2003 ANNUAL REPORT

of the

UNIVERSITY OF BRITISH COLUMBIA
CLINICAL RESEARCH ETHICS BOARD

Issued May 2004

by

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Mission of the UBC Clinical Research Ethics Board

"To protect the interests of human subjects by ensuring high ethical standards in clinical research at UBC."

Introduction & Background

The UBC Clinical Research Ethics Board (CREB) was formed in 1985. Since that time the CREB has been responsible for review and ongoing oversight of clinical research conducted by researchers based at UBC and its affiliated institutions.

The UBC CREB operates according to the principles and standards detailed in the Tri-council Policy Statement for Ethical Conduct for Research Involving Humans (TCPS).

In addition to clinical research conducted by investigators based on UBC's Point Grey campus, the CREB is responsible for review and oversight of research conducted within the Vancouver Coastal Health Authority (all sites & affiliated research institutes), BC's Children's & Women's Hospital (and affiliated research institutes), and until May 2003, the BC Cancer Agency.

This report is one part of the CREB's multi-faceted effort to maintain and increase the integrity, transparency, independence and efficiency of the clinical research ethical review process at UBC.

This report reflects the activities of the CREB for the calendar year 2003. Historical data and comparisons with 2002's operations are provided in selected instances.

Any questions about this document may be directed to the CREB's Manager, Susan Chunick (Susan.Chunick@ors.ubc.ca) or the CREB Chair, Dr. Peter Loewen (ploewen@interchange.ubc.ca).

Membership

As of December 2003, the CREB was composed of 18 members, 11 of which were regular participants and the balance part-time or periodic participants.

Name	Roles	UBC Affiliation(s)
Peter Loewen, Pharm.D.	Chair	VCHA, UBC Pharmaceutical Sciences
Alain Gagnon, M.D.	Associate Chair	C&WH, UBC Medicine (Obstetrics & Gynecology)
James McCormack, Pharm.D.	Associate Chair	UBC Pharmaceutical Sciences
John Russell, Ph.D.	Ethicist	UBC Philosophy
Karen Low Ah Kee, CMA	Lay Member	none
Lynn Beattie, M.D.	Primary Reviewer	VCHA, UBC Medicine (Geriatrics)
Stephen Hoption-Cann, Ph.D	Primary Reviewer	UBC Health Care & Epidemiology
Jolanda Cibere, M.D. Caroline Patterson, M.D. Kam Shojania M.D. Ian Tsang, M.D.	Primary Reviewers	Arthritis Research Centre, UBC Medicine (Rheumatology)
Valia Lestou, Ph.D.	Primary Reviewer	BCCA, UBC Medicine (Genetics)
Caroline Lohrisch, M.D.	Primary Reviewer	BCCA, UBC Medicine (Oncology)

Janessa Laskin M.D.	Primary Reviewer	
Pratibha Reebye, M.D.	Primary Reviewer	C&W, UBC Medicine (Psychiatry)
Ann Hilton, RN, Ph.D	Reviewer	UBC (Nursing)
Laurie Smith, B.Sc., R.N.	Reviewer	VCHA (ICU Research)
Bill Sullivan, Q.C.	Lawyer	none
David Wensley M.D.	Primary Reviewer	C&W, UBC Medicine (Paediatrics)

Dr. James McCormack was appointed as Associate Chair on August 1, 2003 to provide further support to the existing associate chair, Dr. Alain Gagnon, and the overall operation.

Drs. Jolanda Cibere, Caroline Patterson, Kam Shojania and Ian Tsang representing rheumatology within the UBC Department of Medicine completed their terms at the end of 2003, as did Dr. Ann Hilton, UBC Nursing, and Penny Washington who alternated as the CREB's legal representative during that time. Their contributions to the CREB and to the UBC research community are highly valued.

