

Preamble

The Canadian Collaboration for Child Health: Efficiency and Excellence in the Ethics Review of Research (CHEER) Project was granted CIHR funding in 2020 to address the growing need for increased equitable access to health research for children and their families by streamlining ethics approvals for multisite research. CHEER is led by Clinical Trials Ontario (CTO) and the Maternal Infant Child Youth Research Network (MICYRN), in partnership with the Queen's University Faculty of Health Sciences, Office for Professional Development and Educational Scholarship, and investigators and collaborators across the country. Multisite child health research is logistically challenging to conduct, often with many sites needed to reach recruitment targets. Resources for pædiatric research are limited and ensuring that research dollars are spent in the most efficient manner is paramount. A single research ethics review alleviates some of the barriers to timely multisite pædiatric research initiation.

As the CHEER Project nears the end, the leadership team would like to share a brief report on the outcomes of the project, in advance of the final report that will be published later this year.

Deliverable 1: Web-based Collaborative Review Platform

▶ Develop workflows and application forms

The CHEER single research ethics review platform leveraged the existing CTO Stream program. The ethics application forms were reviewed by the research and ethics community, and by the MICYRN consortium. Amendments to the platform, including the addition of fields specific for CHEER, were made the CHEER platform was ready to accept multi-site child health studies by 2021.

Onboarding and training workflows have been developed, implemented and modified as needed. For new users of the system, training and hands-on support have been provided.

▶ Develop consent/assent templates/agreements

A consent working group with representation from across the country was created to develop a pædiatric focused interventional (non-oncology) consent template, with input from the CHEER Patient and Family Advisory Committee (PFAC). The pædiatric oncology

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community requested that oncology specific templates continue to be utilized. This template is accepted at all major paediatric research institutes, where legislation allows.

The need for engaging assent materials was identified. A literature search and environmental scan revealed limited examples of assent forms that are interesting and informative for children. With input from families, 3 assent activities were developed, a space themed mission map and 2 activity booklets.

▶ **Accept first pilot study(s)**

CHEER began accepting multi-site studies in 2021 with sites only in Ontario. In 2023, this expanded to include sites in Ontario and Nova Scotia and in 2025, sites in Newfoundland. Piloted studies have included interventional clinical trials and observational studies.

Formal Board of Record Agreements have been negotiated and executed between institutions to delegate ethics oversight. Some agreements have been specific to a study protocol, while some institutions have opted to use bi-directional blanket agreements where either party can act as the REB or the participating site for a term length of 3 years.

▶ **System open to studies; ongoing evaluation**

Since launching, the CHEER system is open to child health studies that have at least 2 sites. Studies may be investigator-initiated, or industry sponsored and can include interventional and observational studies spanning children from neonates to youth. Data are collected for each study submitted in the system.

In addition to the CHEER system, the CHEER project and MICYRN jointly launched the Ethics Review Consultation Service to facilitate REB review processes for paediatric multi-site, cross provincial studies. This included hands-on support to child health researchers and study teams, helping them to understand and navigate the necessary ethics approvals and preparing and facilitating ethics submission across various electronic platforms, systems and jurisdictions. A network of collaborating-site research ethics navigators was established to assist in customizing child health research ethics applications and materials to meet local and provincial requirements by serving as a repository of knowledge of local needs and nuances.

▶ **Outcomes of Deliverable 1**

Delivery

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- ▶ In the CHEER system: 9 participating REBs with 9 participating institutions across 3 provinces. 7 provinces represented in the CHEER project on various working groups and committees.
- ▶ In the CHEER system:
 - ▶ 19 child health studies accepted
 - ▶ 11 multisite studies with sites in at least 2 provinces,
 - ▶ CHEER ICF has been used in 6 studies in multiple provinces.
 - ▶ 9 research groups
 - ▶ 5 Pan-Canadian networks have utilized the CHEER system and the Ethics Review Consultation Service.
- ▶ Research areas included oncology, rare diseases, public health surveillance, neonates/NICU, blood disorders and cardiology.

Effectiveness

- ▶ Average time from submission to approval for a study wide application is 107 days, average time from submission to approval for study wide applications reviewed at full board is 99 days, average time from submission to approval for study wide applications receiving delegated review is 113 days. Average time for site application approval is 22 days.
- ▶ Preparing multisite submissions with multiple ethics applications is still an onerous task that takes significant time and effort. Use of the CHEER pan-Canadian ICF template has helped to alleviate this.
- ▶ For participation, endorsement from research institutes, REBs, and researchers is beneficial. 6 institutions participating in the CHEER system have delegated ethics oversight to other institutions. The Ethics Review Consultation Service was used by study teams across 6 provinces.
- ▶ Board of record agreements once reviewed and agreed upon by institutions can serve as templates and be re-used. Board of record agreements were established between 5 institutions across 2 provinces.
- ▶ It was not always possible to execute board of record agreements between institutions for the delegation of ethics oversight, the consequence of which was duplication of the ethics review at sites. Additionally, for research with components of a protocol taking place at satellite/sub sites, agreements need to be inclusive to allow participation from these sites.

