



Annual Report on Research
(April 1, 2009 through March 31, 2010)

May 2010

Annual Report on Research
April 1, 2009 through March 31, 2010

Table of Contents

Executive Summary	3
Process Improvements Current Research Projects	3
Mandate of the Research Review Team	4
The Nature of Research at Trillium Health Centre	4
Future Directions.....	4
Profile of Current Research at Trillium Health Centre	4
Current Research Projects.....	4
Research Outcomes, Strengths and Achievements 2009/2010.....	13
Achievements.....	13
Research Review Team	13
Research Administration	14
Research Supports	15
The Nature of Research at Trillium Health Centre	4
Future Directions.....	4
Appendix A: Research Study Reportable Findings	17
Appendix B: Research Review Team – Membership Listing	25
Appendix C: Level’s of Engagement in Research Activity	27
Appendix D: Research Review Team Terms of Reference	32
Appendix E: Trillium Health Centre – Research Principles	34

Executive Summary

Process Improvements

Research Administration

In line with Trillium's sustainable research and innovation strategic initiative, a new research infrastructure was formally developed and implemented organization-wide this fiscal year. The various components of the new infrastructure are aimed at developing and fostering a strong and adept research culture modeled after the infrastructures framework. This new infrastructure is geared to support and encourage the conduct, promotion and endorsement of research by all Trillium staff and physicians, and enhance our Human Research Protection Program. Various research policies and decision charts were developed to frame the backbone of the infrastructure aimed at strengthening Trillium's health research capacity, awareness and coordination efforts, and fostering a skilled and robust research culture at Trillium.

Research Ethics Review

The formal documentation and implementation of a protocol to facilitate our strategic alignment with the Ontario Cancer Research Ethics Board (OCREB) continues to serve as an operational improvement by:

1. reducing unnecessary repetition in work for research teams in the submission, review and approval process, and
2. assuring that oncology clinical trials reviewed by OCREB are done so by a group whose membership includes oncology specialists from across the Province.

A recent enhancement to the Research Review Team membership has been the addition of our Family Medicine Residents. This adaptation serves as one approach at re-establishing physician representation on the team, and collaborating with our Family Medicine Teaching Unit in existing as a research learning forum for Trillium's Family Medicine Residents, all of whom are to conduct a research study during their residency.

Collaborative Approaches

Our recognition as a member of the Toronto Academic Health Sciences Network (TAHSN), and our participation in the Research Ethics Education Portal established by the University of Toronto's Joint Centre for Bioethics continues to enable us to:

1. share our internal research principles, protocols and documents with other TAHSN organizations,
2. access research ethics education documents from other participating organizations, and
3. increase the visibility of research at Trillium.

The connections we have made through the Canadian Association of Research Ethics Boards (CAREB) and the National Council on Ethics in Human Research (NCEHR) have served as vast resources enabling us to network with our national colleagues regarding research ethics review and research administration practices. These connections also assist in enhancing the Research Review Teams current processes and procedures.

Our collaborations with our Finance department to establish a mutually acceptable and financially responsible research financial recovery process has served as a key element to ensuring the financial responsibility of Trillium in conducting and participating in research activity. Our efforts are aimed at ensuring that participation in clinical research is cost neutral to the hospital.

Mandate of the Research Review Team

Trillium Health Centres Research Review Team is composed of staff volunteers spanning across our hospitals health systems, and includes the hospital Librarian, Senior Ethicist, Privacy Specialist, a community member, and a Lawyer. Keeping patient safety and confidentiality at the forefront of the review process, the team thoroughly reviews and identifies all concerns and issues regarding potential studies to ensure the best quality of care is available to Trillium Health Centre's patient population.

The Nature of Research at Trillium Health Centre

As evident in the distribution of studies by discipline, the total number of Oncology studies continues to distinctly outnumber all other health disciplines (Figure 1). This has been a consistent trend for the past 3 fiscal years.

The ratio of studies conducted by Trillium Health Centre Staff and Physicians compared to external Investigators has remained fairly consistent compared to last fiscal year with 52% of research activity conducted this fiscal year being lead by Trillium Health Centre Staff and Physicians (Figure 7). The remaining 48% of studies are lead by Investigators from various research hospitals and Institutions (Table 3).

Future Directions

We continue to pursue methods of enhancing Trillium Health Centre's Research capacity through:

- amending our internal research decision making structure to facilitate formal internal recognition of our Research Review Team as a standalone Research Ethics Board;
- exploring effective approaches to re-establish physician representation on the Research Review Team;
- Leveraging off of the recent formal academic teaching affiliation with the University of Toronto, Mississauga;
- Establishment of an efficient research compliance/auditing process;
- Establishment of an efficient research related privacy breach protocol;
- Enacting our strategic plan to provide research education across the organization through the development and implementation of an effective research education program; and Accreditation of Trillium's research education program through the University of Toronto's Continuing Professional Development program.

Profile of Current Research at Trillium Health Centre

Current Research Projects

During the 2009/2010 fiscal year, there were 123 research studies at various stages of the research cycle at Trillium Health Centre. Of the 123 studies, Trillium actively participated in a total of 115 studies, saw 21 studies to completion, had 7 studies in pending status, 1 study on hold due to safety concerns and had 5 studies in suspension. Currently, there are 94 active studies running at various stages representative of Trillium's health systems (Figure 1).

New Studies

There were a total of 24 new studies submitted for review that cover the spectrum of health systems and study types. However, only 17 of these studies were seen through to initiation at Trillium during this fiscal period.

Of the new studies reviewed, 38% were clinical trials, 4 % were Chart Reviews, 50% were Qualitative/Observational/Registry studies, and 8% were Student/Staff studies (Figure 4A).

Of the new studies initiated, 35% were clinical trials, 6% were Chart Reviews, 47% were Qualitative/Observational/Registry studies and 12% were Student/Staff projects (Figure 4B).

Renewals

Of the 94 studies currently running at Trillium 74 of these studies were initiated prior to this fiscal year. However 25 of these research studies failed to submit applications for continuing approval and experienced a lapse in continuing approval.

Continuing approval was granted for 49 of the research studies that were initiated prior to this fiscal year. Of these 53% are clinical trials, 20% are chart reviews, 23% are Qualitative/Observational/Registry studies and 4% are Student/Staff projects. Of the 49 studies renewed this fiscal year, 47% are still open to accrual, 51% are closed to accrual, and for 2% subject accrual has been suspended.

Closures

Of the 21 studies that were completed this fiscal year, reportable findings are available for 12 of them. These findings are summarized in Appendix A.

In examining the total number of new studies initiated this fiscal year, the distribution by type of new study initiated vs. reviewed, and the demographics of all active studies at Trillium, 4 distinct trends stand out:

- (1)** There is a continuous decreasing trend in the number of new studies initiated since 2006 (Figure 3). This fiscal year has seen a 19% decrease in the total number of new studies initiated compared to last fiscal year, and a 43% decrease compared to the 2007/2008 fiscal year. Although the total number of new studies initiated this year (17 studies) is slightly below that of last fiscal year (21 studies), overall there has been a 36% increase in research activity compared to last fiscal year (Figure 3). Surges in Clinical Trial, Qualitative/Observational/Registry, and Student/Staff research activity contribute to this influx. The dynamics of the study type demographics are illustrated within Trillium Health Centre's current research profile (Figures 2 & 5 and Tables 1 &

2). :

Table 1. Summary of % Δ in all studies by type (increase/decrease)

<i>Study Type</i>	<i>% Δ¹</i>
Clinical Trials	33%
Chart Review	18%
Qualitative/Observational/Registry	93%
Student/Staff	50%

Table 2. Summary of % Δ decrease in new studies by type (increase/decrease)

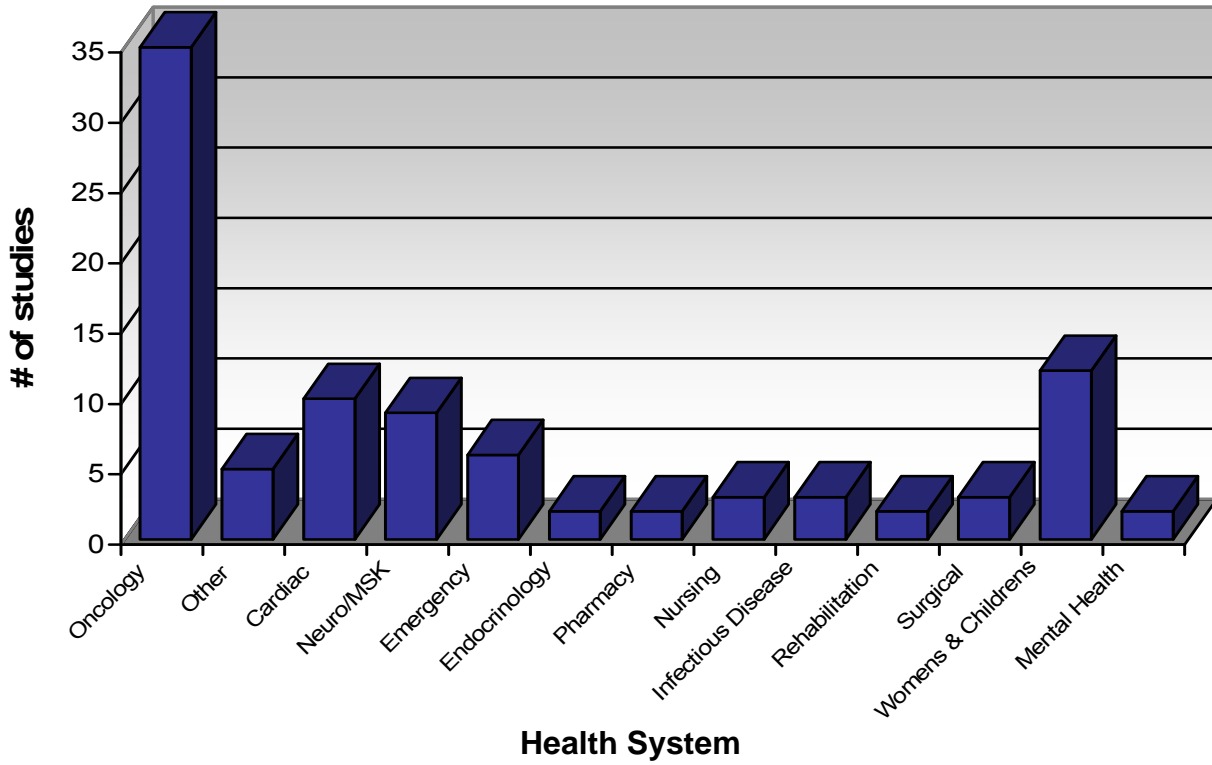
<i>Study Type</i>	<i>% Δ²</i>
Clinical Trials	20%
Chart Review	86%
Qualitative/Observational/Registry	14%
Student/Staff	0%