It is a challenge to maintain the membership needs of the Board to comply with Tri-Council Policy requirements and Health Canada legislation for regulated clinical trials. There is a need for a multi-disciplinary membership with a broad spectrum of expertise and experience. Margaret Shotter, UBC Associate Director, Research Ethics has worked hard to recruit new members to the Board. However, by the end of 2003 there was an urgent requirement for five new members to be primary reviewers on the CREB to cope with the high workload. The recruitment difficulty is unlikely to be overcome without more recognition by the UBC research community of the value of the work done by CREB members.

Operations

In September 2003, Erin Desjardine was hired as Manager of Ethical Pre-Review. In this capacity, Erin enhances the consistency and thoroughness of review of Applications for Ethical Review by being the common reviewer for all new studies going to the Board and for all renewal applications received for Expedited Review. The primary goal of Erin's review is to ensure that a study's consent forms meet current CREB requirements. Alison Stack was hired in July 2003 to provide clerical support to accommodate Erin's promotion. Five nurse reviewers, Heather Abbey, Eleanor Fink, Michelle Jones, Karen MacDonald and Bobbi Zastre were engaged on a part time basis to carry out review of Serious and unexpected Adverse Event (SAE) reports.

Improvements made to enhance the efficiency of correspondence with the research community included the initiation of e-mailed PDF Certificates of Approval, regular e-mail notices to investigators of upcoming renewal deadlines, and simplification of the acknowledgement procedure for SAEs. Furthermore, in order to simplify communication between investigators and the CREB office, Catherine Sutherland was assigned "focal point" responsibilities for responding to and processing all requests for and decisions arising from expedited review. Alison Stack was assigned this role for all full board applications.

Statistics

As of December 31, 2003 the CREB is responsible for ethical oversight of 1,324 ongoing research projects. In 2003 the CREB undertook to clarify the active/completed status of all projects in the CREB database.

The CREB handled 3,527 requests for ethical review in 2003. A breakdown of these requests is depicted in Figure 1.

Figure 1: Requests for ethical review in 2003 (N=3,527).

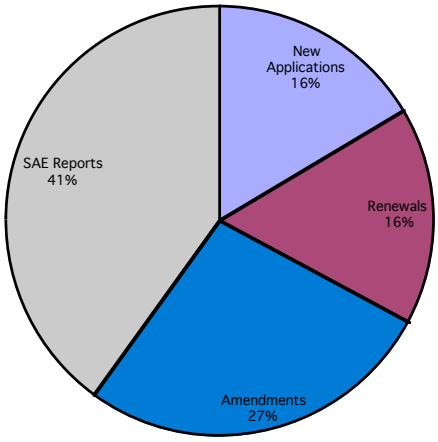


Figure 2: New project applications.

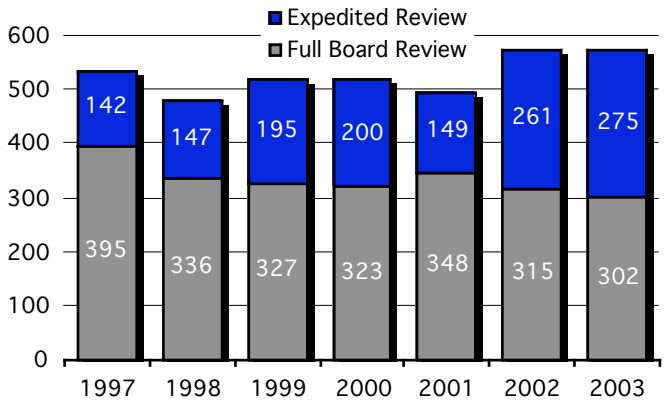


Figure 3: Amendments processed.
Prior to 2003, the method used to estimate the number of Full Board Amendments reviewed provided an overestimate. The 2003 figure is believed to be accurate.

