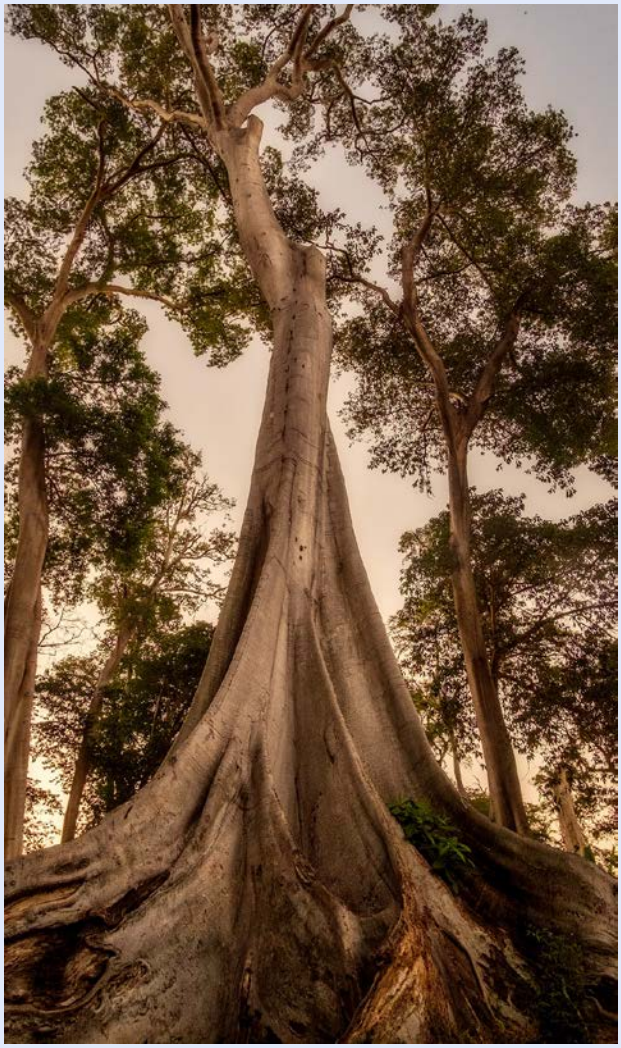
Fraser Health Research Ethics Board



Annual Report

April 1, 2016
to
March 31, 2017

FRASER HEALTH RESEARCH ETHICS BOARD
ANNUAL REPORT

APRIL 1ST 2017 TO MARCH 31ST 2017

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ANNUAL REPORT

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1. INTRODUCTION

The protection of the rights and safety of human research participants who voluntarily agree to participate in research is the keystone of any research study grounded in the principles of scientific validity and reliability. The integrity of the research process itself is dependent on the collection of data that is free from bias and thus must rely on the free and willing participation of research participants. Protecting the rights and safety of these participants is the fundamental purpose of the Fraser Health Authority's (Fraser Health) Research Ethics Board (FHREB); this oversight in turn protects the integrity of the research process.

The FHREB strives to render thoughtful, fair and reasonable decisions that are based on the ethical principles of beneficence, distributive justice, respect and non-maleficence, and in so doing has established relationships with Fraser Health researchers that are based on trust and mutual respect. The outcome of the FHREB's due diligence in carrying out its review of new and continuing research studies is an ongoing improvement in the overall quality of the research conducted in Fraser Health, in addition to researchers' knowledge about the requirements for conducting ethical research.

Over the past year, the FHREB continued to clarify its standard requirements for research submissions, kept abreast of national and provincial changes in guidelines and legislation that affects decisions regarding the ethical approval of research studies, provided ongoing education and continued to be responsive to the inquiries of our research community.

This report is one aspect of the FHREB's effort to maintain the transparency and accountability of the research ethics review process in Fraser Health. The FHREB is very pleased to present its eleventh annual report for the 2016-2017 fiscal year. Any questions about this report may be directed to the board Co-Chairs, Dr. Stephen Pearce and Professor Lindsay Meredith.

2. THE FRASER HEALTH RESEARCH ETHICS BOARD

2.1 Composition of the Board

As of the end of this fiscal year, the FHREB included 11 full time members, two of which shared the role of legal representative. The credentials, roles, affiliation with Fraser Health and terms of office for each member are described in Table 1.

Table 1: 2016-2017 FHREB Membership List

	VOTING MEMBER NAME FIRST LAST	HIGHEST DEGREES EARNED	PRIMARY SCIENTIFIC OR NONSCIENTIFIC SPECIALTY	‡TERM	AFFILIATION WITH INSTITUTION
1	*Dr. Stephen Pearce Male / Canadian Citizen	MD, FRCPC	Cardiology	June 26, 2017 to June 26, 2018	Yes
2	Dr. Allan Belzberg Male / Canadian Citizen	MD, FRCPC	Nuclear Medicine	March 10, 2017 to March 10, 2020	Yes
3	*Prof. Lindsay Meredith Male / Canadian Citizen	PhD	Ethics	January 29, 2017 to September 29, 2017	No
4	** Anu K. Sandhu Female/Canadian Citizen	LLB	Law	June 03, 2015 to June 03, 2018	No
5	** Tamsin Miley Female / Canadian Citizen	LLB	Law	March 08, 2017 to March 08, 2020	No
6	MaryEllen Gillan Female / Canadian Citizen	MA	Community Member	January 29, 2017 to September 29, 2017	No
7	Zhenyi Li Male / Canadian Citizen	PhD	Community Member	March 08, 2017 to March 08, 2020	No
9	Samar Hejazi Female/Canadian Citizen	PhD	Epidemiologist	November 06, 2014 to November 06, 2017	Yes
10	Kim Macfarlane Female / Canadian Citizen	BSN, MA	Tertiary Critical Care	November 22, 2016 to November 22, 2019	No
11	Dr. Jeff Kerrie Male/Canadian Citizen	MD	Internal Medicine, Ethics	June 23, 2015 to June 23, 2018	Yes

* Co-chair
** Alternating members
‡ Date of Appointment Letter
Ex officio: Susan Chunick, Director, Department of Evaluation and Research Services

2.2 Responsibilities of the FHREB

The FHREB is responsible for review, approval and ongoing oversight of all research studies involving humans conducted by Fraser Health researchers at all Fraser Health sites. These researchers include Fraser Health employees, privileged physicians, affiliated academic researchers and any University of British Columbia medical student or resident who is completing research in the health authority as part of their academic requirements.

The FHREB operates according to the principles and standards detailed in the Government of Canada's national standard for research ethics, the "Tri-council Policy Statement: Ethical Conduct for Research Involving Humans" (TCPS2)[1]. In addition, the FHREB complies with

[1] Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada. Tri-council Policy December 2010 and amendments (December 2014). http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/Default/

Health Canada regulations and guidelines concerning the ethical review of clinical drug[2], device[3] and natural health product[4] trials, and with United States (U.S.) government legislation governing the ethical review of studies funded by their government agencies and/or regulated by the U.S. Food and Drug Administration[5]. The FHREB ensures that any other Canadian and provincial legislation that is applicable to the conduct of research by a public institution is adhered to by Fraser Health researchers.

In addition, FHREB members are specifically accountable for ensuring that the requirements of the Fraser Health policy "The Ethical Conduct of Research and Other Studies Involving Human Subjects" are met which includes responsibility for determining the scientific and ethical integrity of each individual research study.[6] Key responsibilities include ensuring that:

1) the study is of value and that the research methodology is sufficient to answer the research question;
2) all ethical norms related to recruitment of study participants, consent and study procedures, safety management and conflict of interest are complied with by the researchers, and that;
3) consent forms and data collection instruments comply with FHREB standards.

An additional role is assigned the FHREB Co-Chairs who conduct the "delegated review" of new studies that meet the criteria for minimal risk as defined by the TCPS2 2014 and FHREB policy. The delegated review process is also used to review:

1) applications for amendment and renewal of previously approved studies that do not require full board review;
2) local and international serious adverse events and protocol deviations;
3) principal investigator responses to requests for modifications arising from full board or delegated review, and;
4) any other study-related correspondence.

Please refer to Appendices 1 and 2 for terms of reference for the FHREB members and FHREB Co-Chairs.

2.3 Conflict of Interest

All FHREB members are required to complete a conflict of interest disclosure form (see Appendix 3) on an annual basis to ensure that any associations with industry sponsors of research or research team members are made known. Any members found to have a conflict of interest are excused from the review of the applicable research study.

2.4 FHREB Education

The annual education session for the FHREB was held on March 04, 2017 for this fiscal year. This session included a presentation by Dr. Nigel Fisher, the previous Regional Department Head/Program Medical Director for Mental Health and Substance Use on the current state of evidence and ethics of research when a risk to research participants is experiencing suicidal

[2] September 1, 2001. Regulations Amending the Food and Drug Act Regulations (1024 - Clinical trials) at http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/clini/cta_documents-eng.php
[3] Part 3 of the Medical Devices Regulations at http://www.hc-sc.gc.ca/dhp-mps/md-im/index-eng.php
[4] Part 4 of the Natural Health Product Regulations at http://www.hc-sc.gc.ca/dhp-mps/prodnatur/index-eng.php
[5] 45CFR and 21CFR at http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html and http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm
[6] Fraser Health Authority. Revised January 2014. The Ethical Conduct of Research and Other Studies Involving Human Subjects. http://research.fraserhealth.ca/media/Research%20-%20The%20Ethical%20Conduct%20of%20Research%20and%20Other%20Studies%20Involving%20Human%20Subjects.pdf

ideation. The session also included a presentation on the topics of use of tissue for future unspecified research and identifiers on lab reports by Susan Chunick, Director, Department of Evaluation and Research Services.

2.5 FHREB Honoraria

The FHREB members are each paid a monthly honorarium of $450.00 for their participation with $850.00 being paid to the Co-Chairs. This honoraria is funded by the $4,000.00 fee for the ethical review of new applications that are paid by industry sponsors for research studies conducted in Fraser Health.

3. ETHICAL STANDARDS AND SERVICES TO FRASER HEALTH RESEARCHERS

3.1 FHREB Standard Requirements

In order to ensure that the FHREB Guidance Notes, application forms and consent form templates meet current ethical standards and best practices for the disclosure of information by researchers, these documents are reviewed and revised on an ongoing basis. See Appendix 4 for the revision status of each document. All changes were communicated to the Fraser Health research community via posting to the health authority's Department of Evaluation and Research Services web site or in direct email communication to clinical trial researchers when a need to ensure regulatory compliance was involved.