- (2) There is a lag in time to initiation of Clinical Trials and Qualitative/Observational/Registry studies (Figure 4 A & B). This lag is due to multiple factors including:
- ◆ Lengthy internal review processes
 - ◆ Termination of projects before site initiation
 - ◆ Poor quality of research submissions
 - ◆ Poor quality of external REB reviews
 - ◆ Lack of knowledge of, or failure to comply with organizational research requirements
 - ◆ Investigators lack of awareness of PHIPA regulations and organizational requirements for the use and dissemination of information for research purposes
- (3) There has been a steady increase in the number of Qualitative/Observational/Registry studies initiated and actively running during each fiscal year since 2006 with the total number of Qualitative/Observational/Registry studies initiated currently sitting at a 4 year high compared to the previous 3 fiscal years (Figure 2). We have seen 93% and 35% increases in the number of these studies initiated this fiscal year compared to last fiscal year, and the 2007/2008 fiscal year respectively (Figure 2).
- (4) Trillium Health Centre maintains continuous involvement in Clinical Trials (Figure 1 & Figure 6), predominantly by means of our Oncology Clinical Trials participation.

¹ When compared to the 2008/2009 fiscal year period.

² When compared to the 2008/2009 fiscal year period.

Figure 1: Active Studies by Discipline (as of March 31, 2010)



Other includes: Critical Care, Health Policy, Medical, Multi-health systems, Pathology and Professional Practice

Figure 2: Distribution of All Active Studies by Type, 2006-2010

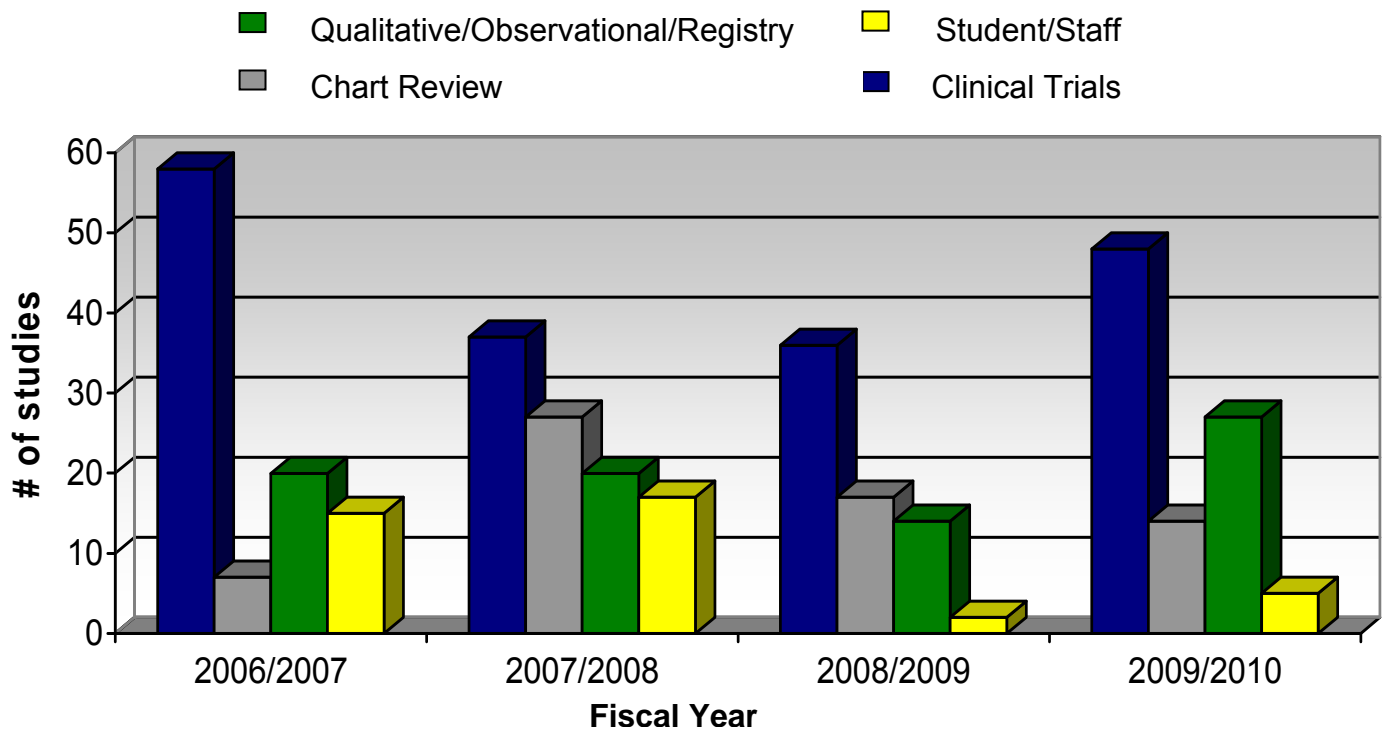


Figure 3: # of New Studies vs. Active Studies/Fiscal Year 2006 - 2010

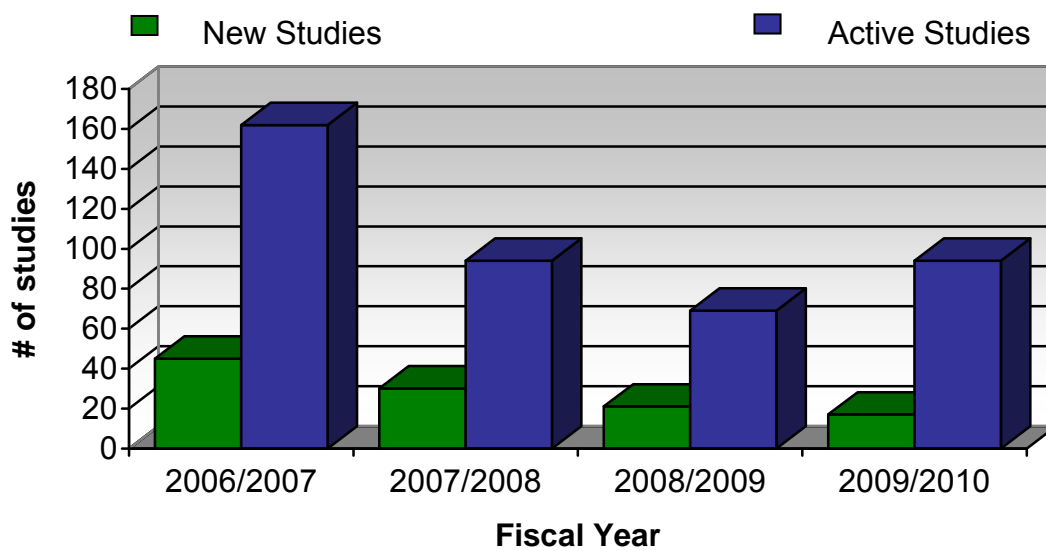
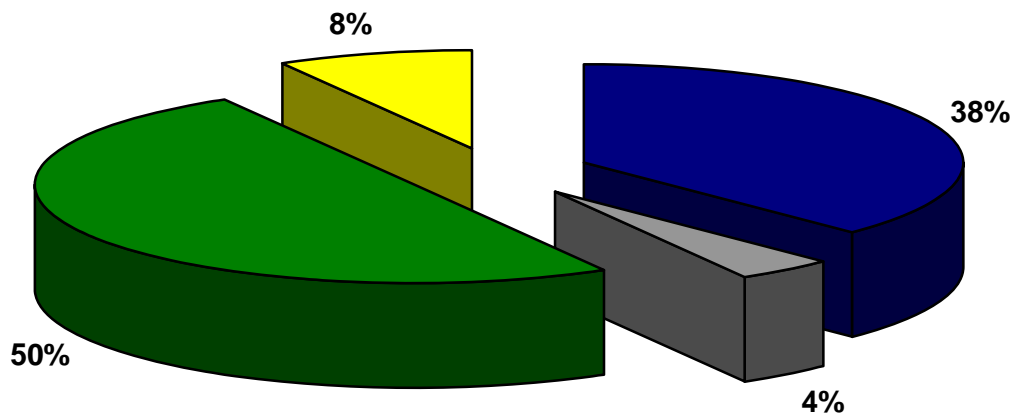


Figure 4. New Project Breakdown

- Qualitative/Observational/Registry
- Student/Staff
- Chart Review
- Clinical Trials

