

Perspectives on Natural Health Products

Population Groups and Issue Areas

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Natural Health Products Directorate
Health Canada

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Preface

Health Canada is committed to ensuring that Canadians have access to natural health products (NHPs) that are safe, effective and of high quality, while respecting freedom of choice and philosophical and cultural diversity. In developing an appropriate regulatory framework for NHPs, the NHPD has maintained an open and transparent process of on-going dialogue and consultation with stakeholders across Canada. The reports that have been created as a result of this consultation process are available in four publications. These documents outline key areas under consideration and also provide information regarding some of the initiatives that are already underway to gather better information about NHPs, to improve professional education and training in this area, to provide reliable and accessible information to people who use NHPs, and to establish the value of these products within the health system. The reports are grouped under four central themes:

- Quality and Safety
- Research
- **Population Groups and Issue Areas**
- Information, Informed Choice and Utilization

During the consultation process, a population health approach was included to identify the unique needs of certain populations and the ways that they intersect with NHP research. *Developing a Research Agenda in Natural Health Products and Complementary and Alternative Health Care in HIV/AIDS: A Discussion Paper*, summarizes key issues concerning the use of NHPs and complementary and alternative health care and the development of research with regard to individuals with HIV/AIDS. A further examination is provided in *The Role of Natural Health Products and Complementary and Alternative Health Care in HIV/AIDS - Developing a Research Agenda: An Invitational Roundtable*. A consideration of the NHP research relative to children and youth is presented in *Natural Health Products Research in Children and Youth: A Priority-Setting Conference*.

The Role of Natural Health Products and Complementary and Alternative Health Care in HIV/AIDS – Developing a Research Agenda: An Invitational Roundtable

*Theodore de Bruyn
Vancouver, March 10-11, 2002*

The views expressed in this document are those of the roundtable participants and do not necessarily represent those of Health Canada.

Executive Summary

A roundtable on developing a research agenda on the role of natural health products (NHPs) and complementary and alternative health care (CAHC) in HIV/AIDS was convened by the Natural Health Products Directorate (NHPD), in collaboration with the Health Human Resource Strategies Division and the HIV/AIDS Policy, Coordination and Programs Division of Health Canada. This roundtable was one of several meetings on research priorities being held with populations known to use CAHC and NHPs.

Objectives

The objectives of the roundtable were as follows:

- to assist in the further development of a research agenda in the area of NHPs, CAHC and HIV/AIDS
- to build capacity to conduct research in Canada in NHPs and CAHC, with

HIV/AIDS serving as an area with readiness to explore ways to accomplish this

- to contribute to the NHPD's process of identifying and advancing research priorities in NHPs and CAHC within the national arena

Process

The roundtable focused on six aspects of research on CAHC and NHPs:

1. NHP research
2. health practices/services research
3. building research capacity
4. methodological development
5. research dissemination and uptake
6. building and strengthening liaisons

In light of potential synergies between the HIV/AIDS field and the broader field of CAHC and NHPs, the instructions to the participants were, for each of the above six areas:

- to identify priorities or opportunities for research or research-related activities

- to select the top three priorities or opportunities
- to identify strategies to advance the top three priorities or opportunities

An Overarching Principle

Participants agreed that consumers need to be involved at all stages of the research process (the design and implementation of the project, and the analysis and dissemination of the results) and in each of the priorities identified below. This overarching principle of access to, and ownership and control of, the research process – which is central to research involving Aboriginal peoples, traditional Aboriginal healers and Aboriginal healing practices – has been endorsed in general by people with HIV/AIDS.

Priorities

Participants identified the following priorities in each of the areas under discussion.

Natural health products research

Priority #1: research on beneficial and detrimental interactions: interactions among NHPs (NHP-NHP interactions) and interactions between NHPs and drugs used by people with HIV/AIDS (NHP-drug interactions)

Priority #2: focus on NHPs used in treatment and support of HIV/AIDS-related conditions (side effects, toxicities, opportunistic infections, etc.)

Priority #3: prioritize the NHPs to be researched first

Health practices/services research

Participants identified an overarching theme for research in this area: research to advance integration across the continuum of health care practices and services, with a special focus on

CAHC and NHPs. Participants also identified guiding principles for the research and possible research projects.

Priority #1: *funding and capacity building of integrative research teams working on CAHC and NHPs with a focus on HIV/AIDS*

Building research capacity

Priority #1:

- a) training in conducting research and using research findings for CAHC practitioners, educators, students and community members
- b) funding for CAHC practitioners to write up case reports
- c) a focus on Aboriginal access to, and ownership and control of, the research process

Priority #2: leveling the playing field to gain equal access to research funds

Priority #3: funding for training awards, research projects and research infrastructure in CAHC and NHP research

Methodological development

Priority #1: establish standards of evidence and research

Priority #2: education and training in standards of evidence and research for CAHC practitioners and educators, and for conventional practitioners and researchers

Priority #3: foster research skills in CAHC and NHPs among practitioners and researchers

Priority #4: educate funding review panels and research ethics boards about CAHC and NHP research, methods and standards of evidence

Research dissemination and uptake

Priority #1: reviews of research on CAHC and NHPs

Priority #2: assessment of information needs of target audiences

Priority #3: dissemination and uptake strategies

Building and strengthening liaisons

Participants identified the sectors in which awareness of and involvement in CAHC and NHP research need to be strengthened – researchers, funders, community organizations, hospitals and clinics, practitioners, professional associations, educational institutions, information providers and the media – and discussed ways to do this.

Priority #1: time, resources and institutional support to work specifically on building partnerships and promoting research on integrative health care

Final Recommendation

To develop research on CAHC and NHPs in the field of HIV/AIDS, it is necessary to have the time and resources to build partnerships, to explore opportunities and to increase the profile of CAHC and NHPs in existing HIV/AIDS networks and programs.

There was overwhelming consensus that funding for a dedicated staff person is necessary to undertake activities to build research on CAHC and NHPs in the field of HIV/AIDS. The following activities were identified but were not prioritized:

- Build on existing HIV/AIDS observational databases (British Columbia Centre for Excellence in HIV/AIDS, the HIV Information

Infrastructure Project) to gather information about the use of CAHC and NHPs among people with HIV/AIDS in relation to conventional health care and treatments.

- Identify and build relations with partners in research on CAHC and NHPs (funders, industry, HIV/AIDS researchers and practitioners).
- Increase the awareness in the HIV/AIDS field of research on CAHC and NHPs at the annual conferences of the Canadian Association of HIV Research and at the XVI International AIDS Conference to be held in Toronto in 2006.
- Disseminate information through existing HIV/AIDS networks about research opportunities and share information about research initiatives in CAHC and NHPs.
- Liaise with broader networks and evolving initiatives in CAHC and NHPs.
- Facilitate the development of research on Aboriginal healing practices in relation to HIV/AIDS.

Introduction

As part of its mandate to facilitate research in natural health products (NHPs) and related areas, the Natural Health Products Directorate (NHPD), Health Canada, has held meetings on research priorities with regard to specific populations with a demonstrated use of NHPs. One of these populations is people with HIV/AIDS. People with HIV/AIDS have used complementary and alternative health care (CAHC) and NHPs since the earliest days of the epidemic. The prevalence and characteristics of this use have been described in studies in British Columbia, Ontario and other parts of Canada. The implications for policy and programs have been considered in a number of reports published under the auspices of the Canadian Strategy on HIV/AIDS. These reports have noted the need for further research on numerous

aspects of the use of CAHC and NHPs by people with HIV/AIDS.

The Invitational Roundtable on the Role of Natural Health Products and Complementary and Alternative Health Care in HIV/AIDS was convened by the NHPD, in collaboration with two other divisions in the department: the Health Human Resource Strategies Division and the HIV/AIDS Policy, Coordination and Programs Division. While the role and responsibilities of the NHPD relate particularly to NHPs, the Health Human Resource Strategies Division is active in the broader field of CAHC, and the HIV/AIDS Policy, Coordination and Programs Division has responsibility for the planning and the programs of the Canadian Strategy on HIV/AIDS.

Objectives

The objectives of the roundtable were as follows:

- To assist in the further development of a research agenda in the area of NHPs, CAHC and HIV/AIDS first established in the document, “Toward Integrative Care – Final Report from a National Strategic Planning Meeting on Complementary Therapies and HIV/AIDS.” This report, along with others referred to above (note 4), have set out the main lines of a research agenda in NHPs, CAHC and HIV/AIDS. The purpose of the roundtable was to further develop this agenda by suggesting specific steps.
- *To build capacity to conduct research in Canada in NHPs and CAHC with HIV/AIDS serving as an area with readiness to explore ways to accomplish this.* There is widespread recognition of the need to build research capacity – to increase the ability and readiness of individuals and organizations to identify, develop and conduct research – in NHPs and CAHC in Canada. Specific steps are

now needed in order to do this in areas where there is sufficient readiness. HIV/AIDS may be one such area.

- *To contribute to the NHPD’s process of identifying and advancing research priorities in NHPs and CAHC within the national arena.* The NHPD is seeking to identify and advance research priorities both through its own funds (intended primarily for developmental purposes) and in collaboration with other funders (such as Canadian Institutes of Health Research, the Hospital for Sick Children Foundation and other funders).

Process

The roundtable began with an overview of the roles and recent activities of the NHPD, the Health Human Resource Strategies Division and the HIV/AIDS Policy, Coordination and Programs Division with regard to CAHC and NHPs. This was followed by an overview of the process for the roundtable, including the proposed topics for the small group sessions:

- NHP research
- health practices/services research
- building research capacity
- methodological development
- research dissemination and uptake
- building and strengthening liaisons

In light of potential synergies between the HIV/AIDS field and the broader field of CAHC and NHPs, the objectives for the small group sessions were:

- to identify priorities or opportunities for research or research-related activities
- to select the top three priorities or opportunities

- to identify strategies to advance the top three priorities or opportunities

Prior to each small group session, a draft synopsis of the topics under discussion was reviewed and revised in plenary. (The synopsis is included under each topic below.) The small groups then discussed the topics – two concurrently in each session – and reported back to plenary. In plenary there was further opportunity to refine the reports and recommendations of the small groups.

