The Toronto Academic Health Science Network

# Task Force on Human Subjects Research

Report:
**February 5, 2007**

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## A. Executive Summary

Human subjects research is central to the academic mission of the Toronto Academic Health Sciences Network (TAHSN). To support TAHSN researchers in their pursuit of human subjects research enabling them to design and implement innovative studies within an appropriate ethical framework, the Hospital University Research Relations Committee (HURRC) recommended to the Vice-Provost Relations with Health Care Institutions that a representative TAHSN committee be struck to examine the current human subjects research review procedures and practices across TAHSN. Further, HURRC recommended that the committee advise on how best practices can be achieved on an ongoing basis to strongly support human subjects research.

In April 2006, in response to this recommendation from the HURRC, the Vice-Provost commissioned a *Task Force on Human Subjects Research* that included representation from the ten affiliated hospitals/research institutes and the health faculties at the University of Toronto. Members of the committee included REB chairs, human subject researchers, research administrators and ethics and legal experts from all fully-affiliated hospitals and health faculties across the network.

The overall goal of the *Task Force* was to recommend mechanisms and processes to improve the quality of human subjects research across TAHSN by identifying key barriers to the achievement of ethical best practices. Further, the committee was charged to identify an enabling infrastructure for TAHSN to overcome these barriers so as to facilitate the conduct of human subjects research of the highest quality in an increasingly stringent regulatory environment.

The *Task Force* conceived a four-phase process to meet its intended goal. In Phase 1, the committee prepared a comprehensive list of barriers and problems, and consolidated these into 16 key barriers that could prevent the conduct of ethical best practices at TAHSN. In Phase 2, the *Task Force* assigned its members to four different working groups to explore and recommend infrastructural needs to address these key barriers. This led to the idea of developing an ethical best practices resource for TAHSN called the *Central Clinical Resource Research Group*.

In Phase 3, the committee developed and sent a survey to the research community of TAHSN (i.e. investigators, research coordinators, REB members, REB chairs, and research administrators) at all ten academic health sciences centres, three community-affiliated hospitals, and the selected departments of the Faculty of Medicine at University of Toronto. The purpose of the survey was to seek stakeholders' opinions on the importance of the 16 key barriers to ethical best practice, and the proposed functions and benefits of the *Central Clinical Research Resource Group* that were proposed by the *Task Force*. Finally, in Phase 4, the *Task Force* synthesized the data collected from the previous phases to formulate recommendations.

Eight hundred and sixteen research stakeholders participated in the survey. Generally respondents endorsed the importance of the key barriers identified by the *Task Force* during the first two phases. Although the list of top five barriers to achieving ethical best

practices differed by research stakeholder group as detailed in section C.4.2, the following five barriers emerged as the most important overall to address initially:

- Need to improve turn-around time of REB approval of research protocols for both single and multi-site trials being conducted at TAHSN.
- Underdeveloped infrastructure to support the conduct of multi-centre studies.
- Need to harmonize REB approval process within TAHSN.
- Underdeveloped strategies to integrate clinical research into routine clinical care.
- Underdeveloped processes to inform investigators of new regulatory requirements.

Although they agreed that REBs must continue to exercise great care in their reviews of potentially invasive or harmful research respondents, stakeholders wanted increased consistency in the ethical review process across the network in particular. Comments from respondents included inconsistent processes for the review of multi-centre studies, different expectations for documents such as the informed consent forms across sites, and varied approaches to proportionate review of research projects across TAHSN REBs.

Failure to increase consistency in review processes across TAHSN is a cause for concern for several reasons. Investigators and research co-ordinators reported that existing processes cause unnecessary delays to studies due to their need to respond to repetitive and conflicting reviews. Similarly, REB members reported spending too much time evaluating proposals that had been reviewed by other TAHSN REBs.

To address this fundamental problem and the other key barriers validated by research stakeholders and to provide support in meeting standards, guidelines and regulations, the *Task Force* recommends the creation of the *Clinical Research Resource Group*. As endorsed by survey respondents, the functions of this group should be to:

1) Create, maintain and coordinate a *web-portal* to support communication with research stakeholders through each hospital intranet and to manage the *Central Clinical Research Resource Group* functions.
2) Work with TAHSN hospitals to develop a central and definitive resource for *education*, courses, workshops-local and web-based-for students, investigators, research staff and REB members at U of T and affiliated hospitals.
3) Provide a *resource* that promotes discussion among the clinical research community and develop recommendations regarding emerging issues in the ethical conduct of clinical research.
4) Create an *information hub* to liaise with external groups on national and international initiatives.

Recognizing the urgency of these issues, the *Task Force* recommends that TAHSN create the proposed *Clinical Research Resource Group* with broad representation from research stakeholders building upon available resources within TAHSN. The *Clinical Research Resource Group* should establish terms of reference to overcome the key barriers to achieving ethical best practices. Specifically, the resource group should first

develop and implement a TAHSN-wide process to overcome the top five barriers identified; next develop strategies to address the remaining barriers, and finally be vigilant to emerging local, national, and international issues pertaining to the conduct of human subjects research.

With the allocation of appropriate TAHSN resources, the *Task Force* recommends that these activities be accomplished within a one-year timeframe.

## B. Terms of Reference of the Task Force on Human Subjects Research

**Preamble:** Human subjects research is central to the academic mission of TAHSN. This Network includes the Health Faculties of the University of Toronto and the nine[1] hospitals fully-affiliated with the University. The Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans has been adopted across TAHSN through the efforts of the University Office of Research and the hospital Research Ethics Boards (REBs). The clinical scientific community engages in translational research often testing new diagnostic and therapeutic interventions that may be in the process of being commercialized. Industry-contracted research supporting single and multi-centre trials are under increased scrutiny by medical journal editors for possible conflicts of interest.

To support our faculty in its pursuit of human subjects research enabling them to design and implement innovative studies within an appropriate ethical framework, strong institutional support and guidance should be provided. This includes support for continuing engagement in industry-sponsored research within an appropriate ethical framework. Therefore, the Hospital/University Research Coordinating Committee recommended to the Vice-Provost Relations with Health Care Institutions that a *Task Force* be struck to examine the current human subjects research review procedures and practices across TAHSN and, importantly, to recommend how best practices can be achieved on an ongoing basis to strongly support human subjects research.

**Purpose:** To propose processes to be undertaken for achieving ethical best practices in human subjects research at TAHSN within the context of current and emerging local, national and international standards and best practices.

**Scope:**

1) Consider current ethical practices/procedures within TAHSN relevant to human subjects research (including clinical trials);
2) Compare TAHSN's current ethical practices/procedures to current and emerging local (e.g. hospital specific), national and international standards and best practices for the ethical conduct of human subjects research;
3) Delineate barriers to achieving ethical best practices and define infrastructure needs within TAHSN.
4) Identify TAHSN-enabling mechanisms for achieving ethical best practices.

[1] The terms of reference were written prior April 1, 2006 when Women's College Hospital was affiliated as an independent institution from Sunnybrook Health Sciences Centre. There are now ten hospitals fully affiliated with the University of Toronto.

**Members of the Task Force on Human Subjects Research**

The Toronto Academic Health Science Network (TAHSN) *Task Force on Human Subjects Research* was commissioned by the Vice-Provost, Catharine Whiteside. The following members represented the affiliated hospitals/research institutes, Health Faculties, REB chairs, human subject researchers, and ethics and legal experts:

**Co-Chairs:**
Valérie Sales/Paula Rochon

**Members:**
Baycrest: Paula Rochon
Bloorview Kids Rehab: Steve Ryan
Centre for Addiction & Mental Health: Padraig Darby, Shitij Kapur, Susan Pilon
Hospital for Sick Children: Michelle Modofsky, Stan Zlotkin
Mount Sinai Hospital: Tamara Birkenheier, Ellen Hodnett
St. Michael's Hospital: Chaim Bell, Julie Spence
Sunnybrook Health Sciences Centre: Anthony Levitt
Toronto Rehabilitation Institute: Angela Colantonio
University Health Network: Ron Heselgrave, Amit Oza, Valerie Sales
University of Toronto Campus: Denis Grant, David Bevan, Rachel Zand

Administrative Support: Leslie Bush, Assistant Vice-Provost, Health Sciences Sector, University of Toronto

## C. Report of the TAHSN Task Force on Human Subjects Research

### C.1. Background

The Tri-Council Policy Statement: *Ethical Conduct for Research Involving Humans* defines human subjects research[2] as a "systematic investigation to establish facts, principles or generalizable knowledge…that involves living humans…human remains, cadavers, tissues, biological fluids, embryos or fetuses." In this context, human subjects research within TAHSN is a very large enterprise. In 2005, it was estimated that some 4300 protocols were reviewed by Research Ethics Boards (REBs) across TAHSN.