3.2 Access to Fraser Health Data

Working with the Fraser Health Privacy Office, a process was implemented to prioritize the review of time-sensitive clinical trials and to minimize the time needed to review minimal risk research when the data is retained within the Fraser Health network on the 'M' drive. In addition, regular meetings are held with the Privacy Office to ensure mutual understanding of requirements for data access and timelines for review of the data requests. The Privacy Office also clarified that research studies review and approved by the FHREB that utilize survey methodology do not have to be submitted to the Privacy Office.

The board is very grateful to the Fraser Health Privacy Office for their support of these initiatives.

3.3 Standard Operating Procedures

A comprehensive review of the standard operating procedures (SOPs) for the administration of the research ethics process is planned for 2017-2018 in order to ensure that these SOPs are consistent with the national standards developed by the Canadian Association of Research Ethics Boards. The revisions are anticipated to be finalized in the 2017-2018 fiscal year.

3.4 Research Quality Improvement Program

No studies were inspected in the 2016-2017 fiscal year.

3.5 Research Ethics Education

Four workshops that included research ethics content were conducted for Fraser Health researchers and for University of British Columbia Family Practice residents; the latter who are required to conduct a research study during their residency in Fraser Health.

3.6 Research Ethics Web Site

All ethics review procedures, including meeting schedules, and applicable guidances, forms and templates are posted and updated on an ongoing basis to the Department of Evaluation and Research Services web site at http://research.fraserhealth.ca/approvals_%26_ethics/forms_and_guidance_notes/ . A feature of this web site is the Research Study Database at http://research.fraserhealth.ca/knowledge_transfer/fh_research_study_database/database .

Comprehensive information on individual studies including their FHREB approval status is available from this database. In addition, a monthly report of the volume of active studies, those pending approval, funding status and classification by program/area is posted at the beginning of each new month to the department's website.

4. ADMINISTRATIVE OPERATIONS

4.1 Support

Susan Chunick is the Director for the Department of Evaluation and Research Services with responsibility for developing, implementing and monitoring ethical review process standards for Fraser Health, providing policy guidance to the FHREB, ensuring that Fraser Health is compliant with all applicable international, Canadian and provincial legislation, guidelines and standards, and for overseeing the administration of the FHREB. In addition, Ms. Chunick conducts workshops on ethical review and the overall conduct of research for Fraser Health employees and privileged physicians and is a member of the provincial Seniors Leaders' Group for the BC Ethics Harmonization Initiative.

The FHREB office was staffed by one full-time Coordinator (Sara O'Shaughnessy up until May 2016 and Sara Birjandian from May 2016 to April 2017) and two part-time Coordinators, (Ann Elvidge up to May 2016 and Sarah Flann from October to April 2017). Ms. Flann's position was created specifically to support the review of harmonized multi-site studies. The FHREB Coordinators perform the essential function of ensuring that the board runs efficiently and effectively. This includes providing support to individual researchers, processing all applications for and decisions of the full board and delegated review, providing assistance to the FHREB Co-Chairs, participating in developing and presenting workshops on ethical review and updating forms, templates, guidance notes, standard operating procedures and policies. In addition to this and as a strategy to improve and sustain the consistency of ethical review, a pre-review of all initial and renewal applications, consent forms and other documentation submitted for full board and delegated review is conducted to ensure standard requirements are met. This information is included in the study documents sent to the board members prior to their attendance at meetings.

In order to ensure the sustainability of the service provided by the FHREB Co-Chairs, in 2015 the board decided that it would be appropriate to expand the duties of the FHREB Coordinator and in congruence with the TCPS2 2014 to include the review and approval of minimal risk studies for the following types of submissions:

a) new minimal risk studies (input from Co-Chairs/REB members solicited as needed at the discretion of the FHREB Coordinator);
b) responses to modifications (if minor);
c) annual renewal applications that do not require full board review;
d) study close-out applications;

e) minor amendment applications that do not constitute a change in the risk-benefit ratio (addition of study site, submission of new recruitment material, consent form language, i.e. change in FHREB contact information); amendments of a clinical nature would usually require review by the clinical REB Co-Chair, and;
f) acknowledgements of administrative letters, e.g. data safety monitoring board reports.

In addition, the FHREB Coordinators represented the FHREB on the British Columbia Ethics Harmonization Initiative (BCEHI) Advisory Committee.

The FHREB acknowledges the very high standards of effectiveness and efficiency with which both Dr. O'Shaughnessy, PhD, Ms. Birjandian, Ms. Flann and Ms. Elvidge carried out their respective duties in support of Fraser Health research.

4.2 Customer Service

The FHREB office provides timely advice in response to inquiries from Fraser Health researchers and assistance in preparing applications for ethical review and related documentation upon request. These researchers include any Fraser Health employee or privileged physician engaged in research as well as academic researchers who have an affiliation agreement with Fraser Health for research purposes. The standard timeline for response to inquiries is within one business day. There were a total of 245 unique active principal investigators for this fiscal year who were engaged with the FHREB office.

4.3 BC Ethics Harmonization

Under the auspices of and with funding from the Michael Smith Foundation for Health Research and involving the Research Ethics Boards for the University of British Columbia, Simon Fraser University and the University of Victoria as well as those for the Interior, Northern Health, Provincial Health Services and Island Health Authorities, a process has been underway for the past five years to develop models of harmonization for ethical review. This process is called the BC Ethics Harmonization Initiative (BCEHI). In order to offset the 'in-kind' contribution of participation by REB administrators, each REB participating in the initiative received $10,000 annually. As mentioned above, this funding was used to hire Ms. Ann Elvidge up until May 2016 after which direct funding to individual REBs ceased.

The most significant achievement over the past year has been the implementation of the model for review of above minimal risk research which means that representatives from multiple REBs participate at one full board meeting to review the research study in question that is to be implemented at more than one site. In addition, a plan to support the individual requirements of all REBs participating in the BCEHI was initiated with input from our FHREB Coordinator for harmonized studies. This plan will provide a drop down menu on the University of British Columbia's RiSE website for ethics applications that will allow any affiliated researcher to access FHREB specific requirements.

In addition, the FHREB continues to be the board of record for initial and ongoing approval of research studies conducted by the University of British Columbia family practice residents who are required to complete a research study during their residency in Fraser Health.

Overall participation in the BCEHI has helped to increase our understanding of the operations and standards of each participating REB and has established much stronger worker relationships.

4.4 Optimizing Document Management and Workflow

The FHREB office has worked with Corporate Information Services to improve the functionality of the initial ethics application form, with the intention of streamlining workflow processes and eliminating manual data entry into the administrative database (i.e., Access) for research and processing data. Key outputs from this project which are expected to be finalized in 2017-2018 are:

1. redesign of the initial application form for visual clarity;
2. alignment of the fields in the Access database with the initial application form to ensure consistency and enable population of data from the form directly into the database;
3. development of a plan to roll out the new PDF version of the application form in the 2017-2018 fiscal year, and;
4. creation of automatic reminders to principal investigators of the one year requirement for annual renewal.

The addition of a .4FTE Coordinator allowed the delegation of responsibility for the pre-review and administration of all harmonized studies and participation on the BCEHI Advisory Committee to be added to this role.

5. RESEARCH ETHICS BOARD OUTPUT

The following section describes the demand for FHREB review in terms of requests for review, the FHREB workload in terms of the number of reviews conducted, and the efficiency of the review process.

5.1 Demand for Review

All Fraser Health researchers with new studies submit an initial application for ethical review which must be reviewed and receive approval by the FHREB before any research-related procedures can be conducted in the health authority or at any other research sites. The types of studies reviewed include clinical drug and device trials which are carried out by Fraser Health privileged physicians only, other types of clinical trials which investigate different types of therapeutic procedures and a variety of population health and health services research which is carried out across many healthcare disciplines.

Applications for amendments to previously approved studies are also received throughout the year for studies that require changes to the research protocol, consent form(s) or other documentation. All amendments must be approved by the FHREB prior to implementation with the exception of those that require immediate implementation in order to ensure participant safety. Both Health Canada and the U.S. Food and Drug Administration require that the review of amendments for regulated clinical trials that meet prescribed criteria be conducted by a meeting of the full board.

In addition, annual renewal of previously approved studies is mandatory for all studies that are continuing to collect data directly from human participants, secondary data sources and/or tissue banks. Studies funded by the U.S. government and/or those regulated by their Food and Drug Administration must also be reviewed by the full board annually.

Other types of correspondence including notification of study closures or terminations, data safety monitoring board reports and protocol deviations, are acknowledged by the FHREB.

Throughout this fiscal year, 106 requests for initial ethical review were received for review by the FHREB, representing a 20% decrease from the previous fiscal year. The overall demand for review of 515 applications of all types also decreased by 17% compared to the 2015-2016 fiscal year. Figure 1 illustrates the volume of requests for review of all types of applications that were received. Figure 2 and Table 2 compares this distribution with the four previous fiscal years.