All the reports and recommendations of the small groups were reviewed in the last plenary session of the roundtable and a specific recommendation was made regarding next steps.

Natural Health Products Research

Synopsis of the topic

Consultations in Canada about research on NHPs have identified a number of recurring priorities. These have included:

- the review and evaluation of existing research
- product standards and quality control methodologies
- the methods to characterize NHPs
- the safety, efficacy, risks, dosage, indications and counter-indications of NHPs
- the pharmacological action of NHPs related to benefits, harms and interactions
- NHP-drug interactions
- the utilization of NHPs, especially widely-used NHPs or NHPs used extensively by specific populations

- the role of NHPs in managing HIV/AIDS and/or HIV antiretroviral therapy
- the role of NHPs in managing hepatitis C

In reviewing these priorities, participants noted, in addition, the importance of:

- investigating beneficial synergies between NHPs and drugs, as well as adverse interactions between NHPs and drugs
- investigating interactions between NHPs and other CAHC practices
- the role of NHPs in managing co-infection with HIV and hepatitis C, which presents unique challenges
- the unexplored field of psycho-neural immunology, which investigates, e.g., how the placebo effect works to improve health or how people's sense of locus of control contributes to the healing process
- the broader context of people's use of NHPs and their concerns within that context, e.g., concerns about effects of conventional drugs, about losing access to NHPs once they are regulated, etc.
- the challenges in communicating research findings about NHPs, particularly preliminary results that can easily be misrepresented and misapplied

Areas for research

The group identified and discussed the following areas that need research (in no particular order of importance):

1. *NHPs used in the treatment and support of HIV-related conditions*

- bone loss
- liver disease
- hepatitis B and C co-infection
- cardiovascular risks (e.g., mitochondrial toxicity)
- lipodystrophy and lipoatrophy
- metabolic disorders (e.g., insulin resistance)
- wasting
- neurological disorders (e.g., peripheral neuropathy)
- depression
- sexual health
- addiction
- immune-based therapies
- hormone dysregulation

2. *Specific priorities in regard to products used by people with HIV/AIDS*

- patterns of use
- cultural context of use
- dietary protocols and basic nutrients
- immunological support: SPV30, immune-based therapies
- l-carnatine: oral versus intravenous, required dosage for different forms
- milk thistle

3. *Research into different formulations, concentrations and routes of administration*

- different formulations have different effects
- different concentrations have different pharmacological properties and different pharmacological effects

4. *Side effects and toxicities*

- use of NHPs in managing side effects and toxicities of antiretroviral therapies
- safety and efficacy of NHPs used to manage side effects and toxicities (both in clinical trials and in the community)

5. *Beneficial and detrimental interactions*

- interactions between NHPs and antiretroviral therapies
- interactions between NHPs and other drugs commonly used in treating HIV/AIDS
- interactions among NHPs

6. *Quality assurance*

- botanical identity of products screening of biological markers
- efficacy of formulas
- quality of NHPs used in clinical trials
- quality control of products sold: Does the product match its description?
- issues related to active ingredients

7. *Screening new antiretroviral drugs*

- include NHPs in pharmacokinetic and pharmacodynamic studies of new antiretroviral drugs

Report to plenary

Priority #1: Research on beneficial and detrimental interactions: interactions among NHPs (NHP-NHP interactions) and interactions between NHPs and drugs used by people with HIV/AIDS (NHP-drug interactions)

Strategies:

- Encourage industry, by identifying champions, to include NHPs when conducting *in vitro* and *in vivo* pharmacokinetic and pharmacodynamic studies.
- Encourage investigators to do pharmacokinetic and pharmacodynamic studies *before* undertaking a clinical trial of an investigational drug.
- Encourage manufacturers of NHPs to identify the metabolic pathways of their products.
- Fund small laboratories to conduct research on interactions by building partnerships in many arenas:
 - domestic and international partnerships
 - partnerships with industry, Canadian Institutes of Health Research, the Natural Sciences and Engineering Research Council of Canada, the Canadian HIV Trials Network, the Canadian Foundation for AIDS Research, health insurance companies
 - partnerships between small laboratories with expertise and structures in place
- Explore, with the Canadian HIV Trials Network, the possibility of pharmaceutical manufacturers adding an

additional arm involving NHPs to their clinical trials of antiretroviral drugs.

- Identify opportunities to incorporate priorities on research on NHPs into the agendas of the Institutes of Canadian Institutes for Health Research.
- Develop and disseminate (particularly to funding agencies) a ‘gold standard’ protocol to be used in research on interactions:
 - Product investigation
 - authenticate the product
 - identify the geographic source of the plant form of the product, if possible
 - identify the formulation(s) most relevant to the user population
 - biomarker concentration or peak profile
 - single or repeated use
 - *In vitro* studies
 - Phase I studies to identify iso enzymes most associated with drug regimen (e.g., cytochrome P450)
 - Phase III studies to identify transport proteins (e.g., ABCB1 or P-glycoprotein)
 - Clinical studies
 - Phase I studies to identify iso enzymes most associated with drug regimen (e.g., cytochrome P450)
 - Phase III studies to identify transport proteins (e.g., ABCB1 or P-glycoprotein)
 - Therapeutic Drug Monitoring to determine drug (and possibly biomarkers) plasma level
- Create a safety board for NHPs to confirm the safety of a product and to review adverse events:
 - base the review procedures on the above ‘gold standard’ protocol
 - seek information on the drug and/or product plasma levels
- Develop a database of NHP interactions.

- Establish a Centre of Excellence in research on NHPs.

Priority #2: Focus on NHPs used in treatment and support of HIV/AIDS-related conditions (side effects, toxicities, opportunistic infections, etc.)

Strategies:

- Involve health care providers who specialize in HIV-related conditions and people with HIV/AIDS in identifying and prioritizing the conditions (see list above) where possible beneficial effects of NHPs need to be investigated.
- Raise awareness of HIV-related conditions among manufacturers of NHPs.
- Communicate priorities regarding NHPs and HIV-related conditions to Canadian Institutes of Health Research and other funding bodies (provincial as well as federal).
- Build on existing observational databases (e.g., the British Columbia Centre for Excellence database of people receiving antiretroviral therapy; the Ontario HIV Information Infrastructure Project) to develop a database of utilization of complementary and alternative products, practices and practitioners by people with HIV/AIDS.
 - Participants observed that it would be worthwhile to explore the possibility of a common data set on use of complementary and alternative products, practices and practitioners, to be used by the British Columbia Centre for Excellence, the Ontario HIV Information Infrastructure Project and other HIV observational databases in the country.
 - Given the constraints of existing databases, it may be necessary to

establish a parallel database (which can make use of the demographic and health care data in the existing databases) to capture more complete information about use of complementary and alternative products, practices and practitioners.

- Lobby for an Office of HIV/AIDS Research within Canadian Institutes for Health Research, which would include a focus on NHPs.

Priority #3: Prioritize the NHPs to be researched first

Strategies:

- Conduct studies of the utilization of NHPs by people with HIV/AIDS.
- Encourage existing observational databases to include information on the use of complementary and alternative products, practices and practitioners (see above).
- Give priority to conditions for which there are few or no conventional medicines.
- Collaborate with researchers, health care providers and professional associations to obtain more information about possible conditions to be studied and to identify what conditions to investigate first.
- Ensure that the research agenda is driven by the needs of people with HIV/AIDS rather than by the needs of industry (community-driven research priorities).
- Provide funding for research grants.

Health Practices/Services Research

Synopsis of the topic

Health practices research includes research to understand complementary and alternative modalities of practices and care, document their

health outcomes, determine their efficacy, establish their cost-effectiveness, etc. Health services research includes research into the ways in which CAHC is provided, different types of combinations of CAHC and conventional health care, the costs of CAHC, etc. Suggested areas of activity have included:

- research on the utilization of complementary and alternative practices and practitioners
- review and evaluation of existing research
- case reports and case series of CAHC
- controlled pilot studies to build bridges between complementary and alternative and conventional practitioners
- research on models of integrated health care
- research on the pathways of decision-making for people with HIV/AIDS in using complementary and alternative practices or services, and the role of various others – friends, community organizations, information providers, health care providers, etc. – in supporting informed decision-making
- research on the efficacy – broadly conceived to include not only biological markers but also quality of life measures – and cost-effectiveness of complementary and alternative practices or services
- role of complementary and alternative practices or services in managing HIV/AIDS and HIV antiretroviral therapy
- role of complementary and alternative practices or services in managing hepatitis C;

- role of complementary and alternative practices or services in managing co-infection with HIV and hepatitis C

In reviewing these suggested areas for research, participants noted the following:

- People use complementary and alternative practices or services for many different reasons, and the perceived benefits do not relate merely to efficacy narrowly conceived as a change in a biological marker. The health outcomes of complementary and alternative practices and services are often broad, and include quality of life as well as clinical improvements. Research must register this broad range of outcomes, particularly outcomes related to quality of life.
- Access to complementary and alternative practices and services is a key issue for people with HIV/AIDS. Integration between systems of health care is a priority.
- It is artificial to separate research on complementary and alternative practices and services from research on NHPs, since people in fact use both and many forms of CAHC combine both.
- It is challenging to translate the philosophy of a complementary and alternative practice into an entity that can be measured in research. ‘Cultural transliteration’ of the complementary and alternative paradigm of health and health care is necessary.
- One cannot assume that conventional research methods cannot be used to investigate a complementary and alternative practice or service.