TAHSN is the largest academic research organization in Canada. The University of Toronto has affiliation agreements with all of the TAHSN-member hospitals - 10 full affiliates and 3 community affiliates. In 2004/05 there were approximately 5,000 faculty with primary appointments in the Faculty of Medicine who together with their colleagues in the other health sciences have been ranked the top over the last 5 years in health sciences publications and citations for publicly funded institutions across North America. It holds the largest number and amount of research funding out of the 17 Canadian Medical Schools; a position that it has maintained for more than 20 years.

Human subjects research is organized differently at the University and at each of the TAHSN sites. Different sites conduct different types of human subjects research. For example, some institutions conduct more clinical trials than others. Moreover, the populations under study often reflect their patient populations and expertise: elderly versus adults versus children and adolescents or chronic versus acute diseases or preventative versus invasive therapeutic procedures. The type of infrastructure available at each site has been adapted to meet their needs. Since a wide range of research can be conducted at each site, certain resources and specific expertise may be developed across sites.

The complexity of clinical studies is increasing, requiring knowledgeable, trained staff for the appropriate conduct of all clinical research and compliance with regulations in clinical trials. Thus, providing the resources for an appropriate infrastructure to support the REB and the overall research system is important in mitigating the risks pertaining to the conduct of human subjects research. There are ongoing efforts about the quality of human subjects research internationally. As high profile issues have arisen in leading academic centres, they highlighted the importance of a concerted prospective approach to address such issues within TAHSN.

[2] In this report, the terms Human Subjects Research and Clinical Research are used interchangeably.

## C.2. Scope

In the preparation of this report, the *Task Force on Human Subjects Research* considered **all ethical practices/procedures within TAHSN relevant to human subjects research**. We considered the entire research system at TAHSN. Research ethics boards (REBs) are an essential and well-established component of this system but other components require further development to support the REBs role and oversight. The research system includes proposal development, scientific review, REB approval, training, quality assurance, monitoring, and eventual publication. The *Task Force* worked on the assumption that there are some exemplary and some more basic standards being followed in the research system across TAHSN.

The *Task Force* worked with the following principles:

1) Human subjects research is essential to the advancement of health care and should be facilitated.

2) Human subjects research conducted within TAHSN institutions should be of the highest quality.

3) Human subjects research within TAHSN institutions will benefit from consistent approaches.

Improving the quality of human subjects research across TAHSN is important on many levels. Research subjects' rights and safety must be protected. They are entitled to participate only in studies, in compliance with regulations and guidelines, meeting the highest scientific rigour as well as ethical and quality standards. From the investigators' perspective, conducting a study within a supportive environment will provide confidence that they can meet or exceed the standards for ethical conduct of human subjects research. Having a supportive and collaborative environment for investigators, research staff and REB members will improve the efficiency of the research process and make TAHSN a very attractive venue in which to conduct research. From TAHSN's perspective, promotion of such an environment will foster advances in knowledge while protecting study participants.

The overall goal of the *Task Force* was to recommend mechanisms and processes to improve the quality of human subjects research across TAHSN by:

1) Identifying key barriers to the achievement of ethical best practices for the conduct of human subjects research within TAHSN; and,

2) Creating an enabling infrastructure for TAHSN to overcome these barriers so as to facilitate the conduct of human subjects research of the highest quality in an increasingly stringent regulatory environment.

## C.3. Process followed by the Task Force on Human Subjects Research

The *Task Force* was struck in April 2006 and met monthly to bi-monthly from late April 2006 to January 2007. The overall four-phase process followed by the *Task Force* is outlined in Figure 1 below.

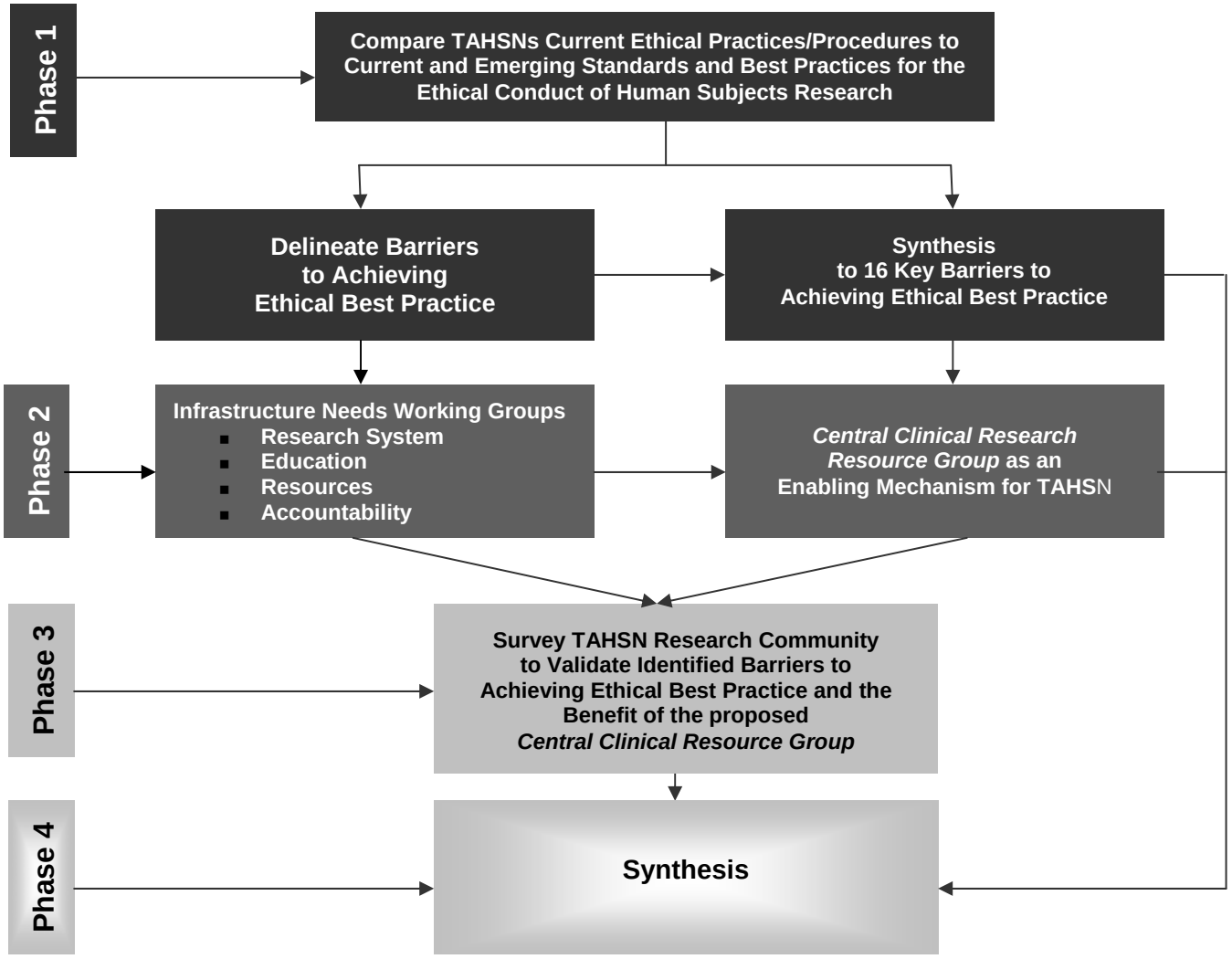



**Figure 1:** Process Followed by Toronto Academic Health Science Network (TAHSN) *Task Force on Human Subjects Research*

### C.3.1. PHASE 1: Identification of Barriers to Ethical Best Practice

In Phase 1, The *Task Force* considered TAHSN's ethical practices/procedures in the context of current and emerging standards and best practices for the ethical conduct of human subjects research. The *Task Force* was designed with representation from all institutions across TAHSN and therefore members brought to the group their understanding of ethical practices/procedures. This process led to the identification of key issues. The *Task Force* members identified *Barriers to Achieving Ethical Best Practice* pertaining to the conduct of Human Subjects Research within TAHSN. These *Barriers to Achieving Ethical Best Practice* were generated based on the experience of *Task Force* members and that of their respective sites. A 20-page list of items was identified (available on request).