A - New Projects Reviewed



B - New Projects Initiated

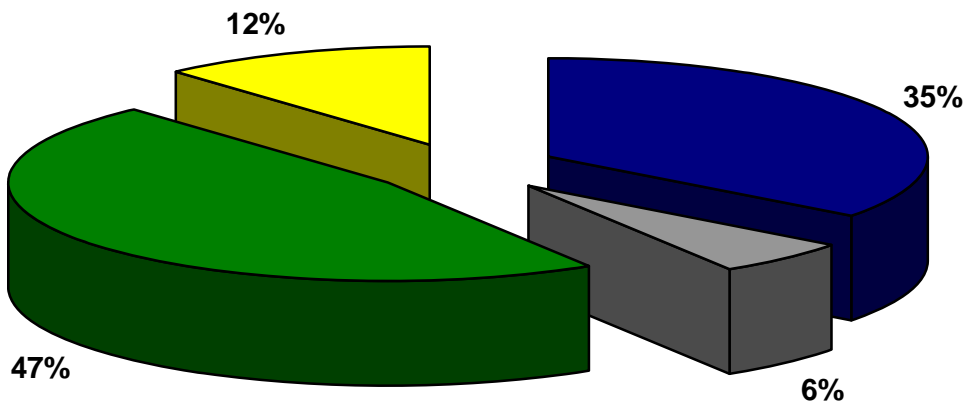


Figure 5: Distribution of New Studies by Type, 2005-2009

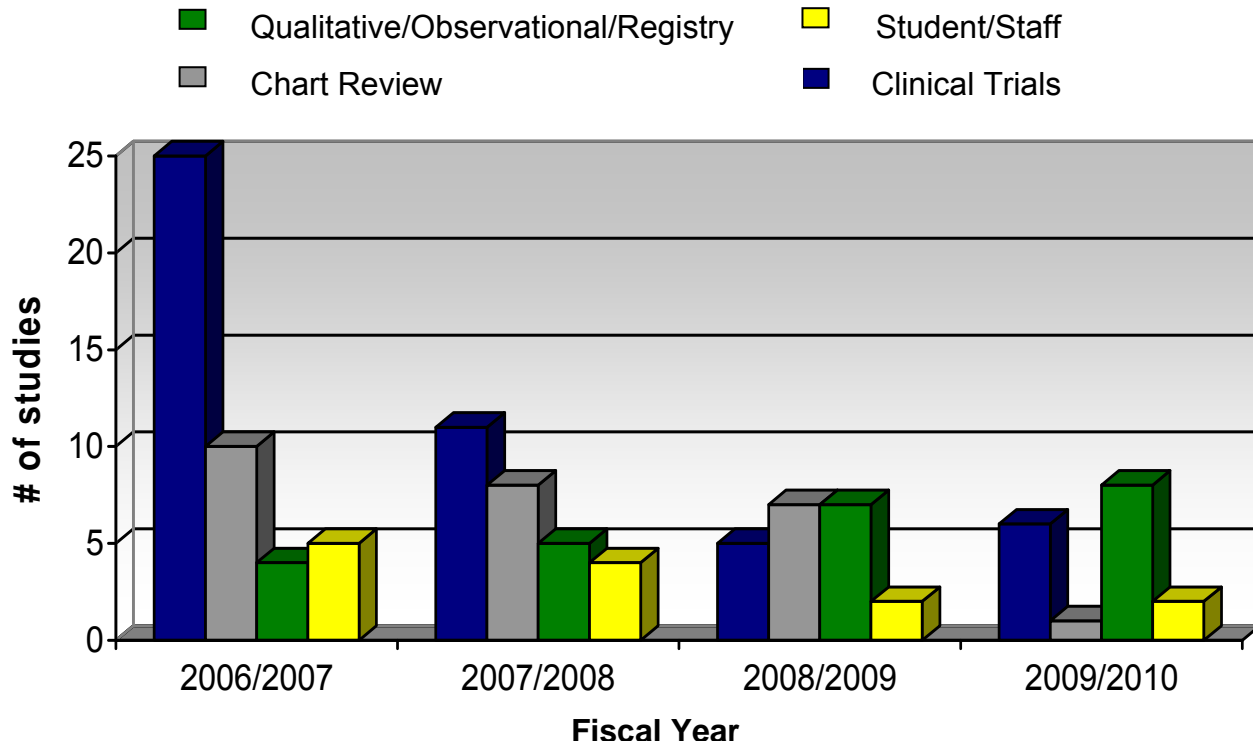


Figure 6: Distribution of Renewals (renewed vs. lapse in continuing approval) by Type – 2009/2010

