July 29, 1997

Barbara M. McGarey
Deputy Director
Office of Technology Transfer
National Institutes of Health
6011 Executive Blvd.
Suite 325
Rockville, MD 20852

Re: Petition of CellPro, Inc.

Dear Ms. McGarey:

On July 2, 1997, CellPro submitted to NIH a 36-page document in support of its march-in petition. We believe that it will be helpful to NIH, in reviewing CellPro's latest filing, to have the benefit of a further submission from Hopkins that takes account both of the CellPro filing and the federal court's rulings on July 24, 1997.

This letter first summarizes the reasons why NIH should decline to initiate a march-in proceeding in the circumstances of this case. It then demonstrates that CellPro's "public health" argument overlooks the steps that have been taken to ensure that public health will not be compromised.

A. A March-In Proceeding is Not Warranted in the Circumstances of this Case.

In considering CellPro's petition, it will be useful to step back and examine the broader context. Although the parties disagree about several matters, there are some fundamental facts that are not disputed, or that are not open to dispute because they have been resolved in a binding federal court litigation. These include the following:

- As soon as Hopkins applied for patent protection on stem cell technology, it took immediate steps to license out the technology for commercialization.

- Hopkins' licensing efforts has resulted in the development of research, diagnostic, and therapeutic products by authorized licensees, just as the Bayh-Dole Act contemplated.

- The exclusive licensee in the therapeutic field, Baxter Healthcare, invested tens of millions of dollars in developing a therapeutic product. It has supported the use of that product in clinical trials throughout the world, has obtained regulatory approval

for sale of the product in Europe, and has applied for regulatory approval to begin commercial sales in the United States.

- Baxter took further steps to make the technology available to the public by offering sublicenses to CellPro and other companies on terms that a jury has found were commercially reasonable.

- CellPro elected to turn down Baxter's repeated a license offers in favor of litigation against the patent holders.

- CellPro is not an innocent infringer. A federal court, in the exercise of its lawful jurisdiction, determined that CellPro engaged in deliberate and bad faith infringement of Hopkins' patents.

- Although CellPro's willful infringement of the patents began as early as 1990, CellPro did not seek a "Bayh-Dole license" until March 1997, after its litigation strategy had failed.

These are not circumstances that could ever justify the exercise of march-in rights under the Bayh-Dole Act. CellPro itself acknowledged in its July 2 filing that under the Act, the government retained march-in rights "where there is nonuse or unreasonable use of a patent." CellPro Response, p. 24; *see* 35 U.S.C. § 200. Here, by contrast, Hopkins and its licensees took reasonable and effective steps to commercialize the patented technology. This is a Bayh-Dole success story, not a failure requiring government intervention in order to protect the public.

CellPro dismisses Hopkins' concern about the future of university-industry partnerships as "scare tactics" and suggests that allowance of its petition would imply nothing more than the prospect of a march-in license being issued "once every 15 or 20 years." CellPro Response, p. 24. In fact, the initiation of a march-in proceeding in the face of the undisputed facts recited above would have far greater consequences. The issue is not simply the impact of a march-in proceeding on Hopkins and Baxter. Even more important is the incalculable number of potential university-industry partnerships that will never come about due to the uncertainties that initiation of a march-in proceeding here would engender.

CellPro says that these concerns are groundless because a co-sponsor of the Act, former Senator Birch Bayh, was hired as a paid lobbyist for CellPro. Of far greater significance are the reactions to CellPro's petition within the university and biotechnology communities, where CellPro's petition is accurately perceived as a profound threat to the future of technology transfer under the Bayh-Dole Act. Some examples:

> *If these "march in rights" were allowed, our technology licensing program would be seriously undermined. This precedent would pose a grave threat to the success*

of the Bayh-Dole Act in encouraging university-industry partnerships and may well put into jeopardy the kind of investments needed today to take medical discoveries through the lengthy process needed to bring them to the public. Gerhard Casper, President, Stanford University.

There is no reason to call upon the "march-in" provisions in a case in which a university-industry partnership has resulted in licensing and product development just as envisioned by the Act. In addition to penalizing those who have acted under the letter and spirit of the Act, a decision to invoke the "march-in" provision would threaten the future effectiveness of the Act by creating an atmosphere in which both universities and industries will be forced to question whether the protections of the Act will, in fact, be provided. Incentives for developing useful technologies that could flow from university research would be weakened and the potential public beneficiaries of the technologies would be the losers. George Rupp, President, Columbia University.