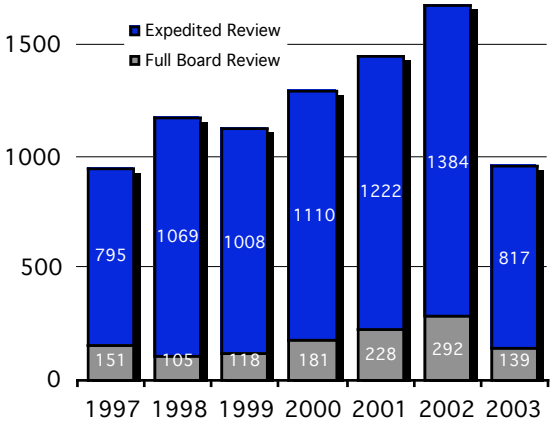
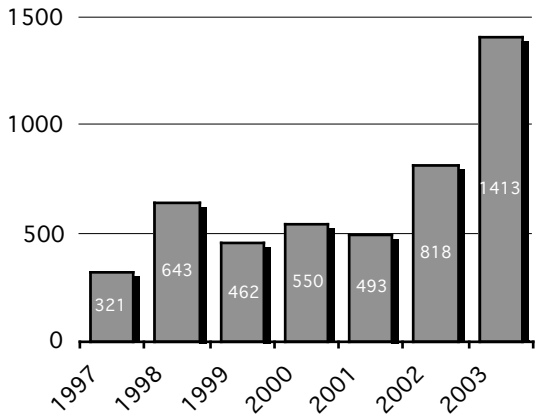


Figure 4: Serious Adverse Event (SAE) reports processed.



Project Disposition

Figure 5: Disposition of Full Board review of new projects in 2003 (N=302).

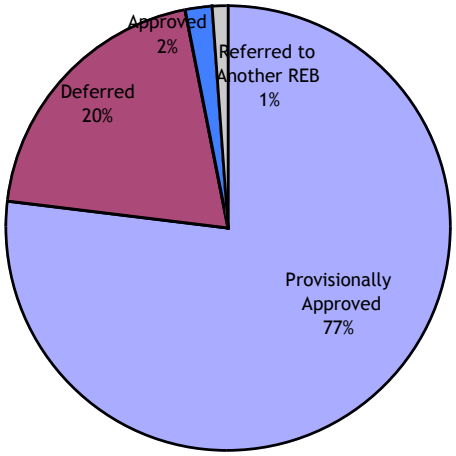


Figure 6: Disposition of Expedited review of new projects in 2003 (N=275).

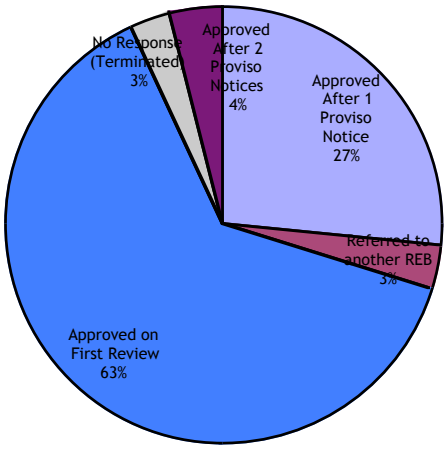


Figure 7: Disposition of Provisionally Approved new Full Board projects in 2003 (N=233).

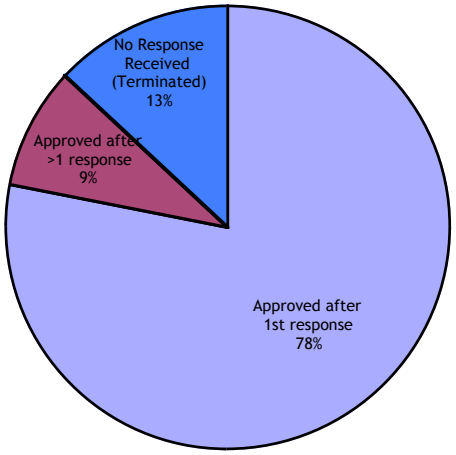


Figure 8: Disposition of Deferred new Full Board projects in 2003 (N=61).

