ANNUAL REPORT

of the

UNIVERSITY OF BRITISH COLUMBIA
CLINICAL RESEARCH ETHICS BOARD

Issued June 2003

by

Dr. Peter Loewen, Chair, UBC Clinical Research Ethics Board
Ms. Susan Chunick, Manager, UBC Clinical Research Ethics Board

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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 are maintained 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.

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 at Vancouver Hospital & Health Sciences Center (all sites & affiliated research institutes), BC's Children's & Women's Hospital (and affiliated research institutes), and until May 2003, the BC Cancer Agency (all sites).

To our knowledge, this document is the first annual report issued by the CREB since its inception. Providing 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 from January 2002 through April 2003. Historical data and comparisons with 2001'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).

2001 External Review Recommendations & Responses

In 2001, at the request of UBC's Vice President, Research, Dr. Indira Samarasekera, the CREB underwent an external review of its operations. The report was issued on August 1, 2001.[1]

Eight recommendations were made. They are paraphrased below, with the addition of the CREBs perspective on how these recommendations have been addressed:

1. **Revise the process of review such that two qualified CREB members review the full protocol of all submissions.**

   Implemented in September 2001.

2. **Appoint an Ethicist to the CREB.**

   Implemented in November 2001.

3. **The CREB should continue to review all biomedical research done by UBC-affiliated investigators, and individual institutions should do independent scientific**

[1] Kinsella TD, Keyserlingk EW. Review of The Clinical Research Ethics Board, University of British Columbia: Final Report. August 1, 2001. On file.

reviews of all submissions, with reports provided to the CREB.

BC Children's and Women's Hospital performs independent scientific reviews in parallel with CREB review. BCCA performed internal scientific reviews prior to CREB submission until May 2003, when their committee was merged with the new BCCA REB. The other organizations served by the CREB (e.g. Vancouver Hospital & Health Sciences Center) have not implemented systematic processes for scientific review. For a large number of industry-funded studies, the CREB acts as the only independent scientific review panel for the project.

4. **Clarify the role of the Providence Health Care REB and its relationship to the University.**

   This issue is not directly related to the CREB. However, since January 2003 the CREB and the PHC-REB have substantially harmonized our application forms and guidance issued to investigators. Cooperation between these two REBs is at an all-time high.

5. **Reform the CREB's recruitment and membership processes in the following ways: (a) expand it; (b) make participation by relevant departments mandatory; (c) have term limits; (d) give more recognition for CREB service; (e) consider payment of fees to members.**

   Thanks to Margaret Shotter (Associate Director of Research Ethics, ORS) and some financial commitment of the University, (a), (c), and (e) have been accomplished, although recruitment is an ongoing challenge (see Membership, page 5). Recommendations (b) and (d) have not been implemented at this time.

6. **Provide a more rapid process of review, more respectful working conditions, additional administrative personnel, and more adequate working space for the CREB support staff.**

   The process of review has been substantially expedited (see Statistics, page 6). Additional personnel and workspace have been secured. (see Operations, page 5).

7. **The CREB should report directly to the Vice President Research of UBC and not to the Office of Research Services.**

   The CREB now reports directly to the Vice President Research of UBC, although operational and resource issues continue to be directed to the Office of Research Services.

8. **The CREB should be an integral participant in research education within the University, affiliated institutions, and the University should strongly support these efforts with funding and other resources.**

   No framework for how the CREB should provide research education to these organizations has been established. The CREB Manager and Chair have provided several education sessions by invitation at UBC affiliated institutions (see Education, page 10)

Membership

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

Name	Roles	UBC Affiliation(s)
Peter Loewen, Pharm.D.	Chair	VHHSC, UBC Pharmaceutical Sciences
Alain Gagnon, M.D.	Associate Chair	C&WH, UBC Medicine (Obstetrics & Gynecology)
John Russell, Ph.D.	Ethicist	UBC (Philosophy)
Penny Washington, LLB	Lawyer	none
Karen Low Ah Kee, CMA	Lay Member	none
Lynn Beattie, M.D.	Primary Reviewer	VHHSC, UBC Medicine (Geriatrics)
Stephen Hoption-Cann, Ph.D	Primary Reviewer	UBC Health Care & Epidemiology
Jolanda Cibere, M.D. Barry Koehler, 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 (Molecular Cytogenetics)
Caroline Lohrisch, M.D.	Primary Reviewer	BCCA, UBC Medicine (Oncology)
James McCormack, Ph.D	Primary Reviewer	UBC Pharmaceutical Sciences
Pratibha Reebye, M.D.	Primary Reviewer	C&WH, UBC Medicine (Psychiatry)
Ann Hilton, RN, Ph.D	Reviewer	UBC (Nursing)
Laurie Smith, B.Sc., R.N.	Reviewer	VHHSC (ICU Research)
Bill Sullivan, Q.C.	Lawyer	none