Research approaches and priorities

1. *Models of integrated care*

A recurring theme in the small group discussion was the need to identify and examine models of integrated health care. Examples mentioned by participants included:

- *Integrated health care at the clinical level for people with HIV/AIDS.* The Sherbourne Health Centre in Toronto has conducted a study of chiropractic care for people with HIV/AIDS that combines biological measures (viral load and CD4 cell counts) with quality of life measures.
- *Integrated health care for Aboriginal people with HIV/AIDS.* Models that promote integrated health care for Aboriginal people with HIV/AIDS include: the Non-Insured Health Benefits administered by the First Nations and Inuit Health Branch, Health Canada, which pays for transportation costs to access traditional healers; the Nine Circles Community Health Centre in Winnipeg, which provides integrated, client-centred primary health care; and models developed for other conditions, such as diabetes, in which traditional healers work alongside physicians.
- *Integration between CAHC and conventional health care.* Integration between these systems needs to happen on several fronts, including health care delivery, research, policy and decision-making.
- *An integrated approach to the management of chronic disease,* including prevention and surveillance, research and evaluation, education of practitioners and consumers, management of care and management of information.

- *Integration at the level of government systems.* There is a dearth of research on the integration of health care at the level of government systems. This includes integration across the determinants of health (research on how action on the determinants of health contributes to improved health and health care); integration across the mandates of government departments (research on integration across departmental mandates for education, employment, housing and health care); and integration across governmental jurisdictions (e.g., research on international models of federal-state collaboration).

2. *Multidisciplinary research teams*

Research on integrated health care requires multidisciplinary research teams that include complementary and alternative practitioners. Practitioners can provide an understanding of the experience of providing and receiving integrated health care (e.g., the synergy between massage and acupuncture). They can advise on how to maintain the integrity of care within the research process. (Research protocols can force practitioners to practice in an artificial way).

Once the infrastructure for such a multidisciplinary approach is established – through integrated clinical services, through collaboration between researchers and practitioners, and through research funding for studies on integrated care – the research projects that emerge are necessarily comprehensive in their approach to health care and the outcomes of health care.

3. *Consumers' ownership of, access to, and control of research*

Consumers need to be involved at all stages of the research process, including the design of the project, the implementation of the project, the analysis of the results and the dissemination of the results. This is true of all communities of people with HIV/AIDS, but was particularly emphasized with regard to

research involving Aboriginal peoples and traditional Aboriginal healers and healing practices.

4. *Consumers' decision-making processes*

The process that the consumer follows in making decisions about health care (including complementary and alternative practices and services) involves more than health care providers: it involves peers, community organizations and other health intermediaries. People especially seek information about how to access services and about how effective the services will be.

5. *Consumers' motivations for using CAHC (products, practices, and practitioners) or integrated health care.*

CAHC meets a range of needs, many of which are broader than the clinical management of HIV infection. In this regard, 'efficacy' can be a problematic concept because it does not fit with the complex factors that make CAHC a good experience for users, or with the philosophy of the complementary and alternative approach to health and health care.

6. *Intervention studies*

Research has to move beyond utilization studies to intervention studies. People with HIV/AIDS want to know what works, not how many people are using a complementary and alternative product, practice or service, or what products, practices or services they are using.

7. *Self care*

Many people with HIV/AIDS use practices that do not need a practitioner. They do many things to manage their health – not all of which are conventionally considered 'health care.' Research into the full range of health care for

people with HIV/AIDS must include practices that do not involve a practitioner.

Report to plenary

Overarching theme: Integrative, culturally appropriate research that adopts the principles of ownership, access, and control to advance the continuum of health care practices and services, with a special focus on CAHC and NHPs.

Some guiding principles:

- an integrative, multidisciplinary approach to the research, one that itself grows out of an integrative team approach to health care
- ownership of, access to, and control of the research for the consumer, so that consumers are involved in the objectives, design and implementation of the research project and the analysis and dissemination of the research findings
- culturally-appropriate research

Some possible research projects:

- models of integrative care that work for people with HIV/AIDS
- consumers' needs and how CAHC can meet those needs
- consumers' decision-making processes and pathways
- models of integration: a) system-wide; b) clinical; c) jurisdictional (across determinants of health and across levels of government)

Priority #1: Funding and capacity building of integrative research teams working on CAHC and NHPs with a focus on HIV/AIDS

Strategies

- Build the concept of integrative research teams:
 - determine existing capacity for integrative research
 - establish principles of integrative research
 - set the goals and the short- and long-term objectives for integrative research
 - develop criteria and review the proposal process for research funding
 - develop a work plan
- Write a draft request for proposals for consideration by research funding agencies (if the agencies are supportive, the draft would form the basis for their own request for proposals).
- Identify possible demonstration projects, drawing on models of integrated care currently in practice (e.g., Tzu Chi Institute, Oak Tree Clinic, Nine Circles Community Health Centre, Sherbourne Health Centre, etc.).

Next steps

- a core working group undertakes the preliminary development of the concept, builds support for the concept and plans a national meeting
- a national meeting to further build the concept and develop the draft request for proposals, involving:
 - clinics and centres with experience in integrative care and research (nationally and internationally)

- consumers (people with HIV/AIDS, Aboriginal people)
 - other relevant networks (Canadian Collaborative HIV/AIDS Pharmacy Network; Canadian Association of Nurses in AIDS Care, Canadian Holistic Nurses Association, networks of researchers in CAHC and NHPs, etc.)
 - CAHC practitioners with experience in research or HIV/AIDS care
- seed funding for a core working group to follow up on the national meeting, prepare the draft request for proposals and build partnerships with research collaborators, industry, Health Canada and research funding agencies

Possible model

One possible model to consider is the Institute for Work and Health. The institute is an independent, not-for-profit organization whose mission is to research and promote new ways to prevent workplace disability, improve treatment and optimize recovery and safe return-to-work. It has been providing evidence-based research and practical tools for clinicians, policy-makers, employees and managers since 1990. It began as a research program of the Workers' Compensation Board. It expanded to an institute with the support of three funders and is currently one of the leading research agencies on work and health in North America. For further information, see www.iwh.on.ca.

Building Research Capacity

Synopsis of the topic

Building research capacity refers to efforts to increase the ability and readiness of individuals and organizations to identify, develop and conduct research on CAHC and NHPs. Some of the needs identified in recent consultations include:

- funding for training awards, research projects and research infrastructure for research in CAHC and NHPs
- mentors, role models and champions for research in CAHC and NHPs
- training in conducting research and using research findings for CAHC practitioners, educators, students and community members
- training and funding for CAHC practitioners to write up case reports
- networks of researchers and practitioners to develop and implement research agendas
- research funding panels with appropriate expertise to review CAHC and NHP research projects, including members from relevant communities
- research ethics boards with appropriate expertise to review CAHC and NHP research projects, including members from relevant communities

Participants in the roundtable especially underscored the importance of drawing in people from the relevant communities (e.g., people with HIV/AIDS, Aboriginal peoples) and consumers of CAHC and NHPs to participate in all stages of the research projects.

Areas for capacity building

1. *Community participation in and control of research*

Community ownership of, access to, and control of the research process is a core value for people with HIV/AIDS and Aboriginal people. To this end, capacity building is required in:

- developing community-based participatory research
- training community members in conducting research and using research findings
- networking between community organizations on research priorities, opportunities and initiatives

2. *Training and engagement of potential researchers*

Specific efforts are needed to find, train or engage people who could potentially conduct research on CAHC and NHPs. This would include:

- training in conducting research and using research findings for CAHC practitioners, educators, students and community members
- specific funding allocations to CAHC educational institutions for research capacity building
- building bridges between research communities and networks
- building research capacity in Aboriginal communities

3. *Access to research funds*

CAHC practitioners are at a disadvantage when applying for research funds. It would help to have peer review panels with appropriate expertise to review research projects on CAHC and NHPs, including members from the relevant communities. It may also be useful to look for funding for research

from unexplored areas such as raw material suppliers of NHPs.

4. *Review of research proposals*

Research proposals should be reviewed as to both their scientific quality and their relevance to consumers. It is important to build the capacity for the peer review of consumer relevance as well as scientific quality, and to ensure that reviewers have the appropriate expertise to review research projects on CAHC and NHPs.

5. *Sustainability of research over time*

To sustain the development of knowledge over time, ongoing funding is required. One-time funding is a barrier to the sustained development and application of knowledge in a continuous learning process.

Report to plenary

Priority #1:

(A) Training in conducting research and using research findings for CAHC practitioners, educators, students, and community members

(B) Funding for CAHC practitioners to write up case reports

(C) A focus on Aboriginal ownership of, access to, and control of the research process

Strategies:

- Use existing best practices in research training and development.
- Fund the development of multidisciplinary educational modules on research.
- Provide training in how to complete a research funding application.

- Pursue strategic funding initiatives with Canadian Institutes of Health Research and other partners (e.g., the Canadian Foundation for AIDS Research, suppliers of raw materials of NHPs, etc.).
- Undertake a needs assessment with Aboriginal communities to identify how they wish to move forward in building research capacity (e.g., consult with the National Aboriginal Council on HIV/AIDS).
- Consider how the Canadian Aboriginal AIDS Network's Aboriginal Capacity-Building Program in Community-Based Research could build capacity in research (e.g., through the Summer Training Awards).
- Support community participation in laboratory research and population-based participatory research.

Priority #2: Leveling the playing field to gain equal access to research funds

Strategies:

- Approach suppliers of raw materials for NHPs, as well as other funders, for research funding.
- Build from where there is currently strength in research on CAHC and NHPs.
- Develop a solid training and mentorship program in research on CAHC and NHPs.
- Examine the reasons for the poor credibility of CAHC and NHPs and undertake research in these identified areas.
- Identify and communicate the high utilization rate of CAHC and NHPs through high-quality research and publications.
- Increase the recognition of research on CAHC and NHPs through publications, presentations, conferences, etc.

- Work with the organizers of the XVI International AIDS Conference (to be held in Toronto in 2006) to get a track devoted to CAHC and NHPs:
 - The Canadian Treatment Action Council will conduct an analysis of the forthcoming XIV International AIDS Conference (to be held in Barcelona in July 2002) to identify coverage of research on CAHC and NHPs.
- Work with the Canadian Association for HIV Research to get time at its annual conference and recognition for research on CAHC and NHPs.