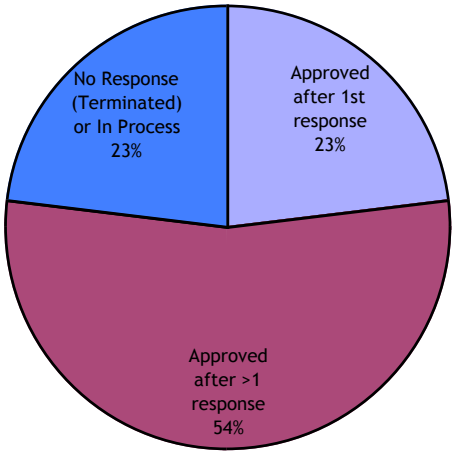
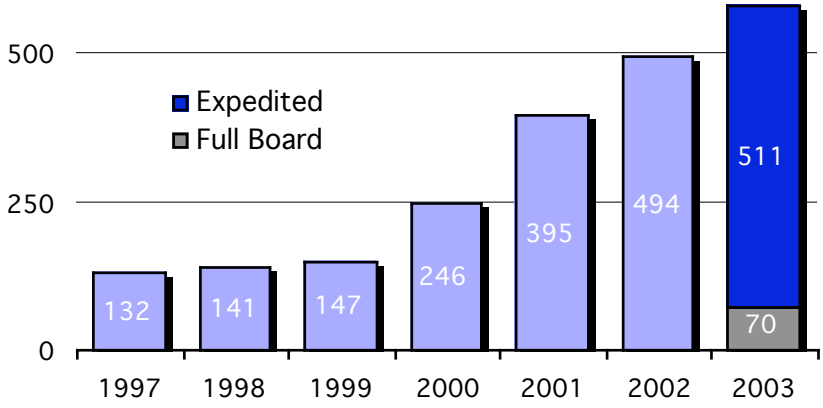


Figure 9: Approved applications for Annual Renewal



Timelines

All times are *median* number of *calendar days* (includes weekend days).

Figure 10: Days from CREB meeting to first Notice of Ethical Review for Full Board applications.

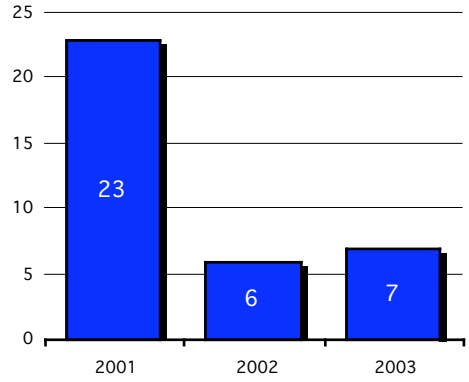


Figure 11: Days to approval for Full Board reviewed applications with 1 Notice of Ethical Review/proviso (60% of all new applications). *(Note: Most of these days are "investigator days", not "REB days".)*

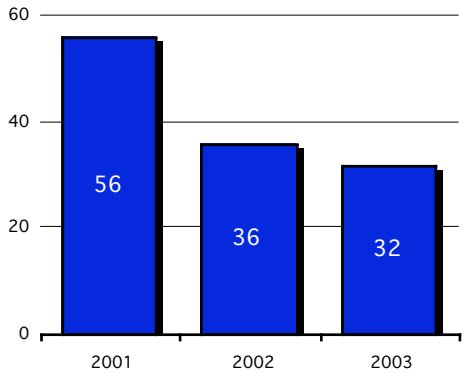
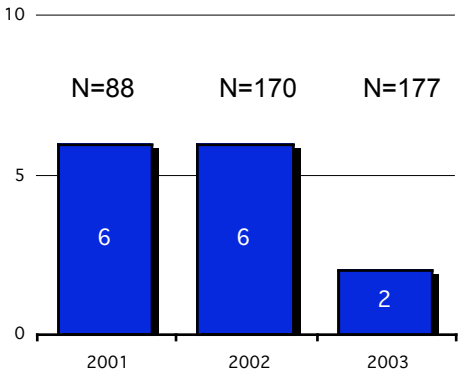


Figure 12: Days from submission to approval of Expedited new applications when no provisos issued (64% of all expedited applications).