Impact

- ▶ The studies received have ranged from interventional clinical trials to chart review and registries. Studies with sites in Ontario and in Nova Scotia have been able to streamline ethics approvals. First time users have been supported to navigate a new

system and style of ethics application and have become comfortable using the platform.

- ▶ Newfoundland and Labrador amended legislation that had historically limited the delegation of research ethics oversight, following sustained advocacy from researchers and institutions and with support from the provincial government. Collaboration with the pædiatric oncology community has identified previously unknown challenges of implementing single ethics review when sub sites and satellite sites, nested under tertiary care centres, are utilized for some aspects of a protocol. Future ethics delegation agreements will need to be inclusive of this.
- ▶ The consultation service has been received positively by the pædiatric research community, who are eager to reduce the administrative burden of REB submissions and review. MICYRN investigators expressed a preference for a single ethics review. With that said, the Ethics Review Consultation Service has highlighted variability in REB review and interpretation of policy, leading to fragmented multisite studies. This variability introduces additional administrative labour and can result in significant disparity between study initiation and recruitment timelines across sites.

Deliverable 2: REB Assessment Program

▶ Develop assessment criteria

The REB assessment program was developed and is available for REBs wanting to become CHEER qualified. Qualification involves the review of standard operating procedures, office organization, REB membership that meets TCPS2 requirements, and application of regulations and policies to the review of 4 selected studies. The qualification team includes an independent auditor, an experienced REB operations professional and an experienced REB Chair. The qualification team is supported administratively by the CHEER project manager. Expertise in pædiatric health research is paramount for the qualification team. The independent auditor has expertise in REB policies and regulations and is final decision maker. The qualification program is at arm's length from other CHEER operations to ensure integrity and independence. The CHEER qualification program is designed to ensure that participating REBs are compliant with applicable regulations and policies, e.g. Health Canada Division 5, FDA, DHHS, ICH-GCP and TCPS2. This process not only builds trust between REBs but also ensures a standard upon which delegation of ethics oversight can be established. In addition to policy and regulation REB membership requirements, CHEER

▶ Pilot assessment(s)

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The program was initially piloted with REBs that had previously undergone qualification by CTO. Support for REBs qualifying for the first time was provided in the form of a pre-review and an honorarium for extra staff time to prepare.

▶ Ongoing REB assessment and evaluation

Each year following qualification, REBs submit an annual report to CHEER which details information of changes to operations, membership or procedures for review by an independent CHEER auditor. Qualification is in effect for 3 years after which REBs are then re-qualified using the same criteria as the initial qualification.

▶ Outcomes of Deliverable 2

Delivery

- ▶ 9 REBs across 3 provinces have undergone CHEER qualification and have been successfully qualified. As of today, 7 REBs have undergone re-qualification.

Effectiveness

- ▶ REBs qualifying for the first time have found the program to be valuable for improving standards and collegial with sharing of best practices.
- ▶ All applicable policies and regulations are used in the compliance assessment of the REB.

Impact

- ▶ REBs that have undergone qualification have ensured that SOPs and other operational practices meet applicable regulations and policies.
- ▶ Researchers have submitted ethics applications to qualified REBs other than their home institution, which has broadened their experiences and understanding of streamlining.
- ▶ Health Canada and TCPS2 acknowledge that streamlining initiatives can be used for multi-site health research and encourage sponsors to consider streamlined approaches to ethics review.
- ▶ Institutions have supported their REBs to engage in the qualification process, seeing the benefit of joining a collaborative environment and creating efficiencies in research initiation.

Deliverable 3: Education Development/Delivery

- ▶ Outreach and prioritization of content

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The paediatric health research community has been regularly consulted for webinar topics and workshops or educational sessions of special interest. CHEER has been able to provide platforms for niche areas of child health research such as access to clinical trials for military connected children, and alternative models of consent for NICU research. Subject matter experts from across Canada have contributed to CHEER educational content, and allied research health and networks have worked to deliver webinars. Researchers with expertise in Indigenous child health research were closely consulted for culturally appropriate consent processes for research with Indigenous communities.

▶ **Delivery and evaluation of online modules**

5 education modules are live and open access on the CHEER website. Each module has been translated into French.

▶ **Delivery and evaluation of webinars**

Webinars have been delivered throughout the lifetime of the project on an array of topics relevant to child health research including Indigenous research, emergency NICU research, child health research in military settings and assent.