Figure 1: Total Requests for Review of All Ethics Applications n=515
April 1, 2016 to March 31, 2017

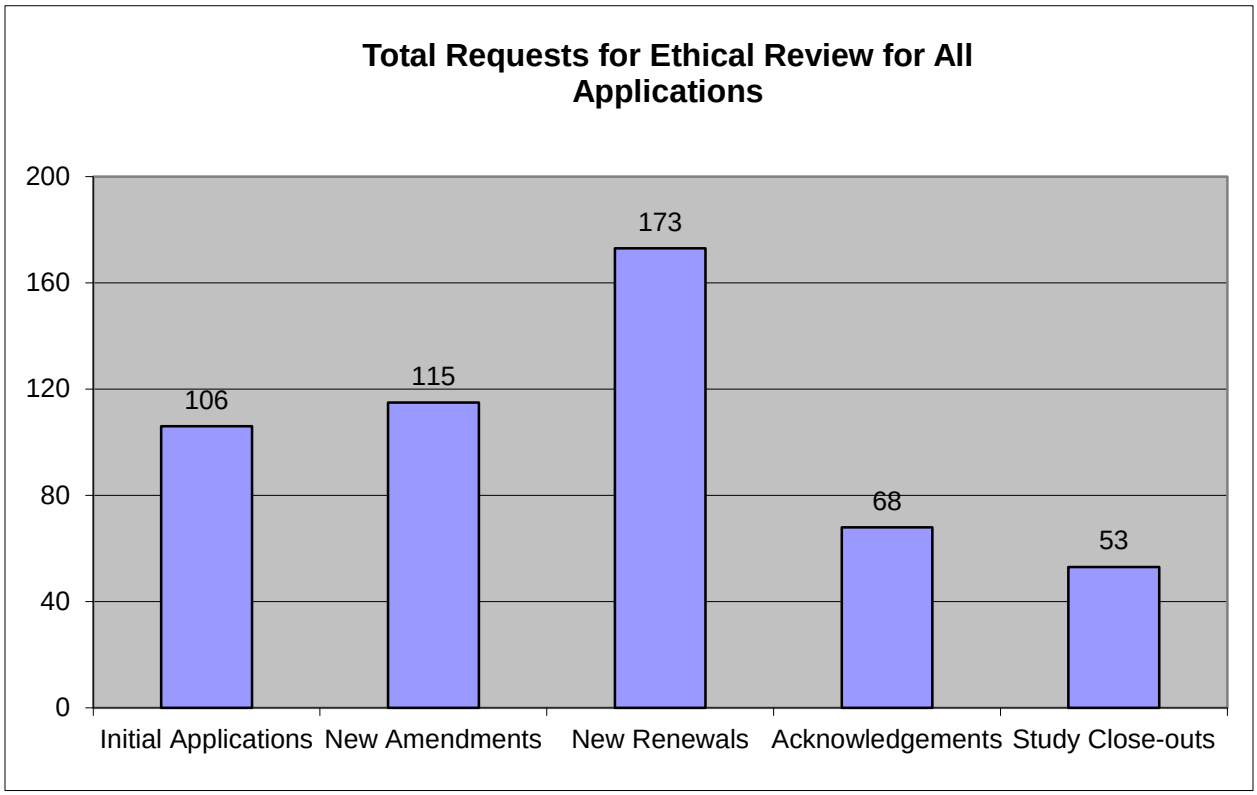


Figure 2: Total Number of Requests for Ethical Review by Fiscal Year April 1, 2012 to March 31, 2017

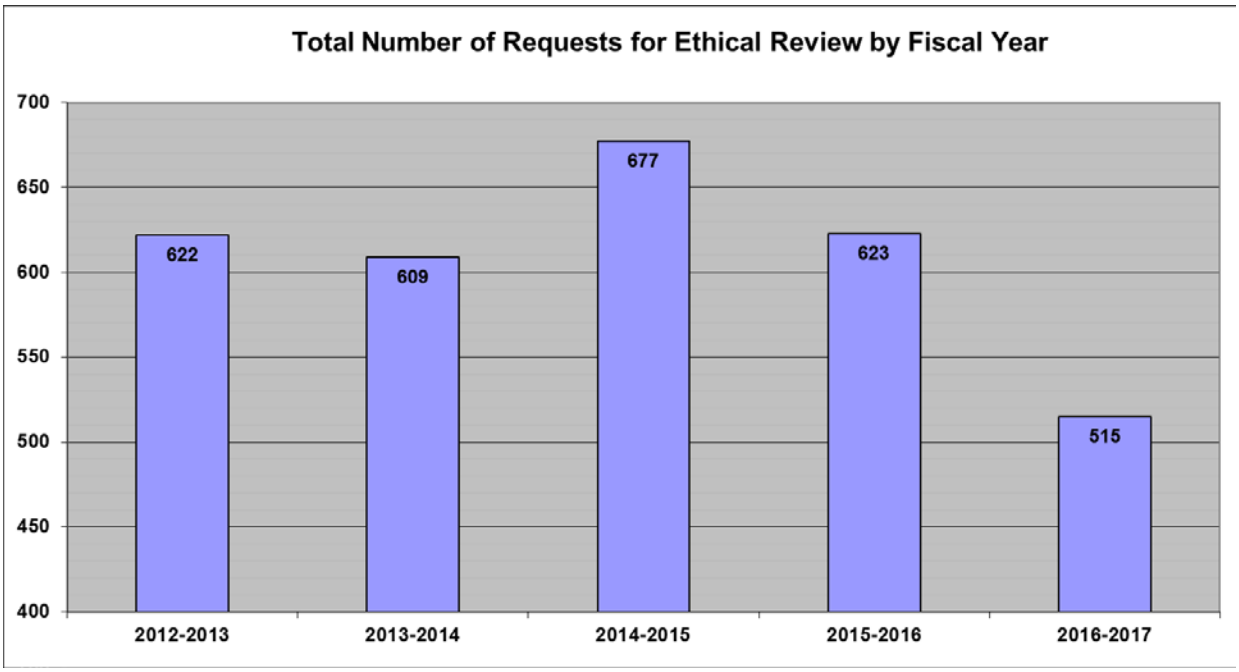


Table 2: Type of Requests for Ethical Review by Fiscal Year from 2012-2017

Type of Application	2012-2013	2013-2014	2014-2015	2015-2016	2016-2017
Initial	152	131	145	132	106
Amendment	155	137	169	147	115
Renewal	135	149	185	192	173
Close-out	73	128	105	83	53
Acknowledgements	107	64	73	69	68

5.2 FHREB Workload

Workload is differentiated from demand in that the data in this section reflects the actual number and type of applications that were reviewed in this fiscal year. The 'work' of the FHREB includes the time to review all of the application documents and to make a determination regarding approval as well as the time taken by the FHREB Coordinators to prepare all pre-review material required for the board's review of each study.

Workload varies from demand data because applications received late in the fiscal year may be reviewed in the following fiscal year. The FHREB reviewed a total of 524 applications (including acknowledgements of serious adverse event reports, protocol deviations, data safety monitoring board reports) for this fiscal year. This reflects a 16% decrease compared to the review of 623 applications for the prior fiscal year.

Figures 3 and 4 highlight the number and type of applications that received full board review and the number and type delegated to the FHREB Co-Chairs for review from 2012 to 2017.

Delegated review occurs for new applications when the study is considered to be of minimal risk to the prospective subject or is retrospective in design, for amendments and renewals of active studies that do not require full board review, and for review of serious adverse events, protocol deviations and close-out reports.

Note that this data does not include subsequent modifications arising from either a delegated or full board review of initial or amendment applications that were conducted in the prior fiscal year. For this workload data, please see 5.2.2.

Figure 3: Number and Type of Applications Receiving Full Board Review April 1, 2016 to March 31, 2017

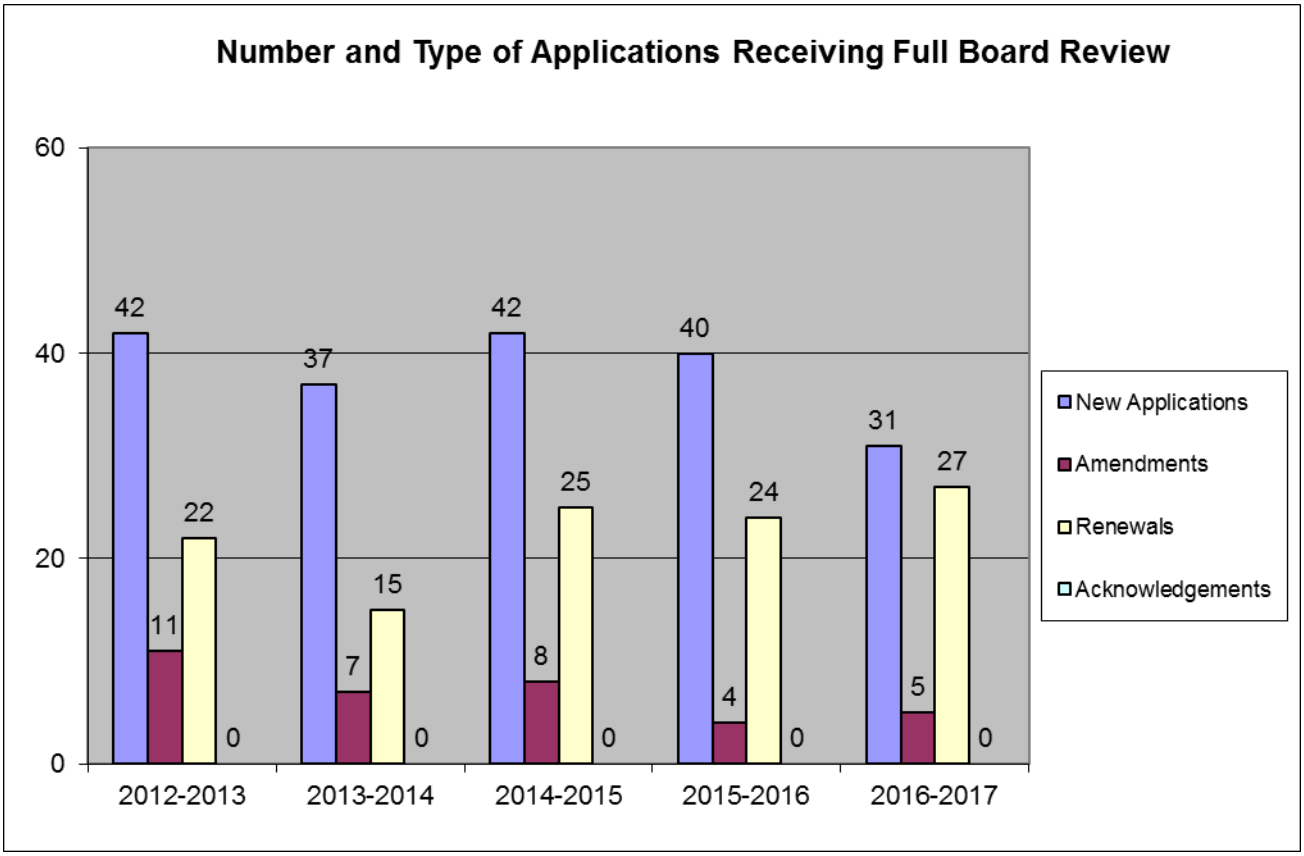
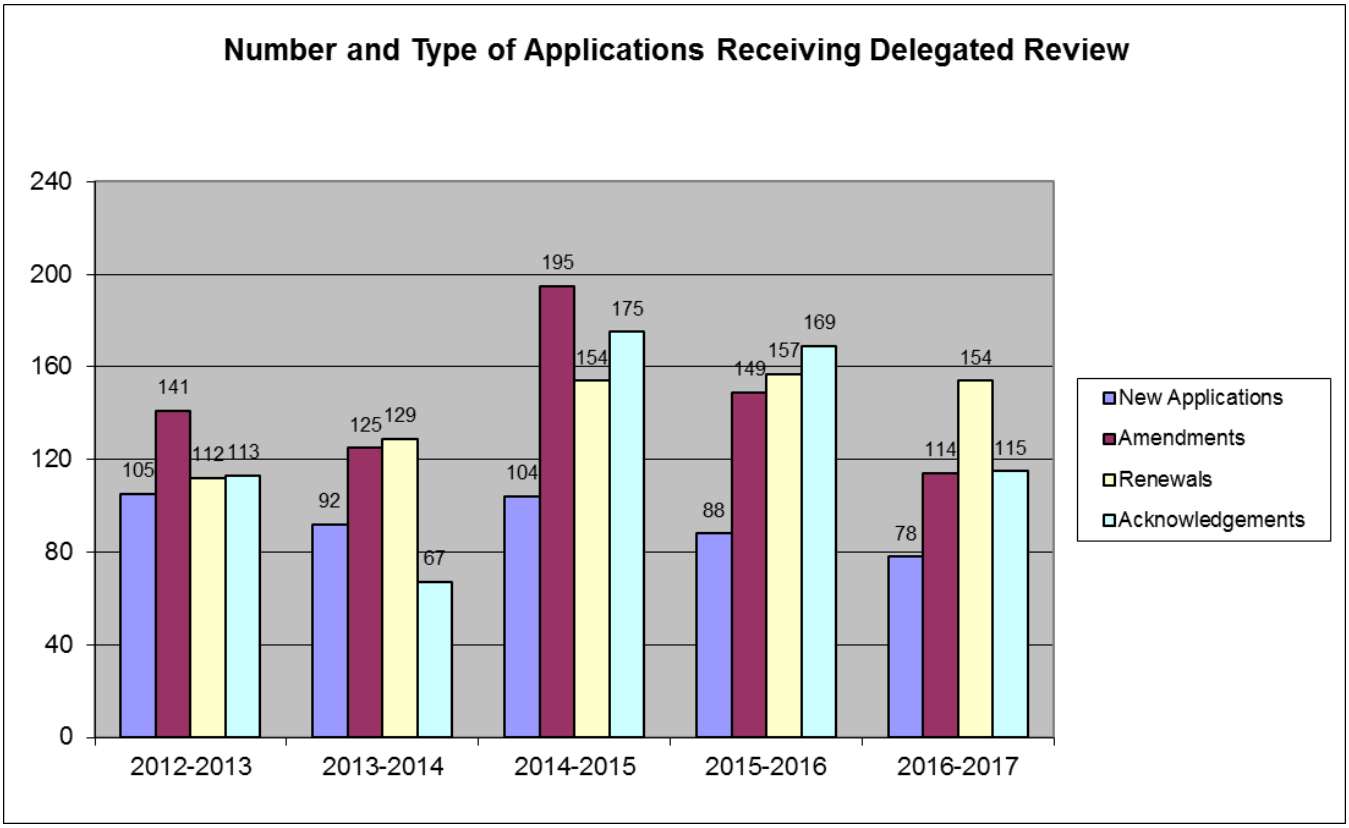