In 2003…

Proportion of projects undergoing Full Board review meeting the CREB's target of having a Notice of Ethical Review issued within 7 calendar days of the meeting: **66%** (same as 2002)

Proportion of projects undergoing Expedited review meeting the CREB's target of having a Notice of Ethical Review issued within 7 calendar days of receipt: **72%** (68% in 2002)

Ethical Standards and Services to Investigators

NCEHR Site Evaluation

The CREB voluntarily requested and underwent a site visit by the National Council on Ethics in Human Research (NCEHR) in October 2003. NCEHR's objectives for such visits are:

- To discuss the process of ethics review with the responsible people, and to identify and exchange information on relevant issues with them;
- To identify issues of concern in the policy area of research ethics review;
- To identify administrative issues related to research review;
- To identify and discuss issues related to the implementation of policies and guidelines, including the Tri-Council Policy Statement, the Good Clinical Practice Guidelines, and international guidelines;
- To identify means by which the quality of ethics review and participant protection may be enhanced;

UBC VP Research, Dr. Indira Samarasekera received the final report of the visit, and it is available upon request from her office.

The recommendations of the NCEHR site visit team were:

- Deans and Department Heads should reflect on the importance of the work of the CREB in the general research enterprise. Without an effective system of protection for human subjects of research, in which the role of the REB is paramount, the entire research enterprise in the Faculty of Medicine would be in peril. Deans and department heads should follow the lead established by the VP Research and develop arrangements that will encourage faculty to take appointments on the CREB.

- The University should consider establishing a link between the REBs and the UBC Board of Governors, so that the ultimate responsibility is seen to lie with the UBC Board of Governors. The REBs could direct their annual reports to an existing, or special, committee of the Board. The existing Learning and Research Committee on the board of governors could be a suitable recipient of reports on the ethics review process.

- In order to decrease the workload for individual members and to assure the recruitment of new members, it may be useful to consider dividing the CREB into 2 panels which would be headed by the same chair person and work in parallel using the same policies and procedures. Distribution of protocols in such a case could be done with consideration of expertise available on each panel.

- CREB preferably should start the next budget year with a balanced budget, the current deficit made up by general research funds of the university.

- It would be useful to enhance the recognition of academic staff serving the CREB by their own individual department and by the university.

- In order to enhance the transparency of the review process, the REB could formally adopt and annunciate a policy inviting researchers to be present and participate when protocols are to be discussed.

- A responsibility for ongoing review or audit should be established in discussion between the university and affiliated institutions in order to assure that this process will be in place in the near future.

- Research protocols registered as ongoing, need to be reviewed in order to establish which in effect, are still active protocols and which ought to be formally closed.

- CREB should recognize the support of the BREB Manager who provides assistance to the patient access telephone line of the CREB.

- The plan to place the entire review process online needs to be accelerated and given full support in order to satisfy the researchers desire for increased transparency and the removal of the 'bottle neck' in handling papers and to delays in the documentation. This platform should be user friendly and easy to navigate.

- Many departments of the Faculty of Medicine have not contributed members to CREB. These departments should be encouraged to consider arranging for reimbursement of any financial loss for individuals who might be asked to serve on the CREB, as the department of dermatology may do if they provide members for the REB. Such arrangements should assure that the faculty members who derive income from fees for service be compensated for lost income engaged in CREB work.

Guidance Notes

Numerous updates, clarifications, and additions to the CREB's Guidance Notes were made throughout 2003 in an effort to assist investigators in meeting current standards for ethical conduct of research and to increase the efficiency of ethical review.

