

FRED HUTCHINSON CANCER RESEARCH CENTER  
**BOARD OF TRUSTEES**

**Patient Protection Oversight Committee Progress Report**  
**April 25, 2002**

**Background**

Fred Hutchinson Cancer Research Center engages in clinical research as part of its mission to save and enhance lives. The safety of individuals who participate in research studies and the confidence of the public in the integrity of clinical research activities are an integral part of fulfilling this mission. With this in mind, the Center's Board of Trustees created a standing committee, the Patient Protection Oversight Committee (PPOC), to recommend improvements to the Center's policies and practices related to conduct of clinical trials and to provide trustee oversight of the Center's policies and practices pertaining to research involving human subjects. Committee members are Mr. Bruce Pym, chair; Mr. Carl Behnke; Mr. Philip Bussey; Ms. Joan Enticknap; Mr. Edward Fritzky; Mr. Jon Runstad; Mrs. Pat Stanford; Rev. William Sullivan, S.J.; Mr. Doug Walker.

As part of its duties, the PPOC was charged with reviewing and implementing the findings of the Committee for Patient Protection in Research Trials (CPPRT), a community-based committee that made recommendations for improving the Center's practices and policies related to the conduct of clinical trials. This report summarizes the activities of the PPOC and the progress made toward implementing the action plans recommended and approved by the PPOC.

**Committee Activities**

The PPOC met from October 2001 through April 2002. Throughout this time, members received updates on external audits pertaining to human subjects research, reviewed current practices and policies, studied background materials and literature on Institutional Review Board activities, protocol data and safety monitoring, informed consent, management of conflicts of interest, and financial disclosure.

The committee's meetings included a session with former patients and a family member who shared their personal experiences of the informed consent process. In its study of conflict of interest policies, the committee reviewed an analysis of the Center's policies compared to the policies of other major research centers, U.S. Public Health Services regulations, and guidelines proposed by the Association of Academic Medical Colleges in December, 2001. The committee met with several members of the CPPRT to discuss their personal views and insights. Also considered were the views of scientific faculty, as collected through informal surveys and staff sessions on the issue of conflict of interest. Margaret Dale, Harvard University's Director of the Office of Research Issues, and

Wylie Burke, Chair of the Department of Medical History and Ethics at the University of Washington, participated in the committee's discussions.

### **Key Action Plans of the Committee**

The Committee for Patient Protection in Research Trials (CPPRT) and the independent experts contracted by the CPPRT to review the Center's practices concluded that the Center is in compliance with government regulations for human subjects research, and that the Center's practices are comparable with those of other major cancer research centers in the United States. The external reviewers did identify areas in which they thought the policies or practices of the Center might be improved. These suggestions form the basis for the recommendations made by the CPPRT.

Two of the recommendations of the CPPRT were implemented immediately by the Board of Trustees and the Center:

1. The Board of Trustees created the Patient Protection Oversight Committee to assure oversight of the Center's activities in conducting clinical trials.
2. The Center posted the CPPRT's and the independent reviewers' reports on the Center's web site. Copies were made available to media and others upon request.

The PPOC is fully engaged in improving the processes involving clinical trials. The PPOC reviewed the recommendations and the suggestions for improvement made by the CPPRT and the independent reviewers contracted by the CPPRT. The PPOC agreed with the conclusion that the Center is in compliance with government regulations and the practices of major research centers in the country for human subjects research. Following a review of the recommendations made by the CPPRT and the external reviewers, the PPOC recommended action plans to address improvements. Many of the action plans for improvement are now being implemented. Some improvements were initiated during the reviews of the community-based CPPRT, and others were based on recommendations of the CPPRT or PPOC. All of the activities are outlined below.

#### ***1. Financial Conflicts of Interest***

The PPOC has examined the management of financial conflicts of interest at length. The PPOC heard from outside experts and reviewed conflict of interest policies adopted at leading research centers and as modeled by the Association of Academic Medical Colleges (AAMC). Additional interactions with former patients and a family representative were also held to seek their insights and feelings regarding conflict of interest issues.