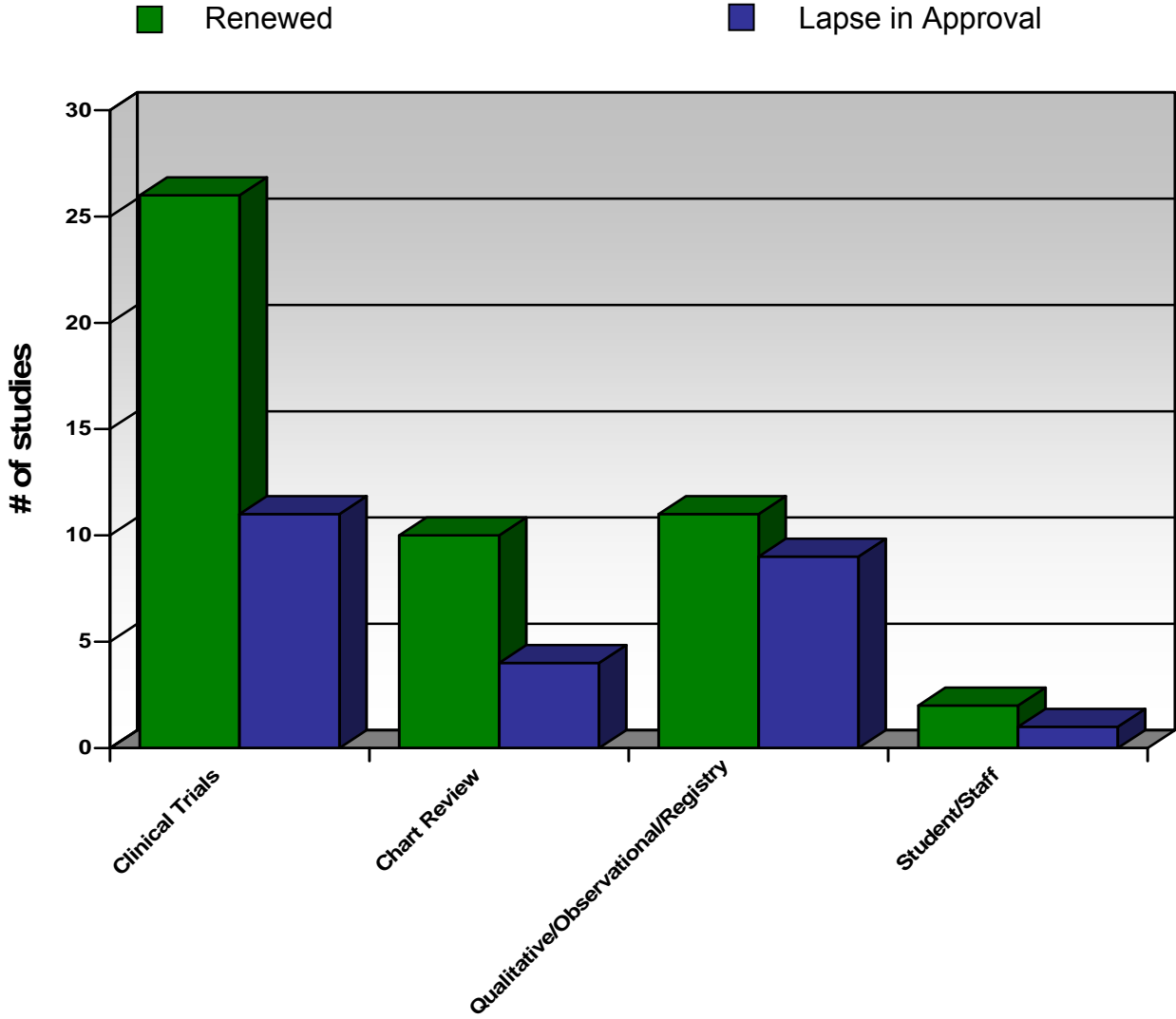


Figure 7. Active Study Distribution by PI status

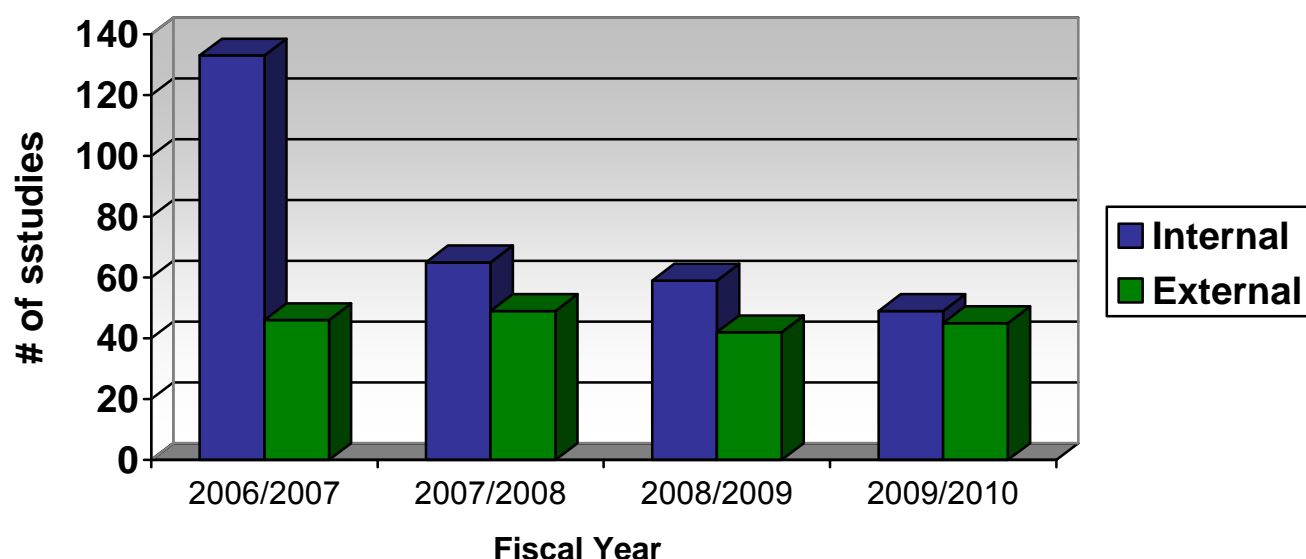


Table 3. Institutions leading Research Activity at Trillium Health Centre

	Institution
1.	Centre for Addiction and Mental Health (camh)
2.	Cardiac Care Network
3.	Hamilton Health Sciences Centre
4.	Humber College
5.	Institute for Clinical Evaluative Sciences
6.	London Health Sciences Centre
7.	Mount Sinai Hospital
8.	Ontario Network of Sexual Assault/Domestic Violence Centres
9.	Peel Children's Centre
10.	Princess Margaret Hospital
11.	University Health Network (UHN)
12.	Queens University
13.	Hospital for Sick Children
14.	St. Joseph's Health Centre
15.	St. Michael's Hospital
16.	University of Toronto
17.	Sunnybrook Health Sciences Centre
18.	University of Guelph
19.	University of Waterloo
20.	University of Western Ontario
21.	Women's College
22.	Toronto Rehabilitation
23.	Sunnybrook-Osler

Research Outcomes, Strengths and Achievements 2008/2009

Achievements

Research Review Team

The Research Review Team is continuously brainstorming and implementing new strategies to enhance the quality and efficiency of the study review process, and to promote research, awareness and education. Highlights include the developments below:

- ◆ **Draft Guidance on Reporting of External (Non-Local) Serious Adverse Events to Research Ethics Boards³**

In 2009 a Serious Adverse Events working group was established among a subset of the Canadian Association of Research Ethics Boards membership. The objective of this working group was to prepare a draft guidance regarding reporting of external serious adverse events to research ethics boards. This guidance would be directed to Health Canada and all sponsors of clinical trials in Canada (e.g. pharmaceutical and biotechnology sponsors, investigator-sponsors, cooperative group sponsors CIHR etc.).

A presentation was given at the 2009 CAREB national Conference and Annual General Meeting which included presentations showcasing perspectives from sponsors, REBs and Health Canada on the current adverse event reporting system. The outcome of the discussions surrounding this topic was an overall agreement that the current system of reporting adverse events in research does not enhance participant protection and may be hindering the REBs capacity to review and respond to safety issues in a timely fashion which ultimately may be harming research participants.

In response to this, the CAREB Board of Directors endorsed the development of this Guidance directed to Health Canada and all sponsors of clinical trials in Canada. Trillium (Research Administration and Research Review Team) was one of fourteen organizations across Canada that provided a position and feedback for this draft guidance during the 90 day consultation period of the various stakeholders. Trillium is in agreement that the current system of reporting contributes a significant workload that is non-productive and affects the RRTs capacity to review and respond to actual situations where participants rights, welfare and safety are threatened, in a timely manner. Trillium also expressed the fact that the current system of reporting is not supportive of the RRTs mandate of conducting meaningful ongoing review of research.

With the development of this draft guidance, CAREB also issued a recommendation to Health Canada to undertake a review of the Food and Drug Act in regard to adverse events in clinical trials. A subsequent meeting took place with representatives from

³ Details summarized from the “Canadian Association of Research Ethics Boards History of Development of the Guidance on Reporting of External (Non-Local) Serious Adverse Events to Research Ethics Boards” document v2010-03-23.

Health Canada's Bioethics, Innovation and Policy Integration Division/Science Policy Directorate/Strategic Policy Branch and the Clinical Trials/Adverse Drug Reaction Unit and CAREBs SAE working group. Health Canada has committed to providing a response to CAREB concerning this draft guidance.

- ◆ Trillium's RRT Adverse Events Subcommittee, established in April of 2006, continues to add value to the review and follow-up of adverse events reported for clinical trials running at our hospital. The Subcommittee members review all Serious Adverse Event (SAE) reports in detail, report the findings, and provide their feedback to the Research Review Team on a monthly basis. For events that involve Trillium patients, further follow-up and assessment of the steps taken to address the event, and ensure that proper care and follow-up are provided to our patients is assured through the actions of our SAE subcommittee. This has allowed for a more efficient means of reviewing all events, and identifying and advising whether specific studies should be reviewed further due to the nature, frequency and/or recurrence of the adverse events reported.

Membership of the Adverse Events Subcommittee is inclusive of pharmacy and clinical representation.

- ◆ As a preliminary introduction and education requirement, this fiscal year, the Research Review Team has incorporated a requirement that all new members complete the Tri-Council Policy Statement *Interagency Advisory Panel on Research Ethics'* *Introductory Tutorial* and the Office for Human Research Protections *Human Subject Assurance Training* modules. The information retained from this resources, combined with the use of the Research Reviewer Checklist assist in enhancing the quality and efficiency of the research review process.
- ◆ A series of Research Decision Charts and Policies were developed and implemented this fiscal year to provide guidance and direction to researchers and research teams in the development and initiation of research studies at Trillium. The Research Decision Charts serve as tools to equip researchers and research teams with knowledge surrounding key regulatory and ethical requirements that should be addressed during the development and initiation of research studies. The Research Policies, while inclusive of the applicable regulatory requirements regarding research, serve as a level of enforcement for research best practice. The decision charts and policies should increase the level of awareness of the regulations and organizational requirements regarding research activity, and will work towards increasing the level of compliance by researchers and research teams.

RESEARCH ADMINISTRATION

Trillium's Research Office has made and continues to develop significant collaborations with Credit Valley Hospital in:

- Aligning our processes, procedures and policies concerning research to ensure consistency between the two hospitals, and

- Leveraging off of CVH's videoconference access to the Society of Clinical Research Associates⁴ (SoCRA) conferences and seminars offered through the Greater Toronto Area Chapter. Our relationship and continuous networking with CVH has enabled us to extend access to these conferences and seminars to our clinical trials staff.

Department of Family Practice and Trillium-Summerville FMTU participation in the development of Trillium's Research Education Program (Cristina Martins, Primary Care Coordinator; Dr. Michael Kates, Chief – Department of Family Practice; Delilah Ofosu-Barko, Research Office) – *Excerpt from the Department of Family Practices' Annual Report*

As a quality assurance and improvement initiative, in November 2009 Trillium approved the development and implementation of a research education program. This program will foster the development of essential elements needed for a strong and efficient research infrastructure at Trillium Health Centre. Moreover, enhancing the quality of research conducted at Trillium and ensuring patient safety.

The Research Education program will be available to all Trillium staff and physicians, and will consist of one in-class certification session and 2 online certification modules courses. In order to conduct any research at Trillium, staff and physicians must participate in this program.

This exciting research education program, which is still in the planning and development stage, has received sponsorship from the University of Toronto's Medical School, Centre for Faculty Development. Trillium will be applying for accreditation through the University of Toronto's Continuing Professional Development (CPD) program, which will allow all physicians to collect CME credits for completing the program components.

A working group, which includes physician representation from Dr. Stephen McKenzie, Dr. Michael Kates, physician members of the Trillium-Summerville FMTU, which include Dr. Bachir Tazkarji, Dr. Ruby Alvi and Dr. Rosy Zafar, as well as clinical representation across Trillium's health systems, is in the process of designing this education program.

This is an exciting educational opportunity for Family Physicians and Resident, as it provides an opportunity to conduct innovative research in an academically affiliated learning environment.

Trillium's mission is to provide, excel and lead in innovation in acute and specialized care, build and strengthen our role in the regional tertiary services and provide an academically affiliated learning environment to teach the next generation of health care professionals. The research education program will serve as a method of meeting the goals of our mission by encouraging and supporting innovative research initiatives lead by Trillium investigators and fostering a robust research culture.

Research Supports

⁴ SoCRA is an international non-profit professional organization dedicated to the continuing education and development of clinical research professionals.

Trillium Health Centre has a unique opportunity to build capacity for research through strategic linkages, as we continue to move forward to implement activities in line with our five strategic themes.

Primarily driven by the “Learning & Innovation” strategic theme, Trillium Health Centres staff and physicians are consistently participating in and leading clinical research initiatives with the goal of ensuring the best quality of care is available to Trillium Health Centre’s patient population. Some examples of these research initiatives are provided in Appendix C which provides a snapshot of the diversity in of the initiatives, and the various degrees of engagement our staff and physicians demonstrate in their research activities.

Guided by the “Quality by Design” and “Operational Excellence” strategic themes, we are working towards enriching our efforts to help researchers at Trillium take advantage of the resources available by eventually providing the following support:

- Knowledge about grant opportunities and expertise in writing successful grant applications.
- Providing education and support to enable ethical and responsible research decision making by clinical researchers at Trillium.
- Developing and conducting meaningful statistical analysis of existing outcome data.
- Providing investigators with research education and access to research education materials.
- Assisting in appropriate, statistically significant sampling strategies.
- Assistance with preparing submissions for publication in peer reviewed scientific journals, including case reports.
- Administering a database to track all ongoing research projects, generate all required documentation on an automated, pre-scheduled basis, and link to the billing function.

In line with our “Integration & Partnership” strategic theme, we continue to work with Credit Valley Hospital with the aim of establishing overarching research guiding principles, and standardized research documents and applications between our hospitals. We continue to connect with other research-focused community hospitals, such as William Osler and Southlake Regional Health Centre, establishing valuable linkages to facilitate improving the quality of Trillium’s research program.

