

Evaluation of the Human Health Therapeutics Research Centre

Office of Audit and Evaluation

September 22, 2020

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Acronyms

- **BRIC:** Brazil, Russia, India and China
- **CDMO:** Contract Development and Manufacturing Organization
- **CGT:** Disruptive Technology Solutions for Cell and Gene Therapy
- **CMO:** Contract Manufacturing Organization
- **CRO:** Contract Research Organization
- **GBA+:** Gender-Based Analysis Plus
- **HHT:** Human Health Therapeutics Research Centre
- **IRAP:** Industrial Research Assistance Program
- **IP:** Intellectual Property
- **MAb-T:** Multi-functional Antibody-based Therapeutics Program
- **MNE:** Multi-National Enterprise
- **NRC:** National Research Council of Canada
- **OGD:** Other Government Department
- **PRC:** Peer Review Committee
- **R&D:** Research and Development
- **SME:** Small and Medium-sized Enterprise



Executive summary

The Human Health Therapeutics (HHT) Research Centre provides technological and scientific support to public and private sector research organizations – particularly Canadian small and medium-sized enterprises (SMEs) – in an effort to de-risk and accelerate the discovery and development of innovative biologic medicines for Canada. HHT is one of the largest research centres at the National Research Council of Canada (NRC) in terms of both budget and staff.

This evaluation covered the period of 2014-15 to 2018-19, inclusively, and drew on a bibliometric study, data review, document/literature review, internal and external interviews, and an expert peer review composed of industry and academia representatives.

Key findings

Supporting business innovation

Support to industry was the primary focus of HHT activities throughout the evaluation period. HHT successfully advanced innovation by de-risking and accelerating the product development cycle, and facilitated technology transfers of manufacturing processes. As a result of working with HHT, clients have grown and improved their capabilities, attracted investments, and increased their market valuation. To date, HHT has helped progress eight products into clinical trials.

Client projects generated significant revenue for HHT, which was an organizational priority at the time. However, given that projects were selected ad-hoc and were centred on clients' needs, they did not necessarily align with a broader strategic objective or public health priority. HHT's industry-focused strategy hindered their relationships with academia and other government departments (OGDs), as well as their ability to publish and advance scientific knowledge in certain areas.

Some research activities were carried out to fill important gaps in the large-scale biomanufacturing landscape. These activities were noted by the Peer Review Committee (PRC) to be resource-intensive and beyond the suggested scope of a research and development (R&D) institution such as HHT.



Supporting government solutions

While not a strategic priority during the evaluation period, some of HHT's research aligned with federal government priorities and contributed to important advancements in public health, such as the development of a vaccine against Haemophilus influenzae type A (Hia). HHT's work has also filled important gaps where industry is not present (i.e., Indigenous health and antimicrobial resistance).

To better position itself to respond to national public health priorities, HHT will require a more systematic approach to engaging with OGDs.

Advancing scientific excellence

HHT holds the largest intellectual property portfolio at the NRC and numerous licensing agreements, demonstrating innovation and the uptake of research beyond the scope of projects. HHT publications have been cited in external best practice documents, clinical practice guidelines, good manufacturing practices and experimental/manufacturing protocols.

HHT's work in therapeutics across the blood-brain barrier is leading edge, according to bibliometric analyses and comments from the PRC. However, there is a risk these efforts will not generate their anticipated impact, should the right industry partner not be secured in a timely way.



Executive summary

Recommendations

The evaluation resulted in six recommendations, which were approved and addressed by HHT in its Management Response and Action Plan.

Recommendation 1 – Strategic focus



Clarify the 2019-24 strategic plan and new program offerings by:

- determining the focus of activities (especially within cell and gene therapy, bioprocessing/biomanufacturing, TRL focus)
- clarifying how, and to what extent, each of HHT's research areas, programs, and initiatives will contribute to each strategic outcome, with specific targets identified
- considering the use of advanced manufacturing technologies for process optimization and efficiency
- monitoring changes in the large-scale biomanufacturing landscape in Canada and adjusting efforts in this area accordingly

Recommendation 2 – Impact on government policy solutions



Increase collaboration with OGDs to address public health R&D needs, and ensure that they are well aware of HHT's strategic plan, including capabilities, expertise and facilities.

Recommendation 3 – Resource planning



Develop a strategic human resources plan and an up-to-date capital investments plan. With regards to human resources, the plan should outline succession planning, training requirements, and consider workload issues and time for exploratory research.

Recommendation 4 – Project selection



Develop a clear project planning process that prioritizes the selection of projects that contribute to the organizational mandate and address government priorities in public health.

Recommendation 5 – Research data management



Ensure that Big data from projects, such as bioprocess automation and genomics, is well exploited (well mined) and integrated into project planning and decision-making (e.g., decision points). HHT should seek bioinformatics support from the Digital Technologies Research Centre and system support from Knowledge, Information and Technology Services.

Recommendation 6 – Impact on research innovation



Ensure that the blood-brain barrier carrier (FC5) is taken to clinical trials with the right, committed industry client (preferably a Canadian client).



INTRODUCTION • HUMAN HEALTH THERAPEUTICS RESEARCH CENTRE

An evaluation of HHT, completed in 2019-20, assessed the relevance and performance of the Research Centre. This report provides an overview of the evaluation findings, conclusions and recommendations.

Introduction

Note re: COVID-19

This evaluation report was finalized in early March, 2020, but its approval was re-scheduled due to HHT's involvement in the Government of Canada's response to the global pandemic. While the outbreak of COVID-19 has not inherently changed the evaluation findings or its recommendations, it has placed greater importance on some activities that were, at the time this report was written, not central to HHT's forward strategy – particularly those of early-stage vaccine research and large-scale biomanufacturing. The long-term impact of COVID-19 on HHT's operating context is still unknown.

An evaluation of HHT was completed in 2019-20. The Research Centre was assessed for the time period spanning from fiscal year 2014-15 to 2018-19, inclusively (herein referred to as the evaluation period). The evaluation was carried out in accordance with the NRC's approved evaluation plan and Treasury Board policies. The last evaluation of HHT was completed in March 2014.

This report begins by providing a profile of HHT, and then presents the evaluation findings on stakeholder engagement, capabilities, performance, and the way forward. Following the conclusion, the evaluation's six recommendations are presented.

Throughout the report, you will see the following symbols:



This symbol indicates information that facilitates understanding of the findings.



This symbol indicates a quote that illustrates or supports the main findings.



This symbol indicates information that supports equity, diversity and inclusion, and Gender-Based Analysis+ (i.e., factors that illustrate how diverse groups may experience policies, programs and initiatives).



Sources: These are the methods from which the findings are drawn. Sources are listed at the bottom of each page.



Evaluation approach

Methods

Mixed methods were used to maximize the generation of useful, valid and relevant evaluation findings. This approach also allowed for cross validation of results based on the following methods:

- document/literature review, including client surveys
- data review (financial, administrative and performance data)
- bibliometric study
- interviews with internal staff and clients and collaborators (n=28)
- external expert peer review

For more detailed information on these methods, including challenges and limitations, refer to Appendix A.

In addition, the evaluation piloted a *Gender-Based Analysis (GBA+) Lens for Evaluation*. See Appendix B for a summary of the findings.

Questions

The evaluation questions were developed based on consultations and a review of key documents. The questions, which guided the conduct of the evaluation, were:

What has HHT achieved over the past five years?

1. How has HHT progressed toward achieving its planned outcomes?
2. Has HHT worked with the clients and collaborators required to achieve its outcomes?
3. How did HHT assist its clients in achieving their objectives?
4. What has been HHT's contribution to scientific excellence?
5. Did HHT have access to the expertise, critical mass and facilities to achieve its objectives?

How has HHT positioned itself for future success (to reach its new objectives)?

6. Does HHT's plan address some of the most important needs of the sector?
7. How will HHT's approach contribute to the advancement of scientific excellence?
8. Does HHT have access to the expertise, critical mass and facilities to achieve its objectives?

Sources: Evaluation matrix



PROFILE • HUMAN HEALTH THERAPEUTICS RESEARCH CENTRE

HHT provides innovative technologies and expertise to Canadian SMEs and other industry partners to help de-risk, accelerate and add value to the development of their products. HHT also strives to promote the development of biomanufacturing capabilities in Canada.

(HHT 2014-19 strategic plan)

Background: The changing NRC context

Then (2014-15 to 2018-19)

In early 2012, in an effort to foster business innovation and economic growth across Canada, the NRC underwent major restructuring and formally rebranded itself as the nation's Research and Technology Organization. This reorganization saw the NRC institutes, previously focused on unique research and technology areas, amalgamated into research centres, focused on broader industry sectors. HHT was established as a part of this process, through the amalgamation of expertise and assets from three former NRC institutes.

In support of this new direction, HHT's 2014-19 strategic plan was heavily industry-focused and revenue-driven, with a vision to contribute to the prosperity of Canada's biopharmaceutical sector through projects centred on clients' needs. This plan included five strategic goals:

1. Position HHT as the "partner of choice" for Canadian SMEs to de-risk and accelerate the development of their products and add value to their pipeline and technologies
2. Build the Programs of the Future – FY2019 and beyond - preparing for diversity in protein modalities, DNA-based therapeutics and vaccines against cancer and chronic diseases, and delivering biologics to the brain
3. Transfer bioprocessing and other enabling technologies to industrial clients to reinforce a strong and prosperous Canadian biomanufacturing sector
4. Align the HHT workforce and streamline its activities in order to support projects with the best returns on investment and respond in a flexible timely manner to evolving industry needs
5. Foster Canadian SME access to global markets (BRIC & Fast Follower markets) through NRC's Strategic International Partnership Initiative

Now (2019-20 to 2023-24)

In 2016, increased federal investments in research and a change in NRC leadership resulted in another significant transformation for the organization and its research centres. The "re-imagined NRC" is focused on science excellence, research innovation and collaboration, and strives to address some of Canada's most pressing socio-economic and health challenges. While business innovation and growing firms remain important aspects of the NRC's new strategy, the organization is scoping its efforts to focus on the areas of greatest importance to Canadians and that align with Government of Canada priorities.

As a key contributor to this new mandate, HHT aligned its activities to address three new and distinct strategic objectives, as outlined in its 2019-24 strategic plan:

1. Apply disruptive technology solutions for advancing cell and gene therapy

HHT will invest in strategic research to advance scientific knowledge and apply disruptive and transformative technologies such as cell and gene therapy to develop innovative medicines that safely and effectively modify disease outcomes.

2. Support business innovation

HHT will enable Canadian SMEs to de-risk the development, testing, and production of multifunctional biologics. HHT will foster biomanufacturing in Canada.

3. Deliver policy solutions for Government

HHT will catalyze (in partnership with other OGDs and research institutions) public health solutions for unmet medical needs such as emerging infections and rare Canadian genetic disorders by engaging partners to develop new health care delivery models and made-in-Canada vaccines and therapeutics.