Figure 4: Number and Type of Applications Receiving Delegated Review April 1, 2012 to March 31, 2017
(n.b. Please note that acknowledgements include the review of close-outs. This was not included in the data for 2013-2014).



5.2.1 Safety Reporting

Under delegated review, the review of safety-related information is one aspect of providing ongoing monitoring of active clinical drug and device trials. The aim of this review is to ensure that any unexpected serious adverse event (SAE) experienced by a local Fraser Health research participant has been handled appropriately and that any significant SAE pattern from other non-local sites is recognized.

Adverse events related to research studies are defined as "*…noxious and unintended responses to a medicinal product related to any dose…".* [7] Non-local (i.e. international) SAE reports are those that are sent by the industry or academic sponsor to the principal investigator from other sites conducting the same study world-wide. The reporting process for these reports changed as a result of an agreement facilitated by the Canadian Association of Research Ethics Boards (CAREB) in July 2010. In accordance with the CAREB Guidance, non-local SAEs are now reported to the FHREB in the form of periodic safety update reports, accompanied by meaningful information that a research ethics board can assess. It is expected that the safety report(s) includes at a minimum, a sponsor analysis of the significance of the adverse event or an analysis from an independent data safety monitoring

[7] Health Canada, Health Products and Food Branch: Clinical Safety Data Management Definitions and Standards for Expedited Reporting, ICH Topic E2A https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/clinical-trials/background.html

board, with (where appropriate) a discussion of previous similar events. Investigators are advised that they may rely on the sponsor's assessment and provide to the FHREB a periodic safety update report prepared by the sponsor. These reports receive a delegated review only because the reports arise from research sites that are not within the FHREB's jurisdiction.

As a result of this change in reporting non-local SAEs, the FHREB reviewed all submitted non-local SAE reports and reviewed two SAE reports submitted for one local research study, none of which required further follow-up.

In addition to SAE reports, the FHREB Co-Chairs also review and follow-up the outcome, if required, of reported protocol deviations related to clinical drug and device trials. A deviation is defined as an "unanticipated or unintentional divergence or departure from the expected conduct of an approved study that is not consistent with the current research protocol, consent document or study addenda".[8] Five protocol deviations were reviewed by the FHREB Co-Chairs. All deviations were managed appropriately by the principal investigators for the respective studies and did not require further follow up

5.2.2 Disposition of the Review

Figure 5 illustrates the result (i.e. the decision) of the delegated and full board reviews. Studies that are not approved after initial review receive either a 'request for modifications' or in the case of some studies receiving full board review where there are substantive concerns, may receive a 'deferral' notice and therefore are deferred to a subsequent full board meeting upon receipt of the principal investigator's response. Note that not all studies are approved within this fiscal year because when the review is not finished it carries on into the following fiscal year; therefore only the activities of the 2016-2017 fiscal year are reported. Review and approval of the principal investigator's response to a 'request for modifications' is delegated by the full board to one of the FHREB Co-Chairs under the delegated review process or if the changes are very minor, to the FHREB Coordinators.

All principal investigators are expected to reply to the request for either modification or deferral within six months of the FHREB's decision, otherwise the study will be closed by the FHREB Coordinator and the principal investigator notified of that decision. The principal investigator may submit the same study at a future time but with a new initial application so that it is reviewed as a new study.

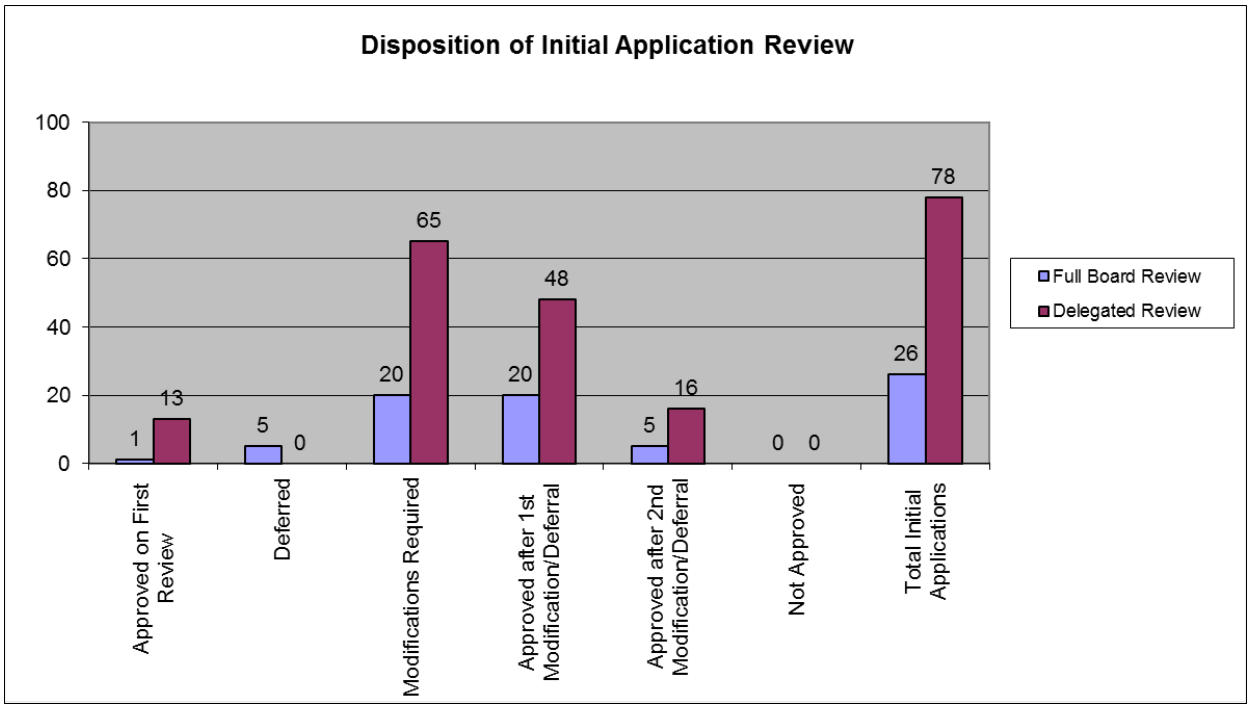
The FHREB has observed that more minimal risk studies require modifications compared to previous years and this change is attributed partially to an increase in the complexity of harmonized studies and the need for more information in research protocols. In contrast, the review of amendment and renewal applications for previously approved studies usually results in an approval decision because the amendment is most often a straight-forward change to the research protocol or consent form and the renewal is simply a report of year to date activity. Statistics for amendments and renewals are depicted in Figures 6 and 7.