Next these barriers were grouped into similar categories resulting in the identification of 16 barriers to achieving ethical best practice being faced at TAHSN (see Section C.4 for list).

### C.3.2. PHASE 2: Task Force Working Groups to Define Infrastructure Needs

In Phase 2 these items were categorized into thematic areas that related to infrastructure needs within TAHSN that would help to address these identified barriers to achieving ethical best practices. Four working groups of *Task Force* members were formed to respond to these barriers: *Research Systems*, *Education*, *Resources*, and *Accountability*. The documents prepared by each of these groups are in Appendix 2. Details of the recommendations based on these documents can be found in Appendices 5 and 6.

The *Research Systems* working group recognized that the current system for human subjects research would benefit from a concerted approach within TAHSN. The working groups recognized that while each institution needs a good research system tailored to its own needs, this system needs to be coordinated with the other TAHSN sites to be more efficient, avoid duplication and ensure that broader issues can be addressed consistently across institutions. As REBs are central to the research systems, they have taken the lead in harmonizing certain submission and review processes across sites.

The *Resources* working group explored the value of central, virtual resources on ethical best practices that all hospital investigators and their staff could access. It was recognized that certain sites such as the current University of Toronto web-site are excellent but are not directly available for the research activities of TAHSN investigators and their staff. Easy access is required to references such as regulations, common processes and tools as the existing harmonized REB submission form or protocol templates. It was also noted that there are no mechanisms in place to track active research studies across TAHSN.

The *Education* working group explored means of educating, training, and informing all those involved in the ethical conduct of human subjects research. Many in the

research community are unaware of the educational opportunities that are available. It is important that researchers, research staff and REB members be appropriately trained for standards and regulations in line with their roles and responsibilities in the conduct of clinical research. This is important to prepare for regulatory authorities as they come to inspect a research site, to manage the risks pertaining to liability issues, and most importantly, operationalize the guiding ethical principles espoused in the *Tri-Council Policy Statement* and following the *Declaration of Helsinki* and *Good Clinical Practices*. Education may well be one of the best interventions to mitigate risks for research institutions as they cannot oversee all activities and maintain best practices in the approach of potential participants and the care provided in the context of the study.

The *Accountability* Working Group focused on "hot issues" related to accountability. Accountability is reflected in all aspects of human subjects research from having a sound design with an acceptable risk/benefit ratio to reporting results, whether positive, negative or neutral. These include issues as broad as registration of clinical trials, publication, research and care, conflicts of interest and relations with industry. The different parties involved in clinical research must be held accountable to each other as well as to the participants and the public at large. It is essential that the parties work together for expansion of our knowledge of disease and evaluation of new interventions.

The Research Systems, Resources, Education, and Accountability Working Groups of the *Task Force* each reported their findings to other members. After considering each of the four reports, *Task Force* members agreed that a consistent theme emerged. This common theme was that there was need for consistent approaches and a common information resource for ethical best practices within TAHSN. This led to the proposed creation of a *Central Clinical Research Resource Group* as an enabling mechanism to support the ethical conduct of clinical research within TAHSN. The four proposed major functions of this group aligned with the needs identified by the four working groups.

The following is a description of how the *Task Force* members envisioned *The Central Clinical Research Resource Group*. The proposed group would provide a common information system, a mechanism for providing common educational opportunities, an opportunity to provide shared resources, and finally, promote accountability by providing common, current and consistent information across the network. The group would act as a resource to research stakeholders, including investigators, research ethics board (REB) members, research coordinators and research administrators.

While the potential scope of operation of the *Central Clinical Research Resource Group* was broad, the *Task Force* proposed a narrower focus. The *Task Force* worked with the understanding that the group:

1) would build on existing resources within TAHSN;
2) not duplicate existing resources; and,
3) add value to existing resources.

Accordingly, *Task Force* members agreed that the *Central Clinical Research Resource Group* should focus on overarching issues that affect TAHSN as a whole. This resource group would allow sharing of best practices between institutions. The group would not

replace local REBs or duplicate existing resources, but rather complement the research resources available at individual TAHSN sites. This group would provide a central, comprehensive resource to address critical issues being faced in the conduct of human subjects research. This group would provide a vehicle to promptly address emerging local, national, and international issues, and would assist in the development of practical strategies targeted at meeting evolving standards in clinical research.

### C.3.3. PHASE 3: Survey to Validate Task Force Findings

Phase 3 was designed to obtain views from the broad TAHSN research community. The *Task Force* developed a web-based survey (see Appendix 1) to solicit feedback from key research stakeholders (i.e. investigators, REB members/chairs/coordinators, research coordinators, and research administrators) across all TAHSN member institutions, community affiliated hospitals and the Faculty of Medicine. The three survey objectives were:

1) To seek members' opinions on the importance of the sixteen identified barriers to ethical best practice*;*
2) To get members' advice regarding the proposed functions of a *Central Clinical Research Resource Group;* and,
3) To get members' advice regarding the potential benefit of the proposed *Central Clinical Research Resource Group*.

The survey was distributed by individual *Task Force* members using email research distribution lists at their respective sites, posted on the Faculty of Medicine intranet, and distributed to members of the Joint Centre for Bioethics.

The description of the methods and analysis used for the survey is provided in Appendices 3 and 4.

### C.4. Phase 4 Synthesis: Barriers to Achieving Ethical Best Practices

Three sources of data were used to identify the barriers and problems to achieving ethical best practices at TAHSN. These were:

1) The *Task Force* members findings;
2) TAHSN survey quantitative data; and,
3) TAHSN survey qualitative data.

### C.4.1. Task Force members findings

The first source of data was from the *Task Force* members findings.

The following is a list of the 16 key Barriers to Achieving Ethical Best Practice identified by the *Task Force* members. These barriers were derived from the thematic review of the 20-page list of obstacles identified by *Task Force* members. The *Task Force* identified that it was important to:

- Harmonize the REB approval process within TAHSN.
- Improve institutional conflicts of interest policies.
- Reduce the turn-around time of REB approval of research protocols.
- Improve policies related to part-time and adjunct faculty doing research in private practices, but using institutional affiliations.
- Develop an appropriate infrastructure (REB, standard operating procedures, training, etc) to support newly affiliated community hospitals that conduct clinical research.
- Develop the infrastructure to support the conduct of multi-centre studies.
- Develop processes and institutional support to facilitate on-site inspections by regulatory and granting agencies.
- Improve the contract review process.
- Develop a centralized process for registering clinical trial protocols.
- Improve the processes to monitor the ethical conduct of research studies.
- Have the infrastructure to develop auditable web-based study databases that will preserve data integrity.
- Develop processes to address emerging ethical issues pertaining to new research activities in areas such as new technologies, genomics, proteomics and bio-banks.
- Develop processes to inform investigators of new regulatory requirements.
- Develop processes to inform potential study participants about ethical practices in clinical research so they understand their rights.
- Develop strategies to integrate clinical research into routine clinical care.
- Provide educational opportunities on the ethical conduct of clinical research.

### C.4.2. TAHSN Survey Quantitative Data

The second source of data was obtained from the TAHSN survey quantitative data. A survey was conducted among research stakeholders across TAHSN. The data obtained from the survey are described below. All tables describing the more detailed results from this survey data can be found in Appendix 4.

A total of 816 research stakeholders responded to the survey from each of the TAHSN sites as outlined below. All ten TAHSN member sites, three community affiliated hospitals, and other members of the university were surveyed as listed in Figure 2.