2002 also saw the departure of several longstanding members of the CREB, including Dr. Alan Hannam (UBC Dentistry), Dr. Joan Bottorf (UBC Nursing), Ms. Brenda Mercier (VHHSC Cardiology Research) and Dr. Richard Klasa (BCCA). The Board and the University are grateful and indebted to these individuals for their valuable service to the Board and the UBC research community.

The Board was pleased at the appointment in July 2002 of Dr. Alain Gagnon as Associate Chair, who now shares critical office-related duties with the Chair, and serves as a backup to the Chair for meetings and other matters.

It is a challenge to sustain the membership needs of the Board to comply with Tri-Council Policy requirements and to maintain a sufficient size and breadth of expertise of the membership. The Board has benefited since Ms. Margaret Shotter was installed as UBC's Associate Director of Research Ethics from her efforts to identify and recruit suitable members to serve on the CREB. To increase the membership of the Boards and ensure continuity of expertise, there is a need to recruit several new members every year. Discussions are taking place with the Faculty of Medicine to create a nomination process to ensure ongoing representation from Departments and Institutes

During 2002, UBC's Vice President, Research implemented term limits for CREB members. Members are normally appointed for a term of 3 years, which is renewable once. A defined term benefits members by providing a guideline as to what is an expected duration of service and allows an amicable departure after it has elapsed. It benefits the CREB operationally by allowing sufficient time for members to become proficient in the complexities of ethical review, which typically takes about one year.

Operations

In December 2001, the CREB administrative office was relocated from UBC campus to a new satellite location at Vancouver Hospital in order to improve the access of investigators to ethics staff. At the same time, a new Manager, Susan Chunick, was hired to administer the operations of the CREB. In addition to the staffing provided by Catherine Sutherland, Erin Desjardine was hired into a new full time position in September 2002. Both Catherine and Erin provide the clerical support required to process the submissions for ethical review of new studies as well as those required for amendments and renewal of previously approved studies. Two nurse reviewers, Eleanor Fink and Heather Abbey were engaged on a part time basis to carry out the review of serious and unexpected adverse events (SAEs).

Statistics

As of April 2003, the CREB is responsible for the oversight of **4,664** ongoing research projects.

Workload

In total, the CREB handled 3,369 requests for ethical review in 2002. A breakdown of these requests is depicted in Figure 1.

Figure 1: Requests for ethical review in 2002 (N=3369)

