to the investigation must be maintained in a manner available for FDA inspection. Reports must be prepared and submitted to FDA if there are unanticipated adverse device effects. Progress reports must also be submitted to the agency at regular intervals. Investigators also have reporting obligations to the IRB, sponsor, and monitor of the study.

7. However, an IDE is not merely a matter of paperwork. Rather, an investigational use of a device presents major restrictions in a physician's ability to treat a patient. Specifically, 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. In contrast, 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, discussed further below, 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 C.F.R. § 801.4.

8. As noted, the purpose of an IDE is not to permit the general use of unapproved device. Rather, an IDE is intended to be used to generate valid scientific evidence to support safety and effectiveness claims for the device. The sponsor of the IDE must demonstrate that the objectives of the clinical investigation are directly linked to developing data for such claims. Even a pilot

study in one patient should be designed to provide basic information on safety and effectiveness of the device that will support the design and conduct of broader definitive clinical studies to support the device claims. Simply put, an IDE should be based upon a scientific rationale and study design -- it is not an excuse to use an otherwise unapproved product.

9. In the absence of an emergency, the sponsor of an investigation may begin an investigation only after waiting 30 days after FDA receives the IDE application. This time period may be extended if FDA orders the sponsor not to begin the investigation. The agency may either approve the proposed investigation, modify it, or disapprove it.

10. An approved IDE is not a license to promote the use of a product, and the commercialization of an unapproved device is generally prohibited under FDA regulations. Thus, investigational devices may not be promoted, test marketed, or sold above cost. An "investigation" or series of "investigations" may not be prolonged to promote the device or for any other reason inconsistent with developing sound scientific data to demonstrate device safety and effectiveness. I am advised that Baxter filed its premarket approval (PMA) application in February 1997. The average elapsed time for approval of an original PMA application in FDA's Fiscal Year 1996 was 25.9 months. See FDA Office of Device Evaluation Annual Report for Fiscal Year 1996 (attached). Assuming the PMA in question is an average submission, based upon FDA's statistics, Baxter is most likely two years away from PMA approval and the Baxter device will remain investigational for the foreseeable future. During this time, it is quite common, for public health reasons, for FDA to limit the number of IDEs it will approve for the Baxter Isolex® 300 device or the total number of clinical sites under one IDE for the same, to what is necessary to gather data to support the device's safety and effectiveness. It is not FDA's

policy to carte blanche approve innumerable IDEs absent some unusual and urgent public health reason. which I do not believe is present in this case.

11. In addition to denying an IDE. FDA has broad authority to withdraw approval of an IDE. Such a withdrawal can occur if there is a failure to comply with any requirement of the IDE regulations. including when the agency deems an investigation to be scientifically unsound or a commercialization of an unapproved device.

12. In certain. very limited circumstances. FDA permits the emergency shipment and use of an unapproved medical device without an approved IDE. This limited emergency use policy 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. FDA requires the patient in such a case to be in a life-threatening condition that needs immediate treatment. There must be no available. generally acceptable alternative for treating the patient. and, because of the immediate need to use the device, no time to use existing procedures to get FDA approval for the use. This policy is to be used only in true emergencies. not where there is a reasonable opportunity to submit or expand the terms of a legitimate IDE. If an emergency does exist. FDA must be notified immediately after the shipment of the device to the physician. and the physician must provide FDA with a written summary of the conditions constituting the emergency, patient protection measures, and the scientific results. If a device is used in a manner that is not appropriately characterized as an emergency, FDA can take regulatory action against the device manufacturer or the physician/investigator.

13. Other important implications of the use of Isolex® 300 IDEs to provide a market substitute for the approved CellPro product only highlight the unreasonable nature of the

suggested scheme. Even if these IDEs were valid under FDA's rules, it is highly unlikely that governmental healthcare programs or insurance companies would pay for an investigational procedure unless very specific criteria were deemed met. Thus, in many cases patients would bear the burden of the Plaintiffs' suggested IDE-based use of the Isolex® 300 device. The liability implications for physicians are also substantial. For example, there is a significant difference between the potential liability exposure to a physician who deviates from an investigational plan under an IDE versus the use of an approved product, such as the CellPro device, in a manner consistent with the practice of medicine. Indeed, it is likely that most courts would view a deviation from the terms of an IDE that results in patient injury to be *per se* negligence by the physician.

14. Overall, the use of IDEs to allow the use of the unapproved Isolex® 300 product is not a feasible option upon which to rest a permanent injunction. Even if legally defensible, this plan could have a detrimental impact upon patient care and severely constrain the practice of medicine. Thus, it is my opinion that the use of the Isolex® 300 device under physician-obtained IDEs does not constitute a reasonable substitute for the availability of the CellPro device.

I certify that all of the foregoing is true and understand that I am subject to penalty for perjury for any falsehood.

April 18, 1997

Date

David F. Weeda

David F. Weeda