Priority #3: *Funding for training awards, research projects and research infrastructure in CAHC and NHP research*

Strategies:

- Help potential applicants learn about and apply for available funds by:
 - publicizing timely information about opportunities through networks (networking is key)
 - maintaining a web-based database of current funding opportunities
 - creating partnerships among researchers and with funding agencies
- Provide training in how to write a research funding application.
- Provide resources for research offices and other research development programs in educational institutions for CAHC practitioners to inform potential researchers of funding opportunities and to help them navigate the funding application process.
- Nurture a research culture in educational institutions for CAHC practitioners.

- Continuously seek new research funding opportunities.

Methodological Development

Synopsis of the topic

Researchers in CAHC and NHPs have emphasized the need to use or to develop research methodologies that are appropriate to the therapy under investigation. This can be challenging. For example, what research methods are appropriate when studying practices based on the mind-body dynamic? What research methods are appropriate when dealing with non-standardized therapies (e.g., individualized treatment regimens, incremental dosing of products, use of non-standard products or unique product preparations)?

While randomized controlled clinical trials may be used or modified in some circumstances, other research methods – such as individual case reports, case series, case-control studies, etc. – may be needed in other circumstances. For instance, randomized controlled clinical trials can be used for many types of research on NHPs, but are not suited to research on NHPs in their cultural context (such as research on individual preparations used in Traditional Chinese Medicine).

Researchers are asking for meetings and mechanisms by which they can address methodological issues and build bridges between different methodological schools. Among the issues to be addressed are types of evidence (What counts as evidence? What evidence is appropriate?) and measures of outcomes (What is being measured? Is the measure appropriate?).

HIV/AIDS-specific methodological challenges

HIV/AIDS, as well as the treatments used to manage it, presents a number of specific methodological challenges, in addition to the more general challenges encountered in research on CAHC and NHPs:

- HIV/AIDS is not a single disease, but a syndrome that involves multiple diseases.
- The syndrome varies from individual to individual.
- The syndrome involves both immunological and virological dynamics.
- The treatment for HIV consists of multiple drugs (antiretroviral drugs, prophylactic treatments for opportunistic infections, treatment for opportunistic infections, drugs to manage side effects) in multiple combinations (there is no standard protocol that every individual follows).
- It is difficult to determine whether an effect is due to an intervention or to the HIV.
- One cannot generalize the results of studies of pharmacologic effects of benefits, harms and interactions of NHPs or CAHC in healthy individuals to benefits, harms and interactions in people with HIV/AIDS.
- Given a life-threatening disease and a standard of care that has been shown to reduce mortality and morbidity, research that departs from the standard of care would require substantial ethical justification.
- People with HIV/AIDS may be reluctant to participate in studies that require them to go to HIV clinics or other institutions that are publicly identified with HIV care because of concerns with the consequences of disclosure of their HIV status (e.g., stigma in the community or at work, loss of housing, refusal of insurance, etc.).

Areas for methodological development

1. Transcultural translation of CAHC – an area for research

Research on CAHC needs to be informed by a complete understanding of the paradigm of health and health care of the modality under investigation. This requires transcultural translation of the paradigm and its constituent concepts, diagnostics and practices. This should be an area of research in and of itself, as well as a necessary preamble to research on the effects of CAHC.

2. Challenges presented by some forms of CAHC

Participants identified aspects of CAHC and use of NHPs that present methodological challenges for researchers. These include situations where a variety of CAHC modalities are used simultaneously to treat an individual or where NHPs are used in an individualized, culturally-specific context (such as in Traditional Chinese Medicine). One suggested approach would be to conduct comparative outcome studies in which two groups receive a complex of treatments based on the practitioners' judgement.

3. Issues related to the use of randomized controlled clinical trials

A number of issues should be addressed with regard to the use of randomized controlled clinical trials. One is the potential for selection bias when study participants include or consist of past users of CAHC or NHPs. Another is the potential for contamination when a product is available for purchase (often in many different formulations) outside of the study.

4. Assumptions about research methods for CAHC and NHPs

It is frequently assumed that research in CAHC and NHPs requires different methods than research in conventional health care. This assumption should be examined. The research methods to be used should

be appropriate to the claim being made and to the evidence required to make that claim. For example, some types of claims for NHPs would require the evidence of a randomized controlled clinical trial; other types of claims would require other forms of evidence.

5. *Measuring a complex set of effects*

It is important to recognize the complexity of what can or should be measured in research on CAHC and NHPs. The effects that need to be measured include not only pharmacologic and pathologic endpoints, but also psycho-social outcomes such as quality of life, as well as psycho-neural interactions such as immune responses resulting for the care process. For some of these effects, there are established methods (such as quality of life scales) but for other effects (such as mind-body dynamics), there are no established methods.

6. *Ethical challenges associated with research on CAHC and NHPs*

The ethical challenges associated with research on CAHC and NHPs may be more perceived than real (e.g., the perception that an NHP is the equivalent of a placebo in a randomized controlled clinical trial). Nevertheless, these challenges – perceived as well as real – must be addressed by educating research ethics boards about CAHC and NHP research, and by educating CAHC and NHP researchers about research ethics.

7. *Collaborative and participatory research methods*

Collaborative and participatory research can require adjustments from researchers, their sponsoring institutions, funding agencies, funding review panels and research ethics boards. Challenges encountered in the development of the Community-Based Research Program of the Canadian Strategy on

HIV/AIDS can provide some insight into the work that is required in this regard.

Report to plenary

Priority #1: Establish standards of evidence and research

The first priority is to establish standards of evidence and research. These standards should address the question of what standard of evidence is required when making a certain claim or investigating a particular effect (e.g., for a claim regarding an NHP, for treatment involving multiple modalities, for self-reported health outcomes, etc.), and what research methods are appropriate when gathering the required evidence. These standards of evidence and research methods can be used in educating practitioners, researchers, funding review panels and research ethics boards about CAHC and NHP research.

Strategies:

- Build on existing work, such as the work of the National Center for Complementary and Alternative Medicine in the United States (<http://nccam.nih.gov/fi/research/centers.html>).
- Suggest to the organizers of the forthcoming workshop on research methods in CAHC and NHPs (scheduled for the autumn of 2002) that one goal or outcome of the workshop be to develop standards of evidence and research in CAHC and NHPs.

Priority #2: Education and training in standards of evidence and research for CAHC practitioners and educators and for conventional practitioners and researchers

Strategies:

- Develop a series of learning modules on research in CAHC and NHPs (as proposed by the August 2001 roundtable on research literacy and capacity).

- Develop and implement research training support programs for faculty in CAHC educational institutions (as proposed by the August 2001 roundtable on research literacy and capacity).

Priority #3: Foster research skills in CAHC and NHPs among practitioners and researchers

Strategies:

- Support research teams of conventional and complementary/alternative researchers (train both established and new researchers in CAHC and NHP research through the process of doing research).
- Work with the Canadian Association for HIV Research to educate its members about CAHC and NHP research through, for example, satellite meetings at its annual conference.
- Promote accredited continuing education events on CAHC and NHPs and related research for health care providers.

Priority #4: Educate funding review panels and research ethics boards about CAHC and NHP research, methods and standards of evidence

Strategy:

- Recognition of different research methods and of the equal contribution of all collaborators (regardless of their order as authors of publications) is essential if integrative research teams are to receive funding.

Research Dissemination and Uptake

Synopsis of the topic

Consumers of CAHC and NHPs are looking for reliable, accessible and easy-to-understand

information about CAHC and NHPs. Health intermediaries and information providers can help consumers in this regard, by evaluating and selecting information, by presenting information in ways that will be accessible to consumers and by increasing the skills of practitioners and consumers in working with information about CAHC and NHPs.

Suggested ways to facilitate the dissemination and uptake of research have included:

- systematic reviews of research
- development of standardized concepts and terminology across CAHC modalities
- directories and networks that facilitate access to experts
- plain-language, culturally-sensitive resources in all required languages
- training for health intermediaries in understanding and evaluating research findings (critical appraisal skills, knowledge of research methods, knowledge of statistics, knowledge of the therapy under consideration)
- use of informal information networks, such as peers, families and friends, community networks, gay men's health centres, etc., to disseminate information
- use of popular print media and the Internet
- education of conventional practitioners about CAHC and NHPs
- education of CAHC practitioners about conventional health care and health research

It is important to note that health care providers are not the primary sources of information about CAHC and NHPs for people with HIV/AIDS. Rather, their primary sources of information include knowledgeable individuals; HIV/AIDS information providers (such as the Canadian AIDS Treatment Information Exchange and Project Inform); national,

regional and local HIV/AIDS organizations; conferences and meetings; and the popular media..

There are concerns about equity of access to information about CAHC and NHPs among certain vulnerable groups (e.g., street youth, injection drug users) and people in rural areas.

Areas of development

1. *Types of resources that could facilitate dissemination and uptake of information about CAHC and NHPs:*

- guidelines for consumers about interpreting information about CAHC and NHPs
- alternative formats of information for people who do not access main sources of information such as the Internet (focus groups can be used to determine the required formats)
- a list of CAHC practitioners and researchers who are working in HIV/AIDS
- a structured format to help academic researchers share the results of research in community fora in language that consumers understand (this could be built into the funding agreement for research projects, with funding set aside for communication at community fora)
- monographs on NHPs

2. *Channels of information that can be used to reach people with HIV/AIDS with information about CAHC and NHPs:*

- existing channels of communication with people with HIV/AIDS, such as:
 - the Canadian AIDS Treatment Information Exchange
 - community organizations (e.g., the AIDS Committee of Toronto

maintains a directory of CAHC practitioners)

- provincial and national health organizations
- the Canadian HIV/AIDS Clearinghouse
- people selling NHPs (pharmacists, health food store staff)
- the health care delivery system, including physicians, public health workers, pharmacists, poison control agencies, etc.