If institutions cannot offer their licensees the protections of the patent system, needed investments necessary to take medical innovations through the product development, clinical trials, and FDA approval process will dry up. Jordan J. Cohen, M.D., President, Association of American Medical Colleges.

If CellPro, Inc. is granted an unwarranted license under the "march-in rights" of the Bayh-Dole Act, it will set a very negative precedent for the future of technology transfer. Such an action will likely have a negative impact on our ability to attract private sector partners for the commercialization of research innovations. Arthur D. Levinson, Ph.D., President and CEO, Genentech, Inc.

If CellPro is able to use the Bayh-Dole Act as a crowbar to pry open our patent system, all nonprofit medical research institutions will suffer the consequences. Because unless they can secure solid rights to their intellectual property, the licenses they grant will be practically worthless. David Gollaher, Ph.D., President, California Healthcare Institute.

Far from being an isolated case of a small company seeking its own brand of justice against the might of a large pharmaceutical company, the case has far-reaching implications for technology transfer and the perceived value of collaborations between industry and universities. . . . Without some guarantee of exclusivity, the reasons for partnering in the first place come into question. Editorial, BioWorld Financial Watch, July 14, 1997.

These statements, and the many more that have been submitted to NIH in opposition to

CellPro's petition,[1] make clear that CellPro's attempted misuse of the Bayh-Dole Act in its own self-interest has broad ramifications for the future of technology transfer. CellPro's effort to belittle the precedent that would be set by a march-in proceeding here should not be credited.

The federal court's rulings on July 24, 1997 make the implications of a march-in proceeding here of even greater concern. In its Opinion, the court found, based on its review of all the evidence, that "CellPro deliberately infringed the patents in bad faith and . . . used the litigation to frustrate plaintiffs and as an opportunity to throw up baseless arguments and defenses to avoid liability." Opinion, p. 24. This finding is not open to challenge before this agency. The court further noted that CellPro's conduct over the past seven years demonstrated "contempt for Dr. Civin and his patents, for the people at Johns Hopkins, at Baxter, and at Becton Dickinson . . . for the law; and for our system of civil justice." Id. at 17.

In the face of the court's findings and the undisputed facts of this case, initiation of a march-in proceeding here would set a chilling precedent. It would mean that a company can deliberately violate federal patent law and still be welcomed by this agency as a "responsible applicant" under the march-in regulations. It would also mean that an exclusive licensee's good faith investment of tens of millions of dollars in product development and clinical trials is not enough to ensure against march-in if an infringer can win the race to FDA approval for even a single narrow indication. And it would mean that a willful infringer's decision to reject the offer of a license on commercially reasonable terms in favor of litigation is not enough to preclude a later march-in proceeding when the infringer loses in court. CellPro's assertion that grant of its petition would "further" the policies of the Bayh-Dole Act is specious.

CellPro's argument that the Patent Act itself contains sufficient disincentives to prevent abuse of the march-in provisions is rebutted by CellPro's own conduct in this case. As the court found, in late 1991 CellPro was projecting $1.6 billion dollars in sales of its stem cell selection products over the next eight years. It knew at the time that its products infringed Dr. Civin's patents. Nevertheless, CellPro's internal planning documents plotted a scenario to "Fight Civin & win", in which case there would be a "0.0%" royalty on its sales. Appendix, Tab N, page 4. If, on the other hand, the outcome was to "Fight Civin & lose," CellPro calculated it could at that point obtain a license at a 15% royalty. Id. Although CellPro could have petitioned DHHS for a "Bayh-Dole license" back in 1991, from its self-interested perspective doing so would have removed the business opportunity for a "0.0%" royalty rate if by chance it prevailed in litigation. Thus, it was not until after losing in court that CellPro filed its Bayh-Dole petition as an alternative, back-up strategy.

This same strategy could easily be followed by other companies where the upside is high

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[1] For NIH's convenience, examples of these letters are included in the supplemental appendix submitted herewith.

enough to warrant the expense. Indeed, in the medical field, the Patent Act facilitates it by providing an exemption from liability for infringement for clinical trial activities directed to obtaining premarket clearance from the FDA. 35 U.S.C. § 271(e).[2] Relying on § 271(e), a company could exploit a university's patented technology with impunity until it obtained FDA approval for its product. Then, unless the exclusive licensee elect to give up exclusivity and grant it a license, it could petition this agency for a "Bayh-Dole license," making exactly the same sort of public health argument that CellPro has asserted here. This is not a theoretical "parade of horrors," as CellPro would have it, but a very plausible scenario, the prospect of which would reasonably lead bio-medical companies to forego investment in university-based medical technology.[3]