Appendix A: Reportable findings⁵

Study Title:	Evaluating the Quality of Sentinel Lymph Node Biopsy Practice in Ontario (ID#363)
Study Findings:	<p>The proportions of patients with a positive node and the use of SLNB in ineligible patients were consistent with the literature. The proportions of cases having appropriate pathology evaluation and reporting were low, as was the proportion of cases with more than one node removed. Both the identification of the SLNB and performance of SLNB concurrently with primary breast surgery were high exceeding 90%. As expected, the rate of completion axillary node dissection increased with the size of metastases identified in the positive SLN.</p> <p>The overall measure of quality in SLNB practice was high in the province. There remains room for improvement particularly in appropriate pathologic evaluation and reporting, as well as the proportion of cases with more than 1 lymph node removed,</p>
THC Practice Changes:	None indicated
Publications:	None indicated

Study Title:	Development and Evaluation of Interprofessional Care Practices (IPC) through Clinical Stimulation (ID#370)
Study Findings:	147 members of the THC clinical staff and physicians participated in a one-day workshop using clinical simulation to develop greater awareness of interprofessional skill including the need to greater understanding of professional culture, communication patterns and respect across professions. Analysis of data is in progress. Initial findings indicate a shift following the workshop in understanding of shared team responsibility for care from a physician directed model.
THC Practice Changes:	At the last workshop, THC stated a strategic priority was Interprofessional Care and the research team offered to attend any meetings to share knowledge.
Publications:	Mary Van Soeren, Kathleen Macmillian, Sandra Cop, Chris Kenaszchuk, Scott Reeves. <i>Development and evaluation of interprofessional care practices through clinical simulation. Journal of Interprofessional Care, Volume 23, Issue 3 May 2009, pages 304-306</i>

⁵ The study details reported in this section are reflective of those details provided by the site investigator in reporting study closure, or those findings publicly accessible through journal articles, health research conference posters and presentations.
Annual Report on Research 2009/2010

Appendix A: Reportable findings (continued)⁶

Study Title:	MA.5 – Intensive CEF versus Standard CMF as Adjuvant Therapy for Breast Carcinoma in Pre-menopausal Patients with Histologically involved Axillary Nodes (ID#220)
Study Findings:	The experimental arm, CEF, was developed in Canada through pilot work conducted by the Ontario Clinical Oncology Group. Between December 1989 and July 1993, 716 women from across Canada entered this trial. The primary results were reported in the Journal of Clinical Oncology in 1998 and showed a 10% increase in 5-year relapse-free survival and a 7% increase in 5-year overall survival associated with the experimental treatment. These results led to regulatory approval of epirubicin for the treatment of breast cancer and adoption of CEF as a standard therapy. This CEF regimen has gone on to be tested further in the NCIC CTG MA.21 trial, in which preliminary reporting demonstrated superior disease free survival as compared with standard treatment with Adriamycin, cyclophosphamide, and paclitaxel.
THC Practice Changes:	None indicated
Publications:	<ol style="list-style-type: none"> 1. O'Malley FP, Chia S, Tu D, Shepherd LE, Levine MN, Bramwell VH, Andrulis IL, Pritchard KI. <i>Topoisomerase II alpha and responsiveness of breast cancer to adjuvant chemotherapy</i>. Journal of the National Cancer Institute, 101:644-50, 2009. 2. Early Breast Cancer Trials' Collaborative Group (EBCTCG), Clarke M, Coates AS, Darby SC, Davies C, Gelber RD, Goodwin J, Goldhirsch A, Gray R, Peto R, Pritchard KI, Wood WC. <i>Adjuvant chemotherapy in estrogen-receptor-poor breast cancer: patient-level meta-analysis of randomized trials</i>. Lancet 371: 29-40, 2008. 3. Pritchard KI, Shepherd LE, O'Malley FP, Andrulis IL, Tu D, Bramwell VH. <i>Cancer to adjuvant chemotherapy</i>. New England Journal of Medicine 354:2103-11, 2006. 4. Levine MN, Pritchard KI, Bramwell VHC, Shepherd LE, Tu D, Paul N. <i>Randomized trial comparing cyclophosphamide, epirubicin, and fluorouracil with cyclophosphamide, methotrexate, and fluorouracil in premenopausal women with node-positive breast cancer: update of National Cancer Institute of Canada Clinical Trials Group Trial MA.5</i>. Journal of Clinical Oncology 23:5166-70, 2005.

⁶ The study details reported in this section are reflective of those details provided by the site investigator in reporting study closure, or those findings publicly accessible through journal articles, health research conference posters and presentations.

Appendix A: Reportable findings (continued)

5. Ouyang Y, Li D, Pater JL, Levine M. *The importance of temporal effects in evaluating the prognostic impact of joint ERPR expression in premenopausal women with node-positive breast cancer.* Breast Cancer Research and Treatment 92:115-23, 2005.
6. Parulekar WR, Day A, Ottaway J, Shepherd LE, Trudeau ME, Bramwell V, Levine M, Pritchard KI. *Incidence and Prognostic Impact of Amenorrhea During Adjuvant Therapy in High-Risk Premenopausal Breast Cancer: Analysis of a National Cancer Institute of Canada Clinical Trials Group Study NCIC CTG MA.5.* Journal of Clinical Oncology 23: 6002-8, 2005.
7. Praga C, Bergh J, Bliss J, Bonnetterre J, Cesana B, Coombes C, Fargeot P, Folin A, Fumoleau P, Guilianni R, Kerbrat P, Hery M, Nilsson J, ONida F , Piccart M, Shepherd L, Therasse P, Wils J, Rogers D. *Risk of acute myeloid leukemia and myelodysplastic syndrome in trials of adjuvant epirubicin for early breast cancer: correlation with doses of epirubicin and cyclophosphamide.* Journal of Clinical Oncology 23: 4179-91, 2005.
8. Crump M, Tu D, Shepherd, L, Levine M, Bramwell V, Pritchard K. *Risk of acute leukemia following epirubicin-based adjuvant therapy: A Report from the National Cancer Institute of Canada Clinical Trial Group.* Journal of Clinical Oncology 21:3066-71, 2003.
9. Levine M, Bramwell V, Pritchard K, Norris B, Shepherd L, Abu-Zahara H, Findlay B, Warr D, Bowman D, Myles J , Arnold A, Vandenberg T, Mackenzie R, Robert J, Ottaway J, Burnell M, Williams CKO, Tu D. *Randomized trial of cyclophosphamide, epirubicin, fluorouracil chemotherapy compared with cyclophosphamide, methotrexate, fluorouracil in premenopausal women with node positive breast cancer.* Classic Papers & Current Comments 5: 694-702, 2001.
10. Levine M, Bramwell V, Pritchard K, Norris B, Shepherd L, Abu-Zahara H, Findlay B, Warr D, Bowman D, Myles J , Arnold A, Vandenberg T, Mackenzie R, Robert J, Ottaway J, Burnell M, Williams CKO, Tu D. *Randomized trial of intensive cyclophosphamide, epirubicin and fluorouracil chemotherapy compared with cyclophosphamide, methotrexate, and fluorouracil in premenopausal women with node positive breast cancer.* Journal of Clinical Oncology 16: 2651-8, 1998.

Appendix A: Reportable findings (continued)

	<p>11. Levine M, Pritchard K, Bramwell V, Shepherd L. <i>Adjuvant chemotherapy with CEF versus CMF for node-positive breast cancer (in reply letter to the editor)</i>. Journal of Clinical Oncology 16: 3917, 1998.</p> <p>12. Shepherd L, Ottaway J, Myles J, Levine M. <i>Therapy-related leukemia associated with high-dose 4-epi-doxorubicin and cyclophosphamide used as adjuvant chemotherapy for breast cancer (letter to the editor)</i>. Journal of Clinical Oncology 12: 2514-5, 1994.</p> <p>13. Sadura A, Pater J, Osoba D, Levine M, Palmer M, Bennett K. <i>Quality of life assessment: patient compliance with questionnaire completion</i>. Journal of the National Cancer Institute 84: 1023-6, 1992.</p>
Study Title:	SC.18 – Phase III Double-blind, Placebo-controlled Randomized Comparison of Megestrol Acetate (Megace) Versus an N-3 Fatty Acid (EPA) Enriched Nutritional Supplement Versus Both for the Treatment of Cancer Cachexia and Anorexia. (ID#221)
Study Findings:	<p>A smaller percentage taking the EPA supplement gained $\geq 10\%$ of baseline weight compared with those taking MA: 6% v 18%, respectively (P =.004). Combination therapy resulted in weight gain of $\geq 10\%$ in 11% of patients (P =.17 across all arms). The percentage of patients with appetite improvement (North Central Cancer Treatment Group Questionnaire) was not statistically different: 63%, 69%, and 66%, in EPA-, MA-, and combination-treated arms, respectively (P =.69). In contrast, 4-week Functional Assessment of Anorexia/Cachexia Therapy scores suggested MA-containing arms experienced superior appetite stimulation compared with the EPA arm, with scores of 40, 55, and 55 in EPA-, MA-, and combination-treated arms, respectively (P =.004). Survival was not significantly different among arms. Global quality of life was not significantly different among groups. With the exception of increased impotence in MA-treated patients, toxicity was comparable.</p> <p>CONCLUSION: This EPA supplement, either alone or in combination with MA, does not improve weight or appetite better than MA alone.</p>
THC Practice Changes:	None indicated
Publications:	Jatoi A, Rowland K, Loprinzi CL, Sloan JA, Dakhil SR, MacDonald N, Gagnon B, Novotny PJ, Mailliard JA, Bushey TI, Nair S, Christensen B; North Central Cancer Treatment Group. <i>An eicosapentaenoic acid supplement versus megestrol acetate versus both for patients with cancer-associated wasting: a North Central Cancer Treatment Group and National Cancer Institute of Canada collaborative effort</i> . Journal of Clinical Oncology: 22(12):2469-76, 2004 Jun 15