▶ **Common ethics sub/review issues interviews**

A needs assessment was conducted, and child health researchers, families and REB members were surveyed and interviewed to provide their views on the ethics review of child health research and opinions on educational materials. Results of this will be published in a peer reviewed journal.

Input and involvement of patient and families The CHEER Patient and Family Advisory Committee (PFAC) have been instrumental in providing lived experiences and perspectives throughout the project. A guidance document for recruitment and orientation of new community REB members was created by the PFAC. Additionally, a workshop was delivered exploring the role of community REB members and how their perspectives can be effectively engaged.

A brochure introducing the concept of research, adapted from work done by the Language Barriers project at BC Children's Hospital, was modified to be applicable to a pan-Canadian context. It is available as a paper trifold, a digital infographic compatible with phone and tablet use, and a digital poster for TV screens in waiting rooms. This has been translated into multiple languages including French and Inuktitut. Additional languages will

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include Spanish and Mandarin, in a collaborative effort between CHEER and the BC Children’s Hospital’s community of patient partners.

A visual study schedule, adapted from work by the Blueprint Translational Research Group in Ottawa, was developed. This is a traditional study schedule that uses pictures to replace text and can be used by children and their families to understand when visits will happen and what the study activities of each visit are. The schedule is available in French and English.

▶ **Outcomes of Deliverable 3**

Delivery

- ▶ 5 modules in English and French
- ▶ 12 workshops and webinars, 2 conferences presentations, regular presentations for various groups in the child health research community.
- ▶ 5 unique resources developed for REB members, families and researchers

Effectiveness

- ▶ Workshops and webinars are well attended and have low attrition rates. Positive feedback was received for an education session proving guidance on common mistakes seen in ethics applications and how to avoid them. Recorded virtual events are posted on the CHEER website and are watched on average 37 times.
- ▶ Education modules align with Health Canada regulations.

Impact

- ▶ Throughout the project, outreach to organizations and groups in the pædiatric research space has been ongoing. Outreach has resulted in collaborations to create resources for families and REBs, including the visual study schedule and brochure, and has provided broader opportunities for community dialogue and assessment of cultural competency during the resource development process.
- ▶ Knowledge mobilization has been key throughout the project and connections to groups who may benefit from the work of CHEER, for example Strategy for Patient Orientated Research (SPOR) groups.

Deliverable 4: Final Report and Recommendations

- ▶ Consultation/drafting of final report

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This primer will serve as the start of knowledge mobilization to disseminate learnings from the CHEER project. A more detailed final report for the pædiatric research community will be released in the coming months along with a shorter version for interested members of the public.

- ▶ Broad consultation re: report and recommendations

Interim progress reports from the CHEER project have been relayed to The Institute of Human Development, Child and Youth Health (IHDCYH) throughout the course of the CHEER project. CHEER hosted annual consortium meeting with the pædiatric research community to provide update on the project and discuss future direction of CHEER. CHEER has engaged in consultation with CanReview and MICYRN to ensure that resources developed by CHEER are long-lasting, creating legacy.

- ▶ Delivery of final report

Prior to the end of the CHEER grant.

Looking Forward

Over the last 20 years, in the absence of a pan-Canadian initiative for single research ethics review, individual jurisdictions reorganized their research ethics processes to create efficiencies. On the one hand, much investment and customization have gone into existing platforms to improve interprovincial streamlining, demonstrating that single ethics review within a jurisdiction positively impacts research. On the other hand, some provinces and territories felt compelled to introduce legislation and regulations to solve local research ethics issues. This inadvertently created obstacles to the implementation of a program of pan-Canadian single ethics review.

As a result, not all jurisdictions in Canada were in a state of readiness for pan-Canadian streamlining research ethics approvals. For all jurisdictions across Canada to reach a state of readiness some modifications will need to happen, including legislative or regulatory reforms to ensure that jurisdictions are able to adopt a new initiative. To expand this across the country, REBs will need to be provided with appropriate support to implement a new ethics workflow, parallel with ongoing local review.

Communicating with study teams as infrastructure for single review becomes available will ensure that studies will increasingly be brought forward for single review. For multi-site

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child health studies to have an internationally competitive start up time, investigators and sponsors need to be confident that the research ethics review is reliable and accepted across all participating sites.

Conclusion

Over the course of the CHEER Project, much has been learned and implementing single ethics review for multi-site research remains a key priority. Regular meetings of REB professionals from across the country were key to creating an atmosphere of collegiality that built trust and improved communication. The CHEER project has achieved several of the goals originally outlined in the grant and has made progress on streamlining. Lessons learned from the CHEER initiative have paved the way to the development and implementation of a pan Canadian streamlined ethics review process and system.

Consistent and high-quality ethical reviews are critical for Canada to become more globally competitive and to attract sponsors, achieved through education, training and community building.