CellPro argues that exclusive licensees should not be alarmed because any "Bayh-Dole license" must be granted "on terms that are reasonable in the circumstances." CellPro Response, p. 22. CellPro misses the point. The promise of exclusivity is a promise that the licensee does not have to grant any license to another party, no matter what the terms. Moreover, even in its latest filing CellPro continues to argue that NIH should award it a license at a 4% royalty -- less than the royalty Baxter itself must pay -- despite the jury's determination that a reasonable royalty for CellPro in 1990 would have been 10%. The mere possibility that such an argument could prevail in a march-in proceeding is more than enough to chill investment in university-based technology.[4]

CellPro's argument is also based on false premises. According to CellPro, it is Baxter's

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[2] In this case, CellPro elected not to raise § 271(e) as a defense to infringement.

[3] In fact, another company, Miltenyi, has developed its own stem cell selection device and recently has begun clinical trial activities in the U.S. If CellPro persuades this agency to exercise march-in rights on its behalf, it can be expected that other companies will promptly follow suit claiming that they too need "Bayh-Dole licenses" under Hopkins' patents to justify continuation of their clinical trials.

[4] CellPro claims it recently proposed a license on terms more favorable to Baxter than the ones it granted other companies. Not only is this characterization untrue as a matter of economics, but CellPro's proposal was so one-sided as to raise doubts about CellPro's motivations. As a condition of its proposal, CellPro insisted on continuing its litigation against Hopkins and its licensees even in the face of the jury's finding of bad faith, willful infringement. Under the proposal, if CellPro eventually won, it would not be bound by any of the terms of the "license." If Hopkins and its licensees won, by contrast, they would be bound by the terms of the license, so CellPro would win either way. CellPro's insistence on continuing its costly litigation strategy in an effort to avoid paying Hopkins anything for the use of its patented technology is disappointing, and can only have the effect of decreasing the funds available for medical research and the development of new therapies for cancer and other diseases.

"refusal to grant a license on reasonable terms" that conflicts with the policies underlying the Bayh-Dole Act. CellPro Response, p. 26. CellPro is wrong on two counts. First, as shown in our June 2, 1997 filing, the Bayh-Dole Act was enacted to encourage exclusive licensing, not to force exclusive licensees to grant sublicenses. Second, as the court found in its Memorandum Opinion of July 24, 1997 rejecting CellPro's patent misuse defense, Baxter in fact offered to grant CellPro a sublicense, on numerous occasions. The jury's verdict in March establishes beyond dispute that the terms of Baxter's offer were reasonable. CellPro's decision to reject Baxter's repeated offers and take its chances in litigation was its responsibility alone. The Bayh-Dole Act was not enacted to reward bad judgment.

B. Initiation of a March-In Proceeding is Not Necessary to Alleviate Public Health Needs.

CellPro's public health argument offers little new in the way of "response" to Hopkins' filings, and instead reiterates assertions previously made. As CellPro's preface makes clear, the argument has as its premise that the court's order will "forc[e] CellPro to withdraw its CEPRATE system from the marketplace." CellPro Response, p. 2. But Hopkins and its licensees did not seek an order forcing immediate withdrawal of CellPro's product from the market, and the court did not order it.

CellPro emphasizes, as it has in previous filings, that its system is approved by the FDA and Baxter's is not. Putting aside whether this distinction is meaningful given that CellPro's approved indication is for a single narrow indication that is now all but obsolete,[5] the court's order permits CellPro to continue selling its system and using it in clinical trials until Baxter's product, or another licensed alternative, receives FDA approval. CellPro's first argument is thus irrelevant.

CellPro's second argument reiterates alleged shortcomings of the Baxter system, citing declarations of several clinicians. These arguments were addressed in Hopkins' June 2 filing. As there demonstrated, CellPro's clinicians have little or no experience with the Baxter system; their declarations merely assert their desire to continue using the product they know best, whether it

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[5] CellPro dismisses the narrowness of its approved indication by emphasizing the potential benefits of using the device "off-label." In the same breath, it denies any promotion of the device for "off-label" use, other than in a Christmas card. Anyone who has read the materials reproduced on CellPro's web site or seen stories in the press or on television placed by CellPro's public relations firm knows that CellPro has incessantly, in every available form of media, promoted the alleged public health benefits of using its system for autologous transplants of peripheral blood stem cells, allogeneic transplants of both bone marrow and peripheral blood stem cells, gene therapy, and a host of other therapies, despite the fact that the FDA has not determined that CellPro's system is safe and effective for any of these treatments.