Figure 5 also indicates that five full board studies were deferred. These studies required re-review by the full board because of substantive concerns regarding the scientific merit, research design or ethical issues relating to subject recruitment, consent or safety. Sometimes the complexity of the ethical issues creates the need for a review process that is lengthy and involves more than one deferral. The FHREB offers the research team every

[8] Fraser Health: Guidance Note for Submitting Protocol deviations to the FHREB, 2008 11 18. http://research.fraserhealth.ca/approvals-&-ethics/forms-and-guidance-notes/

opportunity to satisfy the FHREB of its concerns and does not limit the number of times that the study is submitted for review.

Figure 5: Disposition of Review of Initial Applications by Full Board and Delegated Review
April 1, 2016 to March 31, 2017



Figures 6 and 7 illustrate the disposition of the full board and delegated reviews for amendments and renewals of previously approved studies. As indicated, all but a very few are approved on initial review. Again, note that not all applications are approved within this fiscal year because when the review is not finished it carries on into the following fiscal year; therefore only the activities of the 2016-2017 fiscal year are reported.

Figure 6: Disposition of Review of Amendment Applications by Full Board and Delegated Review
April 1, 2016 to March 31, 2017

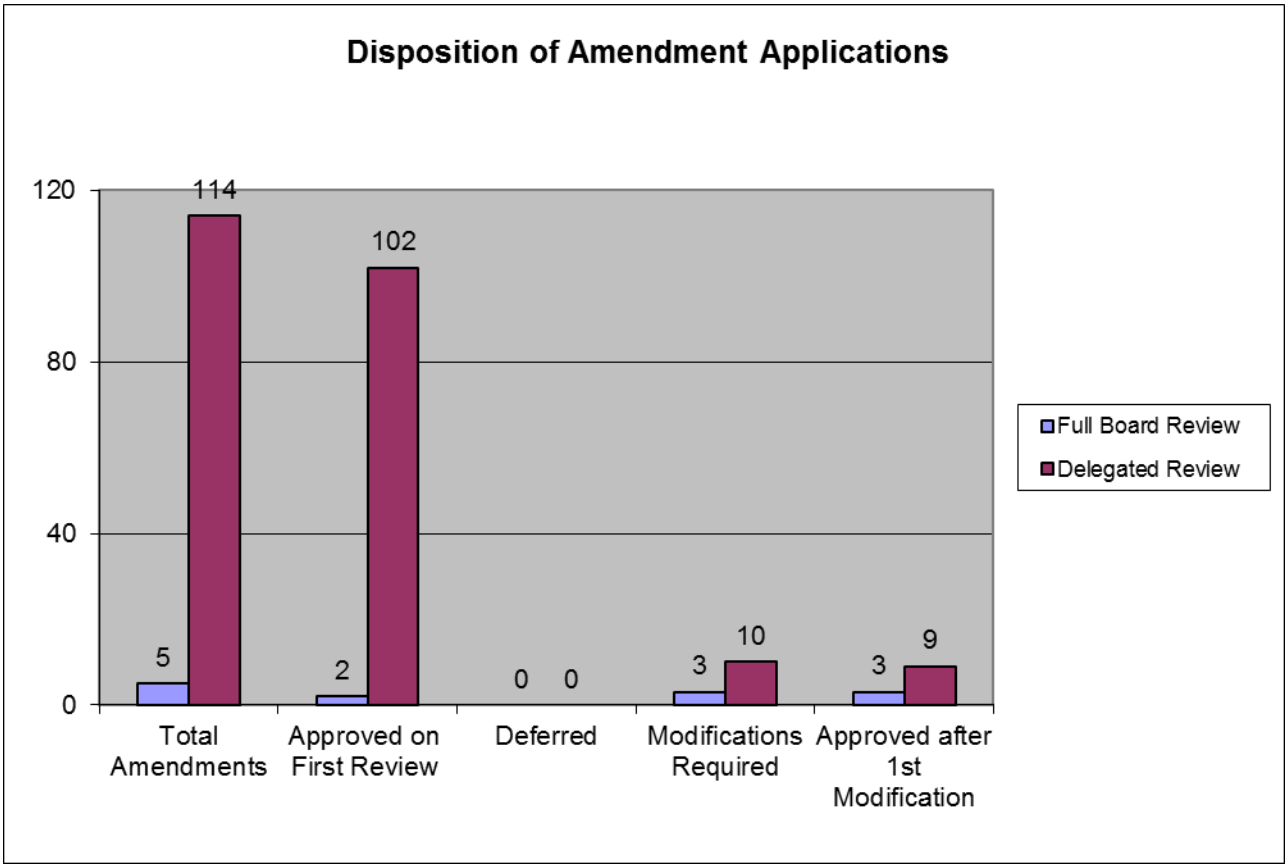
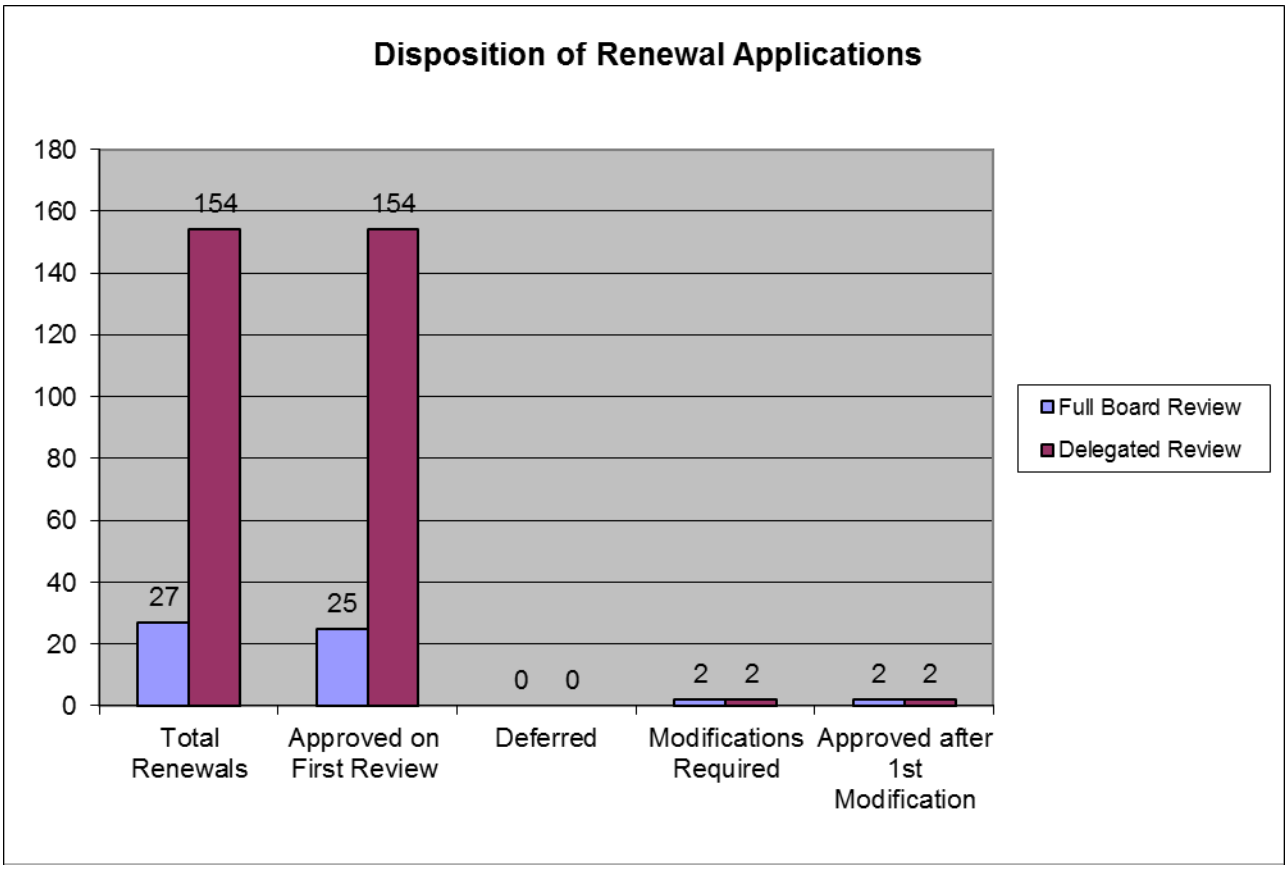


Figure 7: Disposition of Review of Renewal Applications by Full Board and Delegated Review Received from April 1, 2016 to March 31, 2017



5.2.3 Compliance with Annual Renewal

Annual renewal of previously approved studies is a mandatory requirement for all ongoing studies. In order to ensure compliance, a notice is sent to all principal investigators within one month of the expiry of the initial approval or subsequent renewal for their study. Sixty-two studies (i.e. 34%) were renewed outside of the date of expiry which is one year from the initial date of approval or renewal. The primary reason for this statistic is the delay in hiring a new part-time FHREB Coordinator to assume responsibility for the renewal process.

5.3 FHREB Efficiency

The FHREB office strives to issue decisions of the full board or delegated review within five business days of the review. The principal investigator must respond at any time within a six month period following the date of the decision, otherwise the FHREB will close the study.

The applications for full board review are received approximately three weeks prior to the full board meeting date to allow the FHREB Coordinator time to pre-review the documents, coordinate harmonization of the files with partner REBs as applicable, and submit them to the FHREB members for review prior to the board meeting.