Study Title:	PAC.1/S0205: A Phase III Randomized Open-label Study Comparing Gemcitabine Plus Cetuximab (IMC-225) Versus Gemcitabine as First-Line Therapy of Patients with Advanced Pancreatic Cancer (ID#245)
Study Findings:	Results: 766 pts (735 eligible) with a median age of 64 (30–91) were enrolled by SWOG and CTSU between January 2004 and April 2006. Of those, 51% were males, 21.5% had locally advanced disease, and 13% had PS of 2. The study closed with full accrual. The median survival was 6 months in the G arm and 6.5 months in the G plus C arm for an overall HR of 1.09 (95% CI 0.93–1.27, p= 0.14) . The corresponding PFS was 3 months and 3.5 months, for G and G+C arms, respectively (HR =1.13, 95%CI .97–1.3, p=.058). The confirmed response probabilities were 7 % in each arm, and inclusion of unconfirmed responses yielded 14% in the G arm and 12% in the G + C arm.702 pts were evaluable for toxicity. 90 pts experienced at least one grade 4 toxicity; 14% on the G plus C, 11% on G alone. Conclusions: This study failed to demonstrate a clinically significant advantage of the addition of cetuximab to gemcitabine for overall survival, PFS and response in advanced PC.
THC Practice Changes:	No – Cetuximab is not available in Ontario
Publications:	Philip PA, Benedetti J, Fenoglio-Preiser C, et al.: <i>Phase III study of gemcitabine [G] plus cetuximab [C] versus gemcitabine in patients [pts] with locally advanced or metastatic pancreatic adenocarcinoma [PC]: SWOG S0205 study.</i> [Abstract] Journal of Clinical Oncology 25 (Suppl 18): A-LBA4509, 2007

Study Title:	Adherence with Injectable Venous Thromboembolism Prophylaxis Following Total Hip and Total Knee Replacement Surgery (ID#399)
Study Findings:	The Complete Registry is the first Canadian registry that provides key real life data on adherence with injectable VTE prophylaxis and the factors impacting the adherence. Median inpatient and outpatient adherence was over 90% with few instances of under and over adherence.
THC Practice Changes:	None indicated
Publications:	William M Semchuk, David Backstein, John Stewart, Esmat Dessouki, Mary Kwan, Pauline Lavoie, Maria Valois, Allan Mills, and John W Eikelboom. <i>Adherence with Injectibal Prophylaxis for Venous Thromboembolism (VTE) Following Total Hip (THR) and Total Knee (TKR) Replacement Surgery: Complete Registry.</i> Blood (ASH Annual Meeting Abstracts) 114: 558.

Appendix A: Reportable findings (continued)

Study Title:	Transmission of infection in healthcare settings: determining the risk of infections in long-term care facility (LTCF) residents after a visit to the emergency room (ER) (ID#391)
Study Findings:	Visit to ERs, without admission to the hospital, is associated with a 4.5fold increased risk of acquisition of either RTI or GI infections. The ER-returning resident may then become the index case for outbreaks in the LTCF. Following these results, future studies looking into ER organization and compliance with infection control and prevention measures, as well as infection control measures in LTCF will be undertaken.
THC Practice Changes:	None indicated
Publications:	Abstract Presentation: McGill Epidemiology, Biostatistics & Occupational Health Seminar Series 2008/2009 – <i>Emergency rooms – when it is not just about waiting but also about sharing...</i>

Study Title:	Retrospective Observational Study to Assess Canadian Healthcare Institution Resource Utilization Resulting from Skeletal Related Events in Patients with Bone Metastases – Medical Chart Review (ID#401)
Study Findings:	Information collected from the study will be used to calculate costs of treating specific types of Skeletal Related Events in Canada.
THC Practice Changes:	None indicated
Publications:	

Study Title:	EFPECT - Enhanced Feedback for Effective Cardiac Treatment (ID#11)
Study Findings:	The publication of the early feedback hospital report card did not result in a significant systemwide improvement in the early feedback group in either the composite AMI process-of-care indicator (absolute change, 1.5%; 95% confidence interval [CI], -2.2% to 5.1%; P = .43) or the composite CHF process-of-care indicator (absolute change, 0.6%; 95% CI, -4.5% to 5.7%; P = .81). During the follow-up period, the mean 30-day AMI mortality rates were 2.5% lower (95% CI, 0.1% to 4.9%; P = .045) in the early feedback group compared with the delayed feedback group. The hospital mortality rates for CHF were not significantly different. CONCLUSION: Public release of hospital-specific quality indicators did not significantly improve composite process-of-care indicators for AMI or CHF
THC Practice Changes:	None indicated
Publications:	1. Jackevicius CA, Alter D, Cox J, Daly P, Goodman S, Filate W, Newman A, Tu JV; Canadian Cardiovascular Outcomes Research Team. <i>Acute treatment of myocardial infarction in Canada 1999-2002</i> . Canadian Journal of Cardiology. 2005 Feb;21(2):145-

Appendix A: Reportable findings (continued)

	<p>52.</p> <p>2. Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. <i>Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model.</i> Journal of American Medical Association. 2003 Nov 19;290(19):2581-7.</p> <p>3. Tu JV, Donovan LR, Lee DS, Wang JT, Austin PC, Alter DA, Ko DT. <i>Effectiveness of Public Report Cards for Improving the Quality of Cardiac Care: The EFFECT Study: A Randomized Trial.</i> Journal of American Medical Association. 2009 Nov 18;</p>
--	---

Study Title:	RE-DEEM - Randomized Dabigatran Etextilate dose finding study in patients with acute coronary syndromes post index event with additional risk factors for cardiovascular complications also receiving aspirin and clopidogrel: multi-centre, prospective, placebo controlled, group dose escalation trial
Study Findings:	<p>In the RE-DEEM trial studying four doses of dabigatran added to dual antiplatelet therapy vs. placebo, researchers found that the novel oral direct thrombin inhibitor resulted in a low and acceptable bleeding rate in patients post-MI.</p> <p>For the primary endpoint of major and clinically relevant minor bleeds, dabigatran combined with dual antiplatelet therapy resulted in low major bleeding ($P<.001$). In the on-treatment group assigned placebo, 1% experienced bleeding. Major bleeding occurred in 2% of the 50 mg group, 1% of the 75 mg group, 6% of the 110 mg group and 4% of the 150 mg group. Clinically relevant minor bleeding occurred in 7% of the placebo on-treatment group, 9% in the 50 mg group, 14% in the 75 mg group, 23% in the 110 mg group and 23% in the 150 mg group.</p> <p>In the secondary outcome of D-dimer levels, there was a 45% decrease in all dose levels consistent out to 26 weeks. After treatment cessation, D-dimer levels were similar between the placebo and dabigatran groups.</p> <p>For the clinical endpoint — a composite of CV death, nonfatal MI and stroke — there was only stroke in the placebo arm of the study and an overall low event rate.</p> <p>Dabigatran up to 150 mg twice daily seems safe if added to aspirin and clopidogrel in patients with AF and stenting. Dabigatran 110 mg or 150 mg twice daily after ACS needs further</p>

Appendix A: Reportable findings (continued)

	evaluation in a large-scale study before the cardiology community can know its effect on clinical outcomes
THC Practice Changes:	None indicated
Publications:	

Study Title:	Long Term Impacts of West Nile Virus Infection: A Cohort Study (ID#277)
Study Findings:	Physical and mental function, as well as mood and fatigue seemed to return to normal within 1 year of symptom onset. Participants with neuroinvasive disease took slightly longer to recover. Maximum predicted recovery or rate of recovery in any domain did not differ between participants with meningoencephalitis and those with encephalitis. Lack of preexisting comorbid conditions was associated with faster recovery of physical function whereas lack of comorbid conditions and male sex were associated with faster recovery of mental function.
THC Practice Changes:	None indicated
Publications:	Loeb M, Hanna S, Nicolle L, Eyles J, Elliott S, Rathbone M, Drebot M, Neupane B, Fearon M, Mahony J. <i>Prognosis after West Nile virus infection</i> . Annals of Internal Medicine. 2008 August 19; 149(4):232-41

Study Title:	Cardiac CT and MR Assessment of Bioprosthetic Aortic Valves: A Pilot project (ID#266)
Study Findings:	CT and MR are feasible non-invasive modalities for determination of PVA in bioprosthetic aortic valves. SM prosthesis has highest image quality for both modalities. PVA was very highly correlated between CT and MR. PVA by CT/MR had a moderate inverse correlation with peak gradient by echocardiogram.
THC Practice Changes:	None indicated
Publications:	Tarang N. Sheth; Gopal Bhatnagar. <i>Planimetric Valve Area of Bioprosthetic Aortic Valves By Computed Tomography and Magnetic Resonance</i> . [poster presentation] The Society for Heart Valve Disease, 5 th Biennial Meeting, Berlin 2009.