Avoiding conflicts of interest, or even the appearance of conflicts of interest, on the part of individuals involved in human subject trials is of great importance to the Center. It is central to maintaining the trust and confidence of study participants in research studies and the objectivity of researchers. At the same

time, strong collaborations among for-profit life sciences companies, the non-profit and public sectors and individual scientists in the development of new technology are vital to the Center's goals of advancing scientific knowledge to save lives. Current federal policies encourage institutions to seek private investment to translate the ideas of biomedical research into medically useful products.

The community-based CPPRT recommended "an outright prohibition on the part of individuals participating in human subject trials of any financial interest in for-profit corporations which may benefit from the result of such trials." In response, the PPOC proposed revisions to the Center's existing conflict of interest policy that expressly prohibit a Center scientist from being involved in a human subject trial if he/she has certain financial interests in a for-profit sponsor that could be impacted by the outcome of the trial. These prohibited financial interests include shares of stock in any amount, royalty rights on patents or other intellectual property, and payments which exceed \$10,000 per year from a single entity. Payments of any sort based on or related to the outcome of the trials continue to be prohibited. The revised conflict of interest policy requires a scientist who is an author on a publication concerning a trial to disclose any prohibited financial interests that could affect the research.

This new prohibition imposes a more restrictive standard than that recommended in the AAMC guidelines and the policies of several research centers in two key respects. First, the Center's revised policy prohibits researchers, without exception, from participating in human subject trials if they have a prohibited financial interest in the for-profit sponsors of the trials. The AAMC guidelines and the policies of several research centers do not have an absolute prohibition, but allow approved exceptions to this rule. Under these exceptions, a person with a financial interest in a for-profit company may still be allowed to conduct research under exceptions specified by a conflict of interest committee if that person could demonstrate compelling circumstances. Second, the Center's policy prohibits any amount of ownership interest in a for-profit company, except for publicly traded mutual funds. In contrast, a number of other research centers allow equity interests of up to \$10,000.

After extensive and careful consideration, the PPOC recommended that the Center retain the standard of permitting members of the Center's scientific staff to receive honoraria for speeches, compensation for service on scientific advisory boards, fees for general consultation services and reimbursement for travel and other expenses, subject to an aggregate limitation of \$10,000 per year from any single entity. The PPOC considered activities such as meeting to discuss the progress of studies and giving seminars to disseminate the knowledge or research efforts part of the normal course of conducting research trials. The PPOC concluded that the modest compensation for these activities is acceptable. The policy permits reimbursement for expenses incurred in the course of carrying out effective research and education, costs that are normally borne by companies supporting a research study. The U.S. Public Health Services in the "Objectivity

in Research Regulations,” the AAMC guidelines, and a number of research institutions across the United States consider these practices to be acceptable. In fact, the AAMC noted that the practice of scientific staff members receiving financial rewards from research endeavors is not intrinsically unacceptable, as long as it does not adversely influence scientific or clinical decision-making.

The Board of Trustees reviewed and approved the revised conflict of interest policy on April 25, 2002.

**2. *Financial Disclosure***

The PPOC acknowledges the importance of disclosing to participants in clinical trials whatever compensation or other financial interests may be received by a scientist participating in trials from for-profit sponsors of such trials, even though such consideration is permitted by the Center’s conflict of interest policy. The issue of how to disclose in order to promote the best interests of study participants is extremely important. With that understanding, the PPOC has asked that Center staff conduct a more in-depth review by July 2002. Center staff will report back to the PPOC with recommended procedures for implementing disclosures of financial interests to study participants. Center staff will consider options discussed by the PPOC: the inclusion of information in informed consent documents or making information available to study participants through accessing a database. Center staff is charged with reviewing the practices of other research centers and obtaining the views of human subjects experts, ethicists, and clinicians, with the best interests of study participants as a goal.