3. *Strategies to increase recognition of research on CAHC and NHPs:*

- publication of the results of research on CAHC and NHPs in mainstream medical and scientific journals
- presentations or satellite meetings on CAHC and NHPs at the annual conference of the Canadian Association for HIV Research and the XVI International AIDS Conference (to be held in Toronto in 2006)
- systematic reviews of CAHC and NHP research studies (supported by a request for proposals or other forms of funding)

4. *Gaps in access to information*

There are people with HIV/AIDS who do not access information through community-based organizations, through HIV/AIDS conferences or through other commonly used sources of information. It is important to determine how these people access information and to target information strategies accordingly. This may involve evaluation studies of current or future information dissemination programs.

Report to plenary

Key groups to consider

The following groups should be included in strategies and programs to improve dissemination and uptake of information about CAHC and NHPs:

- consumers and consumers' organizations
- conventional and complementary/alternative practitioners
- educators and researchers
- government agencies: federal and provincial/territorial ministries of health; public health agencies; First Nations and Inuit Health Branch, Health Canada

Priority #1: *Reviews of research on CAHC and NHPs*

Strategies:

- Fund systematic reviews of research studies on CAHC and NHPs.
- Prepare guidelines for reviewers to ensure consistency of systematic reviews.
- Build networks of people with the required skills to conduct systematic reviews.
- Simplify the language of reviews so that everyone – reviewers and consumers – use the same language.
- Use the Internet as a clearinghouse for systematic reviews:
 - Canadian Health Network (www.canadian-health-network.ca)
 - CAMline (<http://camline.org>)
 - Canadian Aboriginal AIDS Network LinkUp Connexion (www.caan.ca)
- Link with other review networks, such as:

- the Cochrane Collaboration (for resources on complementary and alternative therapies see www.cochrane.org/cochrane/whatcdsr.htm#CAT and www.cochraneconsumer.com/index.asp?S HOW=Search)
- the University of Exeter Complementary Health Studies Program (see www.ex.ac.uk/chs)

Priority #2: *Assessment of information needs of target audiences (see list of key groups above)*

Strategies:

- Conduct focus groups with target audiences to determine:
 - means to ensure equity of access to information
 - formats for information dissemination
 - language requirements (level of literacy, languages used, etc.)
 - cultural appropriateness of information
 - nature of information needed
- Use questionnaires and other needs assessment methods to determine the above.

Priority #3: *Dissemination and uptake strategies*

Strategies:

- Tap into existing organizations and systems, and use them as conduits of information:
 - CAMline
 - Canadian Aboriginal AIDS Network LinkUp Connexion
 - HIV/AIDS treatment information providers
 - community fora
 - professional organizations
 - HIV/AIDS conferences (community conferences, research conferences, health provider conferences)

- Integrate information dissemination about CAHC and NHPs into health services delivery.
- Create directories of CAHC providers, CAHC and NHP researchers, and CAHC and NHP educational institutions.
- Develop networks of CAHC providers, and CAHC and NHP researchers.
- Develop monographs on NHPs.
- Develop templates or guidelines for interpreting research findings and information about CAHC and NHPs.
- Support knowledge transfer workers.

Building and Strengthening Liaisons

Synopsis of the topic

Efforts to promote research on CAHC and NHPs are gathering momentum in Canada. What are some specific ways to build or strengthen liaisons between the HIV/AIDS field and the broader CAHC and NHPs field?

Participants identified the sectors in which awareness of and involvement in CAHC and NHP research need to be strengthened – researchers, funders, community organizations, hospitals and clinics, practitioners, professional associations, educational institutions, information providers and the media – and discussed ways to do this.

Areas of development

1. *Researchers*

The following ways were suggested to encourage researchers to become involved in research on CAHC and NHPs:

- Identify leaders in relevant organizations, such as the Canadian Association for HIV Research and the Canadian Association of Nurses in AIDS Care.
- Sponsor workshops or satellite meetings at the annual conferences of these organizations.
- Provide funds for a dedicated staff person to build liaisons and to develop ideas emerging from the workshops or satellite meetings.
- Provide funds for researchers as an incentive to them to develop new partnerships or to undertake a new line of research.
- Develop a mentorship program for new researchers to support them in applying for training funds or project funds in CAHC and NHP research.

2. *Funders*

Potential funders include the federal research granting agencies (Canadian Institutes of Health Research, the Natural Sciences and Engineering Council of Canada, the Social Sciences and Humanities Research Council of Canada), banks, insurance companies, industry and foundations:

- The NHPs industry should be encouraged to direct their research into the role of NHPs in HIV care.
- Manufacturers of HIV antiretroviral drugs are interested in the use of NHPs to mitigate side effects associated with their drugs and may be persuaded to support clinical trials on selected interactions.
- Foundations that may provide funds include the Trillium Foundation, the Toronto Wellesley Hospital, the Michael Smith Foundation for Health Research, the Buddhist Compassion Relief Tzu Chi Foundation and the Canadian Foundation for AIDS Research.
- Insurance companies have an interest in promoting wellness and may be persuaded to

support CAHC and NHP research to this end.

It is important to have a well-developed project before approaching a funder. One suggestion was to run a competition for concept proposals for funding applications, and then to award seed money to the successful applicants for the development of a full funding application.

When funding clinical services, it may be possible to require an evaluation of the services. This would provide funding for research on the evaluation of clinical services, including the integration of services.

3. *Community organizations*

Community organizations working in HIV/AIDS are developing their capacity for research. For example, the AIDS Committee of Toronto has dedicated research and evaluation staff. Similarly, the Canadian Aboriginal AIDS Network has a dedicated staff person for research, and recently awarded one of the Summer Training Awards – which it administers under the Aboriginal Community-Based Research Program – to a person studying Aboriginal health practices in Labrador and Quebec.

There are potential resources to support community-based research. The Community-Based Research Program of the Canadian Strategy on HIV/AIDS funds technical support staff in research for community organizations. It is possible that these resources could be applied to research on CAHC and NHPs.

Ongoing funding is key to building capacity in community organizations. Jurisdictional barriers can disrupt funding. For example, the British Columbia Persons With AIDS Society lost provincial funding for its work on CAHC and NHPs because research was deemed to be an area of federal responsibility. As a result, a promising

capacity for research on CAHC and NHPs was stalled.

Community organizations are key to recruitment into and participation in research, as well as to knowledge transfer between community members and researchers. One way to move forward in CAHC and NHP research is to facilitate communication between community organizations about their research activities in this field and related knowledge transfer activities. Another way is to fund training for research staff of community organizations in publishing in peer-reviewed journals and in interpreting evidence presented in these journals.

4. *Hospitals and clinics*

There are a number of hospitals and clinics in Canada that could possibly become a site for research on CAHC and NHPs and HIV/AIDS:

- Oak Tree Clinic, Vancouver, serving primarily women and children with HIV/AIDS and their families
- St. Paul's Hospital, Vancouver, the home of the British Columbia Centre for Excellence in HIV/AIDS and the national offices of the Canadian HIV Trials Network
- Tzu Chi Institute for Complementary and Alternative Medicine, Vancouver
- Nine Circles Community Health Centre, Winnipeg, which provides integrated, client-centred primary health care, including traditional Aboriginal healing
- St. Michael's Hospital, Toronto, which provides HIV care, provides \$5 million for research, and has developed a protocol for CAHC
- Sherbourne Health Centre, Toronto, which provides HIV care, including CAHC

- Mt. Sinai Hospital, Toronto, which provides selected CAHC, including art therapy and Traditional Chinese Medicine
- Hospital for Sick Children, Toronto, which provides HIV care and is involved in research on CAHC and NHPs
- Toronto Western Hospital, the home of the Artist's Health Centre

However, there are relatively few clinics in which conventional and complementary/alternative health care are fully integrated. This is a barrier to research on the integration of care.

5. *Practitioners*

There are relatively few complementary/alternative practitioners who specialize in HIV/AIDS. Those who do are very busy.

The approach of conventional practitioners can overlap with that of complementary/alternative practitioners. It may be possible to work with such practitioners to advance research on CAHC and NHPs. Suggestions as to how to do this include:

- Work with sections of professional associations that focus on CAHC and NHPs.
- Work with professional associations that bridge conventional and complementary/alternative health care, such as the Canadian Complementary Medical Association, the Association of Complementary Physicians of British Columbia and the Ontario Society of Physicians for Complementary Medicine.
- Sponsor continuing education accreditation for educational events about research on CAHC and NHPs.

There is an opportunity to gather more information about the use of CAHC and NHPs through HIV/AIDS observational databases. In Ontario, the HIV Information Infrastructure Project (the successor to the HIV Ontario Observational Database) is about to begin gathering comprehensive data on the health care of people with HIV/AIDS in Ontario (see www.ohtn.on.ca/welcome_hiip.html). There have been discussions about including some information about CAHC in the database. However, time is of the essence, as the software for the database is in the final stages of preparation and installation (for an interactive demonstration, see www.hyperweb.org/dev/CMS/index.html).

6. *Professional associations*

Professional associations – both conventional and complementary/alternative – can be helpful in developing research infrastructure and obtaining research funds. They can facilitate communication and networking through their mailing lists, sections and conferences. They can promote education and awareness about CAHC and NHPs, as well as about research in these fields, at their annual conferences and in their continuing education programs. They can provide credibility and support for funding applications for research projects.

7. *Educational institutions*

In general, participants observed that there is a need for:

- resources for research offices in CAHC educational institutions
- curriculum and faculty development on CAHC and NHPs in educational institutions for conventional health care providers
- curriculum and faculty development on research in educational institutions for CAHC providers

There are a number of initiatives underway to expand research capacity in CAHC and NHPs in Canada:

- Through a Health Canada contract, the Tzu Chi Institute for Complementary and Alternative Medicine is undertaking a survey of three CAHC educational bodies (for chiropractors, massage therapists and naturopaths) as a follow-up to the roundtable on research literacy and capacity convened by Health Canada in August 2001.
- The University of Calgary, in conjunction with Health Canada and a national advisory group, is undertaking a review of NHPs and CAHC in undergraduate medical school curriculum, with a view to identifying effective teaching approaches, curriculum placement and national guidelines for incorporating the necessary level of attention to this area for graduating doctors.