Appendix B: Trillium Health Centre Research Review Team Membership Listing

CHAIR

Allan Mills (Interim)

CO-CHAIR

- Dianne Godkin -

Active Voting Members						
Last Name	First Name	Degrees & License	Primary Speciality or Occupation	Physician Scientist/Other Scientist/Non-Scientist	Gender	THC Affiliation
Hunter	Amanda J.	BA LLB	Lawyer	NS	Female	No
Douloff	Carol	RN BA MHSc	Neuro/MSK	OS	Female	Yes
Nasser	Shirin	CCHRA	Privacy Specialist	NS	Female	Yes
Tugwood	Bruce	BScPharm	Pharmacy	OS	Male	Yes
Mills	Allan	PharmD	Pharmacist	OS	Male	Yes
Woodward	Christina	MA MLIS	Hospital Librarian	NS	Female	Yes
Godkin	Dianne	RN, BScN, MN, PhD	Ethics, End of Life, Gerontology, Qualitative and Quantitative Methodology	OS	Female	Yes
Sumbler	Karen	Ph.D	Child Psychologist	OS	Female	Yes
Walsh	Cathy	RN MScN ACNP CCNc	Cardiac Surgery	OS	Female	Yes
Samuel	Jessy	BSc.Pharm ACPR	Pharmacy	OS	Female	Yes
Rosser	Mary	MA	Community Member	NS	Female	No
McKye	Anne	OT Reg(Ont); BASC; BHSc(OT);	Occupational Therapist: Seniors' Health and Geriatric	OS	Female	Yes

Active Voting Members						
Last Name	First Name	Degrees & License	Primary Speciality or Occupation	Physician Scientist/Other Scientist/Non-Scientist	Gender	THC Affiliation
		MSc	Mental Health			
Ahluwalia	Ravjit	MD, PGY1	*Family Medicine Resident	PS	Male	Yes
Biro	Laurence	MD, PGY1	*Family Medicine Resident	PS	Male	Yes
Corkum	Casey	MD, PGY1	*Family Medicine Resident	PS	Male	Yes
Puri	Gaurav	MD, PGY1	*Family Medicine Resident	PS	Male	Yes
Tazkarji	Bachir	MD, CCFP, ABRM	+Family Medicine	PS	Male	Yes
Members on Leave						
DeBruyn	Joan	MSc. OT BSc. OT	Clinical Educator: Neuro/MSK Rehab	OS	Female	Yes
Non-Voting Members						
Ofosu-Barko	Delilah	BMSc	Research	OS	Female	Yes

* Monthly Rotating Resident Member
+ Ad hoc Member

Trillium Health Centre's Research Review Team operates in compliance with the Tri-Council Policy Statement, ICH GCP Guidelines, PHIPA, Part C, Division 5 of the Health Canada Food and Drug Regulations and maintains active registration with the Office for Human Research Protections.

Appendix C: Level's of Engagement in Research Activity

1. Use of Normal Breast Tissue to Study Basal-like Breast Cancer

Level of Engagement:	Collaboration in leading edge molecular research
Abstract:	Breast cancer is a heterogeneous disease that includes several distinct subtypes. Basal-like breast cancer is one of the most aggressive subtype for which there is no specific treatment. There is therefore a tremendous interest in the identification of novel therapeutic targets. The tumor suppressors Rb, Pten and p53 are often loss in basal-like breast cancer. We have recently inactivated Rb plus p53, or Pten plus p53 in the mammary epithelium of transgenic mice and demonstrated that this leads to mouse tumors that highly resemble human basal-like breast cancer. To develop a model for basal-like BC using human cells, we propose to knock down the right combination of these tumor suppressor genes (Rb/p53, Pten/p53) in normal human mammary epithelial cells, followed by transplantation into the mammary gland of recipient mice. We expect the mice to develop human basal-like breast cancer. This would provide us with a powerful pre-clinical model for human basal-like breast cancer and allow us to identify novel therapeutic drug.
Investigator Collaboration Information	
Investigator	Organization
Dr. Eldad Zacksenhaus	Toronto General Hospital/University Health Network
Dr. Michael Weinberg	Trillium Health Centre
Funding Agency/Organization:	Canadian Breast Cancer Research Alliance

2. A prospective controlled trial comparing photoselective vaporization of the prostate (PVP-120W) to transurethral resection of the prostate (TURP) for the treatment of benign hyperplasia of the prostate (BPH)

Level of Engagement:	Collaboration in leading edge clinical research
Abstract:	In patients with an enlarged prostate (benign prostatic hyperplasia), the standard surgical treatment is transurethral resection of the prostate (TURP). Recently, a high-power (120W) laser system has been approved by Health Canada for the treatment of an enlarged prostate. This treatment, called photoselective

Appendix C: Level's of Engagement in Research Activity (continued)

	vaporization of the prostate (PVP), may offer more efficient removal of prostate tissue with fewer complications and may result in clinical and economic benefits compared to the standard treatment. However, there have been no studies comparing the 120W laser with the standard TURP. This study will provide currently unavailable information for clinicians and decision makers.
Investigator Collaboration Information	
Investigator	Organization
Dr. Jean-Eric Tarride	Program for Assessment of Technology in Health, St. Joseph's Healthcare/McMaster University
Dr. Gary McIsaac	Trillium Health Centre
Dr. Edward Woods	The Scarborough Hospital
Dr. Paul Whelan	McMaster Institute of Urology
Funding Agency/Organization: Ontario Ministry of Health and Long Term Care	

3. Cardiac MR Assessment of Medtronic Mosaic Bioprosthetic Valves

Level of Engagement:	Clinical research initiative developed and initiated by Trillium Physicians
Abstract:	The Medtronic Mosaic valve is among several types of artificial valves currently used to replace an aortic valve. Recent experience at Trillium Health Centre suggests that this type of valve may have a high pressure gradient as measured by echocardiography after it is implanted, which would indicate that valve opening area was not as good as required. In several such clinical cases, imaging with MRI and CT suggested that the valve area was actually normal. This investigation seeks to systemically study a range of Medtronic valves previously implanted at Trillium with both echocardiography and MRI to provide further information about this clinically important discrepancy.
Investigator Collaboration Information	
Investigator	Organization
Dr. Tarang Sheth	Trillium Health Centre
Dr. Gopal Bhatnagar	Trillium Health Centre

Appendix C: Level's of Engagement in Research Activity (continued)

Funding Agency/Organization:	Medtronic, Inc.
-------------------------------------	-----------------

4. Quality Initiative in Rectal Cancer Trial

Level of Engagement:	External Investigator Initiated and Lead Clinical Research
Abstract:	<p>The study includes 18 hospitals across Ontario that will randomized to receive the QIRC strategy (experimental arm) or no intervention (control arm). The QIRC strategy interventions include evidence-based surgery, physician feedback, participation by opinion leaders, and appreciation for the practice environment. This strategy utilizes the surgical principles of total mesorectal excision and the process principles of continuous quality improvement, which emphasizes participatory and incremental improvement at the system level. There is some evidence that rates of permanent colostomy and local recurrence can be improved through the use of total mesorectal excision techniques. However, there is no evidence that for a large group of surgeons and hospitals that this strategy will improve patient outcomes versus current surgical practice.</p> <p><u>Objectives:</u></p> <p>Primary: To test if the QIRC strategy, which is designed to positively influence surgeon practice, can decrease hospital rates of permanent colostomy and local tumour recurrence for surgically treated rectal cancer patients.</p> <p>Secondary: To test if the QIRC strategy can lead to improved quality of life scores, and improved bladder, bowel and sexual function for surgically treated rectal cancer patients.</p>

Investigator Collaboration Information

Investigator	Organization
Dr. Marko Simunovic	Hamilton Health Sciences Centre

Funding Agency/Organization:	Canadian Institutes of Health Research
-------------------------------------	--

Appendix C: Level's of Engagement in Research Activity (continued)

5. MA.24 – HERA: A randomized three arm multi-centre comparison of 1 year and 2 years of Herceptin versus no Herceptin in women with HER2 Primary Breast Cancer who have completed adjuvant chemotherapy

Level of Engagement:	Industry and disease specialty group lead international clinical trial
Abstract:	<p>This is a three arm, randomized, open-label and multicentre study and death. Retrospective data suggests that breast tumours that over express HER2 may be particularly sensitive to certain cytotoxic drugs and less sensitive to others i.e. Tamoxifen. HER2 is a transmembrane Human Epidermal growth factor Receptor, which is over expressed in 15-25% of human breast cancers and is associated in the laboratory, with more aggressive tumour behaviour. HER2 over expression has been independently associated with poorer disease-free survival and overall survival compared with tumours that do not over express HER2. Herceptin is a recombinant humanized monoclonal antibody that binds with high affinity to the HER2 protein and has been show to inhibit the proliferation of human tumour cells that over express HER2 both in vitro and in vivo. In North America and much of Europe, Herceptin is approved as part of the therapy for the treatment of patients with metastatic breast cancer whose tumours over express the HER2 protein.</p> <p><u>Objectives:</u></p> <p>Primary: To compare disease-free survival in patients with HER2 over expressing breast cancer who have completed acceptable adjuvant and radiotherapy if applicable, and who have been randomized to Herceptin for one year or two years, versus no Herceptin.</p> <p>Secondary: To compare overall survival in these patients randomized to Herceptin for one or two years versus no further therapy.</p> <p>To compare the incidence of cardiac dysfunction in patients treated and not treated with Herceptin.</p>
Investigator Collaboration Information	
Investigators	Organization
Dr. Kathleen I. Pritchard	Edmond Odette Cancer Centre, Sunnybrook Health Sciences Centre
Dr. Martine J. Piccart-Gebhart (study chair)	Institut Jules Bordet

Appendix C: Level's of Engagement in Research Activity (continued)

Dr. Robert E. Coleman (study chair)	Cancer Research Centre at Weston Park Hospital
Dr. Karen A. Gelmon (study chair)	British Columbia Cancer Agency
Dr. Olivia Pagani (study chair)	Ospedal Beata Vergine
Dr. John Gapski (lead site investigator)	Trillium Health Centre
Collaborating Organization	European Organization for Research and Treatment of Cancer
Collaborating Organization	National Cancer Institute of Canada Clinical Trials Group
Collaborating Organization	International Breast Cancer Study Group
Funding Agency/Organization: Breast International Group & Hoffman La-Roche	

6. Stroke CARE & ACT

Level of Engagement:	Trillium Physician initiated Clinical Research (grant-in-aid)
Abstract:	While cardiac studies are routinely conducted in the work-up of stroke patients, the impact of these studies lies not so much in the identification of abnormalities but more so with the ability of these findings to influence clinical change. Our recent data suggests that exhaustive use cardiovascular investigations in the work-up of stroke patients have little clinical impact in the medical management of our stroke patients. In contrast to over utilization of cardiovascular investigations we have observed under utilization of antiplatelets, antihypertensive and statin agents in this patient population. A prospective study is required for assessment of cardiovascular investigation in stroke management in order to try to determine if there is a specific stroke population that can truly benefit from these tests. The evaluation of medical management regarding antiplatelet, BP and cholesterol on admission, and post discharge will also provide an accurate picture of how stroke patients are medically managed outside a controlled environment.
Investigator Collaboration Information	
Investigator	Organization
Dr. Andre Douen	Trillium Health Centre
Funding Agency/Organization: Pfizer Canada Inc.	