**3. *Institutional Conflict of Interest***

The PPOC discussed policies for institutional conflict of interest, but determined that the subject is evolving and that policy changes should not be developed at this time. There are currently no federal requirements for research centers on how to manage institutional financial conflicts of interest. Policies regarding aspects of these issues such as the management of investment funds, technology transfer activities, or the use of licensing income vary among institutions. In the upcoming year, the AAMC will review the management of institutional conflict of interest and will issue guidelines. The PPOC recommended that the Center monitor and participate in national discussions on institutional conflict of interest as they unfold, and then adopt appropriate policies.

**4. *Institutional Support***

The Center has allocated additional resources of \$1 million to help support activities noted in the CPPRT report and the action plans approved by the PPOC.

**5. *National Discussions***

Center staff will be further involved in national discussions regarding Institutional Review Board activities and protocol safety and data monitoring, and will increase participation in discussions on informed consent and the management of conflict of interest.

**6. *Regulatory Compliance***

The Center is in the process of creating a Research Trials Office that reports to the Director of the Center. This office will be operational in 2002, and will track ongoing regulations that relate to trials involving human subjects.

Regulatory compliance is a function of the General Counsel's office. To provide increased support of this function, an Associate General Counsel has been added to Counsel's staff.

The Center has hired a consultant to advise on Food and Drug Administration (FDA) regulatory compliance.

The Center will hire an additional trainer whose main role will be to address increased federal requirements for ongoing research integrity training.

**7. *Informed Consent***

The Center has improved the ethnic diversity of the Institutional Review Board membership that will serve to enhance sensitivity to cultural, racial, and language differences in the informed consent process.

A Physician Assistant has been hired in the Protocol Development office to help with standardization and simplification of language for the informed consent documents used for adults and children.

An external consultant will be engaged to assist in evaluating the language and format of the informed consent documents for improvements.

The PPOC will continue to evaluate ways to enhance the availability of patient advocacy in the informed consent process. The issue will be referred to a group that includes the ethics committee and other staff. This group will review the informed consent process and make recommendations to the PPOC.

**8. *Protocol Compliance and Data Integrity***

The Center has recently updated its ongoing system for protocol data and safety monitoring. The National Cancer Institute has approved this new system. For some studies that benefit from specialized review, monitoring continues to be overseen by data safety monitoring boards, bodies consisting of internal or outside experts who are independent of the study.

Due to the evolving regulatory and auditing requirements of the National Cancer Institute and the Food and Drug Administration, the Center has hired an outside contract research organization to perform monitoring of protocol data. This year the Center will put into place an internal monitoring function to assume the duties of the contract research organization, as recommended by the independent reviewer contracted by the CPPRT.

**9. *Recognition of the Members of the Institutional Review Board***

The Center continues to recognize the importance of the contributions made by Institutional Review Board (IRB) members in assuring the welfare of study participants and the integrity of research activities. The Center Director has re-affirmed the important roles of the individuals who serve as IRB members, and will continue to meet with members to learn how to increase support and recognition for their service.

The Center has also sent a letter to supervisors of IRB members emphasizing the importance of their staff's participation in the IRB, and reinforcing the fact that this is considered a work-related activity.

**10. *Ethics Expertise***

The Center has a strong commitment to ethical principles in the conduct of human subjects research. The Center is creating a new research ethics committee under the Research Trials Office. The ethics committee will provide consultative services to researchers and staff designing or reviewing research studies, offer advice to Institutional Review Boards upon request. The committee will provide an open forum for the discussion of ethical issues that may arise during the design and implementation of research studies.

**11. *Follow-up Review***

The Center will engage independent reviewers for a follow-up review of the Center's practices and policies related to the conduct of clinical research in 2002.

The PPOC will continue to review and monitor work plans in progress and the suggestions for operational improvements made by the independent reviewers. Some of the issues such as informed consent and the management of conflict of interest are complex and the focus of ongoing evaluation and debate in research centers across the country. The Patient Protection Oversight Committee will continue to oversee activities in the Center's conduct of clinical trials as national discussions unfold and regulations evolve and, when appropriate, the Center will modify its policies and practices. The ongoing work of the Patient Protection Oversight Committee will continue to be based on the commitment of the Fred Hutchinson Cancer Research Center to the care and safety of participants of clinical trials.