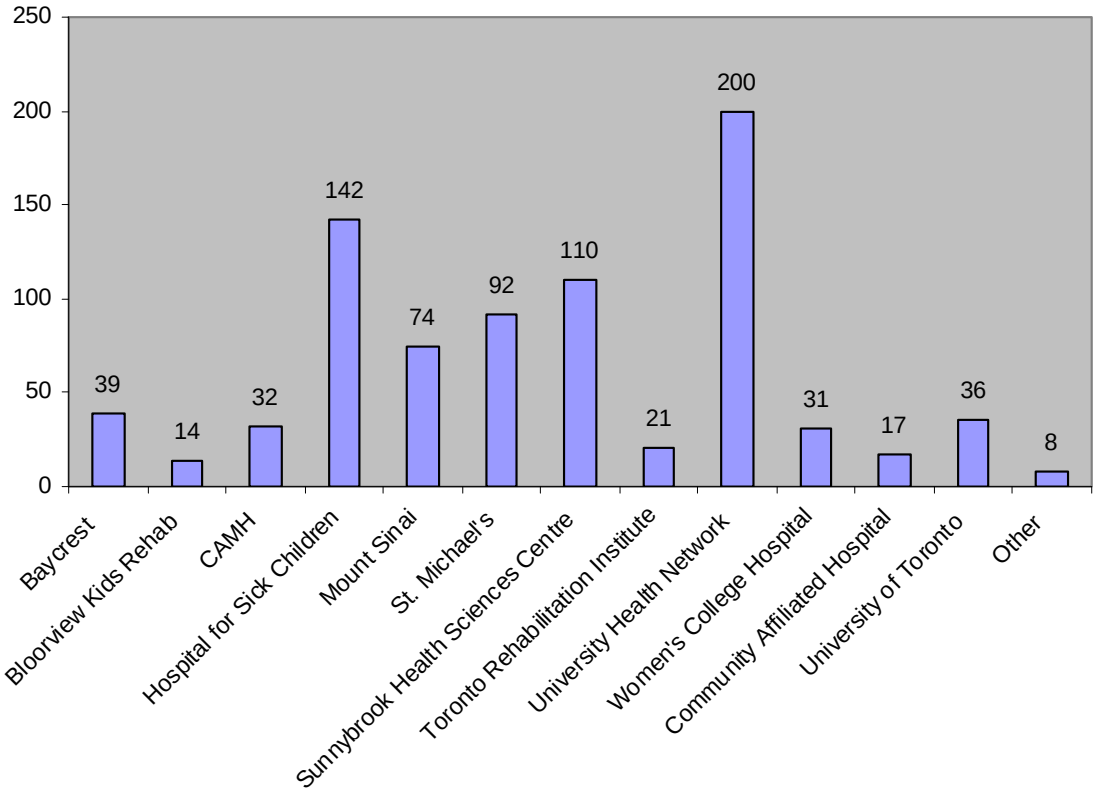



**Figure 2:** The distribution of survey respondents by site.

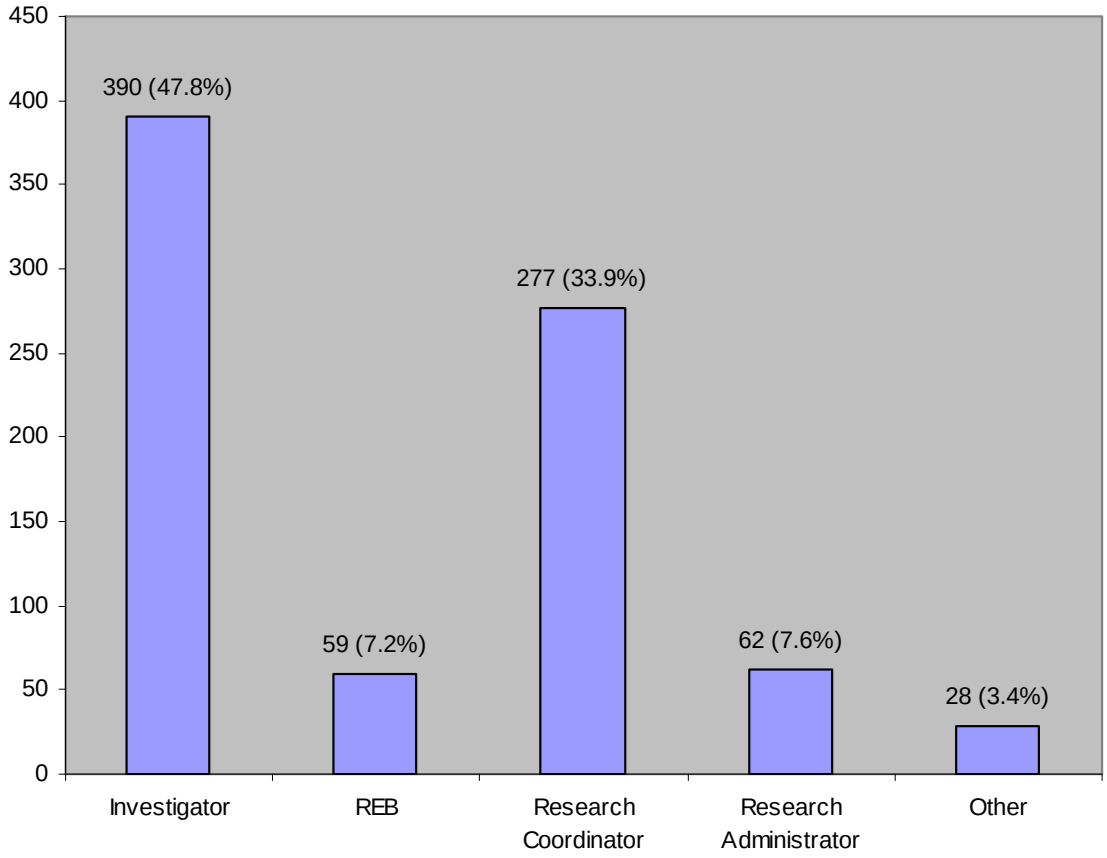



**Figure 3**: The distribution of survey respondents by their primary research role. More than 80% of the research stakeholders surveyed were either investigators or research coordinators.

On average 78% of the respondents agreed or strongly agreed that the barriers identified were important. Mean scores ranged from 3.62 (SD = 0.91) to 4.58 (SD = 0.50) across all items out of a maximum score of 5.

**Figure 4** lists the 16 barriers to ethical best practice. These items are ranked based on the overall rank of importance derived from the mean ratings from all respondents.

**The Top Five Barriers:**

| Survey | Investigator | REB | Coordinator | Administrator |
|---|---|---|---|---|
| 1. It is important to reduce the turn-around time of REB approval of research protocols. | 91.6% | 86.5% | 91.6% | 82.7% |
| 2. It is important to develop the infrastructure to support the conduct of multi-centre studies. | 86.8% | 71.2% | 88.9% | 82.7% |
| 3. It is important to develop processes to inform investigators of new regulatory requirements. | 89.1% | 100% | 94.7% | 100% |
| 4. It is important to harmonize the REB approval process within TAHSN. | 84.0% | 86.6% | 88.2% | 72.6% |
| 5. It is important to develop strategies to integrate clinical research into routine clinical care. | 82.3% | 69.4% | 83.8% | 77.6% |

**The Remaining Eleven Barriers:**

| Survey | Investigator | REB | Coordinator | Administrator |
|---|---|---|---|---|
| 6. It is important to provide educational opportunities on the ethical conduct of clinical research. | 76.1% | 94.3% | 93.4% | 94.1% |
| 7. It is important to develop an appropriate infrastructure to support newly affiliated community hospitals that conduct clinical research. | 80.3% | 92.5% | 88.3% | 87.5% |