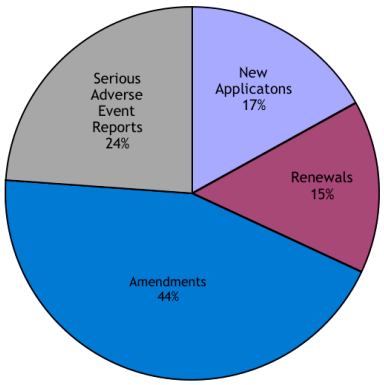


Figure 2: New project applications

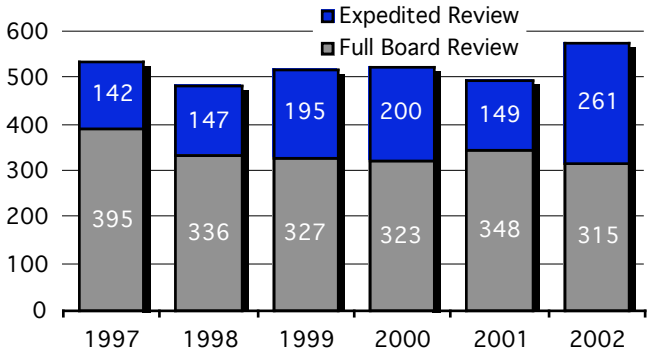


Figure 3: Amendments processed

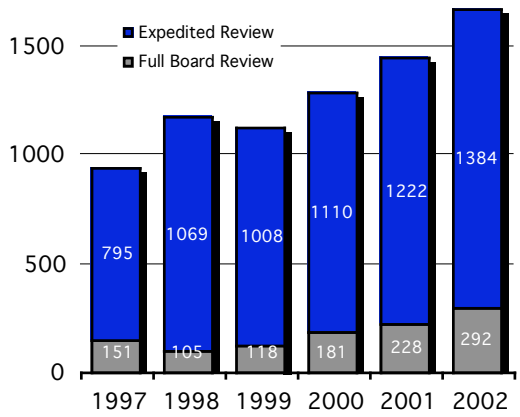
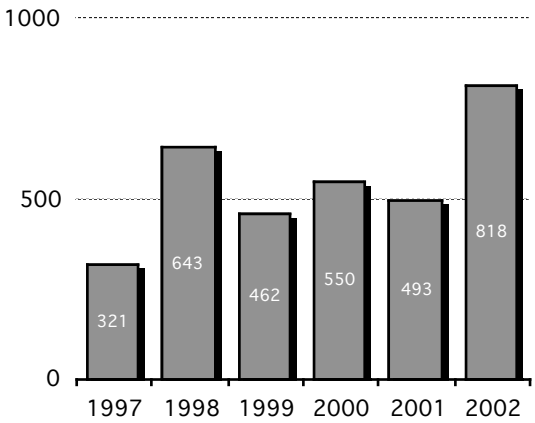


Figure 4: Serious Adverse Event (SAE) reports processed



Project Disposition

Figure 5: Disposition of Full Board review of new projects in 2002 (N=315)

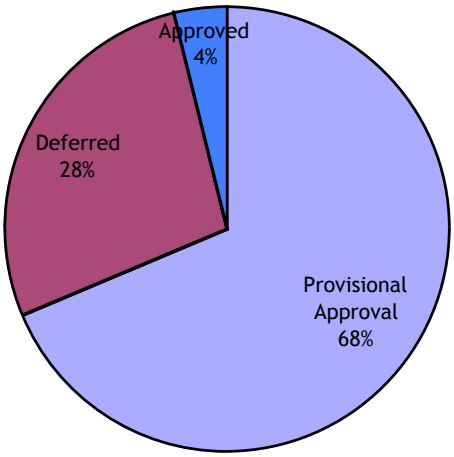


Figure 6: Disposition of Expedited review of new projects in 2002 (N=261)

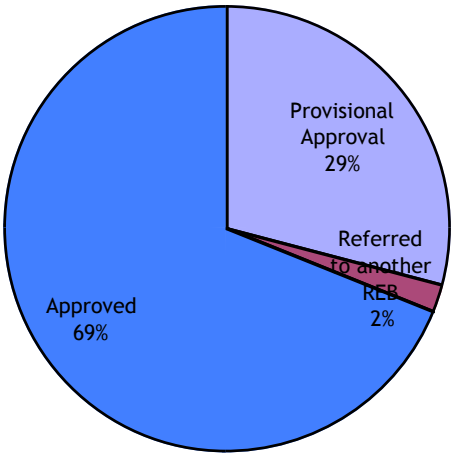


Figure 7: Disposition of Provisionally Approved new projects in 2002 (N=216)

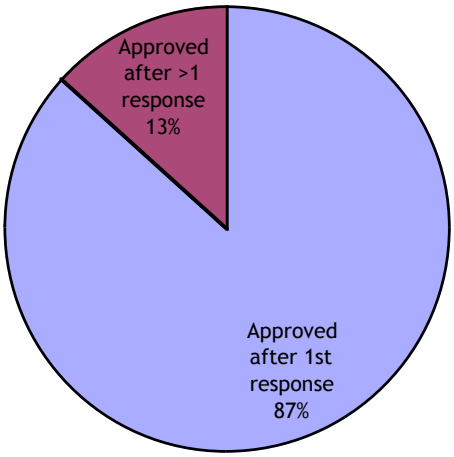


Figure 8: Disposition of Deferred new projects in 2002 (N=87)