Sources: Internal documents

Research activities

Programs and activities

Prior to 2019, HHT had three active research programs. As part of its strategic planning for 2019-20 to 2023-24, the Research Centre is moving forward with two programs and three special initiatives. Several elements of the previous programs are part of these new programs and initiatives. For more detailed information on HHT activities, please refer to the logic model in Appendix D.

Programs prior to 2019 (2014-15 to 2018-19)

Biologics and Biomanufacturing program:

Development of biotherapeutics against cancer, infectious diseases, as well as inflammatory and auto-immune diseases.

Vaccines and Immunotherapeutics program:

Development of prophylactic and therapeutic vaccines against cancer and emerging infections.

Therapeutics Beyond Brain Barriers program:

Development of biotherapeutics against central nervous system diseases.

Further details on these programs are provided in Appendix C.

Programs and initiatives starting in 2019 (2019-20 to 2023-24)

Multi-functional Antibody-based Therapeutics (MAb-T) program:

An amalgamation of the Research Centre's three former programs; focused on expanding the Canadian SME biotechnology pipeline of multifunctional biotherapeutics that address unmet needs in cancer and neurological diseases.

Disruptive Technology Solutions for Cell and Gene Therapy (CGT) program:

Advancing disruptive technology solutions for the design, development, and delivery of affordable and accessible engineered cell and gene therapy to treat cancer and rare genetic disorders of importance to Canada; part of the NRC's suite of Challenge Programs.

Biomanufacturing initiative:

Supporting a prosperous Canadian biomanufacturing ecosystem.

Vaccines and Emerging Infections Readiness Innovation initiative:

Disruptive technologies for development of vaccines against emerging infections and combating anti-microbial resistance.

NRC-Centre hospitalier universitaire Sainte-Justine Collaborative Unit for Translational Research:

Development of biomarkers, biotherapeutics and engineered cell therapies for unmet medical needs in children.

Sources: Internal documents

Financial resources

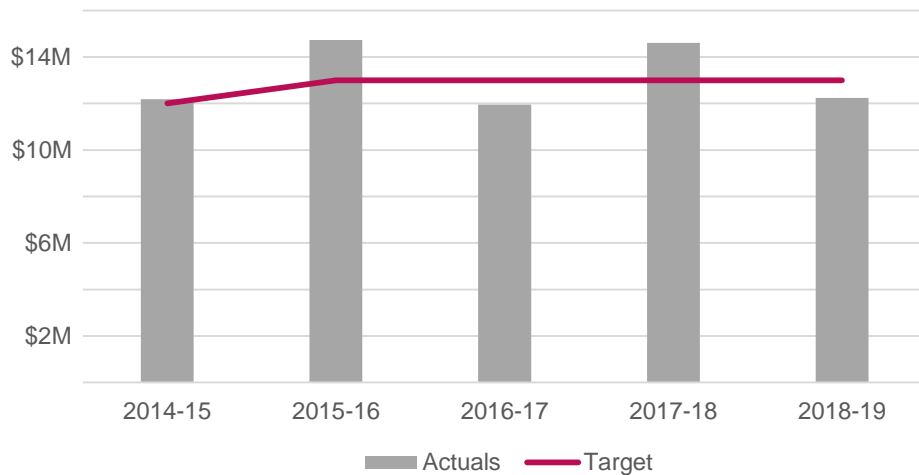
Revenues and expenses

Throughout the evaluation period, HHT had expenditures totaling \$168.95 million and generated \$65.72 million in revenues. HHT earned an average of \$13.14 million per year, while expenses averaged at \$33.79 million per year.

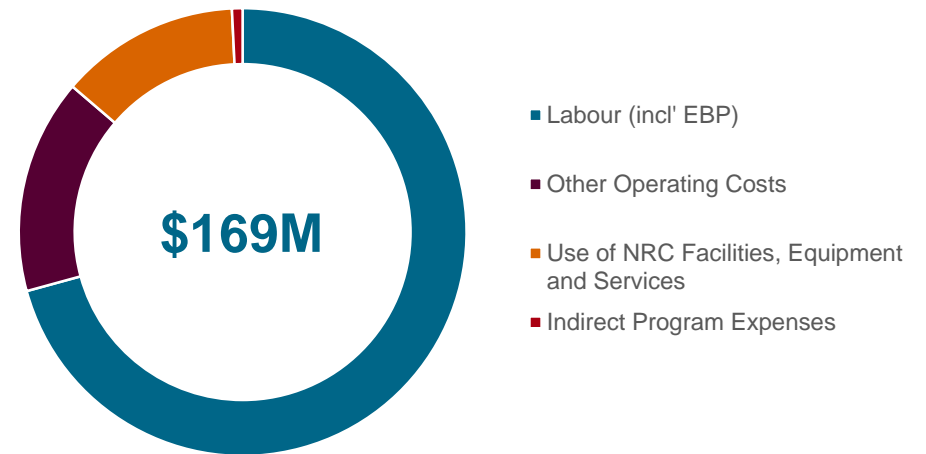
The majority (55%) of HHT's earned revenues were generated through activities under the Biologics and Biomanufacturing program, while the remainder are attributable to the Vaccines and Immunotherapeutics (20%) and Therapeutics Beyond Brain Barriers (24%) programs. All programs generated revenues predominantly from strategic research projects.

HHT exceeded their revenue target by nearly \$2.0 million in fiscal years 2016 and 2018, but fell short of its target by nearly \$1.0 million in fiscal years 2017 and 2019.

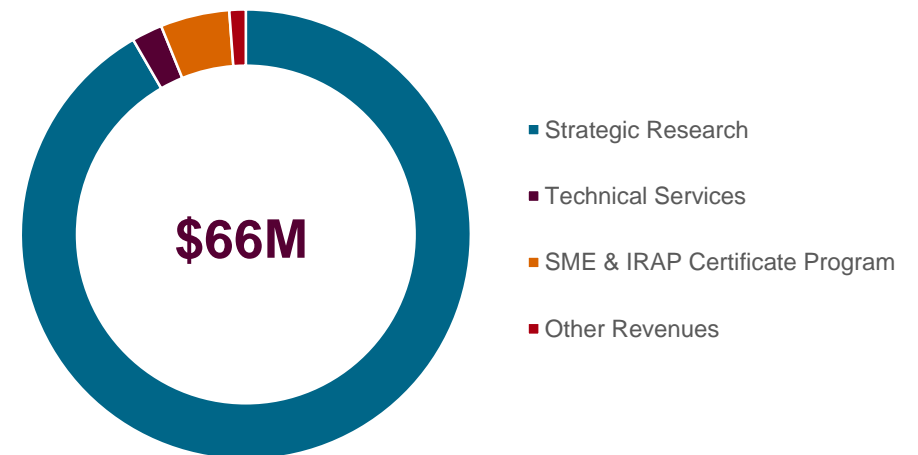
HHT's revenues remained relatively stable over the years



The majority of HHT expenses are drawn from labour



Most revenues were generated from strategic research projects



Sources: NRC financial statements, HHT administrative data, internal documents

Human resources

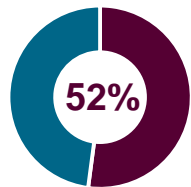
Human resources

As of March 31, 2019, HHT had a total of 340 employees, with the majority located in either Ottawa (46%) or Montreal (52%), and a small subset (2%, 7 full time equivalent employees) located in Halifax. HHT is the second largest of NRC's 14 research centres.

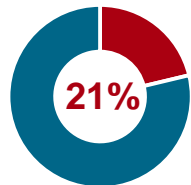
HHT employees are organized into four R&D departments, each headed by an R&D director, namely: Immunobiology, Bioprocess Engineering, Translational Bioscience, and Downstream Processing and Analytics. Within each R&D department, staff are further organized into distinct teams or sections by area of specialization. The Research Centre also has an operations department.



Gender, diversity & inclusion



Women make up more than half of HHT's workforce, including 33% of all research staff, 60% of all technical staff, and 57% of the management team. HHT exceeds its representation target for women by 3.3%.



Nearly a quarter of HHT employees self-identified as **visible minorities**. HHT exceeds this representation target by 2.4%.



The self-identification results for both **people with disabilities** (target: 4%) and **Indigenous people** (target: 3%) were redacted for privacy reasons, which suggests a value of less than 1.5%. HHT therefore does not currently meet its representation targets for those groups. This is a trend that is observed across the NRC.



Sources: NRC financial statements, HHT administrative data, internal documents

Facilities

HHT maintains and operates facilities in four locations, each with specific capabilities listed below:

MONTREAL: **Royalmount Avenue**

- cell culture pilot plant
- functional in vitro assay platforms
- mammalian scale-up biomanufacturing (production and purification)
- microbial fermentation pilot plant
- molecular modelling
- monoclonal antibody production
- quality attributes and characterization



OTTAWA: **Montreal Road**

- animal resources
- electrophysiology
- genomics
- immune monitoring core
- immuno-oncology
- in vitro pharmacology
- pre-clinical imaging and in vivo pharmacology



OTTAWA: **Sussex Drive**

- advanced analytics (mass spectrometry)
- bacteriology and virology
- glycochemistry
- mucosal immunology
- single domain antibodies
- surface plasmon resonance



HALIFAX: **Oxford Street**

- biomarker quantification
- validation of clinical assets for industry partners



Sources: Internal documents

Projects and clients / collaborators

Over the course of the evaluation period, HHT started and/or completed a total of 685 projects with 224 unique clients. The majority (**54%**) of these projects were strategic or collaborative R&D projects, while the remaining **46%** were technical or testing services projects. HHT's clients and collaborators were mostly Canadian organizations, with Canadian industry making up 46% of the Research Centre's total client base and generating 64% of all project revenues.



Industry, including 101 Canadian and 60 international companies.

- 573 projects: 58% R&D, 42% technical services
- \$43.3 million in revenues (average revenue per project: \$76,000)



Academia and others, including 35 Canadian and 22 international universities, colleges, hospitals, research institutes, and other organizations.

- 97 projects: 34% R&D, 66% technical services.
- \$3.0 million in revenues (average revenue per project: \$31,000)



OGDs, Health Canada, Public Health Agency of Canada, Canadian Food Inspection Agency and Agriculture and Agrifood Canada.

- 12 projects: 42% R&D, 58% technical services.
- \$1.8 million in revenues (average revenue/project: \$150,000)



Provincial Government, including 2 provincial health authorities.

- 3 projects: 100% R&D, 0% technical services.
- No revenue was attributed to these three projects.



What's the difference between strategic research and development (R&D) projects and technical services?