There may also be opportunities to include education about CAHC and NHPs in training programs in HIV care:

- Department of Family Medicine, McMaster University, third-year residency in HIV care, being developed under the direction of Dr. Dale Guenter
- School of Nursing, University of British Columbia, course on HIV Prevention and Care

Report to Plenary

Priority #1: Time, resources and institutional support to work specifically on building partnerships and promoting research on integrative health care.

The group reported on the areas for development summarized above. The group then emphasized the importance of having dedicated staff to work specifically on building partnerships and on promoting research on integrative health care. This work requires time, resources and

institutional support. There are a number of possible models:

- a Centre of Excellence in integrative health care
- a research network on integrative health care
- research staff in community organizations
- an office of CAHC and NHP research in Canadian Institutes of Health Research.

Final Recommendation

To develop research on CAHC and NHPs in the field of HIV/AIDS, it is necessary to have the resources and time to build partnerships, explore opportunities and increase the profile of CAHC and NHPs in existing HIV/AIDS networks and programs.

There was overwhelming consensus that funding for a dedicated staff person is necessary to undertake activities to build research on CAHC and NHPs in the field of HIV/AIDS. The following activities were identified but were not prioritized:

- Build on existing HIV/AIDS observational databases (British Columbia Centre for Excellence in HIV/AIDS, the HIV Information Infrastructure Project) to gather information about the use of CAHC and NHPs among people with HIV/AIDS in relation to conventional health care and treatments.
- Identify and build relations with partners in research on CAHC and NHPs:
 - funders, such as the Canadian Foundation for AIDS Research
 - industry, such as suppliers of raw materials of NHPs and pharmaceutical companies interested in the role of NHPs in relation to antiretroviral therapies
 - HIV/AIDS researchers and practitioners who are open to work on CAHC and NHPs

- Increase awareness in the HIV/AIDS field of research on CAHC and NHPs:
 - at the annual conferences of the Canadian Association of HIV Research, through presentations and satellite meetings
 - at the XVI International AIDS Conference to be held in Toronto in 2006, through a separate track or presentations across the tracks
 - Disseminate information through existing HIV/AIDS networks about research opportunities, and share information about research initiatives in CAHC and NHPs.
 - Liaise with broader networks and evolving initiatives in CAHC and NHPs, such as:
 - the follow-up to the research priority-setting conference on drug interactions with NHPs
 - the forthcoming workshop on methodological issues related to research on CAHC and NHPs
 - the initiative to develop curriculum for undergraduate medical education on CAHC and NHPs
 - initiatives to improve the dissemination and uptake of information about CAHC and NHPs
 - Facilitate the development of an integrative research team on integrative health care by:
 - liaising with health centres that provide integrative health care to people with HIV/AIDS
 - establishing a working group to identify research opportunities in integrative health care
 - developing a draft request for proposals
- liaising with Canadian Institutes of Health Research and other funders to explore funding opportunities for research on integrative health care
 - Facilitate the development of research on Aboriginal healing practices in relation to HIV/AIDS, in consultation with:
 - the Canadian Aboriginal AIDS Network
 - the First Nations and Inuit Health Branch, Health Canada
 - the Institute of Aboriginal Peoples' Health, Canadian Institutes of Health Research

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Developing a Research Agenda in Natural Health Products, Complementary and Alternative Health Care and HIV/AIDS: A Discussion Paper

*Theodore de Bruyn
February 27, 2002*

The views expressed in this paper are those of the author and/or conference participants and do not necessarily represent those of Health Canada

Executive Summary

This discussion paper provides a broad overview of issues concerning the development of a research agenda in the area of natural health products (NHPs), complementary and alternative health care (CAHC) and HIV/AIDS. The purpose of this report is to facilitate discussion and the identification of priority needs at the Invitational Roundtable on the Role of Natural Health Products and Complementary and Alternative Health Care: Developing a Research Agenda. The roundtable is being convened in March 2002 by the Natural Health Products Directorate (NHPD), in collaboration with the Health Human Resource Strategies Division and the HIV/AIDS Policy, Coordination and Programs Division of Health Canada.

The objectives of the roundtable are:

- **to assist in the further development of a research agenda in the area of NHPs, CAHC and HIV/AIDS, building on the priorities first established in the**

document “Toward Integrative Care: National Strategic Planning Meeting on Complementary Therapies and HIV/AIDS.”

This report, along with others referred to in this discussion paper, have set out the main lines of a research agenda. The purpose of this roundtable is to develop this agenda further by suggesting specific steps.

- **to build capacity to conduct research in Canada in NHPs and CAHC, with HIV/AIDS serving as an area with readiness to explore ways to accomplish this.** There is widespread recognition of the need to build research capacity – to increase the ability and readiness of individuals and organizations to identify, develop and conduct research – in NHPs and CAHC in Canada. What is needed now are specific steps to do this in areas where there is sufficient readiness. HIV/AIDS is one such area.
- **to contribute to the NHPD’s process of identifying and advancing research priorities in NHPs and CAHC within the national arena.** The NHPD is seeking to identify and advance research priorities both through its own funds (intended primarily for developmental purposes) and in collaboration with other funders (such as the Canadian Institutes of Health Research, the Hospital for Sick Children Foundation and other funders).

The groundwork for the roundtable began in previous consultations within the HIV/AIDS field and the CAHC/NHP field. Drawing from these consultations, this discussion paper:

- summarizes key aspects of the use of CAHC/NHPs by people with HIV/AIDS
- summarizes research priorities that have been identified in the area of NHPs, CAHC and HIV/AIDS
- summarizes the outcomes of Health Canada's consultations on building research capacity and advancing research priorities in CAHC/NHPs
- outlines a process for considering next steps

Next Steps

There is growing momentum in Canada to build research capacity and to advance the research agenda with regard to CAHC and NHPs. Researchers, practitioners, consumers, information providers, industry, government, and research funders are actively looking at specific and concrete ways to move forward.

In this context, there is a potential for synergy between the HIV/AIDS field and the broader CAHC/NHP field. With their considerable experience in the use of CAHC/NHPs, research, community organization, industry relations, and consultation and lobbying, people and organizations in the HIV/AIDS field have much to contribute to CAHC/NHP research.

At the same time, the momentum in the broader CAHC/NHP field may help to strengthen the capacity of the HIV/AIDS field to identify, participate in, and advance research on CAHC and NHPs, particularly research that is of special relevance to people with HIV/AIDS.

The roundtable on March 10-11, 2002 is intended to explore the potential for mutual strengthening and collaboration in the following areas:

- building research capacity
- methodological development
- NHP research
- health services research
- knowledge dissemination and uptake
- building and strengthening liaisons

In HIV/AIDS consultations and/or in CAHC/NHP consultations, these areas have been identified as areas for action. The overall objective of the roundtable is to identify and select top priorities and opportunities for each of these areas and to identify strategies to move forward in advancing these priorities.

Introduction

The purpose of this discussion paper is to provide background information and stimulate strategic planning to advance a research agenda in natural health products (NHPs), complementary and alternative health care (CAHC) and HIV/AIDS. It is intended to be a resource for participants in the March 10-11, 2002 Invitational Roundtable on the Role of Natural Health Products and Complementary and Alternative Health Care in HIV/AIDS – Developing a Research Agenda. The roundtable is being convened by the Natural Health Products Directorate (NHPD), in collaboration with the Health Human Resource Strategies Division and the HIV/AIDS Policy, Coordination and Programs Division in Health Canada.

The objectives of the roundtable are:

- **To assist in the further development of a research agenda in the area of NHPs, CAHC and HIV/AIDS first established in the document "Toward Integrative Care:**

National Strategic Planning Meeting on Complementary Therapies and HIV/AIDS.” This report, along with others referred to in this discussion paper, have set out the main lines of a research agenda. The purpose of this roundtable is to develop this agenda further by suggesting specific steps.

- **To build capacity to conduct research in Canada in NHPs and CAHC with HIV/AIDS serving as an area with readiness to explore ways to accomplish this.** There is widespread recognition of the need to build research capacity – to increase the ability and readiness of individuals and organizations to identify, develop and conduct research – in NHPs and CAHC in Canada. What is needed now are specific steps to do this in areas where there is sufficient readiness. HIV/AIDS is one such area.
- **To contribute to the NHPD’s process of identifying and advancing research priorities in NHPs and CAHC within the national arena.** The NHPD is seeking to identify and advance research priorities both through its own funds (intended primarily for developmental purposes) and in collaboration with other funders (such as the Canadian Institutes of Health Research, the Hospital for Sick Children Foundation and other funders).

The groundwork for the roundtable has been laid in previous consultations, both within the HIV/AIDS field and within the CAHC/NHP field (see References, below). This discussion paper draws on these consultations to:

- summarize key aspects of the use of CAHC/NHPs by people with HIV/AIDS

- summarize research priorities that have been identified in the area of NHPs, CAHC and HIV/AIDS
- summarize the outcomes of Health Canada’s consultations on building research capacity and advancing research priorities in CAHC/NHPs
- outline a process for considering next steps

Definitions and Context

Complementary and alternative health care

The United States National Center for Complementary and Alternative Medicine describes CAHC (also referred to as complementary and alternative medicine or CAM) as follows (<http://nccam.nih.gov/fcp/faq>):

- Complementary and alternative medicine (CAM) covers a broad range of healing philosophies, approaches, and therapies. Generally, it is defined as those treatments and health care practices not taught widely in medical schools, not generally used in hospitals, and not usually reimbursed by medical insurance companies.
- Many therapies are termed “holistic,” which generally means that the health care practitioner considers the whole person, including physical, mental, emotional, and spiritual aspects. Many therapies are also known as “preventive,” which means that the practitioner educates and treats the person to prevent health problems from arising, rather than treating symptoms after problems have occurred.
- People use these treatments and therapies in a variety of ways. Therapies are used alone (often referred to as alternative), in combination with other alternative therapies, or in addition to conventional therapies (sometimes referred to as complementary).

- Some approaches are consistent with physiological principles of Western medicine, while others constitute healing systems with a different origin. While some therapies are far outside the realm of accepted Western medical theory and practice, others are becoming established in mainstream medicine.