infringes Hopkins' patents or not. In contrast, Hopkins submitted declarations of clinicians who have worked with both the CellPro and the Baxter systems. These clinicians, who practice at such leading transplant centers as New York Blood Center and the Fred Hutchinson Cancer Research Center, attest to the consistently superior stem cell purification results provided by the Baxter system.[6]

CellPro's argument that clinical trials will be disrupted by the court's order reiterates an argument made last April, before Hopkins and its licensees expressly asked the court to permit CellPro to continue its clinical trials, including those underway at the point of FDA approval of an alternative system. CellPro's citation of clinician declarations describing the impact of an injunction on their clinical trials were drafted in March and April on the assumption that the court's order would force the immediate cessation of those trials. For CellPro to cite them now in a different context is highly misleading.

CellPro's claim that substituting the Baxter system in ongoing clinical trials would require "scores of investigators to start their research all over again" and cause delays of "many months and probably one to two years" is addressed in Hopkins' letter to NIH dated July 2, 1997. CellPro forgets that the these trials are directed to evaluating the safety and therapeutic benefit of transplanting purified stem cells. The investigators' research can go on as long as they have available a device that provides purified stem cells, which is exactly what Baxter's Isolex® 300 system does. Moreover, CellPro's suggestion that obtaining FDA and IRB approval to substitute one device for another in an ongoing trial would take one to two years is unsupported by any evidence and is an insult both to the FDA and to the doctors who make up local IRAS. Where patient care is at stake, both the FDA and the IRBs are prepared to act quickly and conscientiously.[7]

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[6] The data submitted to the FDA in support of Baxter's PMA showed median CD34+ purities of 89-90% in autologous stem cell transplants, representing 100-fold or better depletion of non-target CD34- cells. By way of comparison, in obtaining FDA approval of its device, CellPro demonstrated median CD34+ purities of only 75%. Hopkins Supplemental Response to Petition of CellPro, Inc., June 2, 1997, Appendix, Tab C, p. 2. Although the FDA has not finally decided the efficacy criteria for approving stem cell selection devices like Baxter's and CellPro's for use in autologous stem cell transplantation, the FDA's advisory panel has voted overwhelmingly in favor of a determination that Baxter's system yields a highly purified stem cell population that is safe and effective for transplantation and engraftment.

[7] CellPro questions whether Baxter can perform its commitment if it completes the proposed transaction with VIMRX Pharmaceuticals, noting that VIMRX has fewer employees than CellPro. This is misleading. The proposed transaction involves the creation of a new joint venture, which will have the personnel and resources of Baxter's current Immunotherapy Division, the financial support of both VIMRX and Baxter, and the manufacturing, sales,

In any event, the court's decision, and the terms of the court's order, effectively remove these issues from the case. The court specifically found, after considering all the evidence, that CellPro had not demonstrated any adverse public health consequences arising from the terms of its order. It nevertheless retained jurisdiction over the case and undertook to entertain future applications for modification of the injunction if CellPro demonstrates a public health need to do so. The court thus established a mechanism for ongoing monitoring of the situation to address any public health issues if and when needed.

There is a more general fallacy in CellPro's argument. In substance, CellPro is arguing that it is always better to have two companies engaged in clinical studies rather than one. At any given moment in time, either company might be sponsoring a study directed at a potential benefit that is not the subject of a study by the other. But this is really an argument against exclusive licensing. That debate took place in Congress in 1980, and Congress came down on the side of exclusive licensing as the best means to promote medical research and product development. Superficially, it may seem that making new medical technology available through two companies rather than one would benefit patients, but Congress recognized that this approach was shortsighted. The risk of following that course and denying companies the protections of exclusive licensing is that rather than having two companies providing commercial embodiments of the technology, there will be none. It is this risk to public health that is utterly ignored in CellPro's petition.

CellPro's final argument is that the terms of the proposed order would as a practical matter force it to shut down its operations. But the actual terms of the order as entered are considerably more favorable to CellPro than was assumed in CellPro's July 2 submission. The court did not order CellPro to pay all of its incremental profit on infringing sales to plaintiffs, and instead ordered a 60-40 profit split. This will give CellPro added economic incentive to continue selling its Ceprate® SC products while it pursues its appeal.[8] The court even left open the possibility of adjusting the profit split, assuming CellPro decides to disclose its actual sales and cost data. Memorandum Opinion, p. 24. The court's order also permits CellPro to manufacture

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marketing and distribution capabilities of Baxter behind it. Baxter's commitment is addressed specifically in our letter to NIH dated July 2, 1997.