Strategic R&D consists of collaborative research projects undertaken with partners to de-risk R&D and accelerate commercial development timelines or to advance knowledge that is of interest to the NRC. Technical services make use of NRC's existing knowledge and technology to assist clients in solving immediate technical problems through the delivery of specialized fee-for-service support.

Sources: HHT administrative data, internal documents



CLIENTS AND COLLABORATORS • HUMAN HEALTH THERAPEUTICS RESEARCH CENTRE

HHT worked mostly with Canadian industry and international partners, which was appropriate given the client-focused and revenue-driven operating context of the time. Under its new strategy, HHT has plans to increase collaboration with other collaborators, including NRC research centres. A more strategic and selective approach may be needed.

Stakeholder engagement

HHT was successful in engaging with targeted clients and collaborators.

Planning

Throughout the evaluation period, HHT kept an up-to-date stakeholder engagement plan. Although this plan targeted primarily Canadian SMEs developing protein therapeutics, vaccines and/or immunotherapies, it also highlighted the importance of working with multi-national enterprises (MNEs) to facilitate product entry into clinical trials and commercialization, and to sustain revenue through high-value contracts. OGDs, centres of excellence and research institutes were also considered for co-development projects in areas of mutual interest.

During this period, HHT adjusted its stakeholder engagement plan to include collaborations with contract research organizations (CRO), contract manufacturing organizations (CMO), and contract development and manufacturing organizations (CDMO), in an effort to strengthen the biomanufacturing ecosystem in Canada.

In addition, HHT kept an ongoing outreach plan to attract new or potential clients. Internal documents show that HHT did indeed engage with stakeholders by regularly participating in high-profile conferences and organizing workshops, seminars, and meetings, particularly in the areas of biomanufacturing, vaccine development and Indigenous engagement.

Engagement and outreach responsibilities

Internal documents outlined the general roles and responsibilities of staff across NRC:

- **Research and Technical Staff:** attend and/or present at conferences; host information booths at industry events
- **Business Management Services Team:** seek and build relationships with clients and stakeholders; manage agreements; promote products and services
- **Communications Team:** prepare promotional materials and presentations; draft media/press releases

Sources: HHT administrative data, internal documents, peer review



Clients and collaborators – Industry and international

HHT worked mostly with Canadian industry clients and also maintained strong relationships with international organizations.

Canadian industry

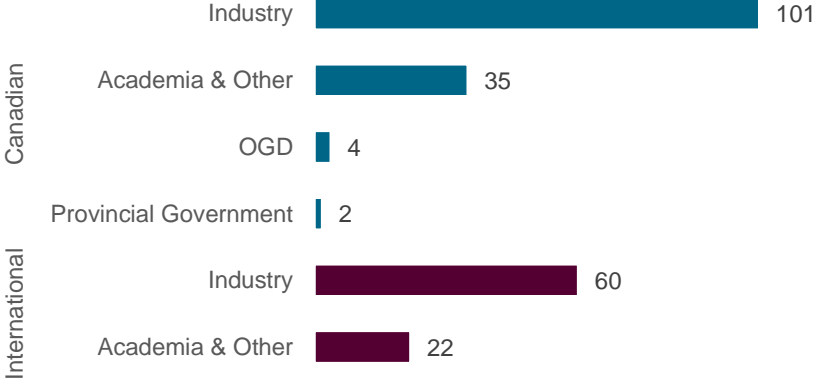
HHT’s 2014-19 Strategic Plan was heavily industry-focused, prioritizing collaborations with Canadian SMEs in an effort to de-risk and accelerate the development and commercialization of biologics, vaccines and biomarkers, as well as to contribute to the strength and prosperity of the Canadian biopharmaceutical and manufacturing sectors.

The mix of HHT’s 224 clients and collaborators appears to align with these strategic objectives as well as HHT’s stakeholder engagement plans, with nearly half (46%) of its clientele representing Canadian industry.

International organizations

International organizations, particularly foreign industry, were another important source of collaboration for HHT, contributing to more than a quarter of all project revenues. HHT also frequently interacted with international organizations by way of non-exclusive material transfer or technology license agreements, for assets that – while likely co-developed with a Canadian industry partner – attracted interest worldwide.

HHT clients and collaborators were largely from industry



Immediate consideration

The PRC recognized that HHT’s Therapeutics Beyond Brain Barriers program has been very active in working with key players in their field, particularly international partners, and has developed a number of important and fruitful relationships. However, the committee also noted that HHT has yet to find the right client who will commit to taking their primary platform, the FC5 carrier, into clinical trials. Given that much of HHT’s success in central nervous system research is dependent on the success of this platform, the PRC recommends that clinical validation with an industry partner be of top priority.

Sources: HHT administrative data, internal documents, peer review

Clients and collaborators – OGDs, academia and others

HHT worked with OGDs in some areas, but there is potential to collaborate more broadly. Relationships with other collaborators, such as academia, are being rebuilt.

Other government departments

HHT collaborated with four OGDs on 12 projects over the past five years. Some of those projects included work with the Public Health Agency of Canada on Ebola and Tuberculosis, a project with Health Canada on synthetic cannabinoids, and research for the Department of Agriculture and Agri-Food on antibodies against Intimin (e.g., E coli).

HHT also collaborated with OGDs via interdepartmental committees and national associations. For example, HHT's Director General is co-chair of the Vaccine Research Innovation and Development committee, which – according to OGD interviewees – plays an important role in identifying priority health issues and informing vaccine R&D in Canada. Additionally, in partnership with OGDs and other national stakeholders, HHT has been involved in the Canadian Cancer Research Alliance, and has provided in-kind support to the Genomics Research and Development Initiative.

It is recognized that, under HHT's former strategy, OGDs were not the focus of the Research Centre's stakeholder engagement efforts. While HHT maintained collaborations with OGDs in some research areas, particularly vaccines, the Research Centre could increase its visibility and engagement with these key partners moving forward, in order to succeed in delivering public policy solutions for Government.

Academia and others

While collaborations with academia and other organizations, such as research institutes and hospitals, were not encouraged under HHT's previously industry-focused and revenue-driven strategy, the Research Centre has gradually increased these collaborations over the last two years. Moving forward, HHT intends to increase and actively seek out collaborations with academia and other organizations, particularly as part of the CGT Program and the Collaboration Unit for Translational Research.

The PRC agreed that collaboration with academia will be an important factor in HHT's success under the new strategy. According to the PRC, academic institutions generate a wealth of cutting-edge, early-stage research that HHT could then transform into possible solutions by increasing the readiness of a new technology approach. These types of collaborations will better position the Research Centre to achieve scientific excellence and deliver impact.

The PRC also saw an opportunity for HHT to leverage and strengthen its relationships with universities by bringing on PhD or post-doctoral students to help fill gaps in capacity or expertise in novel areas. This is aligned with strategies outlined in HHT's 2019-24 strategic plan.

Sources: HHT administrative data, internal documents, peer review



Collaboration across NRC

Collaboration with other NRC research centres was limited, but will increase under HHT's new strategy.

Limited collaboration with other research centres

The evaluation found that HHT has not relied on NRC's matrix management as much as most other research centres. Of NRC's 14 research centres, HHT ranks 10th in terms of the number of hours spent supporting programs hosted by other research centres, and 9th in terms of the amount of support received from other research centres to deliver on its own programs.

Interviews suggest that this may be due to the nature of HHT's work. While some interviewees reported synergies and facility-sharing with the Aquatic and Crop Resource Development, Medical Devices and, more recently, Digital Technologies research centres, many stated that projects with other research centres often do not "fit" within HHT's focused mandate to address human health.

The future looks promising

Recent initiatives such as the NRC Challenge Programs and Small Teams initiative will provide an opportunity for HHT to increase its collaboration with other research centres.

HHT is host to one of NRC's Challenge Programs, the CGT Program, which will draw on the resources and expertise of seven research centres across the NRC. While collaboration with research centres will be an inherent part of program delivery, some interviewees suggest that the initiative may result in new and unforeseen opportunities for joint projects.

Additionally, HHT was recently awarded funding under NRC's Small Teams initiative to collaborate with the Nanotechnology and Aquatic and Crop Resource Development research centres on engineered immunobiotic delivery systems to combat the antimicrobial resistance crisis.



*The NRC uses a **matrix organizational structure** that includes research centres as its vertical structure, and programs as its horizontal structure. While research centres are permanent organizational units with identified resources (i.e., personnel and facilities), programs are specialized, time-limited efforts focused on addressing specific business-identified priorities and/or challenges. While each research centre is responsible for managing its own resources, programs can draw on resources from within their host research centre or from others in an effort to fill gaps in capabilities and/or expertise.*

Sources: HHT administrative data, internal documents, peer review



CAPABILITIES • HUMAN HEALTH THERAPEUTICS RESEARCH CENTRE

HHT is recognized for the breadth and quality of its expertise and capabilities. However, recent increases in workload, budget reductions, aging facilities, and a workforce nearing retirement threatens its ability to stay relevant and achieve objectives. HHT is responding to these challenges through targeted hiring and investment strategies.

Capabilities

HHT is recognized for the breadth and quality of its expertise and capabilities.

Expertise

The PRC and clients recognize HHT's highly qualified and experienced personnel in bioprocessing, biomanufacturing and blood brain barrier technology research. Specific areas of expertise include: neurodegenerative disorders; cancer immunology and inflammation; emerging infections; glycoconjugate vaccines and adjuvants; and, antibody engineering and bioprocess development.

Some clients sought to work with HHT because they wanted to collaborate with researchers renowned for their expertise in a particular field. Clients also appreciated the industry expertise of HHT staff, which can be critical for understanding the market feasibility and relevance of potential products.

Unique service offering

Few other organizations in North America have the capabilities and/or expertise necessary to carry a product through the entire development chain, from early discovery through to the pre-clinical phase. One half of all client interviewees reported that, while the same capabilities and/or expertise may exist across several companies/organizations in North America, the complete suite of services offered by HHT are difficult to find elsewhere.



"In terms of Bioprocessing, the committee found HHT to have excellent, experienced staff."

Peer Review Committee



Sources: Interviews, peer review, internal documents

Capacity challenges and response

HHT's increasing workload, coupled with a workforce nearing retirement, threatens its continued high-performance. It is responding through targeted hiring and support for next generation researchers.

Retirements

Loss of expertise due to retirement has been, and continues to be a concern. Over the evaluation period, close to 12% of HHT's staff retired (40/340). Further, more than a quarter (90/340) of HHT's remaining staff are eligible to retire over the next three years.

While HHT does not currently have a formal succession plan in place, it is responding to these challenges by using natural attrition to fill capability gaps in areas critical to its new programming. For example, in 2019-20 HHT is targeting recruitment in the areas of genomics and bioprocessing.

HHT also plans to develop expertise through hiring and training new researchers. To do so, it plans to:

- be proactively involved in doctoral training with universities
- leverage NRC's post-doctoral program
- increase hires for summer students
- pilot a new graduate student program for NRC



"This is an excellent opportunity to develop next generation scientists and also allow transfer of expertise to younger generations employed by HHT."