The CREB's Guidance Notes & Model Consent are available at:
http://www.ors.ubc.ca/ethics/clinical/

Reciprocal Review between UBC Research Ethics Boards

Since some research is conducted at multiple sites within the UBC system (e.g. at two different hospitals under two different UBC REB jurisdictions), the UBC REBs formalized a policy permitting investigators to submit to the UBC REB of their choice for initial review and the REBs subsequently organize an

expedited review of the project by the corresponding REB for the other site(s). This arrangement has mainly been exercised between the UBC CREB and the UBC/Providence Health Care REB.

Refer for more details to:
http://www.ors.ubc.ca/ethics/forms/GNinitialapp.htm#What1.2

Emergency Ethical Review for Time Sensitive Studies

The CREB formalized its policy and procedures for providing emergency expedited review of applications involving research of an extremely time-sensitive nature, such as infectious disease outbreaks.

Details of the policy and procedures can be obtained by contacting the CREB office.

HIPAA Guidance

In April 2003, the United States' HIPAA Privacy Rule governing health information collection and transmission came into force. This resulted in significant uncertainty and concern about how this legislation might affect research being conducted in Canada by US-based sponsors.

The UBC CREB and UBC/Providence Health Care REBs collaborated in preparing and issuing guidance to UBC investigators interacting with sponsors about this issue.

The guidance issued on 2MAY03 is available at:
http://www.ors.ubc.ca/ethics/clinical/c-forms.htm

Stem Cell Research and Ethical Review

To assist UBC investigators in complying with CIHRs requirement that any research involving stem cells undergo REB review (regardless of whether humans are involved as research subjects), the CREB collaborated with the UBC/BCCA REB in developing and communicating a procedure for these reviews.

The guidance issued is available at:
http://www.ors.ubc.ca/ethics/forms/GNinitialapp.htm#Guide2.1

Education

Throughout 2003 and the first quarter of 2004, 8 education sessions were held at Vancouver Hospital, Children's and Women's Hospital, G.F. Strong Rehabilitation Centre, and UBC to update the research community on the CREB's policies as well as its requirements for completing application forms and formulating consent forms. These sessions have been provided by the CREB Manager, Associate Director, Research Ethics, and Heather Abbey, SAE reviewer.

In April 2003, the Chair provided the first-ever "CREB Update" to UBC researchers and coordinators to talk about the CREB's activities since 2001 and to receive feedback. This was followed by the first-ever "CREB Open House", which allowed researchers to meet the members of the CREB and discuss common concerns. Both events were extremely well attended.

Financial Statement for Fiscal Year 2003-2004

Revenue	*Projected*	*Actual*
Fees Collected[1]	$ 252,000.00	$272,328.77
Fees Outstanding as of 31MAR2004	0.00	$ 37,692.00
Total Revenue	$ 252,000.00	$310,020.77

Expenses	*Projected*	*Actual*
Administrative staff salaries[2]	$ 214,807.00	$206,542.89
Direct Committee Expenses	$ 61,806.00	$ 59,350.52
Education (attendance at conferences/workshops + travel)[3]	$ 7,000.00	$ 7,999.50
Office Expenses	$ 42,000.00	$ 24,681.96
Total Expenses	$325,613.00	$298,574.87

[1] Fees are collected for industry-sponsored applications only. Projected revenue was based on a fee of $1750.00 per new application. This fee was increased to $3000.00 per new application as of 01SEP03. There were 141 industry sponsored studies for fiscal year 2003-2004. The fees collected take into account refunds for 4 withdrawn studies.
[2] Includes wages + benefits for full time and casual staff, wages for serious adverse event reviewers, and honoraria for workshop participation.
[3] Includes conference attendances by CREB members and staff.

The direct cost for ongoing administrative operations of the CREB office, including committee expenses, are recovered entirely by fees collected from industrial sponsors of research. Initially set at $1750.00 per new application, this fee was increased to $3000.00 per new application as of September 2003.