Figure 8 illustrates that the median number of business days for full board review from the date of the board meeting to approval is 46 days, with 37 days for delegated review. A portion of this time is attributed to the length of time it takes for the principal investigator to

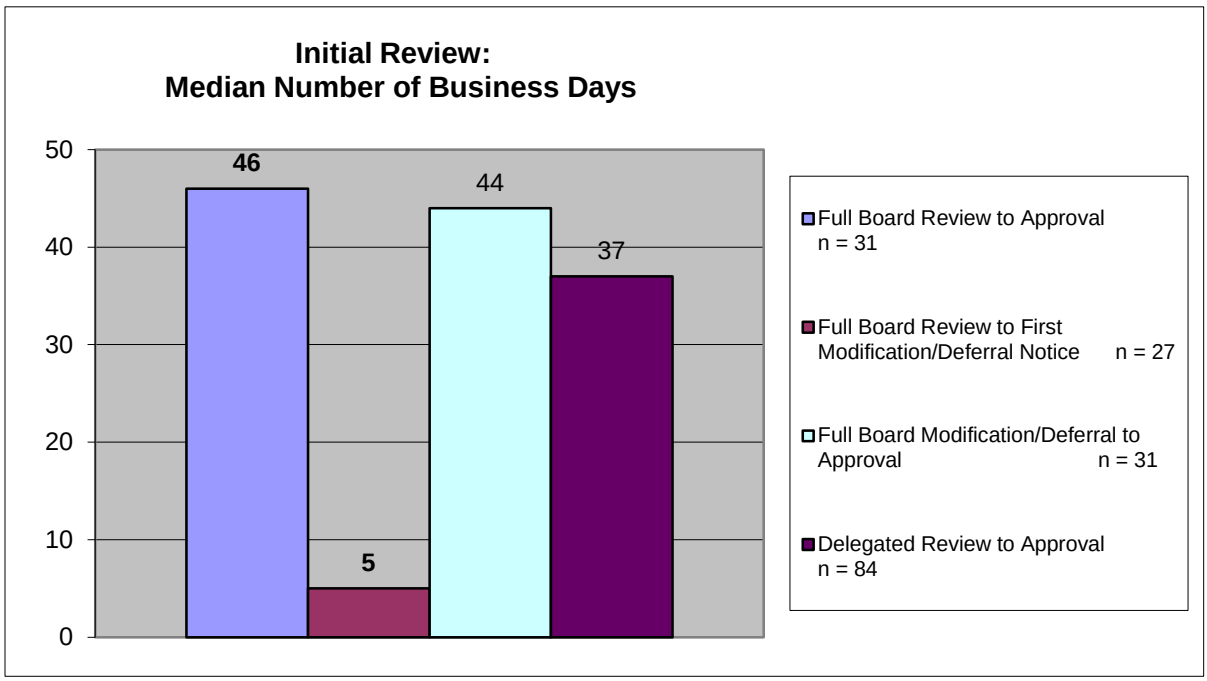
respond to the modification or deferral notice. It is important to note that this may also reflect the time it takes for an industry or academic sponsor to review and accept the required FHREB changes and to communicate their approval to the local Fraser Health principal investigator. As can be seen from the figure, the approval timeline is substantially shorter for delegated review.

In order to ensure oversight by the full board, a summary of all delegated reviews is sent to the members for any comment or questions that they may have before the ethics certificate of approval is issued to the principal investigator. All decisions are ratified at the next full board meeting.

Timelines are affected by the time spent by the FHREB Coordinator on non-review tasks, such as participation in the BCEHI, updating forms and other ethics documentation, coordination with the Fraser Health privacy office and managing ongoing administrative issues.

All timelines in the following figures are reported in median number of business days. Studies that were reviewed but did not receive final approval in this fiscal year are not included.

Figure 8: Initial Review: Median Number of Business Days for Full Board and Delegated Review
April 1, 2016 to March 31, 2017



The timeline for amendment approvals shown in Figure 9 was similarly longer for full board submissions that received a modifications/deferral notice, than for delegated submissions. The median number of business days for amendments for delegated review received to approval is fourteen business days (n = 112). The median number of business days for amendments for full board requiring modifications received to approval is 61.5 business days (n = 3). It is important to note that this number is influenced by the small sample size, and the long response time from the principal investigators.

Figure 9: Amendments: Median Number of Business Days for Full Board and Delegated Review
April 1, 2016 to March 31, 2017

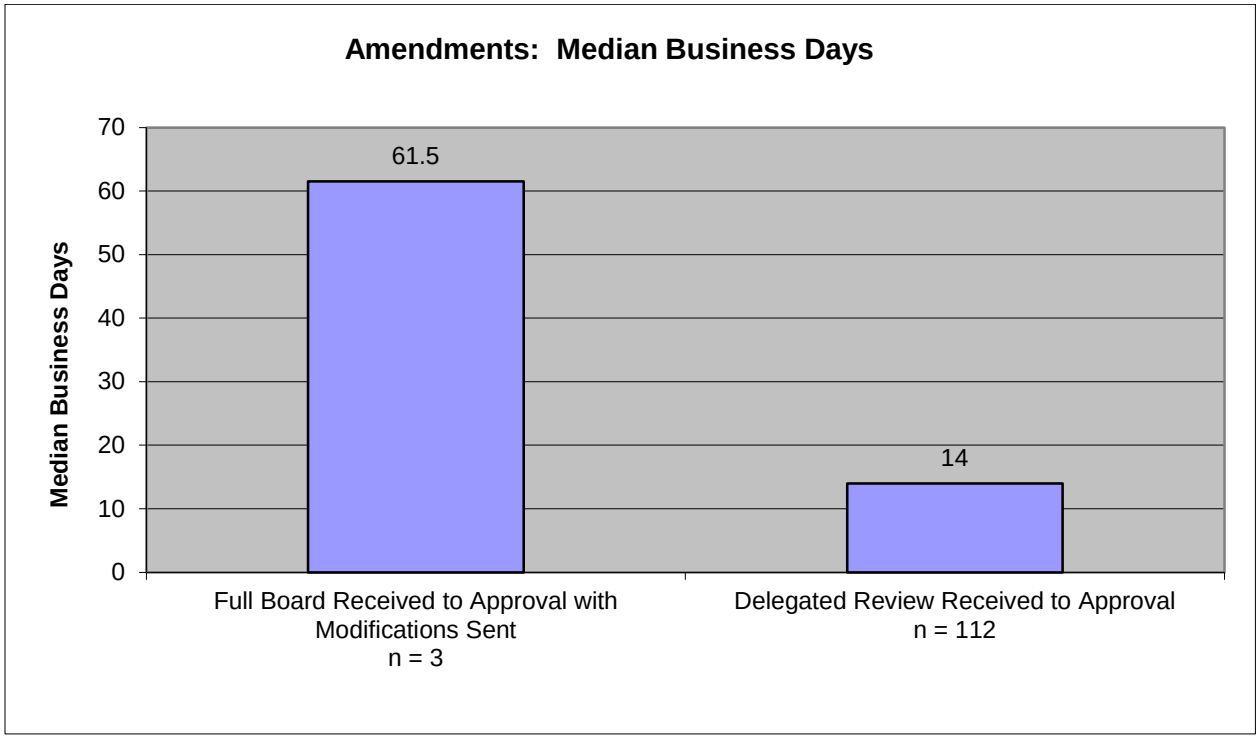
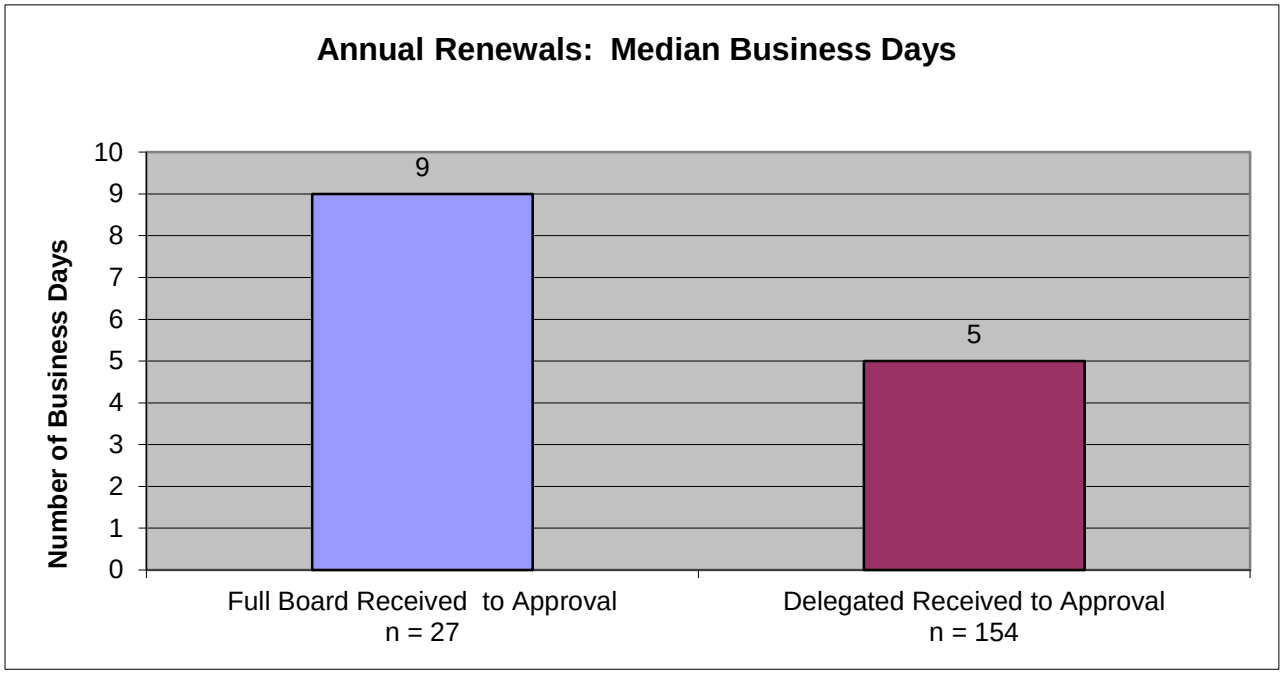


Figure 9 illustrates the timelines for review of renewal applications. Two full board renewals required modifications. The timeline for full board review also includes the time spent by the FHREB Coordinator to conduct the pre-review of documents prior to submission for the review of the members before the meeting occurs. This usually is done over a three week period prior to the actual meeting of the full board.

Figure 10: Annual Renewals: Median Number of Days from Date of Full Board and Delegated Review to Approval
April 1, 2016 to March 31, 2017



6. COMPLIANCE WITH FHREB REQUIREMENTS

6.1 Fraser Health Authority Research Inquiry and Investigation Committee

There were no referrals of research misconduct to the Fraser Health Research Inquiry and Investigation Committee for this fiscal year.

6.2 Breaches

There were no research-related privacy preaches reported to the Fraser Health Privacy Office and the FHREB in the 2016-2017 fiscal year.

6.3 Participant Complaints

There was one complaint from a patient participant concerning the payment of their honoraria in cash as this affected their income from social assistance, in addition to an unintended expense which placed a financial burden on the participant. The participant also wished to withdraw from the study. The REB Office notified the study team who immediately contacted the participant to offer a gift card in lieu of cash and reimbursement for the other expense and to reassure the participant of their right to withdraw from the study. The issue was resolved to the satisfaction of the participant. In addition, the issue was reviewed by the FHREB at its July 13, 2016 meeting with the recommendation that the FHREB Guidance Notes be updated to recommend alternate forms of honoraria in lieu of cash.