Appendix D: Research Review Team Terms of Reference

RESEARCH REVIEW TEAM Terms of Reference

Role and Responsibilities:

The Research Review Team advises the Chief of Staff with respect to acceptability of new and ongoing research proposed by researchers affiliated with Trillium Health Centre. It does so in accordance to Trillium's Research Principles and Protocols (5000 & 5010), and specifically by:

- Reviewing and evaluating all research applications against accepted ethical, scientific and organizational standards (Tri-Council Policy and Trillium protocols).
- Ensuring affected Health Systems and SBUs have completed an impact analysis, and any issues or questions have been discussed and resolved with the Principal Investigator.
- Ensuring site agreements have been reviewed and accepted.
- Arranging for a dispute resolution meeting if required.
- Reviewing and evaluating all ongoing ethical, scientific and organizational concerns during the research period, and advising the Chief of Staff of any unanticipated events.
- Reviewing compliance with Trillium's principles and protocols on Research.
- Providing annual research reports based on the database of all research activities maintained by the Chairperson.

Frequency of Meetings:

- A minimum of 10 (ten) meetings per year
- Third Thursday of the month

Operating Procedures:

- Members who are directly involved in an application under discussion are non-voting.
- Quorum is 51% of voting membership.
- Chairperson is appointed by Chief of Staff and Senior Administrator in charge of Research.
- Minutes will be prepared and maintained by the Chairperson or their delegate, and will clearly document all research review activities which led to any recommendations.
- Members will attend regularly, and the Chairperson will address any attendance issues.

Accountability:

The team is accountable to the Chief of Staff and the Senior Administrator in charge of Research.

Reviewed by Team: November 21, 2002

Approved by Chief of Staff: November 26, 2002

Revised – December 2003, April 2004, October 2004, May 2009

The membership will reflect requirements articulated by the Tri-Council Policy Statement and PHIPA as follows:

Membership meets the requirements defined in the Tri-Council Policy on Human Research and the Personal Health Information Protection Act as follows:

1. at least two members with broad expertise in the methods or in the areas of research that are being covered
2. at least one member knowledgeable in ethics
3. at least one member knowledgeable in relevant Canadian laws
4. at least one non-scientific member
5. one independent community member
at least one member knowledgeable in Privacy (according to PHIPA)

Appendix D: Research Principles

Principle Title:	Research
Section:	Provider of Choice
Number:	5000
Approved By:	Board of Directors
Approval Date:	January 30, 2001
Effective Date:	January 20, 2001
Review/Revisions:	February 25, 2004; November 17, 2004

Upon which Principles is Research based...?

1. Trillium Health Centre supports basic and applied sciences research focused on the organization's core services and strategic priorities by providing a supporting environment and resources.
2. The Board of Directors at Trillium Health Centre is responsible for all research involving human subjects, with the mandate to ensure that a process is in place to approve, reject, propose modifications to, or terminate any proposed or ongoing research involving human subjects, which is conducted within, or by members of the institution.
3. The Board of Directors expects that each proposed research study would be evaluated against the highest existing standards to ensure sound ethical and scientific conduct. This is enabled through a standard review process.
4. All research that involves living human subjects must submit to an ethics review to ensure compliance with Good Clinical Practice Guidelines, the Tri-Council Policy Statement, and best practices to protect personal health information. This also applies to research involving human remains, cadavers, tissues, biological fluids, embryos or fetuses. Quality assurance studies, performance reviews or testing within normal educational requirements should not be subject to such a review.
5. Trillium Health Centre has adopted a proportionate approach to research review, based on the general principle of minimal risk: if potential subjects can reasonably be expected to regard the probability and magnitude of possible harms implied by participation in the research to be no greater than those encountered by the subject in those aspects of his or her everyday life that relate to the research then the research can be regarded as within the range of minimal risk. Above the threshold of minimal risk, the research warrants a higher degree of scrutiny and greater provision for the protection of the interests of the prospective subjects. (Tri-Council Policy Statement)
6. In keeping with this principle, proportionate review at Trillium implies two different levels of Research review:
Full Research Review - default requirement for all research, unless deemed to meet Expedited Review Requirements. Approval of these studies requires Medical Advisory Committee approval. The Chief of Staff may grant temporary approval following review by

the Research Review Team, when the MAC is adjourned for regular business. The MAC will be informed of these decisions.

Expedited Research Review – categories of research that are confidently expected to involve minimal risks. Examples of such categories might include: Research protocols and staff/student projects that involve no more than minimal risk; Annual renewals of approved projects in which there has been little or no change in the ongoing research; Research involving review of patient records. The Chair of the Research Review Team, will provide expedited approval following review by the Research Review Team for these studies. The Chair of the Research Team, in consultation with the Chief of Staff, may grant temporary approval, when the Research Review Team is adjourned for regular business. The Research Review Team will be informed of these decisions.

7. Proposed research that is funded by a sponsoring agency must undergo an ethics and scientific review by an External Ethics Committee. Documentation of this external review is a required component of the Application and approval process. Research without such funding will be reviewed by the Trillium Health Centre Research Review Team, which will submit its findings to the Chief of Staff.
8. The Principal Investigator must:
 - disclose financial interest as a result of participating in the proposed study;
 - ensure that all impacted systems and services understand and support the proposed study and that arrangements are in place to reimburse them for any incurred operating costs;
 - ensure that any financial and/or site agreements are reviewed and approved by Trillium Health Centre, before a study can proceed.
9. Each active project will be reviewed annually. The Principle Investigator will ensure than an annual report is provided to Trillium, which includes an update on the progress of the study, and costs and any changes in protocol.

What is the overall context ...?

- The World Medical Association Declaration of Helsinki summarizes recommendations guiding physicians in biomedical research involving human subjects, noting that the purpose for such research must be to improve diagnostic, therapeutic and prophylactic procedures and understanding of the etiology and pathology of the disease.
- Any sponsoring agency wishing to undertake a clinical trial in Canada must seek approval from Health Canada's Therapeutic Products Directorate (TPD). TPD applies its *Good Clinical Practice: Consolidated Guidelines* (1997) to evaluate such proposals. GCP is based on international guidelines adopted by regulatory bodies of the European Union, Japan and the USA. GCP articulates in detail:
 - Roles and responsibilities of the Investigator and the Sponsor
 - International standards for preparation of Investigator's Brochures and Clinical Trial Protocols
 - Investigator's and Sponsor's responsibilities regarding the development, filing and maintenance of "Essential Documents"

- Responsibilities and functions of an Institutional Review Board/Independent Ethics Committee

- Health Canada has the legal authority to audit/inspect clinical trials.
- In addition to GCP, the Tri-Council Policy Statement “Ethical Conduct for Research Involving Humans” provides an ethics framework and processes to guide organizational decision-making in this area. (Authored by Medical Research of Canada, Natural Sciences and Engineering Research Council of Canada and Social Sciences and Humanities Research Council of Canada).
- The Personal Health Information Protection Act (PHIPA) sets a legal context for protection of personal health information associated with research involving human subjects
- In the U.S., the Health Insurance Portability and Accountability Act (HIPAA) sets a legal context for management of health-related electronic transactions.
- Other Acts affect the standards and conduct of research involving human subjects in a variety of ways, such as intellectual property, and competence.
- The Management Regulations of the Public Hospitals Act grant the Board of Directors the authority to permit access to health records for the purpose of scientific research. Scientific research to be conducted by a member of medical, dental, midwifery or extended class nursing staff requires the additional approval of the Medical Advisory Committee.
- The Canadian Council on Health Services Accreditation expects a process for reviewing research applications, with an emphasis on ensuring that information is disclosed appropriately to patients and that informed consent is sought.
- Trillium Health Centre’s core value of Excellence articulates a focus on innovation and evidence, both of which are supported by research.

What are the protocols to support the principles...?

- Research Applications & Reporting Requirements, (#5010)

Where can I find more information...?

Research Office	Medical Staff Office	Management Regulation 22 (6), Public Hospitals Act
Tri-Council Policy Statement, Ethical Conduct for Research Involving Humans, 1998	Canadian Council on Health Services Accreditation, 2004 AIM Standards	Trillium’s Core Commitments
Trillium Policies on Consent, Access to Information, Intellectual Property	Good Clinical Practice: Consolidated Guideline, Health Canada 1997	Guidelines to Research Consent Documents and Guidelines to Research Protocol Development
Personal Health Information Protection Act	Personal Health Information Protection Act Regulations	iCARE portal: My Workspace, Information Resources, Toolkit Documents, Research folder

Health Insurance Portability and Accountability Act	Health Insurance Portability and Accountability Act Regulations	Research Ethics Web portal offered through the Joint Centre for Bioethics and the University of Toronto
---	---	---