Peer Review Committee

These efforts will increase HHT's student complement from 26 in 2019-20 to 45 in 2023-24.

Workload

HHT has been able to meet its objectives with current staffing levels. However, the Biologics and Biomanufacturing, and Therapeutics Beyond Brain Barriers programs have stretched their staff resources and work/life balance was a concern for managers and their employees. While most projects were not affected, several clients experienced delays or missed deadlines due to lack of capacity, including one client who took a project to another organization.

Budget reallocation across NRC

All NRC research centres are required to reduce spending by 10% over the next five years as part of NRC's budget reallocation for strategic investment. This is an issue of concern for HHT, if it is to balance workload challenges and retain the same level of programming and revenue targets.

Sources: Interviews, peer review, HHT administrative data, internal documents

Facilities

Unable to secure the needed funds to invest in facilities and equipment in the past, HHT is now pursuing an incremental investment plan through multiple strategies.

Current state

Like many of NRC's research centres, HHT faces a critical need for capital investment in its facilities. While many facilities were once state-of-the-art, a lack of capital investment in key pieces of equipment (e.g., mass spectrometers, nuclear magnetic resonance machines, microbial pilot plant) has resulted in inefficiencies, instrument downtime, and missed opportunities with clients and collaborators.

Throughout the evaluation period, HHT consistently highlighted their capital investment needs in its annual operational plans, however, most of these planned upgrades still have not occurred. Of note, one of those unsuccessful proposals, submitted in 2015, related to the implementation of an Electronic Laboratory Notebook platform for comprehensive data management and analysis – capabilities that were identified by the PRC as essential in today's data-driven reality.

Those significant needs were also noted in the recent NRC-wide review of facilities where it was found that HHT's Biomanufacturing Facility is growing increasingly outdated and inefficient. A continued lack of capital funding to bring the facility's technology up-to-date threatens its ability to serve its clients and seize potential opportunities.



“In order to remain competitive and respond to industrial needs, HHT should pay attention to capital investment in its facilities.”

Peer Review Committee

Incremental investment plan

In the absence of major capital funding, HHT developed a three-pronged strategy for addressing its facility and equipment needs:

Interim investments: For its analytics, animal, Biomanufacturing, pre-clinical imaging, immune monitoring and pharmacology facilities, HHT will seek minor capital investment for short-term improvements or use leases or collaborations to fulfill its needs.

Longer-term funding proposals: HHT is pursuing funding for its Biomanufacturing Facility as a result of NRC's Facility Review Initiative. It is also pursuing funding through a horizontal government initiative that supports the construction of new, collaborative research facilities for federal science-based departments. Through that initiative, funding will be sought for the analytics facilities (e.g., mass spectrometry and nuclear magnetic resonance) and Combined Containment Level 3 facility.

Partnership investments with other research institutions: In preparation for the launch of the CGT program, NRC invested \$2.7 million in areas essential for program delivery with selected universities, including:

- support for new capacities in mammalian cell genome editing
- investments in biodevices and microfluidic technologies
- support for a new translational research platform

Sources: Internal interviews, document review, data review, peer review

PERFORMANCE • HUMAN HEALTH THERAPEUTICS RESEARCH CENTRE

HHT was successful in achieving its outcomes – after working with HHT, companies reported increased capabilities, attracting investments and increased market valuation. Further, although not the focus at the time, some advancements were made in scientific knowledge and in public health R&D.

Impact on business innovation

By way of its innovative platform technologies and processes, HHT has helped its clients de-risk products and progress through the value chain.

Throughout the evaluation period, HHT consistently met or exceeded its target for the number of products progressed through the development value chain, and was successful in achieving its target of five 'new and improved' products or processes transferred to clients in two of the last five years. Additionally, HHT assisted 10 products in filing Investigational New Drug submissions or Clinical Trial Applications.

Feedback from clients also suggests that HHT's accomplishments in product development are well-recognized:



Some client interviewees reported that, due to the breadth of expertise and capabilities offered, collaboration with HHT allowed them to more easily progress their product through the value chain.



39% of respondents to a 2017 client survey noted that risk-sharing with HHT was either very or extremely important for them.



53% of respondents to the same survey noted that working with HHT decreased the time for their product to get to Investigational New Drug submission or clinical development.

To date, HHT has helped progress eight products to clinical trials, including:

Year	Milestone	Molecule / Technology	Indication / Application
2018	Licensed	Ad5-based vaccine	Ebola
2018	Phase 1-2a	Virus-like particule	Glioblastoma
2017	Phase 1	Antibody-drug conjugate	Solid tumours
2016	Phase 1	Bi-specific antibody	Breast, gastric and ovarian cancer
2016	Phase 1	Virus-like particle	Cytomegalovirus
2016	Phase 2	Monoclonal antibody	Metastatic carcinomas
2015	Market	Hormonal therapy	Hypoparathyroidism
2012	Phase 3	Oncolytic virus	Cancer

Source: Internal documents, external documents



Impact on business innovation

HHT's clients have increased their market valuation, grown and improved their capabilities. Impacts were greatest for smaller SMEs.



Increased market valuation

Nearly half of clients responding to the 2017 client survey reported that HHT had a positive impact on their market value, attributing more than \$100 million in growth to HHT.



Increased investment

Half of clients responding to the 2017 survey said their work with HHT had a positive impact on investment. They said that investments valued at \$16.4 million were directly attributable to HHT support.



Improved capabilities

Clients said that HHT allowed them to fill gaps in expertise and technology and to access knowledge and information. It also helped them develop their own skills so that they could perform work themselves in the future.

The survey also found that smaller companies were more likely to attribute impact to HHT with regard to changes in market valuation, ability to attract investments as well as increased capabilities and performance. Given the long product development lifecycle in the domain of novel therapeutics, the PRC commented on the importance of developing short- and medium-term impact indicators as these changes often take years to be realized.

Success stories

- Since its first collaboration with HHT in 2009, a Canadian company has grown from seven to more than 175 employees, attracted more \$266 million in financing, and secured 11 deals with MNEs to develop biologics for conditions such as cancer.
- Another Canadian company co-developed two anti-cancer biotherapeutics with HHT (one of which is proprietary to NRC), which saw successful financing, rapid development, and approval by the US Food and Drug Administration for clinical trials.
- A third Canadian collaborator has taken two products to clinical trials with HHT support and has invested in their R&D unit in Ottawa, growing from less than 5 staff to a total of 28 employees.

Sources: Impact survey, external interviews, internal and external documents



Impact of research

While research excellence was not a key measure of success at the NRC in the past five years, HHT continued to publish and demonstrated scientific impact in some domains, particularly that of the Blood-Brain Barrier.

Citation impact*

HHT's scientific impact is less than that of both the NRC and Canada. This finding was supported by comments from the PRC, and internal documents which suggest that it may be reflective of the prolific and highly competitive nature of human health research domains.

HHT's greatest research impact is seen in the domain of Blood-Brain Barrier – the area in which it has the fewest publications but an impact score greater than the both Canadian and global scores. The PRC described HHT's work in this area as leading-edge, and suggested that their work is “the strongest asset within HHT”, with “the potential to deliver a platform useful in humans”.

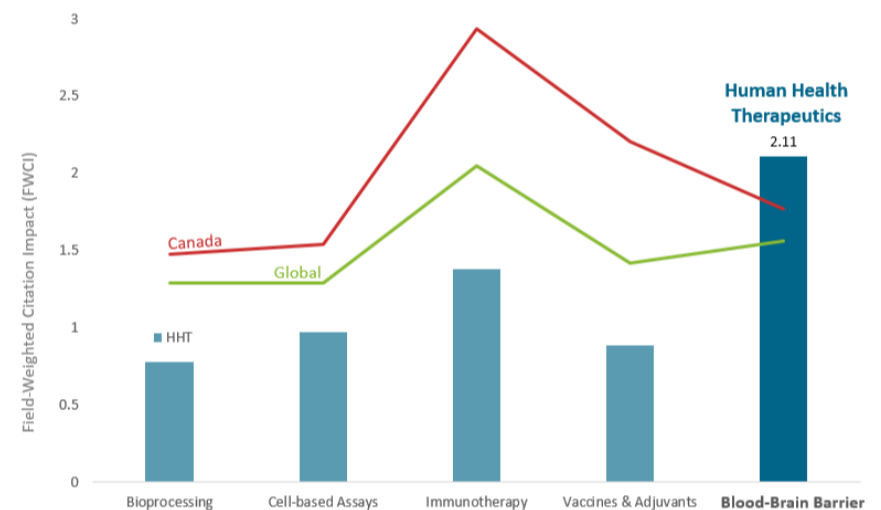
HHT publications have been referenced in best practices, good manufacturing practices and manufacturing protocols, often with respect to scalable industrial production of viral vectors and other biological materials. Many of these citing publications were authored by researchers from large pharmaceutical companies, such as Boehringer, Lonza and Sanofi-Pasteur.

Internal documents suggest that, in the past five years, HHT delivered more than 250 presentations at international conferences, including several keynote and plenary speeches, and that their researchers were frequently invited to give lectures at recognized academic conferences.

* Note: bibliometric data may not be representative of all HHT research area publications. This limitation is noted in Appendix A.

Sources: HHT administrative data, internal documents, peer review

HHT's scientific impact is greatest in Blood-Brain Barrier



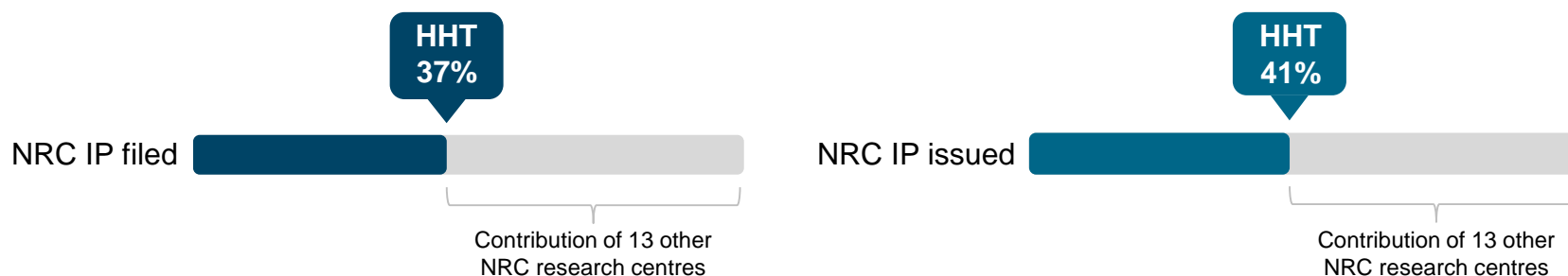
Achieving research excellence

Research excellence has been re-emphasized as a strategic priority in HHT's 2019-24 strategic plan, and the majority of its programs and initiatives will include early-stage, strategic research focused on disruptive technologies.