The CREB acknowledges the ongoing "in kind" support it receives from the Vancouver Coastal Health Research Institute through the provision of office and meeting space.

In addition, as one of the UBC's Research Ethics Boards, the CREB is supported by the university's continued funding of Margaret Shotter (Associate Director, Research Ethics), the development and maintenance of information technology systems and "once only" funding of initial CREB office set up costs.

Outlook & Challenges for 2004

The CREB will continue to enhance the ethical oversight of research at UBC in 2004.

The primary objectives of any changes made will continue to be:

- improve the quality of subject protection provided by the CREB
- maintain the integrity and independence of the process
- improve the efficiency of ethical oversight of research
- maintain the transparency of the process

CREB Membership

The ability to provide ethical review and oversight is dependent on the participation of individuals with clinical and/or research experience in the ethical review process. Identifying, recruiting, and maintaining members on the CREB remains a challenge for several reasons. Both external review groups who have evaluated UBC's ethical oversight operations recently have commented on the lack of formal recognition and support of REB members by the faculties and departments whom they serve. The CREB remains hopeful that support and recognition of REB service will increase in the very near future. This is essential for UBC to maintain or enhance its standing in the increasingly competitive clinical research environment in North America.

In the meantime, the CREB will continue to strive to support its members as much as possible.

Enhanced Continuing Review of Ongoing Research

The CREB is hopeful that an enhanced process of Continuing Review of ongoing research at UBC will be implemented in 2004. Having staff dedicated to performing audits of ongoing projects will close a substantial gap in the research oversight process at UBC and will bring UBC in line with other major research institutions in Canada. Research subjects will benefit from knowing that UBC has such a process in place and that their interests are being actively protected by the University and its affiliated institutions. The CREB will benefit from receiving reports from these reviewers and assurance of subject protection. Researchers will benefit by having an opportunity to prepare for these reviews, which at other institutions has been shown to enhance success with external reviews (e.g. Health Canada, NIH, FDA, sponsors).

Tissue Banks and Research

The UBC community must continue to strive to improve its compliance with the Tri-Council Policy Statement and provincial and federal privacy legislation related to collection and subsequent use of human tissue for research. In 2003 the CREB became actively involved in several instances where improved compliance was required and will continue to work with investigators to ensure that the expectations of research subjects, UBC and its affiliated institutions, and prevailing legislation and guidance documents in this area are met.

Financial Conflicts of Interest in Research

The CREB encountered several cases of individual financial conflicts of interest in research during 2003 and frequently faces the reality that UBC has no contemporary policy on this issue. In the absence of such a policy, the CREB is guided by the Association of American Medical Colleges policy and guidelines (of which UBC is a member institution). The CREB has created a financial declaration as part of the application for ethical review, and includes basic budgetary scrutiny in the review process.

The CREB will continue to manage detected individual financial conflicts of interest on a case-by-case basis using external policy documents until UBC establishes a policy to guide investigators and the REBs.

Privacy Issues

Several levels of privacy legislation are in force in British Columbia which affect public and private organizations differently with respect to research. The addition of the federal PIPEDA act in January 2004 has added to the uncertainty in the research, ethics, and legal communities about what practices and procedures are required of researchers. There is currently no consensus in Canada about how recent changes in privacy legislation affect research.

The CREB has robust policies designed to protect the privacy of research subjects and the confidentiality of information collected from them in the course of conducting research. We will continue to refine those policies as the legislative and ethical requirements become clearer. The CREB will continue to actively participate in the process of clarification through education sessions and focused inquiries with relevant stakeholders and advisors.

Research Ethics Education

Ongoing education activities are planned with Vancouver Coastal Heath Authority Research Services and Children's & Women's Hospital to increase awareness of research ethics issues in the research community.

Electronic Application and Review System

The CREB remains hopeful that the planned implementation of an electronic submission and review process for researchers by the Office of Research Services proceeds and encompasses the CREB as soon as possible.