Natural health products

CAHC may involve the use of NHPs. According to the proposed Natural Health Products Regulations (*Canada Gazette, Part I*, December 22, 2001, p. 4939), “natural health product” refers to a substance or combination of substances, a homeopathic preparation, or a traditional medicine that is manufactured, sold, or represented for use in:

- the diagnosis, treatment, mitigation, or prevention of a disease, disorder, or abnormal physical state or its symptoms in humans;
- restoring or correcting organic functions in humans; or
- maintaining or promoting health or otherwise modifying organic functions in humans.

For the purposes of the regulations, certain substances are included (Schedule 1) and others are not included (Schedule 2) within the scope of the regulations.

Context

This roundtable, and other initiatives like it, are taking place in a context in which the use of CAHC and NHPs is growing among Canadians. Many people practice or use CAHC as a form of self-care, and may combine several products and/or practices at once. Although more people are disclosing the fact that they use CAHC or NHPs to their physicians and pharmacists, many

still do not do so. More people are, in fact, taking NHPs instead of filling a prescription or seeing a physician. There is a widespread desire for reliable information about CAHC and NHPs – What is it? Will it work? Where can I get it? How much will it cost? Who will pay for it? – also a corresponding lack of ready access to information. Because of the uncertain and often negative status of CAHC and NHPs within the prevailing conventional (or Western) medical health care system, relationships are not fostered in which people who use CAHC and NHPs discuss this with their health care providers, disclose adverse reactions, and obtain helpful information from their health care providers. But there are initiatives under way – some of which are described below – to gather better information about CAHC and NHPs, to improve professional education and training in CAHC and NHPs, to provide reliable and accessible information to people who use CAHC and NHPs and to establish the value of CAHC and NHPs within the health system.

Within this context, this roundtable is focusing on how to advance research on CAHC and NHPs in Canada – specifically, how to advance research on CAHC and NHPs in relation to HIV/AIDS.

The Sponsors of the Roundtable

The sponsors of the roundtable have distinct roles in relation to the focus of the roundtable: namely, how to advance research on CAHC and NHPs in relation to HIV/AIDS. These are described below.

Natural Health Products Directorate

The NHPD (originally known as the Office of Natural Health Products), Health Products and Food Branch, Health Canada, was created in 1999 with the mandate to “ensure that all Canadians have ready access to natural health products that are safe, effective, and of high quality, while respecting freedom of choice and philosophical and cultural diversity.” In keeping with its primary role as a product regulator, the NHPD published a proposed

regulatory framework for NHPs in December 2001.

Although the directorate's primary role is as a product regulator, provisions were made for it to support NHP-based research. The research budget for the directorate currently stands at \$1 million per year. To date, the directorate has been consulting on how best to use its research funds. These consultations have been both general – developing an overall research agenda for the directorate – as well as focused – exploring a number of specific areas through a series of priority-setting conferences. These specific topics include drug interactions with NHPs, the role of NHPs in child-and-youth health, and NHP standards and quality control. The directorate has explored these subjects alone or in partnership with both community-based organisations and government partners. The intention is that the directorate will be in a position to actively support research projects and initiatives within the very near future both directly and in partnership with other funding agencies. While CAHC has a contextual impact on some NHPs, the research agenda of the directorate is focused more on products than on practice.

While the directorate has no specific mandate in HIV/AIDS, NHPs have long been a health care option chosen by people living with HIV/AIDS. As part of its mandate to build partnerships within the community, the directorate is keen to facilitate ways in which research can be conducted investigating the use of NHPs in the prevention and treatment of HIV/AIDS.

Health Human Resource Strategies Division

The Health Human Resource Strategies Division, Health Policy and Communications Branch, Health Canada, has developed a policy file on CAHC, looking at broad health system

impacts of this emerging health issue and at future health system implications.

In 2001/2002, the areas receiving attention include:

- health human resources: investigating labour market and human resource issues for CAHC practitioners
- information and informed choice: investigating information quality, appropriateness, and balance; understanding prerequisites of informed health choices at multiple levels
- health law and ethics: investigating practitioner-, practice- and product-related issues, including consideration of regulatory policies and impact of value systems on service delivery
- education: investigating curriculum approaches related to CAHC integration; promoting balanced program activity across health sciences and CAHC education
- health care system: exploring the role of CAHC in health care delivery
- encouraging the development of an information framework that includes CAHC practices and practitioners

The CAHC policy file will be transferred to the NHPD as of April 1, 2002, providing an enhanced opportunity for the consideration of inter-related practice, practitioner and product issues. Within its ongoing mandate in relation to health human resource and health system issues, the Health Human Resource Strategies Division will continue to provide an opportunity for attention to CAHC in relation to allied health and interdisciplinary approaches, and to support the current initiative focused on CAHC in health sciences curriculum.

HIV/AIDS Policy, Coordination and Programs Division

The HIV/AIDS Policy, Coordination and Programs Division of the Centre for Infectious Disease, Prevention and Control, Health Canada, is responsible for coordinating the Canadian Strategy on HIV/AIDS (CSHA). The CSHA was launched in 1998, based on extensive national consultations. As a sequel to the previous two national AIDS strategies, the CSHA is not time limited, thus permitting long-term planning.

As part of the national consultations, recommendations were made regarding CAHC. Projects, which Health Canada funds to this end, include:

- the Canadian AIDS Treatment Information Exchange, which disseminates information on treatment issues in this field
- the Canadian HIV/AIDS Legal Network's project on CAHC, which has resulted in a report by Crouch et al., *Complementary/Alternative Health Care and HIV/AIDS: Legal Ethical and Policy Issues in Regulation*

Many people living with HIV/AIDS use CAHC and NHPs as part of health maintenance and/or as the significant modality in health promotion and maintenance. The CSHA will continue to evolve in this field, guided by the recommendation to remove barriers to access to complementary and alternative treatments and treatment information.

Of the \$42.2 million allocated annually for the CSHA, \$13.5 million is allocated to research. Of this allocation, the Canadian Institutes of Health Research administers \$11.7 million. Of this amount, \$3.5 million supports the Canadian HIV Trials Network. The HIV/AIDS Policy, Coordination and Programs Division administers the remaining \$1.8 million of the allocation, which is dedicated to community-based research.

Of this amount, \$800,000 must be spent on Aboriginal community-based research.

Key Aspects of the Use of CAHC/NHP by People with HIV/AIDS

A shift in approach to health care

There has been a shift in the approach of people with HIV/AIDS to their care, treatment and support (MacDonald et al, v; MacAmmond, 13; Cain et al, v):

- They are making choices on the basis of a global assessment of their health and wellness, rather than on the basis of more narrowly defined medical interventions. Health encompasses not only the physical, but also the mental, emotional, spiritual and sexual aspects of life.
- They are taking an active role in decisions about their health care. They are seeking to make informed choices through collaborative, empowering consultations with health care providers.

This shift has been associated with the advent of multidrug antiretroviral therapy (Kendall, 1; Cain et al, 9). Positively, the success of these drugs in suppressing viral load and preventing disease progression has encouraged people with HIV/AIDS to think about long-term health promotion and disease prevention. Negatively, the side effects of the drugs have required that people with HIV/AIDS look for ways to manage the toxicities of these drugs and to make decisions about treatment in light of their overall health.

Use of complementary/alternative products, practices and practitioners

CAHC and NHPs are an integral component of the health and wellness strategies of people with HIV/AIDS. The range of therapies used is wide. Frequently mentioned therapies include vitamins

and minerals, nutrition and special diets, mind-body techniques, physical therapies and massage, and herbal and medicinal agents (including marijuana). There are important differences between women and men in the use of CAHC/NHPs. For a summary of Canadian studies, see Crouch et al, 122-124 (cf. Achilles et al, 269; MacAmmond, 11; Kendall, 5).

The number of people with HIV/AIDS who report using a complementary/alternative therapy is greater than the number who report consulting a complementary/alternative practitioner (Cain et al, 20). For some, this is because they cannot afford to consult a practitioner (Kendall, 12). It may also be because many complementary/alternative therapies do not require a practitioner (Cain et al, 21). Self-medication with NHPs is one strategy used by people with HIV/AIDS when their funds for CAHC are limited. Another strategy is to rotate the use of CAHC/NHPs, using one product one month, another the next. Some people with HIV/AIDS limit their food intake to pay for NHPs (Kendal, 12-13).

Perceived benefits and risks

The most common reasons given by people with HIV/AIDS for using complementary/alternative therapies include (Crouch et al, 16; Kendall, iv, 5-10; MacAmmond, 12):

- to take active control over one's health care
- to improve general well-being
- to boost immune function
- to lower viral load and prevent, delay, or treat symptoms of HIV disease progression or opportunistic infections

- to help with side effects of conventional therapies (especially antiretroviral therapies),
- which facilitates adherence to a prescribed regime
- to manage hepatitis co-infection
- to help relieve stress, depression and fatigue
- to cope with addiction

Risks associated with the use of CAHC and NHPs by people with HIV/AIDS include (Kendall, iv, 12-13):

- limiting food intake and self-medicating because of the cost of CAHC and NHPs
- lack of communication about use of CAHC and NHPs with conventional practitioners
- the potential for adverse interactions between NHPs and drug

Access to information

It is challenging for both people with HIV/AIDS and for health care practitioners (both conventional and complementary/alternative) to get reliable and useful information about CAHC and NHPs, particularly on the safety and efficacy of therapies and on potential interactions between NHPs and drugs (MacDonald, 14, 27, 29, 33). In addition, many people with HIV/AIDS have difficulty understanding information because it is not in an easily understood format at an appropriate level of literacy (MacDonald, 17).

For people with HIV/AIDS, primary sources of information include knowledgeable individuals, national AIDS organizations, local/regional AIDS organizations, conferences and meetings, and the popular media (MacDonald, 23; Kendall, 15). Lay networks of people with HIV/AIDS – which combine knowledge of HIV/AIDS with knowledge of CAHC and NHPs – are an important source of information (Kendall, 17). Many people with HIV/AIDS prefer to receive treatment information in person from someone with whom they have developed a

relationship of trust, such as their health care provider, a staff member or volunteer with an AIDS service organization, or another person with HIV/AIDS (MacDonald, 16).