Additionally, HHT has planned for internal projects that will focus both on capacity development and fundamental research. The PRC spoke to the importance of allowing investigators to pursue research ideas.

Advancement of scientific knowledge

HHT holds the largest intellectual property (IP) portfolio at the NRC, but should focus its efforts primarily on the development of processes and technology platforms, rather than products. Licensing of IP has generated revenue and demonstrated the uptake of HHT's scientific efforts.



Throughout the evaluation period, HHT disclosed 82 new invention records and filed, on average, 101 intellectual property applications per fiscal year – accounting for approximately 37% of the total number of applications made across the NRC. Additionally, HHT was responsible for 41% of the NRC's total IP issued between 2014-15 and 2018-19, with a total of 351 IP issued under 105 unique titles. Of these titles, however, only two stemmed from inventions disclosed during the evaluation period – a finding that is representative of both the lengthy intellectual property application process as well as the lengthy product development lifecycle in biological sciences. In fact, more than 50% of titles stemmed from inventions disclosed between 2003-04 and 2007-08.

The PRC was impressed with the size of HHT's IP portfolio, but suggested that – with the exception of their Blood Brain Barrier carriers that are leading edge – HHT should steer away from developing proprietary products and focus its efforts solely in their areas of greatest strength: the development of technology platforms and processes. Currently, HHT's portfolio is split between products (40%), technology platforms (50%), methods (4%) and other (6%).

HHT has been successful in licensing its IP, having signed a total of 136 technology license agreements with Canadian and international clients throughout the evaluation period. On average, these agreements accounted for \$3.43 million in annual revenues and more than a quarter of total revenues. These agreements also provide evidence of HHT's scientific efforts being used beyond the scope of initial R&D projects. The PRC commented on the benefits of using non-exclusive licensing agreements as a way to maximize uptake of processes and technology platforms.

Sources: HHT administrative data, peer review

Government policy solutions

While not a strategic priority at the time, HHT's activities addressed some federal priorities, and collaboration with other federal departments contributed to important advancements in public health R&D.

Major government priorities: Indigenous people's health and aging populations

Throughout the evaluation period, the Government of Canada consistently funded efforts to address gaps in health outcomes between Indigenous and non-Indigenous people as well as addressing aging populations concerns. Other commitments included investments in genetics, cell and gene therapy as well and immunization. Although none of the government's announcements were directed at HHT's R&D activities, all of the investments were in areas covered by HHT programs.

Indigenous people's health

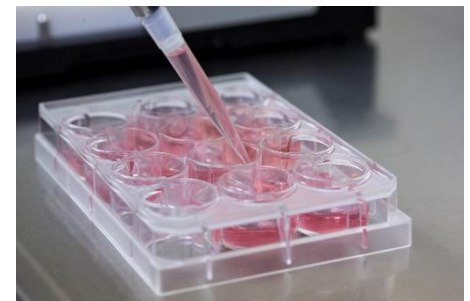
As part of the Vaccines and Immunotherapeutics program, and in partnership with the Public Health Agency of Canada and other federal and community partners, HHT worked on developing a vaccine against Haemophilus influenzae type A (Hia) – a strain of influenza prevalent in northern Indigenous communities. Hia has been identified as a critical public health issue, but its relatively low incidence rates and concentration within minority population groups makes a vaccine unlikely to become commercially lucrative and, therefore, unattractive to private industry. It is for these reasons that government intervention was deemed necessary.

The project resulted in a successful pre-clinical proof of concept by HHT and the Public Health Agency of Canada, which has since been licenced to a GMP manufacturer. HHT and its partners are currently exploring various possibilities to fund the next phases of the vaccine's development. Once Good Laboratory Practice toxicology is completed, it is expected that the vaccine could be made available for clinical trials in other regions of Canada and abroad. To ensure that the project is well received by Indigenous communities, there has been ongoing engagement with community groups. (For more information, see Appendix B)

Aging populations

One of HHT's former programs, Therapeutics Beyond Brain Barriers, was entirely focused on treatment of central nervous system diseases and the delivery of therapeutics to the brain, which have an impact on aging populations. These research efforts will continue under the umbrella of the MAb-T program.

Sources: Internal documents, interviews



Government policy solutions cont'd



Immunization

Budget 2016 identified immunization as a federal priority.

HHT's Vaccines and Immunotherapeutics program aligned with Government's immunization commitment. A notable example of the HHT's work in this area came in response to the outbreak of the Ebola virus in 2014-15 in West Africa, when they partnered with the Public Health Agency of Canada to produce and purify investigational antibodies to accelerate the development of Ebola therapeutics.

Genetics, gene and stem cell R&D

Budget 2016 called for greater efforts in strengthening Canada's international leadership role in stem cell research and in genomics while Budget 2019 committed \$1 billion to the creation of a national strategy to ensure Canadians have access to high-cost drugs for rare diseases.

HHT research aligns with those areas as shown by the CGT Challenge Program, and HHT's projects that support the interdepartmental Genomics R&D Initiative. Of note, one of the major projects that will be undertaken by the CGT program is on rare diseases.

Lack of coordination

Although some of HHT's research has aligned with federal priorities, the evaluation found that this was not due to strategic intention but rather because its research domains are in areas of importance to the advancement of human health that are also aligned with industry priorities (e.g., biopharmaceuticals). While HHT's participation on the Vaccine Research Innovation and Development Committee has led to coordinated interdepartmental efforts in vaccine development (noted earlier in the report), engagement with OGDs has been not been consistent in other research areas.

Sources: Internal documents, interviews



Projects

Research projects generated significant revenue, but there is an opportunity for HHT to better align its projects with strategic outcomes and use data mining to inform project planning and decision-making.

Project selection

HHT's project selection approach was identified by the PRC as an area for improvement. Following a review of key project profiles, it was unclear to the committee why certain projects were undertaken or how they contributed to the overall achievement of strategic objectives, short of generating revenue.

The PRC highlighted the importance of a rigorous project selection process that prioritizes those in line with organizational and federal priorities of greatest importance to Canada.

Opportunity for better data management

Additional collaboration with the NRC's Digital Technologies Research Centre is essential. The PRC spoke to the increasing popularity of the "quality by design" approach in the development of biopharmaceuticals, and highlighted an opportunity for HHT to leverage the expertise of the Digital Technologies Research Centre to improve their in-house capabilities in bioinformatics, data management, and data mining. One committee member described HHT's pool of high-quality raw data as a "gold mine".



Sources: HHT administrative data, internal documents, peer review

WAY FORWARD • HUMAN HEALTH THERAPEUTICS RESEARCH CENTRE

HHT's 2019-24 strategic plan addresses the most important needs of the biopharmaceutical sector and public health priorities. Although there is alignment with available resources, some issues may impact the ability of HHT to deliver on its plan.

Way forward

HHT's new strategy is aligned with global and national trends, and addresses some of the most important needs of the biopharmaceutical sector as well as public health priorities.

Determining priorities – multiple considerations

As part of the Government of Canada's Innovation, Science and Economic Development portfolio, the NRC and its research centres are mandated to support business innovation across Canada and address the needs of their respective industry sectors, which, in the case of HHT, includes nearly 300 SMEs with unique challenges and capability gaps. In order to fulfill this mandate and contribute to the NRC's 2019-24 strategic goal of 'supporting a healthier future' for Canada, HHT's research efforts must also address the latest national public health priorities. Moving forward, HHT has positioned itself to align with both industry trends and public health needs:

Trends – Industry



Rising economic burden of healthcare in Canada, driven by an aging population, increased preference for drug therapy over other treatments, and the development of more effective drugs



Rising popularity of biopharmaceuticals (biologics) over traditional chemical products, due to lower risk of side effects and higher approval rates; in 2017, seven of the top ten global best-selling drugs were biopharmaceuticals

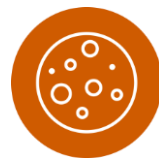


Rising popularity of next generation biotherapeutics and personalized medicines (e.g., cell therapies, gene therapies and regenerative medicines); within 5 years, it is estimated that these substances will represent 20% of the New Active Substances launched globally

Needs – Public health



Neuropsychiatric conditions are ranked as the #1 contributor to economic burden, at more than \$50 billion annually



Cancer is the leading cause of death in Canada; 1 in 2 people will be diagnosed with cancer in their lifetime



Emerging and re-emerging infectious diseases are a leading public health concern worldwide



Antimicrobial resistance is deemed an increasingly serious global public health threat by the World Health Organization

Sources: Internal & external documents, peer review

Way forward

HHT has aligned its new strategy with its strengths in antibodies, bioprocessing, and translational research, but will need to further define the boundaries of certain activities.

A clear vision for the future

Following a review of key documents and presentations by HHT management, the PRC concluded that HHT's strength lies in its core technology platforms: antibody engineering, bioprocess development, and translational research. These three platforms are inter-connected, aligned with the expertise of HHT staff, and provide a strong foundation for its future programs and initiatives.

While the committee felt that HHT's strategic plan is ambitious and would benefit from being defined at a more operational level, they endorsed the Research Centre's areas of focus and its overall technology-driven agenda.

By limiting client projects to those that rely on core competencies and technologies that have already been developed and validated internally and focusing internal projects on technology discovery, innovation, and validation, the PRC agreed that HHT should be able to clearly differentiate itself from both academia (focused on product discovery) and from industry (focused on clinical trials and commercialization).

Considerations

Given the already competitive and crowded nature of the cell and gene therapy domain, the PRC suggested that HHT scope its efforts in this area by focussing only on specific aspects that play to its strengths in antibodies and viral vectors (e.g., CRISPR, a gene-editing technology) rather than attempting to cover a broader spectrum.

The PRC also noted that HHT's efforts in large-scale biomanufacturing may no longer be a logical fit given its defined TRL scope, and that the Research Centre should consider re-allocating its resources in this area to small-scale production and process development, which are more in line with its overall strategy. However, the PRC agrees with HHT management that activities in this area address a critical gap, given that there are very few organizations in Canada with large-scale capabilities. HHT aims to promote the development of these capabilities across the country through its Biomanufacturing initiative, but has yet to see impactful results according to the PRC.

With respect to HHT's efforts in small-scale manufacturing and process development, the PRC stressed the importance of implementing advanced manufacturing technologies for enhanced process control and optimization. While HHT has identified several advanced manufacturing technologies that it intends to incorporate into bioprocessing work, the PRC felt that a clear implementation strategy is needed.