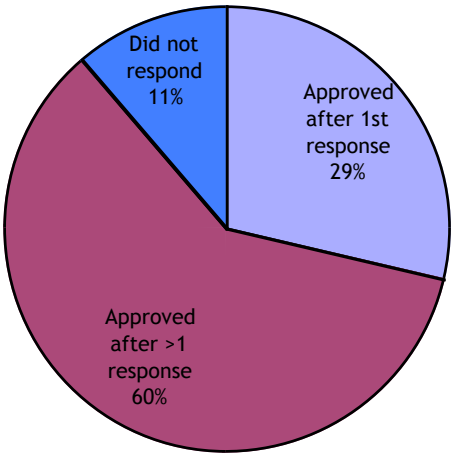
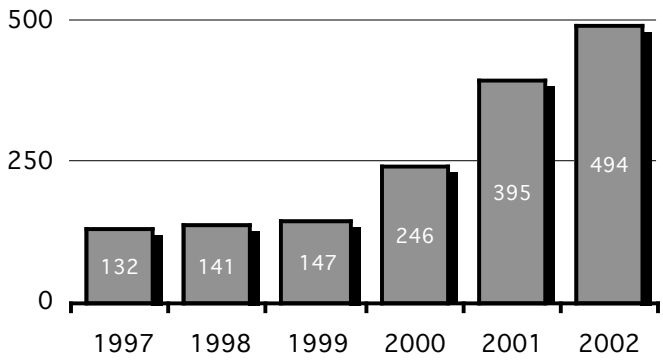


Figure 9: Applications for Annual Renewal



Timelines

All times are *median* number of *calendar days*, which includes weekend days.

Figure 10: Days from CREB meeting to first Notice of Ethical Review for Full Board applications *(Note: Deadline for submission is 10 calendar days prior to each meeting.)*

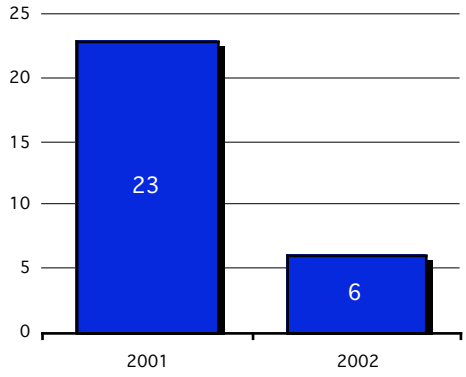


Figure 11: Total days to approval for Full Board reviewed applications with 1 Notice of Ethical Review/proviso (60% of all new applications) *(Note: Most of these days are "investigator days", not "REB days".)*

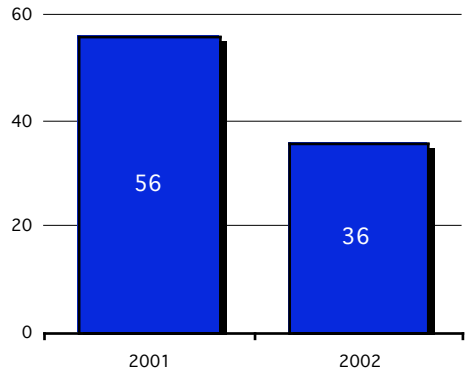
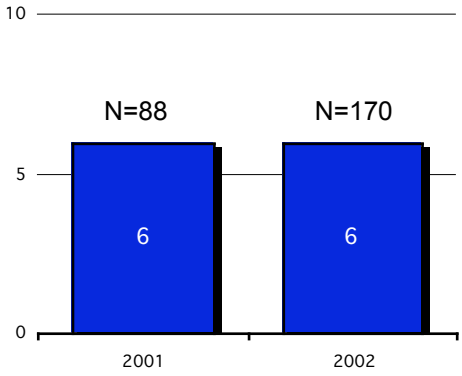


Figure 12: Median days from receipt to approval of Expedited new applications when no provisos issued (69% of all expedited applications).



In 2002…

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%**

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: **68%**

In January 2002, the CREB office streamlined the process for notifying investigators of modifications requested by the CREB as a result of a Full Board or an Expedited review. All written comments from a Full Board review are documented by CREB staff for final approval by the Chair within three calendar days from the board meeting. This has allowed the final notification (Notice of Ethical Review) to be emailed to the study investigators within 7 calendar days (5 business days). In addition, Expedited review of new studies on a weekly basis by the CREB Chair has ensured that Notices of Ethical Review can be emailed to investigators within 7 calendar days from receipt of the study.