7. KEY PERFORMANCE INDICATORS

The FHREB has developed the following key performance indicators (KPIs) as measures of compliance with ethical standards and overall safety of research conducted in FH.

a. Compliance with the requirement for annual renewal of research studies set by Health Canada, the Canadian Institutes of Health Research, the U.S. Food and Drug Administration and the U.S. Department of Health and Human Services in order to maintain eligibility to either conduct clinical trials or receive funding for research. This KPI in addition applies to all research conducted in Fraser Health as it reflects adherence to ethical standards and Fraser Health research policies.
   - % of all regulated and non-regulated studies continuing to recruit and collect data from participants, access secondary data or tissue that are renewed within one year from date of initial ethical review or subsequent annual renewal: 66%

b. Serious Adverse Events.
   - # of Local Serious Adverse Events: 2

c. Participant Complaints, Appeals and Privacy Breaches: There was one participant complaint made to the FHREB, as noted on page 18. There were no requests for appeals of FHREB decisions brought forward by Fraser Health principal investigators to the Island Health Research Ethics Board; the Island Health Research Ethics Board functions as the appeal board for the FHREB.

8. CHALLENGES AHEAD

The FHREB continues to evolve and keep current with best practices in the ethical review of research. As research ethics is always in "evolution", the FHREB is sensitive to the desire of researchers for the application of consistent standards while at the same time striving to ensure that absolute requirements regarding ethical review continue to be implemented.

Provincial legislation, specifically the Freedom of Information and Protection of Privacy Act, includes research specific articles that are open to interpretation which therefore appear to be restrictive to Fraser Health researchers. The FHREB continues to work with the Fraser Health Privacy Office and our Legal Counsel to identify solutions to these issues so that research is not delayed. In addition, these have also been brought to the attention of the BC Ethics Harmonization Initiative as clarification of the legislation is imperative for the review of multi-jurisdictional research.

Although there was a decrease in the total number of applications reviewed, the workload of the FHREB and the FHREB Coordinators is significant, in particular, as the type of research reviewed increases in sophistication and multiple jurisdictions are involved in studies requiring multiple sources of data. Involvement in the BC Ethics Harmonization Initiative has also taken a significant amount of time because of the amount of communication that the FHREB Coordinators undertake between their counterpart REB administrators for multi-jurisdictional research. Maintaining efficiency of review for our researchers, including those academic researchers that are affiliated with Fraser Health, is important with respect to customer service. The addition of a .4 FTE Coordinator since October 2016 has significantly improved the efficiency of the FHREB workflow and timelines.

9. CONCLUSION

The undersigned are pleased to confirm that the Fraser Health Authority Research Ethics Board has been in compliance with the *Tri-Council Policy Statement: Ethical Conduct for Conducting Research Involving Humans* and other regulatory requirements, as applicable, for the 2016 to 2017 fiscal year. The FHREB approved the 2016-2017 annual report at its September 13th 2017 meeting.

Respectfully submitted,

Dr. Stephen Pearce
FHREB co-Chair

Professor Lindsay Meredith
FHREB co-Chair

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APPENDIX 1

TERMS OF REFERENCE

FH RESEARCH ETHICS BOARD MEMBERS

APPROVED: 2007 August 09
1st revision: 2007 October 17
2nd revision: 2011 December 13
3rd revision: 2015 December 09

The members of the FH Research Ethics Board [FHREB] are responsible for carrying out the following activities and functions. The board operates under the authority of the FH Policy "The Ethical Conduct of Research and Other Studies Involving Human Subjects".

1. Complete the "Introductory Tutorial for the Tri-council Policy Statement: Ethical Conduct of Research Involving Human Subjects" at http://www.pre.ethics.gc.ca/english/tutorial/

2. Review all submissions that meet the criteria for full board review that are assigned for a full board meeting prior to the meeting date. These include applications for initial ethical review, applications for amendment and renewal of previously approved studies that meet specific criteria for full board review, and responses to studies that have been deferred from a previous board review.

3. Submit written comments to the FHREB office at the conclusion of the REB meeting for compilation into the modifications or deferral memoranda.

4. Ensure that the study complies with the applicable Canadian federal and provincial and U.S. regulations when applicable and that all research complies with the current version of the Tri-Council Policy for Ethical Policy Statement: Ethical Conduct for Research Involving Humans and other non-regulatory requirements.

5. Make a decision about the outcome of the review for each study as follows:
    a) approve if all FHREB requirements have been met satisfactorily, or
    b) request that the investigator modify the study and/or respond to questions concerning the study prior to approval, or
    c) refer to an external source for review, or
    d) not approve.

6. Develop guidance notes, policies and procedures for ethical review in collaboration with the Director, Department of Evaluation and Research Services, REB ex officio member.

7. Participate in educational activities, evaluations, audits or investigations related to the oversight of research ethics at FH.

8. Declare any conflict of interest pertaining to studies on the full board agenda before discussion begins.

9. Declare conflict of interest on an annual basis.

10. Specific responsibilities according to the expertise and role of individual members are:

a. All Non-Scientific Members: are expected to provide input to areas relevant to their knowledge, expertise and experience, professional and otherwise. These members should advise the FHREB if additional expertise in a non-scientific area is required to assess whether the research protocol adequately protects the rights and welfare of subjects, and to comment on the comprehension of the consent document.
   i. Community Member(s): are not affiliated with the Fraser Health Authority. They are expected to provide input regarding their knowledge about the local community, as it may relate to prospective subjects recruited from the local community, and be able to discuss issues and research from that perspective.
   ii. Member(s) knowledgeable in relevant law: are expected to alert the FHREB to legal issues and their implications, and to present the legal views of specific areas that may be discussed, such as exculpatory language or provincial requirements regarding consent.
   iii. Member(s) knowledgeable in research ethics**:** are expected to alert the FHREB to potential ethics issues basing their recommendations on a balance of ethics theory, practice and experience.

b. Scientific Members: are expected to contribute to the evaluation of a study on its ethical, scientific and statistical merits, and standards of practice. These members should also advise the FHREB if additional expertise in a scientific or non-scientific area is required to assess whether the research protocol, consent document and other research materials adequately protect the rights and welfare of subjects.
   i. Methodologist: is appointed from the Department of Evaluation and Research Services staff. The methodologist provides analysis of the scientific merit of the study to ensure that the research design is appropriate for the stated research objectives and to ensure that the methodology and statistical analysis is commensurate with the study design.
   ii. Pharmacist: is appointed from FH Pharmacy Services and ensures that the drug toxicity information included in Investigator Brochures and other relevant research related documents is included in the study consent form. This position also identifies flaws in study methodology.
   iii. Other clinical experts: are appointed as needed according to the type of research reviewed by the REB on an ongoing basis. For example, a nurse researcher with expertise in qualitative research may be appointed. From time to time, ad hoc reviewers may be consulted for specific expertise or knowledge that is required in order to review the ethical acceptability of a proposal competently.

c. Ex-officio Member: Department of Evaluation and Research Services Director

11. **[Approved 2015 December 09] Honoraria:** All REB members, excluding the co-Chairs, are paid $450.00 per meeting attended.

   i. **Honoraria Paid to Non-FH Employees:** Cheques for the honoraria are sent directly to the REB members, who are physicians or non-FH employees by FH Finance, at the address of their choice. There are no restrictions on the use of the honoraria by REB members who are non-FH employees or who are physicians.

   ii. **Honoraria Paid to FH Employees:** Honoraria for REB members who are FH employees may be claimed by that member with the submission of the following documentation to the Research Ethics Co-ordinator:
      a. expense receipts,
      b. as per FH “Travel and Business Expense” policy, the expense claim must be filled out on an “Employee Expense Report”, and,
      c. a written justification for that expense made to the Director, Department of Evaluation and Research Services who will approve the request.

A cheque requisition form is sent to FH Finance for reimbursement of the approved funds to that REB member.

Honoraria to REB members who are FH employees may be used for the type of expenses that FH employees would normally be able to claim and that are related to the work of the Research Ethics Board. This would normally include expenses related to education, conferences, and other out-of-pocket expenses. Other expenses may be considered upon presentation of an adequate written justification.

Any purchase of equipment and supplies that is approved by the Director, Department of Evaluation and Research Services must comply with the FH Research Policy Section 4.3c.

Reference: Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada. Tri-Council Policy for Ethical Policy Statement: Ethical Conduct for Research Involving Humans. 2010. Articles 6.4 and 6.5

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APPENDIX 2

TERMS OF REFERENCE

FRASER HEALTH RESEARCH ETHICS BOARD CHAIR

APPROVED: 2007 August 09
1st Revision: 2007 October 17
2nd Revision: 2011 December 13
3rd Revision: 2015 December 09

The Chair(s) of the FHREB is responsible for carrying out the following activities and functions, and operates under the authority of the FH Policy "The Ethical Conduct of Research and Other Studies Involving Human Subjects". The terms of reference for the FHREB co-Chairs, in addition, to those of the FHREB Members, are listed below.

1. Chair the full board meetings of the FHREB and ensure that the board meets the current version of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans and Health Canada requirements for quorum at each meeting.

2. Review and edit as required the comments submitted by board members following a meeting and prior to distribution to the investigators as requests for modification or deferral memoranda.

3. Review all applications for initial review, amendments and renewals of previously approved research, that qualify for expedited review under the minimal risk criteria and:
   a) approve if all FHREB requirements have been met satisfactorily, or;
   b) request that the investigator modify the study and/or respond to questions concerning the study prior to approval, or;
   c) refer to the FHREB for review and approval.

4. Review investigators' responses to requests for modifications that arise either from a full board meeting or from an initial expedited review of minimal risk studies, amendments and renewals and approve if all FHREB requirements have been met satisfactorily.

5. Develop guidance notes, policies and procedures for ethical review in collaboration with the board members and the Coordinator, Research Ethics Board and the Director, Department of Evaluation and Research Services, ex officio REB member.