Sources: HHT administrative data, internal & external documents, peer review

CONCLUSION AND RECOMMENDATIONS •
HUMAN HEALTH THERAPEUTICS
RESEARCH CENTRE

Conclusion

HHT was successful in achieving its planned outcomes at a time when industry support was at the center of NRC's research activities. In order to deliver on its new mandate, HHT should focus on its technology strengths and leverage collaboration with OGDs and other stakeholders. Sound planning will be key.

Supporting business innovation

Over the evaluation period, HHT was successful in helping clients de-risk their products and processes and progress through the value chain. Many HHT clients have increased their market valuation, grown and/or improved their capabilities. These impacts were greatest for smaller SMEs, which is important to note given that SMEs were the target clientele of HHT programs.

Project selection throughout the evaluation period did not appear to consider projects' strategic contributions or outcomes. Further, the industry gap filled by HHT in large-scale biomanufacturing is important, but falls outside of the scope of a typical research and technology institution, as noted by the PRC. Given the breadth of activities and research areas covered by the 2019-24 strategic plan, there is an opportunity for HHT to be more selective in its efforts, focussing on projects in priority areas and monitoring changes in the large-scale biomanufacturing ecosystem.

Supporting government policy solutions

HHT's collaboration with OGDs has contributed to important advancements in public health, including the production of investigational antibodies in 2014-15 to accelerate the development of therapeutics against Ebola, an emerging infectious disease.

While HHT's forward strategy and research activities have been aligned with public health priorities, that alignment does not appear to be achieved in a systematic way through discussions and priority-setting exercises with key OGDs, with the exception of vaccine R&D.

Advancing scientific excellence

While research excellence was not identified as a key measure of success during the evaluation period, researchers continued to publish and demonstrated scientific impact in some domains, particularly that of the Blood-Brain Barrier. In addition to holding the largest intellectual property portfolio at the NRC, HHT has also licensed its products and platforms to clients, demonstrating the scientific impact and uptake of its research.

The PRC noted the importance of HHT focussing its efforts on the development of processes and technology platforms, rather than products, to better align with its research scope and maximize uptake.

Moving forward

HHT's forward strategy is aligned with the competencies and capabilities of its staff, considers industry trends, and addresses the most important public health needs, including some research areas where government intervention is essential given the lack of interest from industry (e.g., H1N1 vaccine, antimicrobial resistance). However, the PRC noted that this strategy is very ambitious. While it became clear through discussions with HHT management that the Research Centre plans to focus its efforts in specific areas, this was not well communicated through internal documentation.

There are many challenges that may affect HHT's ability to implement its 2019-24 strategy, including upcoming retirements of key research staff and the lack of investments in facilities. Clear communication and operationalization of HHT's strategic, human resource and investment plans will be key to mitigating these risks.



Recommendations

Recommendation 1

Strategic focus

Clarify the 2019-24 strategic plan and new program offerings by:

- determining the focus of activities (especially within cell and gene therapy, bioprocessing/biomanufacturing, TRL focus)
- clarifying how, and to what extent, each of HHT's research areas, programs, and initiatives will contribute to each strategic outcome, with specific targets identified
- considering the use of advanced manufacturing technologies for process optimization and efficiency
- monitoring changes in the large-scale biomanufacturing landscape in Canada and adjusting efforts in this area accordingly

Rationale: HHT's 2019-24 strategic plan identifies clear areas of focus, but may be too ambitious. HHT knows how and where it has impact. Expectations should be managed by clarifying that with other partners/collaborators. The particular outcomes to be achieved by programming must also be clarified – some areas clearly contribute to business innovation (i.e., biomanufacturing) while others might be best to focus on research excellence (e.g., blood-brain barrier activities) or strictly support government policy solutions (e.g., vaccine activities). Finally, HHT is filling a critical gap in large-scale biomanufacturing; however, close attention must be paid to the landscape should new players emerge, so that HHT can leave this activity area.

Recommendation 2

Impact on government policy solutions

Increase collaboration with OGDs to address public health R&D needs, and ensure that they are well aware of HHT's strategic plan, including capabilities, expertise and facilities.

Rationale: The interdepartmental committee on vaccine R&D has proven to be successful in identifying areas of needs where government has a role to play, and from there important advancements were made. That is not the case for other research areas in the realm of public health where engagement with OGDs does not appear to be consistent. As well, stakeholder engagement efforts to date seemed to have focussed on industry partners and academia – more could be done to ensure that OGDs are well aware of HHT's capabilities and that their needs are addressed.



Recommendations

Recommendation 3

Resource planning

Develop a strategic human resources plan and an up-to-date capital investments plan. With regards to human resources, the plan should outline succession planning, training requirements, and consider workload issues and time for exploratory research.

Rationale: HHT has the critical mass required to carry out its work; however, there are imminent departures due to retirement, which would have an impact on capabilities. There is not currently an up-to-date strategic human resources plan nor is there an up-to-date capital investments plan that identifies how facilities and equipment are aligned with current needs of the sector and the 2019-24 strategic plan.

Recommendation 4

Project selection

Develop a clear project planning process that prioritizes the selection of projects that contribute to the organizational mandate and address government priorities in public health.

Rationale: There was limited strategic linkages between projects selected and their contributions to governmental and organizational priorities and needs. Given the many grounds covered by the 2019-24 strategic plan, there is a need to ensure that projects are aligned to priorities.



Recommendations

Recommendation 5

Research data management

Ensure that Big data from projects, such as bioprocess automation and genomics, is well exploited (well mined) and integrated into project planning and decision-making (e.g., decision points). HHT should seek bioinformatics support from the Digital Technologies Research Centre and system support from Knowledge, Information and Technology Services.

Rationale: HHT's previous attempts to secure the platform required to mine its research data were unsuccessful. HHT's high-quality raw data, noted to be a 'gold mine', could result in gained efficiencies through the integration of data mining and management into the lifecycle of projects, which was absent in the past.

Recommendation 6

Impact on research innovation

Ensure that the blood-brain barrier carrier (FC5) is taken to clinical trials with the right, committed industry client (preferably a Canadian client).

Rationale: The Therapeutics Beyond Brain Barriers program made considerable advancements in the field of central nervous system diseases over the years on both the national and international scene. To ensure that this work continues on and has an impact, it is crucial for HHT to find a committed industry partner to take the FC5 carrier to clinical trials.



Management Response and Action Plan

Recommendation 1		Risk-level associated with not addressing recommendation	
Clarify the 2019-24 strategic plan and new program offerings by: <ul style="list-style-type: none"> determining the focus of activities (especially within cell and gene therapy, bioprocessing/biomanufacturing, TRL focus) clarifying how, and to what extent, each of HHT’s research areas, programs, and initiatives will contribute to each strategic outcome, with specific targets identified 		MEDIUM	
Management response	Measure of achievements	Proposed person(s) responsible	Expected date of completion
Recommendation accepted. Action 1 HHT will prioritize projects under each of its three mandates (science excellence, public good and business innovation) and assign, monitor and rebalance as needed dedicated resources in achievement of its strategic goal. <ol style="list-style-type: none"> HHT Research framework will map the primary focus of its programs and initiatives to one of the three strategic goals, and TRL level targeted. HHT’s key performance indicators will be further developed to align with program and organizational goals Project prioritization is implemented and decision making includes tracking and deployment of resources to priority objectives as needed. 	<ol style="list-style-type: none"> Updated research framework is implemented Yearly achievement of both leading and lagging indicators Resource deployment in alignment with strategic goals 	Director Operations	Action 1a & b June 2021 Action 1c June 2021



Management Response and Action Plan

Recommendation 1 (Contd)		Risk-level associated with not addressing recommendation	
Clarify the 2019-24 strategic plan and new program offerings by: <ul style="list-style-type: none"> considering the use of advanced manufacturing technologies for process optimization and efficiency monitoring changes in the large-scale biomanufacturing landscape in Canada and adjusting efforts in this area accordingly 		MEDIUM	
Management response	Measure of achievements	Proposed person(s) responsible	Expected date of completion
Action 2 HHT will do a strategic review of the scope of its bioprocessing/biomanufacturing activities with respect to process innovation, industry support, and capacity building in support of government priorities such as response to a public emergency. <ol style="list-style-type: none"> Advanced biomanufacturing will be addressed through HHT's Biomanufacturing Initiative which will launch specific projects (e.g., digital twinning) in collaboration with the Digital Technology Research Centre. HHT will leverage a feasibility study to determine the investment needed to align with strategic needs in bioprocessing support versus biomanufacturing to address government needs. HHT will rebalance its bioprocessing/biomanufacturing research focus in agreement with the conclusion of the reviews. 	<ol style="list-style-type: none"> Implementation of projects addressing advanced Biomanufacturing Feasibility study completed Strategic review of the bioprocessing versus biomanufacturing project scope completed & Rebalancing plan implemented 	Director R&D (Bioprocessing engineering)	Action 2a, b September 2022 Action 2c March 2023



Management Response and Action Plan

Recommendation 2		Risk-level associated with not addressing recommendation	
Increase collaboration with OGDs to address public health R&D needs, and ensure that they are well aware of HHT's strategic plan, including capabilities, expertise and facilities.		MEDIUM	
Management response	Measure of achievements	Proposed person(s) responsible	Expected date of completion
<p>Recommendation accepted.</p> <p>Action 1</p> <p>HHT will foster linkages with OGD partners by identifying key areas for collaboration. A shift towards increased OGD collaboration may result in an overall decrease in revenue for HHT (decrease in industrial research service).</p> <p>a. Workshops conducted with OGDS to encourage collaborations.</p> <p>b. Leadership in the VRID (Vaccine Research Innovation Development) committee resulting in responsiveness of HHT to public health & policy solutions</p> <p>c. HHT contributes to OGD priorities and R&D needs in public health; e.g. emerging diseases, rare diseases, dementia.</p>	<p>a. HHT has hosted scientific workshops with OGDs that have a public health mandate (e.g. Health Canada, PHAC, CFIA) & Increased number of interdepartmental agreements (ILAs)</p> <p>b. HHT is invited by OGDs to various action plan/consultation working groups (e.g., AMR, COVID-19)</p> <p>c. HHT is invited to contribute its expertise by participating to projects for emerging public health needs</p>	<p>Director General</p> <p>With</p> <p>Directors (R&D)</p>	<p>Action 1a</p> <p>September 2021</p> <p>Action 1b & c</p> <p>March 2022</p>