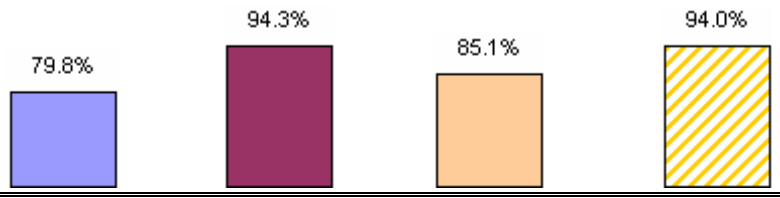
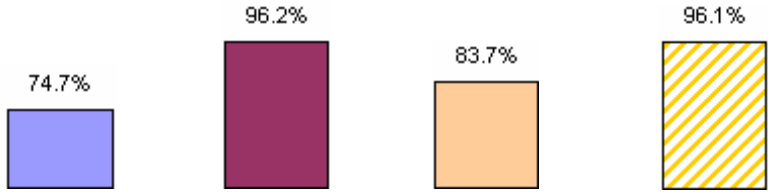
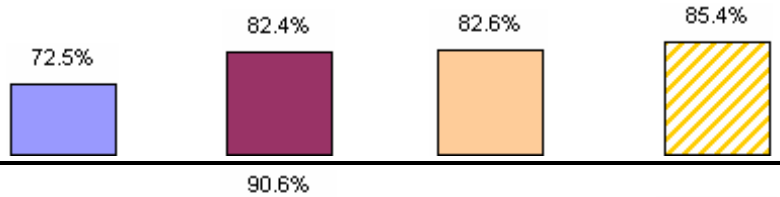
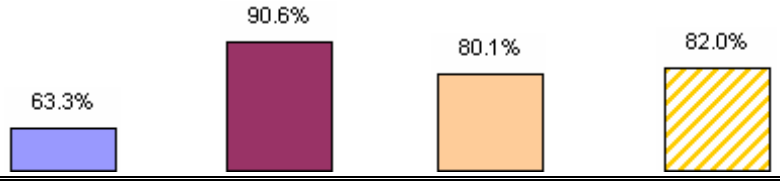
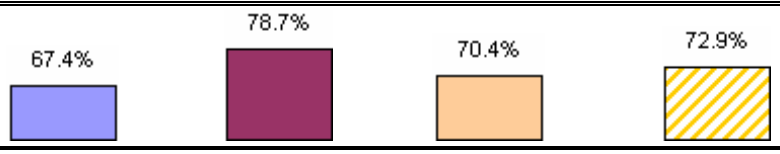
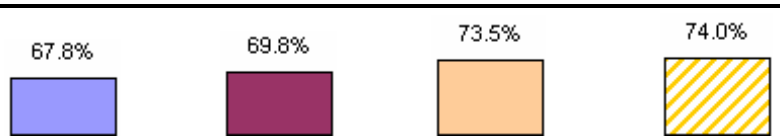
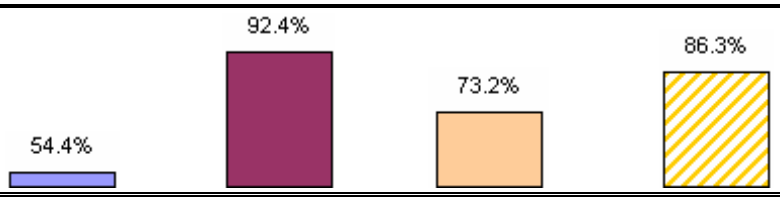
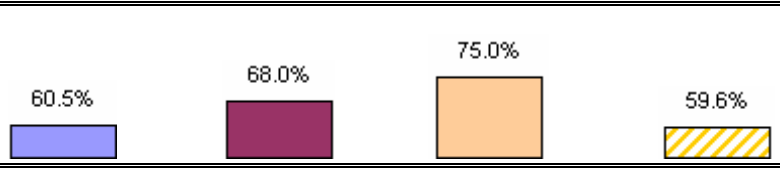
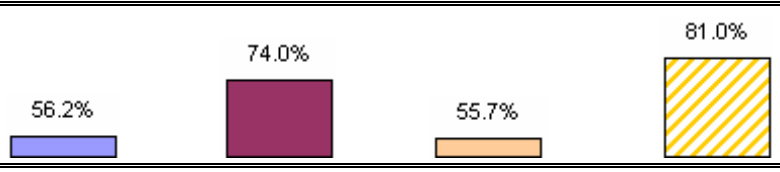
| | |
|---|---|
| 8. It is important to develop processes to address emerging ethical issues pertaining to new research activities in areas such as new technologies, genomics, proteomics and bio-banks. |  |
| 9. It is important to develop processes to inform potential study participants about ethical practices in clinical research so they understand their rights. |  |
| 10. It is important to develop processes and institutional support to facilitate on-site inspections by regulatory and granting agencies. |  |
| 11. It is important to improve institutional conflicts of interest policies. |  |
| 12. It is important to improve the contract review process. |  |
| 13. It is important to develop a centralized process for registering clinical trial protocols. |  |
| 14. It is important to improve the processes to monitor the ethical conduct of research studies. |  |
| 15. It is important to have the infrastructure to develop auditable web-based study databases that will preserve data integrity. |  |
| 16. It is important to improve policies related to part-time and adjunct faculty doing research in private practices, but using institutional affiliations. |  |

**Figure 4:** The scale ranged from 1 to 5 with: 1= “Strongly disagree”, 2= “Disagree”, 3= “Neutral”, 4= “Agree”, 5=”Strongly agree”. The histograms (and the numbers written above) illustrate the percentage of research stakeholders who either agreed or strongly agreed with a barrier statement within each group. Each group represents the primary research role of the respondents. Refer to Appendix 3 for additional tables of results.

The relative importance (ranking) of the items varied between the research stakeholders' role. The highest association of ratings was between the investigators and the research coordinators ($r=0.85$, $p<0.01$). REB members' ratings were correlated with those of research administrators ($r=0.68$, $p<0.01$). Investigators and REB members were most divergent in their ratings of the importance of barriers ($r=0.07$, $p=0.81$).

The following are the five most important barriers to ethical best practice based on mean ratings by investigators:

- Need to improve the turn-around time of REB approval of research protocols.
- Underdeveloped infrastructure to support the conduct of multi-centre studies. *
- Need to harmonize the REB approval process within TAHSN. *
- Underdeveloped strategies to integrate clinical research into routine clinical care.
- Underdeveloped processes to inform investigators of new regulatory requirements. *

Research coordinators placed three of these items (indicated with an asterisk) in their top five most important list. They also identified in their top five barriers the need to:

- Provide educational opportunities on the ethical conduct of clinical research.
- Develop an appropriate infrastructure (REB, standard operating procedures, training, etc.) to support newly affiliated community hospitals that conduct clinical research.

It is expected and important to consider the REB perspective and to recognize that it likely would be different in some areas to that of the investigators and other research stakeholders. REB members represented a smaller number of stakeholders in this survey. In total 59 (7.2%) of the respondents were REB members. The five most important barriers identified by the REB members were the need to:

- Develop processes to inform investigators of new regulatory requirements.
- Develop processes to inform potential study participants about ethical practices in clinical research so they understand their rights.
- Develop processes to address emerging ethical issues pertaining to new research activities in areas such as new technologies, genomics, proteomics and bio-banks.
- Provide educational opportunities on the ethical conduct of clinical research.
- Develop an appropriate infrastructure (REB, standard operating procedures, training, etc) to support newly affiliated community hospitals that conduct clinical research.

### C.4.3. TAHSN Survey Qualitative Data

The third source of data was obtained from the TAHSN qualitative survey comments.

A total of 174 (21%) of the respondents provided written comments related to the barriers to ethical best practice. Comments were categorized by the primary role of respondent. Two *Task Force* members read all comments independently, then identified, compared and agreed upon underlying themes.

The following are the key barrier-related themes that emerged:

1) There is a need to reduce the time it takes to receive full ethical clearance for multi-site research projects.
2) Although REBs should continue to exercise great care in their reviews of potentially invasive or harmful research, the rigour of the review for lower risk research should be proportionate.
3) Common processes should be developed to create consent forms that are truly understandable by prospective research volunteers.
4) New investigators need opportunities to learn about research ethics, REB members need opportunities to learn about research methods, and research coordinators need opportunities to be trained about good clinical practice, research methods and ethics.
5) Regulatory requirements should be harmonized with ethics review processes to facilitate research.

Additionally, two minor themes emerged:

1) REBs should consider the expertise they need to review research protocols appropriately.
2) Additional resources would help REBs/Research Ethics Offices to do their jobs better.

Illustrative examples of respondents' comments for each of the identified themes are available in Appendix 4.

## C.5. Synthesis: Identify TAHSN-enabling mechanisms for achieving ethical best practices.

Three sources of data were used to identify TAHSN-enabling mechanisms for achieving ethical best practice. These were:

1) The *Task Force* members findings;
2) TAHSN survey quantitative data; and
3) TAHSN survey qualitative data.