6. Inform investigators of subject safety related issues that may arise during the course of a study and that require a response from the investigator. These may include, among others, following up serious adverse event reports, protocol violations and data safety monitoring board reports upon reviewing studies using interventions for which regulatory authorities (e.g. Health Canada, FDA) have issued safety alerts.

7. Review and respond to investigator's reports of serious adverse events and protocol deviations.

8. Acknowledge close-out notices from investigators.

9. Participate in Health Canada inspections or NCEHR site visits as required.

10. Participate in investigations related to breach of compliance with Tri-Council policy FH policy on "The Ethical Conduct of Research and other Studies Involving Human Subjects' and the "FH Research Policy".

11. Prepare the FHREB annual report in collaboration with the Director, Department of Evaluation and Research Services.

12. Respond to investigator's inquiries as appropriate.

13. **[Approved 2015 December 09] Honoraria:** REB co-chairs are paid $850.00 per meeting. This also includes the expedited review of minimal risk applications which is conducted on a weekly basis.

iii. **Honoraria Paid to Non-FH Employees:** Cheques for the honoraria are sent directly to the REB members, who are physicians or non-FH employees by FH Finance, at the address of their choice. There are no restrictions on the use of the honoraria by REB members who are non-FH employees or who are physicians.

iv. **Honoraria Paid to FH Employees:** Honoraria for REB members who are FH employees may be claimed by that member with the submission of the following documentation to the Research Ethics Co-ordinator:

a. expense receipts,
b. as per FH "Travel and Business Expense" policy, the expense claim must be filled out on an "Employee Expense Report", and,
c. a written justification for that expense made to the Director, Department of Evaluation and Research Services who will approve the request.

A cheque requisition form is sent to FH Finance for reimbursement of the approved funds to that REB member.

Honoraria to REB members who are FH employees may be used for the type of expenses that FH employees would normally be able to claim and that are related to the work of the Research Ethics Board. This would normally include expenses related to education, conferences, and other out-of-pocket expenses. Other expenses may be considered upon presentation of an adequate written justification.

Any purchase of equipment and supplies that is approved by the Director, Department of Evaluation and Research Services as per the FH Research Policy Section 4.3c.

Reference: Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada. Tri-Council Policy for Ethical Policy Statement: Ethical Conduct for Research Involving Humans. 2010. Articles 6.4 and 6.5

The Chair(s) of the FHREB is responsible for carrying out the following activities and functions, and operates under the authority of the FHA Policy "The Ethical Conduct of Research and Other Studies Involving Human Subjects". The terms of reference for the FHREB co-Chairs, in addition, to those of the FHREB Members, are listed below.

14. Chair the full board meetings of the FHREB and ensure that the board meets the current version of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans and Health Canada requirements for quorum at each meeting.

15. Review and edit as required the comments submitted by board members following a meeting and prior to distribution to the investigators as requests for modification or deferral memoranda.

16. Review all applications for initial review, amendments and renewals of previously approved research, that qualify for expedited review under the minimal risk criteria and:
    d) approve if all FHREB requirements have been met satisfactorily, or;
    e) request that the investigator modify the study and/or respond to questions concerning the study prior to approval, or;
    f) refer to the FHREB for review and approval.

17. Review investigators' responses to requests for modifications that arise either from a full board meeting or from an initial expedited review of minimal risk studies, amendments and renewals and approve if all FHREB requirements have been met satisfactorily.

18. Develop guidance notes, policies and procedures for ethical review in collaboration with the board members and the Coordinator, Research Ethics Board and the Director, Department of Evaluation and Research Services, ex officio REB member.

19. Inform investigators of subject safety related issues that may arise during the course of a study and that require a response from the investigator. These may include, among others, following up serious adverse event reports, protocol violations and data safety monitoring board reports upon reviewing studies using interventions for which regulatory authorities (e.g. Health Canada, FDA) have issued safety alerts.

20. Review and respond to investigator's reports of serious adverse events and protocol deviations.

21. Acknowledge close-out notices from investigators.

22. Participate in Health Canada inspections or NCEHR site visits as required.

23. Participate in investigations related to breach of compliance with Tri-Council policy FHA policy on "The Ethical Conduct of Research and other Studies Involving Human Subjects' and the "FH Research Policy".

24. Prepare the FHREB annual report in collaboration with the Director, Department of Evaluation and Research Services.

25. Respond to investigator's inquiries as appropriate.

26. **Honoraria:** REB co-chairs are paid $850.00 per meeting. This also includes the expedited review of minimal risk applications which is conducted on a weekly basis.

v. **Honoraria Paid to Non-FHA Employees:** Cheques for the honoraria are sent directly to the REB members, who are physicians or non-FH employees by FH Finance, at the address of their choice. There are no restrictions on the use of the honoraria by REB members who are non-FH employees or who are physicians.

vi. **Honoraria Paid to FHA Employees:** Honoraria for REB members who are FH employees may be claimed by that member with the submission of the following documentation to the Research Ethics Co-ordinator:

a. expense receipts,
b. as per FHA "Travel and Business Expense" policy, the expense claim must be filled out on an "Employee Expense Report", and,
c. a written justification for that expense made to the Director, Department of Evaluation and Research Services who will approve the request.

A cheque requisition form is sent to FHA Finance for reimbursement of the approved funds to that REB member.

Honoraria to REB members who are FHA employees may be used for the type of expenses that FHA employees would normally be able to claim and that are related to the work of the Research Ethics Board. This would normally include expenses related to education, conferences, and other out-of-pocket expenses. Other expenses may be considered upon presentation of an adequate written justification.

Any purchase of equipment and supplies that is approved by the Director, Department of Evaluation and Research Services as per the FHA Research Policy Section 4.3c.

Reference: Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada. Tri-Council Policy for Ethical Policy Statement: Ethical Conduct for Research Involving Humans. 2010. Articles 6.4 and 6.5

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APPENDIX 3

POTENTIAL CONFLICT OF INTEREST DECLARATION FOR FRASER HEALTH RESEARCH ETHICS BOARD MEMBERS

Please complete the sections below to provide information to the FHREB Co-Chairs and Director of Research Services about circumstances concerning **you and/or your partner(s) and/or immediate family members (including children, whether living in the household or not)** that could lead to a conflict of interest with the business of Fraser Health Research Ethics Board (FHREB). Include any relevant details from the past two years of your life, including your current situation. Exact details of remuneration are not required.

1. Personal Details:

Surname:
Given Names:
Hospital Department (if applicable):

Hospital Division (if applicable):

Citizenship: ☐ Canadian
☐ Landed Immigrant
☐ Other:

Postal Address:

Phone Number:
Fax Number:
E-mail Address:

2. Research Support: ☐ Yes ☐ No

Provide brief details, including names of sponsors and types of support (e.g. salary, grants, equipment, fees).

- Self:
- Partner and/or Immediate Family members:

3. Consultancy Activities: ☐ Yes ☐ No

Provide brief details, including name(s) of companies who have utilized your services and amount of time spent on consulting.

- Self:
- Partner and/or Immediate Family members:

4. Fees or honoraria for writing research proposals or publications: ☐ Yes ☐ No

Provide details about the organization from which you received the fees.

- Self:
- Partner and/or Immediate Family members:

5. Speaker fees and/or educational awards/honoraria: ☐ Yes ☐ No

Provide details about the organization from which you received the fees.

- Self:

- Partner and/or Immediate Family members:

6. Travel assistance to attend conferences or meetings: ☐ Yes ☐ No
Provide details about the organization from which you received the assistance.
- Self:

- Partner and/or Immediate Family members:

7. Membership(s) on Research Professional Boards or Institutional Boards (for profit and not-for-profit): ☐ Yes ☐ No List memberships.
Provide details about the organization from which you received the fees.
- Self:

- Partner and/or Immediate Family members:

8. Ownership of stock, stock options, or other equity holdings: ☐ Yes ☐ No
No declaration is expected for managed or mutual funds.
- Self:

- Partner and/or Immediate Family members:

9. Any additional financial or other relationship which could be a potential conflict of interest (such as patent rights, intellectual property rights): ☐ Yes ☐ No
- Self:

- Partner and/or Immediate Family members:

10. I understand that it is my responsibility to indicate to the FHREB Co-Chairs when I have a conflict of interest with an application coming before the committee.

Signature: _____ **Date:**

Printed Name:

APPENDIX 4

REVISIONS TO FHREB DOCUMENTATION

Documents	Most Recent Version # Date
Application for Initial Ethical Review Form revised to incorporate Privacy data access agreement	Final: 2016 11 21 Revision: 2016 11 16
Application for Initial Ethical Review Form_Affiliated Researchers revised to incorporate Privacy data access agreement and for RiSE studies	Final: 2016 11 17 Revision: 2016 05 18
Researcher Response Form	Version 14: 2016 05 06
Integrated Post-approval Application Form for Amendments, Renewals, Close-outs, Acknowledgements of Previously Approved Research	Final: 2016 11 16 Revision: 2016 05 06
Change of Principal Investigator Form	Version 4: 2015 05 06
Guidance Notes for New Applications for Ethical Review	Final: Version 27: 2017 03 13 Revision: Version 26: 2016 11 17
Guidance Notes for Amendment	Version: 2016 11 17
Guidance Notes for Renewal	Version: 2016 11 17
Guidance Notes for Reporting Unanticipated Problems to the FHREB	Version: 2011 12 15
Subject Information and Consent Form Requirement Template	Replaced with BCEHI Common Clinical Consent Template Version: 2015 10
Temporary Optional Consent Form	Version #6: 2012 03 28
FHREB Assent Form Template	Version #2: 2011 10 13
Case Report Consent Form Template	Version #1: 2010 05 10
Consent Form Checklist	Version: 2012 03 27
Consent to Contact and Use Data Template	Version: 2011 10 13
Consent to Contact for Future Participation in Research	Version #2: 2011 10 13
Consent to Review Records and Contact Template	Version #2: 2011 10 13
Consent to Review Records to Determine Eligibility	Version #4: 2012 03 28
Non-clinical (i.e. survey, focus groups, observational) Consent Form Template for Patients	Version #5: 2016 01 25
Non-clinical (i.e. survey, focus groups) Consent Form Template for Staff	Version #5: 2016 01 25
Department Agreement for Providing Research-related Services Form	Final: Version #22: 2016 11 17 Revision: Version #21: 2016 05 06