Management Response and Action Plan

Recommendation 3		Risk-level associated with not addressing recommendation	
Develop a strategic human resources plan and an up-to-date capital investments plan. With regards to human resources, the plan should outline succession planning, training requirements, and consider workload issues and time for exploratory research.		MEDIUM	
Management response	Measure of achievements	Proposed person(s) responsible	Expected date of completion
<p>Recommendation accepted.</p> <p>Action 1 Completion of the capacity management initiative and launch of an action plan to address workload issues and balanced deployment of resources to priority areas.</p> <p>Action 2 Along with the completion of its programs and initiatives plans, HHT will update a mapping of its long term HR and capital needs.</p> <p>a. HHT will develop an HR plan for succession; addressing mentoring, training and recruitment.</p> <p>b. HHT will develop a long term capital investment plan that will take into account the 3 year facility reviews and Laboratory Canada clusters developments.</p>	<p>1. Capacity action plan launched & used for resource prioritization.</p> <p>2a. Targeted recruitment, and training alleviates workload issues and results in increased staff engagement evident through the public service employment survey</p> <p>2b. HHT's annual capital procurement is aligned with its long term capital investment plan</p>	<p>Director General with Directors R&D and Director OPS</p>	<p>Action 1 June 2021</p> <p>Action 2a March 2022</p> <p>Action 2b March 2023</p>



Management Response and Action Plan

Recommendation 4		Risk-level associated with not addressing recommendation	
Develop a clear project planning process that prioritizes the selection of projects that contribute to the organizational mandate and address government priorities in public health.		LOW	
Management response	Measure of achievements	Proposed person(s) responsible	Expected date of completion
<p>Recommendation accepted.</p> <p>Action 1</p> <p>HHT will define and implement project selection criteria based on its 5 year strategic goals and current public health priorities.</p> <p>a. Building on its newly developed research framework and leveraging its internal scientific expert panel (DG Research Excellence Advisory Committee), HHT will further refine its governance structure and decision-making process to fully integrate/align project prioritisation at the Program/RI and RC level</p> <p>b. Through the successful implementation of actions proposed in Recommendation 2, HHT will ensure that public health priorities are given proper weight in project selection criteria and ranking.</p>	<p>a. Project selection method determined and criterion defined; Project Evaluation (Ranking) Template created; Governance process for project evaluation/prioritisation established and implemented; Roles & Responsibilities (Terms of Reference) for Program/RI and HHT management governing bodies defined;</p> <p>b. Projects addressing public health priorities are launched and prioritized.</p>	<p>Director General with Director Operations</p>	<p>Action 1a March 2021</p> <p>Action 1b March 2022</p>



Management Response and Action Plan

Recommendation 5		Risk-level associated with not addressing recommendation	
Ensure that Big data from projects, such as bioprocess automation and genomics, is well exploited (well mined) and integrated into project planning and decision-making (e.g., decision points). HHT should seek bioinformatics support from the Digital Technologies Research Centre and system support from Knowledge, Information & Technology Services.		LOW	
Management response	Measure of achievements	Proposed person(s) responsible	Expected date of completion
<p>Recommendation accepted.</p> <p>Action 1</p> <p>HHT will formulate its Data Strategy under the larger umbrella of NRC Data Strategy and implement AI assisted data mining.</p> <p>a. HHT Data Strategy applied for managing centralized data repositories in collaboration with the Digital Technologies Research Centre and Knowledge, Information & Technology Services.</p> <p>b. HHT's Programs (CGT and MAb-T) will deploy AI-assisted data mining and modeling in support of their R&D strategies for target selection, digital twinning and bioamufacturing process development.</p>	<p>a. Data centralized and curated (e.g., HHT CARTA cloud based searchable repository available)</p> <p>b. Knowledge/intelligence mined from data (R&D disclosures) & Knowledge modeled and designed through AI (R&D disclosures)</p>	<p>Action 1a: Directors R&D Translational Bioscience & Bioprocessing Engineering</p> <p>Action 1b: Program Directors CGT Challenge & MAb-T Program</p>	March 2022



Management Response and Action Plan

Recommendation 6		Risk-level associated with not addressing recommendation	
Ensure that the blood-brain barrier carrier (FC5) is taken to clinical trials with the right, committed industry client (preferably a Canadian client).		MEDIUM	
Management response	Measure of achievements	Proposed person(s) responsible	Expected date of completion
<p>Recommendation accepted.</p> <p>Action 1</p> <p>NRC BBB carriers are being partnered with multiple Canadian Biopharma and are evaluated in diverse products (different cargos) on fast-track to clinical evaluation.</p> <p>a. Co-development projects of BBB-Carriers are prioritised and resourced adequately in the MAb-T Program</p> <p>b. HHT provides continued support to partners to accelerate preclinical development and achieve clinical trial application (CTA) and clinical trial initiation in 2021 (e.g. IRAP certificate program; support in fund raising; chemistry, manufacturing, and control (CMC) technology transfers to CROs/CMOs)</p> <p>c. Risk of failure of a single therapeutic is mitigated by developing collaborations with HHT BBB carriers from the second and third generation and with other cargos (e.g., targeting radio-immunotherapeutics)</p>	<p>a. Resource deployment matches planned priorities</p> <p>b. FC5 enters clinical trials</p> <p>c. Additional licensing agreement for HHT BBB carriers with Canadian Biopharma</p>	<p>Director R&D</p> <p>Translational Bioscience</p>	<p>June 2022</p>



APPENDICES • HUMAN HEALTH THERAPEUTICS RESEARCH CENTRE

Appendix A – Methodology

Document / literature review

Internal and external documents, such as business and operational plans, the research centre's strategic plan, presentations, progress reports, industry studies, and documents relating to government priorities, were reviewed to provide context and to complement other lines of evidence in assessing relevance and performance. Of note, the client surveys commissioned by HHT in 2015 and 2017 served as a key source of information as it provided information about satisfaction, outcomes, and client impacts.

Data review

Research Centre and Program administrative and performance data for 2014-15 to 2018-19 were reviewed to provide information on program inputs (e.g., resources), outputs, client reach, capacity and capabilities. This included data on finances, human resource, projects and intellectual property. Data on finances, human resources and intellectual property were provided by NRC corporate branches.

Bibliometric study

NRC's Library and Information Management Services conducted a bibliometric assessment of HHT's peer-reviewed publications indexed in Scopus for the period 2014-2019. This analysis was used to assess scientific excellence and impact (both within academia and beyond academia).

Interviews

Interviews were conducted with a total of 28 stakeholders. This included 14 Research Centre management and senior staff and 14 clients/collaborators. Data collected through the interviews were analyzed by question and by theme, allowing common themes as well as nuances between responses to be identified.

Peer review

A peer review committee was convened to assess the Research Centre's stakeholder engagement, performance, scientific excellence, capabilities and future plans. The committee was composed of five members with expertise in each of HHT's key research areas. Members included international representatives from academia, research organizations and industry. Members were expected to participate in the review process in an objective, unbiased and credible manner, with no apparent or perceived conflict of interest. All members signed a conflict of interest agreement.

The process included:

1. Reviewing background material produced by the research centre and by the NRC evaluation team.
2. Participating in a pre-site visit teleconference to discuss the committee's initial assessment of the research centre, information gaps and questions.
3. Participating in a two day site visit to the NRC.
4. Writing a peer review report.

Appendix A – Methodology

Limitations and mitigation strategies

Availability of data and documents

The evaluation did not carry out a survey of clients given that HHT clients were recently surveyed by an external firm in 2015 and 2017 in addition to having potentially been surveyed through NRC's annual satisfaction survey. In lieu of a survey, 14 targeted client interviews were conducted to provide further information and context. The sample selected included clients who have worked with HHT on multiple projects, and clients from each of HHT's programs.

Valid and reliable data on facility use was not available. As such, the evaluation was not able to assess facility use.

Use of publications to measure excellence

The challenge with bibliometric analysis is that there is a time lag of citation of published work. As a result, the actual use of more recent publications is likely underestimated in the current study. Additionally, the list of HHT publications by research area is not necessarily representative of all research area publication outputs, given that it was based on a keyword search only. NRC-Evaluation was carrying out a more in-depth exercise as part of an internal review; however, those results were not available at the time of writing this evaluation report.

To mitigate these limitations, other lines of evidence were used to assess the excellence and scientific impact of HHT, including the use of an expert peer review.

Comparative review

The evaluation did not gather information on other similar organizations to provide a comparative analysis. Instead, where applicable, other comparators were included. For instance, the bibliometric assessment included comparisons with NRC overall and other international organizations in the field. Some administrative and performance data compared HHT results to other NRC research centres.

Appendix A – Methodology

Limitations and mitigation strategies (continued)

Challenges associated with peer review committee

In order to provide an objective, independent assessment of the Research Centre, arms-length experts were sought to participate in the peer review process. Given the need to be independent and objective, experts selected for peer review committees may not have in-depth knowledge of the research centre and its activities, or the NRC. Additionally, each member comes to the peer review exercise with their own experience, expertise and associated biases.

In order to ensure the needed expertise on the committee, and to select the best possible committee composition, the project team consulted with HHT's senior management and with the Knowledge, Information and Technology Services branch to identify and invite the peer review chair and members. All peer review committee members were vetted and approved by the Research Centre VP and DG.

To mitigate any bias throughout the peer review process, the evaluation team tries to ensure the inclusion of experts from various areas of expertise, including different genders, geographic locations, and representatives from various types of organizations (industry, academia and other governmental organizations). In addition, at least one Canadian representative is sought in order to bring an understanding of the Canadian context. In the case of the HHT peer review however, while some members had an understanding of the Canadian context from previous interactions and/or tenures with Canadian organizations, no Canadian representative was available to participate.



Appendix A – Methodology

Peer review committee members

A peer review committee was convened in Montreal from November 3-5, 2019, to assess the relevance and performance of the Research Centre. The PRC was composed of five international experts with a range of expertise.



Dr. Nathalie Garçon
Chair

Chief Executive Officer
and Chief Scientific
Officer,
BIOASTER

Vaccine and
Immunotherapy Expert



Dr. Mario Feldman

Associate Professor in
Molecular Microbiology,
Washington University

Glycobiology Expert



Dr. Per-Ola Freskgård

Vice Director and
Distinguished Scientist in
Neurovascular Biology,
Roche

Blood-Brain Barrier
Expert



Dr. Danuta Herzyk

Distinguished Scientist,
Merck & Co.

Pre-Clinical Evaluation
of Biologics Expert



Dr. Eli Keshavarz-Moore

Professor of Bioprocess
Science and Enterprise,
**University College
London**

Bioprocessing Expert



Appendix B – Case study in Gender-Based Analysis (GBA+)



What is GBA+?

The Department for Women and Gender Equality define GBA+ as an analytical process used to assess how diverse groups of women, men and non-binary people may experience policies, programs and initiatives. The “plus” in GBA+ acknowledges that GBA goes beyond biological (sex) and socio-cultural (gender) differences, and considers many other identity factors (e.g., race, ethnicity, geography).

How were HHT’s GBA+ contributions assessed?

The evaluation piloted the *GBA+ Lens for Evaluation*, initially developed by the Public Health Agency Canada and Health Canada, to guide the assessment. NRC’s Hia vaccine was identified as a good project for a case study on GBA+ given that it is an ongoing project and is linked to current Government of Canada priorities.