[8] Plaintiffs' original proposal had requested a $2000 per unit minimum payment, which they believe to be less than CellPro's incremental profit. As entered, the court's order retains the $2000 minimum, unadjusted for the 60-40 profit split. When they discovered this apparent inconsistency, plaintiffs wrote to CellPro's counsel expressing their willingness to adjust the amount of the minimum payment if it in fact exceeds 60% of CellPro's incremental profit. (A copy of our letter is included in the Appendix at Tab O). CellPro has not responded to our offer. Incredibly, CellPro sent out a press release today (Tab P) denouncing the $2000 minimum and yet failing to disclose our offer to modify it as may be appropriate.

and sell products abroad if it switches to a noninfringing CD34 antibody made outside the U.S., which we expect it will do. Overall, the terms of the order, together with CellPro's asserted belief that it will prevail on appeal, give CellPro significant economic incentive to continue operations.

Initiation of a march-in proceeding based on CellPro's argument that it needs a license to facilitate financing down the road would set a peculiar precedent. The implication of CellPro's argument is that there should be a special march-in standard for infringers that are undercapitalized and in need of additional financing. A better managed company (or one that did not squander more than $10 million on unjustifiable litigation), on the other hand, would not be entitled to march-in because it would not face the same financial exigencies.

CellPro's latest variation of its economic argument is suspicious. CellPro has known throughout the litigation that plaintiffs were seeking both damages and an injunction against infringement. By February 1997, the federal court had rejected all of CellPro's defenses, and CellPro (and its investors) well knew it faced the prospect of an injunction. CellPro also knew its current cash position and could project its future cash needs. Yet only now has CellPro made the claim that any form of injunction will prevent it from raising necessary capital. This assertion is presented through an unsworn "opinion" of a self-interested, recently hired financial advisor (Alex. Brown) which contradicts the "Strong Buy" recommendation of CellPro's long time financial advisor (Hambrecht & Quist) as expressed in March, which recommendation had assumed the court in fact would enter an injunction. *See* Supplemental Decl. of Dr. Jerry A. Hausman, June 12, 1997, Exh. A. CellPro never presented the Alex. Brown argument in court, and never disclosed it to its stockholders, despite CellPro's publicly announced expectation that a judgment against it would soon be entered.

The federal court properly concluded that the risk of CellPro's shutting down its business if an injunction were entered was "highly speculative" and not supported by any evidence. Memorandum Opinion, p. 23. It also made a finding of fact that "CellPro possesses adequate cash reserves to allow it to continue operations during the pendency of its appeal." Id. at 24.

It is well to step back and recall that this is a company actively initiating new clinical trials, spending millions of dollars on litigation, lobbying and public relations, and having access to $54 in cash as of the end of March. Moreover, CellPro's most recent balance sheet accompanying its July 2 submission shows inventory of over $5 million, more than half of which constitutes finished goods. If, as CellPro has recently hinted, CellPro's year-to-date sales are less than planned, then the inventory figure in all likelihood has increased since March. Indeed, we suspect that CellPro's current inventory of disposable kits numbers in the thousands. The inventory alone should prevent any disruption in access to stem cell technology: surely, CellPro would not refuse to supply a clinical site where it has inventory already manufactured and on hand?

CellPro's economic argument is suspicious also because CellPro has repeatedly refused requests to provide back-up information and documentation to support its assertions. CellPro's

insistence that NIH commence a march-in proceeding based entirely on the alleged financial impact of a proposed injunction, while at the same time it refuses to subject its financial data to outside scrutiny, is enough by itself to warrant denial of its petition.

CellPro's shifting economic argument is not a proper basis for the initiation of a march-in proceeding. If it were, any company that initiates clinical trials involving patented technology activities could trigger a proceeding simply by announcing that without a license under the patents, it will be unable to finance the continuation of those trials. It was not the intent of Congress to authorize the exercise of march-in rights in these circumstances.

CellPro has not demonstrated that there is any statutory basis for initiation of a march in proceeding. The undisputed facts show that Hopkins took prompt and effective steps to commercialize Dr. Civin's patented stem cell technology. Moreover, the federal court carefully crafted its order to ensure that the public will continue to have access to that technology, and retained jurisdiction to ensure that any conceivable public health concern that may arise will be effectively addressed. There is no need for this agency to initiate a parallel proceeding, and to do so would inappropriately interfere with the court's exercise of its lawful jurisdiction. NIH should reaffirm the principles that have made the Bayh-Dole Act the success it is today and promptly deny CellPro's petition.

Respectfully submitted,

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