### C.5.1. Task Force Members Findings

The *Task Force* proposed the creation of a *Central Clinical Research Resource Group* to support the ethical conduct of clinical research within TAHSN and, when appropriate, to take a leadership role on a national and international level. The proposal for the *Central Clinical Research Resource Group* was based on the *Task Force* and working groups' discussions to identify a common enabling mechanism. The functions of the *Central Clinical Research Resource Group* reflect the overlapping thematic areas of the working groups and their perspectives. These include the need to develop a system to provide information, a mechanism to provide educational opportunities, the processes to share resources and finally the means to promote accountability.

Thus, the *Task Force* members proposed four potential functions for the *Central Clinical Research Resource Group*:

1) **Web-portal:** Creating, maintaining and coordinating a *web portal* where all involved in clinical research at TAHSN institutions could readily access policies, procedures, general information, and guidance pertaining to the ethical conduct of human subjects research within TAHSN institutions
2) **Education:** Advising TAHSN members of local and web-based *educational activities* that relate to the ethical conduct of human subjects research
3) **Resource:** Promoting *discussions* among investigators, research coordinators and REB members regarding emerging research ethics issues.
4) **Information Hub**: Acting as an *information hub* where external groups can liaise with TAHSN institutions on new national or international initiatives on the ethical conduct of human subjects research

### C.5.2. TAHSN Survey Quantitative Results

In the TAHSN survey, the *Task Force* introduced the *Central Clinical Research Resource Group* and its four proposed functions. Responders rated the relevance of each function on a scale of 1 strongly disagree) to 5 (strongly agree), and provided additional suggestions for functions of the proposed *Central Clinical Research Resource Group*.

Survey respondents generally endorsed the functions as being important. The overall scores ranged from 3.68 (SD = 0.79) - 4.42 (SD = 0.79).

| Survey | Investigator | REB | Coordinator | Administrator |
|---|---|---|---|---|
| 1. Coordinating a web portal where members could readily access policies, procedures, general information, and guidance pertaining to the ethical conduct of human subjects research within TAHSN institutions should be a function of the resource group. | 85.4% | 87.2% | 90.6% | 84.0% |
| 2. Acting as an information hub where external groups can liaise with TAHSN institutions on new national or international initiatives on the ethical conduct of human subjects research should be a function of the resource group. | 72.6% | 74.5% | 76.8% | 78.0% |
| 3. Promoting discussions among investigators, research coordinators and REB members regarding emerging research ethics issues should be a function of the resource group. | 68.9% | 74.5% | 76.3% | 68.0% |
| 4. Advising TAHSN members of local and web-based educational activities that relate to the ethical conduct of human subjects research should be a function of the resource group. | 62.5% | 76.6% | 75.9% | 68.0% |

**Figure 5** lists the proposed functions of the *Central Clinical Research Resource Group* with the percentage of research stakeholders who either agreed or strongly agreed with a proposed function within each group. Refer to Appendix 3 for additional tables of results.

Among these four potential functions, the idea of a central web-portal was ranked for all groups as being the most important function. The other functions' ranks varied among the groups. However, since the differences in the scores for each of these other functions were small, the *Central Clinical Research Resource Group* would need to consider the implementation of each of the functions in part or in full as it evolves.

TAHSN stakeholders were asked for their overall opinion about the potential benefit of the *Central Clinical Research Resource Group*. Overall mean ratings ranged from 3.83 (SD = 0.88) to 4.14 (SD = 0.87) for the above questions, inferring that there is general

agreement that a *Central Clinical Research Resource Group* could be valuable. There was an endorsement with 73% of respondents indicating that the *Central Clinical Research Resource Group* could be valuable to support ethical best practices and 77% agreeing that it could be valuable for ethics-related issues not previously addressed by their institution. Comments pertaining to these questions provided informative nuances (see section C.5.3).

Figure 6 outlines this information.

| Survey | Investigator | REB | Coordinator | Administrator |
|---|---|---|---|---|
| 1. Overall, the *Central Clinical Research Resource Group* could be a valuable resource if I encountered a research ethics-related question or problem that has not been previously addressed at my institution. | 75.1% | 74.5% | 81.3% | 78.0% |
| 2. Overall, a *Central Clinical Research Resource Group* could be a valuable resource to support ethical best practices in the conduct of human subjects research within TAHSN. | 67.6% | 78.7% | 81.7% | 72.0% |

**Figure 6** lists the potential benefit of the *Central Clinical Research Resource Group* with the percentage of research stakeholders who either agreed or strongly agreed with each statement within each group.

### C.5.3. TAHSN Survey Qualitative Results

Although comments only represent a small percentage of respondents' opinions, they provide important details on the perception of the proposal. A total of 101 comments were received from the 816 survey respondents for question 12.

Overall comments on the creation of the *Central Clinical Research Resource Group* were supportive with cautionary advice to ensure that the *Central Clinical Research Resource Group* would not become an "additional layer of bureaucracy" or "another layer in the REB process". "The *Central Clinical Research Resource Group* should have some decision-making power to facilitate the realization of projects and it should have accountability to the research community". The *Central Clinical Research Resource Group* would "greatly facilitate multi-institutional clinical research and collaboration". The *Central Clinical Research Resource Group* may be able to encourage quality improvement research, promoting evidence-based care for patients to access the best quality of care possible. The composition of the group was suggested to be broader than REB members only, to offer "new points of view".

1) **Web-Portal:**
   Two major themes came from the survey comments. First, the web-portal must not duplicate but build on existing resources. Second, this resource should be accessible to all involved in human subjects research across TAHSN.
   Also, the web-portal could be used for other purposes such as to facilitate sharing of comments/review among REB members and between REBs.[3]

2) **Education:**
   The survey comments highlight recognition of the need of continuing education for all involved in clinical research. The following were requested: REB members on research methods; new investigators on research ethics, and research coordinators on Good Clinical Practice (GCP), research methods and ethics.

3) **Resource:**
   The *Central Clinical Research Resource Group* could promote consistency in REB review approach towards a study or certain types of studies, supporting common interpretation and enactment of requirements across participating institutions. An investigator commented that the *Central Clinical Research Resource Group* could provide timely access to expert support to conduct ethical research more effectively.

[3] This comment was based on a CIHR funded research project headed by Heather Sampson (A Study to Assess the Utility of a Canadian Web-based Research Ethics Board (REB) Protocol and Consent Review Template). This project is investigating a web-based system that provides a process for documentation of REB reviews and the ability to return to each reviewers concerns and comments not only for the review of one study but also during future reviews of similar studies. This could increase consistency of comments and/or requests made by REBs to deal with concerns. It may also help to keep track of frequently asked questions and develop processes to allow the information to be provided to the REB on the initial submission.

4) **Information Hub:**
A key function would be that the *Central Clinical Research Resource Group* would address emerging local, national and international issues and would assist in the development of practical strategies targeted at meeting evolving standards in clinical research. The *Central Clinical Research Resource Group* should be active in defining issues and operationalizing consistent solutions across TAHSN, including scanning of the environment, addressing policy issues and defining consistent interpretation of regulatory guidelines. However, there were also reservations expressed that the *Central Clinical Research Resource Group*'s advice/policy would not be transmitted to the REBs in a timely manner or that the REBs may not have the same understanding, particularly for new research for which the REB would not yet have the expertise for review.

See Appendix 5 for further details.

## C.6 Discussion

The overall goal of the *Task Force* was to recommend mechanisms and processes to improve the quality of human subjects research across TAHSN by:

a) Identifying key barriers to the achievement of ethical best practices for the conduct of human subjects research within TAHSN; and,
b) Creating an enabling infrastructure for TAHSN to overcome these barriers so as to facilitate the conduct of human subjects research of the highest quality in an increasingly stringent regulatory environment.

Through the compilation of the *Task Force* members proposal and the survey quantitative and qualitative results, clear directions emerged for a focus area. The most important barriers to ethical best practice identified pertain to need to increase consistency in the review process across TAHSN sites. This issue includes the inconsistent review process for review of multi-centre studies, different expectations for documents such as the informed consent forms and the need to develop a consistent approach to a "risk-proportionate" review process across REBs. Resolving these process issues are fundamentally important and will prepare TAHSN to take a leadership role on national and international issues related to human subjects research.

The *Task Force* findings were based on the views of *Task Force* members and results of a survey of over 800 research stakeholders (investigators, research coordinators, research administrators and REB members/chairs) from across TAHSN.

Results of the survey of the TAHSN research stakeholders suggest the following:

1) The sixteen barriers to ethical best practice identified by the *Task Force* members and endorsed by survey data from more than 816 research stakeholders across TAHSN are all considered important although *to varying degrees*.