Evidence informing this case study was collected through a review of project documents and interviews with two researchers from NRC and two researchers from the Public Health Agency of Canada.

What is Hia, and how does it relate to GBA+?

Haemophilus influenzae type A (Hia) is a bacterial disease that primarily impacts northern Indigenous communities, with increased incidence in young children. Hia is known to cause severe illness such as meningitis, and has a fatality rate of approximately 9%. Interviewees noted that, even when patients survive, there are often severe consequences, in addition to the impact on the children and their families, such as hearing loss, paralysis, developmental challenges and limb amputation. It was also noted in interviews that these consequences are expensive for the health care system in the long term. In particular, it is very costly to get every child who contracts invasive Hia disease out of their community and into treatment because they must be evacuated by helicopter (due to their remote location and how quickly Hia progresses and increases in severity). At a cost of \$55,000 per evacuation, the total transportation costs related to Hia quickly reach \$330,000 per year simply to start treatment for the average of six cases per year in Nunavut.

According to the Public Health Agency of Canada, the national incidence rate for invasive Hia has risen to more than 300 cases per year, and internal documents suggest that these rates may in fact be underreported. Hia has been identified as a critical public health issue, but its relatively low incidence rates and concentration within minority population groups makes a vaccine unlikely to become commercially lucrative and, therefore, unattractive to private industry. It is for these reasons that government intervention was deemed necessary.

Sources: Internal documents, interviews



Appendix B – Case study in Gender-Based Analysis (GBA+)



How were GBA+ considerations addressed by this project?

Northern Indigenous communities are facing a number of important issues. By listening to these groups, and building relationships in the communities, it was discovered that other medical issues like tuberculosis and addiction are of high priority, and social issues such as housing and clean water are of greater concern than Hia. Interview respondents noted that their approach is to listen to what the needs of these communities, and to propose how the Hia vaccine can be part of the solution. For example, one respondent who often works in these communities heard from residents that their concern was that their sick children needed to be sent to Winnipeg for care. While not resolving the issue in its entirety, the Hia vaccine would help decrease cases of diseases that require displacement for treatment. One interviewee noted that while being sensitive to the larger issues at play, researchers have a responsibility to tell communities that a vaccine may be available, and how it could help them. The challenge is to present it as a solution that addresses the needs and concerns of individual communities.

Early in the development process, collaborators met with groups representing First Nations, Inuit and Metis to initiate dialogue about Hia and to understand the needs of communities. Several workshops were held with these groups and other partners to discuss engagement with communities, and an engagement plan was developed. While the national groups agreed on the importance of a vaccine, they admitted not having the pulse of individual communities - they stressed the importance of engaging with the different communities, to listen to their needs and concerns, and to propose how a vaccine can help. It was found that the current strategy is to seek out people, such as Indigenous doctors, who can champion the vaccine in their communities. Although this is a lengthy process, it is necessary time to appropriately engage and listen to communities.

To what extent have HHT's contributions made a difference?

In partnership with the Public Health Agency of Canada's National Microbiology Laboratory, HHT has been successful in producing a pre-clinical proof of concept that has been licensed to InventVacc Biologicals Inc. – a facility that complies with Good Manufacturing Practices.

While InventVacc has demonstrated initial success in optimizing conjugation methodologies using antigens also provided by HHT, internal documents suggest that any next steps in vaccine development will be dependent on the partners' ability to secure funding. One interviewee noted that InventVacc can only progress the vaccine so far because they do not have the funds to invest in a clinical trial. Interviewees also suggested that a federal policy gap may exist, given that no federal agency has a mandate to fund these types of activities beyond de-risking the development of vaccines.

HHT and its partners are currently exploring various possibilities to fund the next phases of the vaccine's development. Once Good Laboratory Practice toxicology is completed, it is expected that the vaccine could be made available for clinical trials in other regions of Canada and abroad.

Sources: Internal documents, interviews



Appendix C – Program profile

Biologics and Biomanufacturing

Description: development of biotherapeutics against cancer, infectious diseases, as well as inflammatory and auto-immune diseases.

Areas of expertise:

- Candidate design, selection and optimization
- Bioprocess development
- Preclinical development

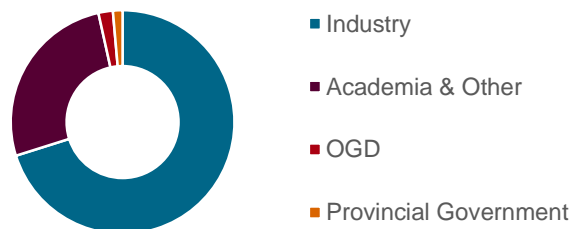
Two business/project streams:

- Biologics co-development
- Industrial solutions for a broad (local and international) clientele

Projects started or completed: 475

- Strategic R&D: 48%
- Technical services: 52%

Program clients (n=144)



Vaccines and Immunotherapeutics

Description: development of prophylactic and therapeutic vaccines against cancer and emerging infections.

Areas of expertise:

- Vaccine formulation and immunomodulation
- Biomanufacturing
- Biophysical characterization

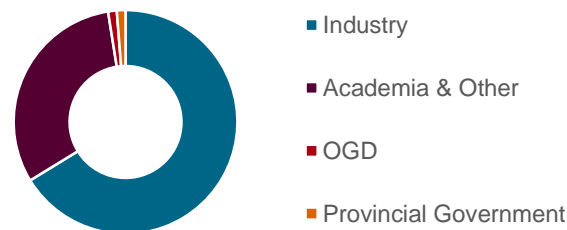
Three business/project streams:

- Vaccine and immunotherapeutic candidate co-development
- Provision of industrial solutions through R&D agreements and licenses
- Targeted projects in key disease areas

Projects started or completed: 150

- Strategic R&D: 65%
- Technical services: 35%

Program clients (n=80)



Therapeutics Beyond Brain Barriers

Description: development of biotherapeutics against central nervous system diseases.

Areas of expertise:

- Blood brain barrier (BBB) carriers
- Coupling therapeutics with BBB carriers
- Evaluating BBB-enabled therapeutics

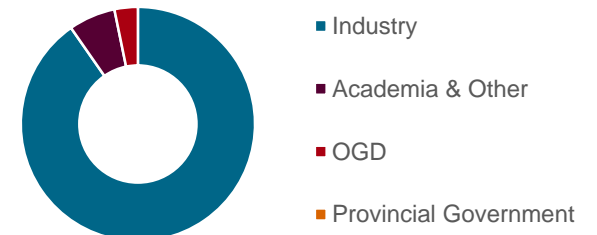
Three business/project streams:

- Product co-development: coupling products with NRC blood brain barrier carriers
- Industrial solutions to overcome technological roadblocks
- Incremental services: evaluating clients' candidates in BBB and central nervous system models

Projects started or completed: 475

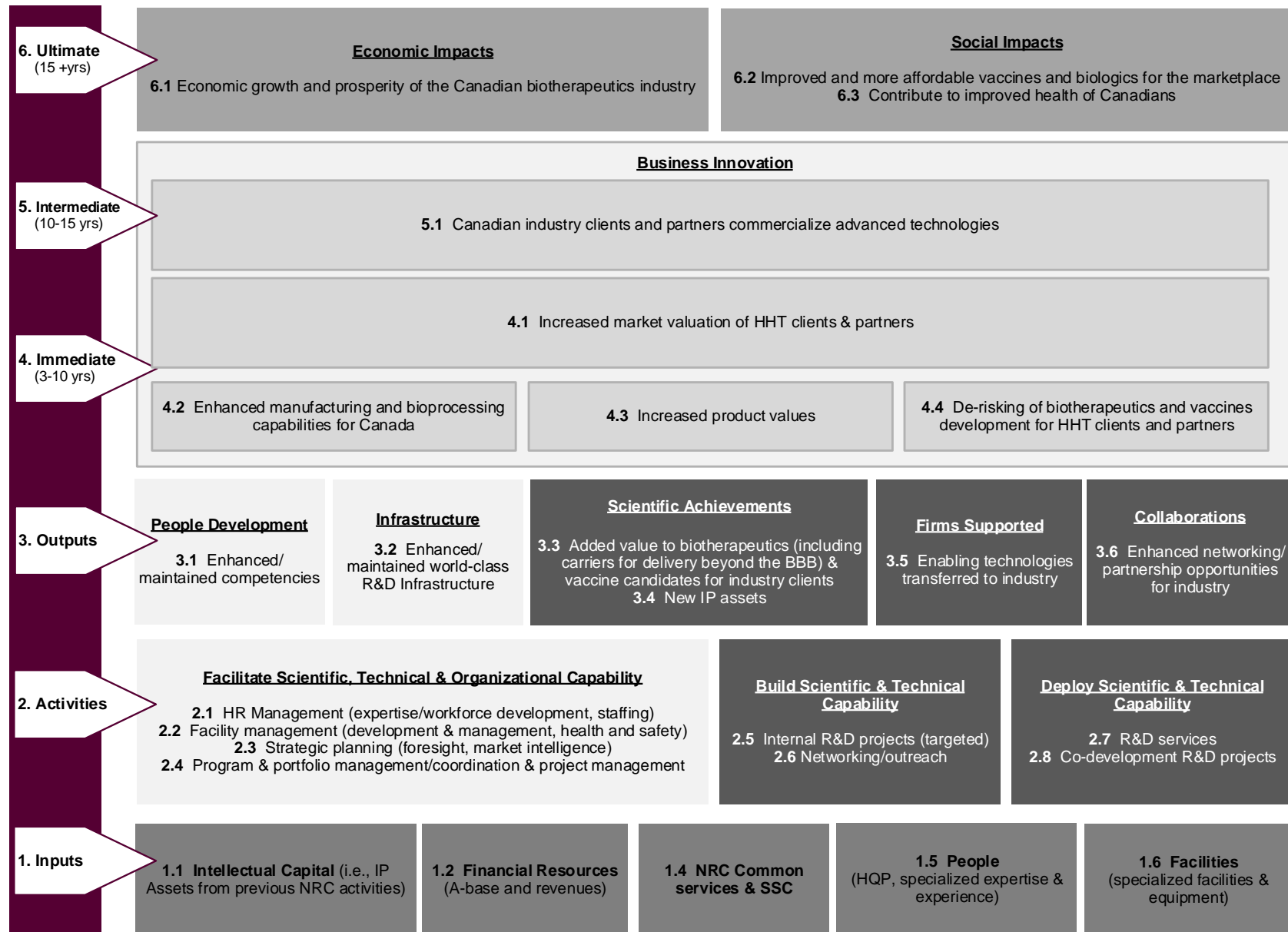
- Strategic R&D: 76%
- Technical services: 24%

Program clients (n=31)



Source: Internal documents, HHT administrative data

Appendix D – DRAFT HHT Logic model (2017)



Legend (activities and outputs): Portfolio-level Program-level