More recently, the CREB office has encouraged investigators to email responses to Notices of Ethical Review directly to the CREB office in order to decrease the delay between notice and final approval.

Ethical Standards and Services to Investigators

Guidance Notes

In 2003 and 2003, the CREB undertook a major revision and clarification of its Guidance Notes to Investigators. This comprehensive full online "living document" is intended to fulfill the need expressed by many investigators to have a clear set of the CREB's *expectations* for the wide variety of research ethics issues encountered in the process of application and ongoing review. It also enhances the CREB's ability to meet another frequently cited investigator request for *consistency* between decisions made on projects with similar ethical issues. Accompanying the Guidance Notes is a newly generated model consent form which provides an explicit template for an acceptable consent form for subject participation in research. Both of these documents are based on the most current national and international standards, policies, and legal requirements for the ethical conduct of human subjects research.

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

Application Forms

New forms for submitting annual renewals, amendments and serious and unexpected adverse events were designed. Accompanying each form is a set of Guidance Notes that instruct investigators on how the forms should be completed and on the submission criteria for each. Investigators are now notified a minimum of one month in advance of an upcoming renewal so that application can be submitted in a timely manner.

Policies

The CREB undertook to create or update several of its policies during 2002. The most notable of these were:

- Creation of Canada's first comprehensive policy and guidance on enrollment of incompetent subjects in research. This meets the needs of investigators conducting research on subjects who cannot provide consent on their behalf, regardless of their age. This policy contains the only explicit guidance that we are aware of on creation of "Assent" documents for incompetent subjects.

- Creation of a policy on compensation for injury which prohibits sponsors from using language which could be construed as asking subjects to waive their legal rights to compensation of any type should they be harmed as a result of participating in a research project.

- Creation of a policy and standard wording informing subjects in pharmaceutical trials of what might happen after the study is completed with respect to their ability to obtain the drug.

- Creation of a policy forbidding mandatory donation of tissue for unspecified future research uses as a requirement for participation in a therapeutic trial.

- Implementation of a comprehensive Conflict of Interest declaration as part of the application process. By default, the CREB is currently acting as a Conflict of Interest Committee in managing financial conflicts of interest according to the widely adopted Association of American Medical Colleges Policy on Individual Financial Conflicts of Interest in Research.[2]

[2] Association of American Medical Colleges. Protecting Subjects, Preserving Trust, Promoting Progress-- Policy and Guidelines for the Oversight of Individual Financial Interests in Human Subjects Research. December 2001. www.aamc.org

In creating and implementing these policies, the CREB undertook a collaborative and consultative approach, giving the research community several weeks to review and provide feedback before approval, and a staged implementation timeline over several months so researchers had sufficient time to incorporate these changes into their research and avoid creating approval delays.

Education

Throughout 2002 and the first quarter of 2003, **seven** education sessions were held at Vancouver Hospital, Children's and Women's Hospital and the Arthritis Research Centre to update the research community on the CREB's policies as well as its requirements for completing application forms and formulating consent forms.

In addition, in April 2003, the Chair provided the first-ever "CREB Update" to the Vancouver Hospital research community to update them on the CREB 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.

Vancouver Coastal Heath Authority Research Services has been active in involving the CREB in its research education efforts in 2002-03.

Outlook for 2003

The CREB will continue to enhance the ethical oversight process at UBC throughout 2003/04.

The primary objectives of these changes continue to be:

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

Some of the initiatives planned to achieve these objectives are described below.

The CREB plans to implement an internal "pre-review" process whereby new applications will be evaluated for technical issues and adherence to CREB policies by a trained CREB Manager. This is expected to greatly enhance the consistency, quality and efficiency of the overall review process and will allow REB members to focus more on the ethical issues that arise. This, in turn, is expected to improve CREB membership recruitment and retention efforts.

The CREB is hopeful that an enhanced process of Continuing Review of ongoing research at UBC will be implemented in 2003. 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).

The CREB plans to invite the National Council on Ethics in Human Research (NCEHR) to perform a voluntary site visit/accreditation during 2003-04.

The UBC VP Research gave approval for the BC Cancer Agency to begin operation of its own REB in May 2003, under the delegated authority of UBC Policy #89. The CREB will be affected in the form of a reduction in new submissions from BCCA. Existing projects will continue to be overseen until completion by the CREB.

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