2) The top five barriers to achieving ethical best practices, for different groups based on the primary research role of respondents are listed in Section C.4.2. Overall, amongst all the respondents, the top five barriers were:

- Need to improve turn-around time of REB approval of research protocols for both single and multi-site trials being conducted at TAHSN.
- Underdeveloped infrastructure to support the conduct of multi-centre studies.
- Need to harmonize the ethical review process within TAHSN.
- Underdeveloped strategies to integrate clinical research into routine clinical care.
- Underdeveloped processes to inform investigators of new regulatory requirements.

Failure to address inconsistent review processes across TAHSN REBs is cause for concern for several reasons. TAHSN investigators and research coordinators report that this causes unnecessary delays to studies due to the need to respond to repetitive and conflicting reviews from other REBs. From the REB members' point of view, they spend inordinate time re-evaluating proposals that have been reviewed by REBs at other facilities, including other TAHSN sites.

Targeting the problems identified by the inconsistent review process is a priority to use as a focus around which to establish the *Central Clinical Research Resource Group*. This is an attractive short-term objective to provide a focal point to use to move forward in a progressive fashion to address the barriers identified to ethical best practice at TAHSN.

3) The *Central Clinical Research Resource Group* could be an important enabling mechanism for the TAHSN research community by facilitating education and communication.

The *Task Force* recognizes that addressing all of the barriers to ethical best practice and creating a *Central Clinical Research Resource Group* that has educational, resource, information hub, and web portal functions needs to be approached in a step-wise manner. The *Task Force* recognizes the importance of prioritizing and starting with a focus on the key barriers identified and moving next to address the other high priority barriers to ethical best practice.

a) This could be accomplished by advising members of local and web-based *educational* activities and providing a *resource* to promote discussions among research stakeholders regarding emerging research ethics issues. This group would act as an *information hub* where external groups can liaise with TAHSN institutions to identify critical issues being faced in the conduct of human subjects research by providing a vehicle to promptly address emerging local, national, and international issues. This would assist in the development of practical strategies targeted at meeting evolving standards in clinical research. Finally, the resource

group would provide a *web portal* where members can easily access policies, procedures, general information and guidance pertaining to the ethical conduct of human subjects research.

b) Committees that can work with the *Central Clinical Research Resource Group* will be identified. Appropriate subcommittees and working groups will be created to focus their expertise to address areas of the research system.

Research stakeholders across TAHSN differed in their overall ratings of the functions of the *Central Clinical Research Resource Group* that they think would be most useful. However, stakeholders agreed that all proposed functions are important to varying degrees.

In addressing the consistency issues, the *Central Clinical Research Resource Group*, could initiate most of its functions: develop collaboration among research stakeholders in developing consistent REB processes, disseminate the process through educational sessions, and provide common tools and consistent information through the U of T portal via each institution's intranet.

## C.7. Recommendations

The *Task Force* advises that, when implementing recommendations, the following be adhered to where possible:

1) Do not duplicate but build on and add value to existing resources within TAHSN, nationally and internationally;
2) Do not create additional hurdles but facilitate clinical research;
3) Ensure representation from key stakeholders involved in clinical research in a Central TAHSN Committee, to provide different opinions on the research systems;
4) Include all study designs within scope; and,
5) Provide resources required to support the proposed activities and meet deliverables.

**The TAHSN Task Force on Human Subjects Research recommends the following:**

Create a TAHSN Committee, referred to in the survey as the *Central Clinical Research Resource Group,* with broad representation from key research stakeholders from across TAHSN.

**Membership of the Committee and general structure:**

The *Central Clinical Research Resource Group* should include core members of committees with similar mandates and expand membership appropriately to include a variety of expertise able to represent research stakeholders. It is desirable for the *Central Clinical Research Resource Group* to build its membership with representation from existing Committees (such as the REB Harmonization Committee; the Clinical Study Agreements Working Group, which is made up of a number of Toronto area hospitals; and the University of Toronto REB administrators working groups) and by adding representation from other TAHSN research stakeholders (such as Investigators, Research Coordinators and Research Administrators with regulatory experience).

1) The *Central Clinical Research Resource Group* will not be an REB or a central REB, thus it will not add bureaucratic layers for protocol reviews by the institutional REBs. The *Central Clinical Research Resource Group* would be a separate and independent committee.

2) The *Central Clinical Research Resource Group* must not only deal with issues pertaining to the REB but the whole research enterprise, thus it must not only be constituted of REB members/chairs/staff.

3) The *Central Clinical Research Resource Group*, a TAHSN Committee, should report directly to the TAHSN Research Committee to provide recommendations pertaining to human subjects research and support the institutions in their implementation of these recommendations.

4) It is anticipated that where required, the *Central Clinical Research Resource Group* will identify current committees and create new subcommittees and working groups to focus on issues, requiring specific expertise, related to human subjects research and advise the *Central Clinical Research Resource Group*. Subcommittees would lead certain initiatives; develop policies; and create common tools akin to the current REB Harmonization Committee.

5) The *Central Clinical Research Resource Group* will liaise with internal and external groups to avoid duplicating available resources and current initiatives. The *Central Clinical Research Resource Group* may adopt and adapt existing resources or collaborate in their development.

**Functions of the Committee:**

TAHSN should commission and support the *Central Clinical Research Resource Group* to develop, implement, operate and maintain a proposed virtual ethical best practices resource for the TAHSN research community. The *Central Clinical Research Resource Group* should incorporate four functions Web-portal, Education, Resource and information Hub (detailed below and in Appendix 5), endorsed by TAHSN stakeholders:

1) Create, maintain and coordinate a *web-portal* to support communication with research stakeholders through each hospital intranet and to manage the *Central Clinical Research Resource Group* functions.
2) Work with TAHSN hospitals to develop a central and definitive resource for *education*, courses, workshops-local and web-based-for students, investigators, research staff and REB members at U of T and affiliated hospitals.
3) Provide a *resource* that promotes discussion among the clinical research community and develop recommendations regarding emerging issues in the ethical conduct of clinical research.
4) Create an *information hub* to liaise with external groups on national and international initiatives.

The *Central Clinical Research Resource Group* should be provided with the resources required to create the four functions and to meet their deliverables.

**Scope of the Committee:**

The new *Central Clinical Research Resource Group* should establish terms of reference to overcome the key barriers to achieving ethical best practices, identified by the *Task Force* and endorsed by the TAHSN research stakeholders. The scope of the *Central Clinical Research Resource Group* can be divided in 3 main categories:

1) Address the top five barriers to achieving ethical best practices identified by the *Task Force* and endorsed by the research stakeholders. The *Task Force* recommends that the group initially focus on identifying strategies to make the review process more consistent across TAHSN sites and to develop consistent processes in the conduct of human subject research.

2) Address in a systematic manner the remaining 11 barriers to achieving ethical best practices identified by the *Task Force* and endorsed by the research stakeholders. Some of these additional barriers will require complementary resources to facilitate the work of the REBs in oversight of clinical research conducted at each institution. These include resources to proactively address emerging ethical issues pertaining to new research areas and for education of investigators and their staff on current and future requirements as well as potential study participants on their rights. In addressing these issues, it is expected appropriate functions to support implementation and maintenance of systems and the infrastructure to minimize or eliminate these barriers will be established.

3) Maintain vigilance with regard to local, national and international emerging issues that can affect TAHSN ability to conduct research within current and future ethical and legal frameworks. This should be a priority of the *Central Clinical Research Resource Group* and its expert sub-committees, to ensure that TAHSN is as well positioned to respond rapidly and completely to changes in the research environment and to be in a position to influence the direction of such changes. This group will identify new requirements for compliance with regulations governing human subjects research put forward by national and international regulatory agencies. It is clear that research ethics is integral to the entire research enterprise and that there has been a rapid evolution in ethics practice and procedures. With the rapid expansion of the responsibilities of those involved in the conduct of human subjects research, the *Central Clinical Research Resource Group* would be streamlining the framework to maintain best practices across TAHSN.

While we also expect the committee to develop a strategy to address the remaining barriers to ethical best practice and a strategy for identifying new and emerging issues in the conduct of human subjects research, we have focused on the key barriers in the discussion above and the related table. It is anticipated that, in addressing the initial barriers to ethical best practices, the *Central Clinical Research Resource Group* will establish processes and functions that will be optimized to obtain the systems and infrastructure to address the remaining barriers identified and future issues.

To address the initial key barriers related to consistency, the *Central Clinical Research Resource Group* should (also see Table 1 below):

a) Review the previous TAHSN report from the Subject Research Harmonization and Implementation Committee (December 2000) and revisit the recommendations in view of the issues identified by the *Task Force*. While this Human Subject Research Harmonization and Implementation Committee focused on the issues related to University and the associated Hospitals, many of the recommendations equally apply to TAHSN hospitals alone and should be considered in light of the current TAHSN context. The *Task Force* recognizes that the REB Harmonization Committee has done considerable work in this area. Many recommendations from the Human Subject Research Harmonization and Implementation Committee have not yet been implemented and thus should be

revisited in light of the *Task Force* findings and the current TAHSN context. It is also clear that harmonized processes need to be developed for all types of study designs not only clinical trials.

b) Develop review standards, processes and training of REB members for coordinated, consistent and timely reviews of

   i) Similar studies reviewed by the REB, and
   ii) Multi-centre studies and the associated informed consent forms, among REBs at different TAHSN sites to avoid redundancy and delays.

c) Provide processes, common tools and education for investigators and research coordinators to provide appropriate and complete documentation to the REBs facilitating the review and approval process.

d) Develop clear, common and consistent application of principles for proportionate ethical reviews and rules across TAHSN based on the framework provided by the Tri-Council Policy Statement on Ethical Conduct of Research Involving Humans.

It is expected that The *Central Clinical Research Resource Group* will continue to identify new and emerging issues and prioritize barriers that need to be addressed on a yearly basis for greatest impact on the clinical research community. This will provide the ability for TAHSN institutions to take a leadership role, to mitigate risks by resolving issues proactively across institutions and to maintain compliance with the rapidly evolving requirements and standards for the conduct of clinical research.

Recognizing the urgency of these issues, the *Task Force* recommends that: (a) TAHSN create the proposed *Clinical Research Resource Group* with broad representation from research stakeholders building upon available resources within TAHSN; (b) the *Clinical Research Resource Group* establish terms of reference to overcome the key barriers to achieving ethical best practices; and, (c) the resource group develop and implement TAHSN-wide processes to overcome the top five barriers identified; and, (d) develop strategies to address the remaining barriers and emerging issues. It will be essential for the *Clinical Research Resource Group* to collaborate in external initiatives to adopt and adapt them for TAHSN and to work closely with its subcommittees and other local committees leading certain initiatives. With the allocation of appropriate TAHSN resources, the *Task Force* recommends that these activities be accomplished within a one-year timeframe.

As part of its terms of reference, the *Clinical Research Resource Group* will be required to conduct an on-going annual evaluation of progress made toward overcoming the key barriers to ethical best practices for human subject research within TAHSN and prioritize future projects.

**Table 1: Proposed Activities, Outcomes and Timelines of the *Central Clinical Research Resource Group***

**Address Five Key Barriers to Achieving Ethical Best Practice: Develop Consistent Processes in Human Subjects Research**

| ***Central Clinical Research Resource Group* activity** | **0utcome** |
|---|---|
| Review the TAHSN report from the Subject Research Harmonization and Implementation Committee (Dec 2000) in light of *Task Force* findings and current TAHSN context | ➢ Identify recommendations and define implementation plan (activities, timelines, responsibilities, resources) to address the key barriers identified by the *Task Force* |
| Develop review standards, processes and training of REB members to optimize consistency in review | ➢ Increased communication among the REBs.<br>➢ Coordinated, consistent, timely reviews of multi-centre studies & informed consent form within and among REBs<br>➢ REBs can review previous comments, questions and resolution on similar studies<br>➢ Institutional REBs consider other appropriate TAHSN REBs full board reviews by reviewing through an expedited process. |
| Develop processes for risk-proportionate ethical reviews | ➢ Consistency in definition of minimal risk studies within and among REBs<br>➢ Institutional REBs consider other appropriate TAHSN REBs full board reviews by reviewing through an expedited process.<br>➢ Recognition of considerations for vulnerable populations and other risk-issues. |
| Develop common tools and education for investigators and research coordinators | ➢ Better understanding of REB review process and requirements.<br>➢ Appropriate and complete document submission facilitates REB review and approval process |

| ***Central Clinical Research Resource Group* activity** | **0utcome** |
|---|---|
| Develop common tools such as:<br>• REB application form for non-clinical-trial studies<br>• Informed consent form templates for different types of studies<br>• Budget templates<br>• Protocol or Investigators' Brochure Templates | ➢ Benefit from expertise of developers<br>➢ Avoid duplication of resources for development of tools<br>➢ Facilitate adherence to principles and guidelines in the ethical conduct of clinical research<br>➢ Promote compliance with regulations |
| Develop a standard informed consent process* | ➢ Promote patient safety<br>➢ Avoid duplication of resources for development<br>➢ Facilitate adherence to principles and guidelines in the ethical conduct of clinical research<br>➢ Promote compliance with regulations |
| Train research stakeholders in the conduct of clinical research**<br><br>Define mandatory training for different roles in study conduct | ➢ Promote patient safety<br>➢ Facilitate adherence to principles and guidelines in the ethical conduct of clinical research<br>➢ Promote compliance with regulations<br>➢ Promote collaboration among institutions based on their expertise and available programs.<br>➢ Risk management |

**Note:** Provided sufficient resources, the activities stated above should be conducted in parallel and initial deliverables met within 12 months. Many activities will be on-going thereafter. The *Central Clinical Research Resource Group* will require administrative support and a part-time project manager.
*Standard Operating Procedures: timelines can be shortened by adopting available SOPs such as the UHN Clinical Research SOPs or when available those of the Network of Networks.
**For Training in GCP, budget preparation, consenting process etc: the *Central Clinical Research Resource Group* may adopt/adapt existing web-based programs or live courses through collaboration among the institutions and participation in initiatives such as the Network of Networks.
[The Network of Networks: new initiative including disease-based networks (Oncology, Rheumatology, etc) and University Health Network (UHN). The *Central Clinical Research Resource Group* could recommend that TAHSN join UHN in the initiative for further representation of the institutions and the ability to use the common tools and standards developed by this Network of Networks.]

## C.8. Conclusions

Recognition of clinical research, as central to the improvement of clinical care and innovation leading to translation of basic research, should remain integral to the culture of academic hospitals. As Clinical Research continues to expand with increasing numbers of protocols submitted to REBs and as the complexity of the studies increases, it becomes essential to provide appropriate infrastructure support for the spectrum of research systems and empower the REBs.

The most important barriers to ethical best practice to be addressed, according to TAHSN research stakeholders, pertain to the need to increase consistency in REB reviews including the development of similar risk-proportionate review processes among TAHSN REBs. The *Task Force* recommends creating the *Central Clinical Research Resource Group* to overcome these five top barriers and to address the additional barriers identified by the *Task Force* and validated by the research stakeholders across TAHSN. Some of these additional barriers will require complementary resources to facilitate the work of the REBs in oversight of clinical research conducted at each institution. These include resources to proactively address emerging ethical issues pertaining to new research areas and for education of investigators and their staff on current and future requirements as well as potential study participants on their rights. Provided adequate resources and in recognition of the importance of the issues, it is expected that the *Central Clinical Research Resource Group* will implement processes to overcome the five key barriers and have clear plans in place to address the remaining barriers within a year.

The *Task Force on Human Subjects Research* recommends a stepwise approach in the establishment of a *Central Clinical Research Resource Group* for TAHSN institutions. This group could be a TAHSN committee built on existing committees and resources to address immediate issues and improve TAHSN processes and research systems. The *Central Clinical Research Resource Group* would evolve into a sustainable enabling mechanism of clinical research within TAHSN through performance of several key functions to address barriers in the conduct of clinical research.

The *Central Clinical Research Resource Group*, with representatives from each TAHSN institution, offers the potential for synergies in establishing best practices, streamlining processes, addressing emerging issues proactively and sharing expertise, thus increasing the coordination of the research system. The *Central Clinical Research Resource Group* also presents an opportunity of leadership on national and international matters relevant to clinical research.