Some people with HIV/AIDS work intensely with the Internet, but there are populations who do not access the Internet (MacDonald, 12, 17). It is, however, difficult and time-consuming to assess the quality of any given website (MacDonald, 41). Critical skills in assessing and applying information are required.

Relationships with practitioners

While people with HIV/AIDS look to health care providers for information in making decisions about their health, both conventional practitioners and complementary/alternative practitioners are often of limited help. Conventional practitioners may not be knowledgeable about, interested in, or supportive of CAHC and NHPs. Complementary practitioners are often not knowledgeable about HIV/AIDS (Kendall, 18). However, when conventional practitioners are prepared to engage in a dialogue with their patients about CAHC and NHPs, they have the confidence of their patients, help to reduce the possibility of interactions between NHPs and drugs, and help to reduce the cost and pill burden associated with CAHC (Kendall, 24).

Both conventional practitioners and complementary/alternative practitioners underscore the need for more evidence-based information on complementary and alternative therapies (MacDonald, 31, 33). In addition, complementary/alternative practitioners desire information as to when various therapies might or might not be appropriate in relation to a particular stage of HIV disease or a particular opportunistic infection (MacDonald, 32).

Research Priorities in CAHC, NHP and HIV/AIDS

The consultations on CAHC, NHPs and HIV/AIDS have identified numerous ways in which research in this area should be advanced (“Toward Integrative Care,” 9-11; Crouch et al, 107-116; MacAmmond, 35-42; Kendall, viii). These are summarized here under the following headings:

Develop research infrastructure

- increase funding and expand the funding base for CAHC/NHP research
- increase priority for CAHC/NHP research within Canadian Institutes of Health Research
- increase priority for CAHC/NHP research within the Canadian Association for HIV/Research
- provide funding for community-based research on CAHC/NHPs
- include NHPs in post-approval product surveillance systems
- develop a research agenda in CAHC/NHPs and HIV/AIDS
- develop mechanisms to set research priorities in CAHC/NHPs and HIV/AIDS
- develop mechanisms for multi-stakeholder ethics review
- develop protocols to govern conduct of health research with and within Aboriginal communities in accordance with principles determined by Aboriginal communities
- develop a ‘virtual’ institute or Centre of Excellence for research in CAHC/NHPs

Build capacity to conduct research

- training and personnel awards and research grants in CAHC/NHP research

- community-based skills development in research methodologies and critical skills in assessing information
- conferences on research questions and methodologies
- networks to facilitate networking and collaboration among researchers
- develop, test and promote acceptance of a wider range of research methods required to investigate complementary/alternative therapeutic approaches
- increase conventional practitioners' knowledge of research methods other than the randomized control trial

Research areas

- use of CAHC/NHPs by people with HIV/AIDS (see Crouch et al, 107-108 for details)
- health care interventions aimed at enhanced well-being and quality of life
- measures of efficacy that recognize a broad range of desirable outcomes
- barriers to integrative care (at the systemic or structural level, at the clinical level, and with respect to specific populations or remote areas)
- models and best practices of integrative care (pilot projects and applied research on different models of collaborative clinical practice)
- delivery of integrative care to specific populations (e.g., women, Aboriginal peoples, drug users, remote areas)
- models of informed consent, shared decision-making, and shared liability in effective therapeutic relationships

- safety, efficacy, risks, dosage, indications and counter-indications of NHPs
- NHP-drug interactions
- role of CAHC/NHPs in preventing or moderating side-effects from drugs and in managing antiretroviral therapy
- role of CAHC/NHPs in managing hepatitis co-infection
- cost-effectiveness of integrative care including specific products and practices
- cost-benefit and cost-effectiveness analysis of extending public and private insurance coverage to CAHC/NHPs (for health promotion; for disease prevention; as an alternative to more expensive conventional therapies)
- regulatory, legal and ethical questions associated with CAHC/NHPs (see Crouch et al, 115 for details)
- consumer information and knowledge (see Crouch et al, 108 for details)

Dissemination and uptake of research findings

- promote resources such as EMBASE, the Cochrane Collaboration and the Canadian Health Network
- develop and expand CAHC/NHP information provided by CATIE, the British Columbia Persons with AIDS Society, AIDS service organizations and other stakeholders
- consolidate and synthesize existing knowledge and evidence
- establish linkages between information providers and the CAHC/NHP research field
- develop capacity for critical analysis, interpretation and synthesis of evidence

- needs assessments with consumers regarding their information needs
- needs assessments with practitioners regarding their information needs

Building Research Capacity and Advancing Research Priorities in CAHC/NHP: Outcomes of Health Canada Consultations

The Natural Health Products Directorate (NHPD) and the Health Human Resource Strategies Division, Health Canada, have held consultations on many aspects of CAHC/NHPs: research priorities, research capacity and literacy, NHP-drug interactions, information and informed choice, and health law and ethics. These consultations provide a picture of the broader context of CAHC/NHP research, as well as information about suggested strategies to move forward.

Building research capacity

Canadian Institutes of Health Research

Canadian Institutes of Health Research (CIHR), as the main funder of health research in Canada, has a central role in building research capacity in CAHC/NHPs. The objective of CIHR is to excel, according to internationally accepted standards of scientific excellence, in the creation of new knowledge and its translation into improved health for Canadians, more effective health services and products, and a strengthened Canadian health care system.

CIHR funds research in the following broad range of areas:

- biomedical research
- clinical research
- research with respect to health systems and services

- research with respect to the social, cultural, and other factors that affect the health of populations

Regular funding opportunities within CIHR include:

- operating grants
- personnel support
- trainee support
- clinical trials
- group grants (infrastructure support for three or more investigators with CIHR grants involved in an integrated program of research that would benefit from shared resources)

Strategic funding opportunities within CIHR include:

- future training program competitions
- Institute developmental meetings/workshops
- Institute strategic requests for applications
- cross-Institute strategic requests for applications (multiple Institutes partner in a priority area of common interest)
- pan-CIHR crosscutting initiatives (engaging a majority of Institutes)

While CIHR did not agree to establish an institute for CAHC/NHP research, as was initially hoped for, it is taking an interest in the field. Several Institutes are collaborating with the NHPD in identifying strategic research priorities in CAHC/NHPs. Important considerations regarding CIHR's involvement in the field include:

- review procedures and panels for training, personnel and grant applications: will there be sufficient expertise in CAHC/NHPs?
- methodological innovation: how will it be developed and evaluated?

- strategic initiatives: where should the research begin?

Natural Health Products Directorate

Since its creation in 1999, the NHPD has allocated \$1 million per year of its budget to supporting NHP research. As the primary role of the NHPD is as a product regulator and not as a funder of research, it has acted to date as a facilitator and partner in research. When acting alone, the NHPD has a mandate to support research activities related to NHPs alone. To address broader CAHC research issues, the NHPD is collaborating with other partners.

The NHPD has been bringing together stakeholders to identify NHP research needs and has been building partnerships with CIHR and other research foundations. It is also in a position to undertake specific projects to ‘jump-start’ NHP research. These include CIHR/NHPD personnel training awards, curriculum development, seed grants for research projects, etc.

Through its consultations, the NHPD has identified four strategic initiatives (Smith, 4-5):

- building research capacity in an interdisciplinary way (complementary/alternative and conventional, researchers and practitioners) through such initiatives as graduate training programs, network support, training centre grants and curriculum development
- supporting research that is clinically relevant to Canadians, addressing such topics as NHP product standards and quality control, NHP-drug interactions, new research methodologies and the role of NHPs in children
- fostering collaboration and partnership building with other units in Health

Canada such as the Canadian Strategy on HIV/AIDS, CIHR and other health research foundations

- supporting information retrieval and knowledge transfer (database development, patient/practitioner communication) to ensure that Canadians have access to quality information and that research-based information is translated into language that is appropriate for consumers

The NHPD recently sought the advice of stakeholder on its future activities in the area of NHP research. The consultation suggested that, in the short term, the NHPD (O’Hara, i-ii):

- continue to ensure community and practitioner input at all levels (without repeating work that has already been done)
- form a central advisory committee with members who have a wide variety of NHP expertise or experience, and have sub-committees feed into this committee
- continue to focus on the wellness model of health care
- facilitate a process to develop research projects that might be funded in part by the NHPD
- continue to forge partnerships and collaboration that leverage funding from other agencies and encourage them to be more receptive to NHP research
- fund workshops that lead to the sharing of perspectives between conventional and complementary/alternative researchers/practitioners on research methodology
- fund workshops on research methodology in NHP
- establish a network for information exchange and knowledge transfer, especially to facilitate training of NHP researchers

- continue to maintain a priority on product-related matters such as quality control and standardization of NHPs

The NHPD's activities with regard to NHP research are intended to support the proposed new regulatory framework for NHPs in Canada, which includes such activities as generating new information about NHPs, building research capacity, etc. Proposed Natural Health Product Regulations were published in *Canada Gazette, Part I*, December 22, 2001, pp. 4912-4971 (available at <http://www.canada.gc.ca/gazette/part1/pdf/g1-13551.pdf>). The regulations would apply to products falling within the definition of an NHP (see above). NHPs would be considered a subset of drugs under the *Food and Drugs Act*. The main components of the proposed regulations are:

- definitions
- product licensing
- adverse reaction reporting
- site licensing
- good manufacturing practices
- clinical trials
- labelling and packaging

Under the new regulations, the NHPD will be the agency responsible for approving clinical trials involving NHPs.

Workshop on Research Literacy and Capacity

A barrier to research in CAHC/NHPs is lack of awareness, knowledge, experience and skill in research and research methods among complementary/alternative practitioners and educators. A recent workshop identified four key needs (Boon, 2, 10-13):

- a need for more awareness and understanding of the value of research in CAHC/NHP educational institutions, among practitioners and with undergraduates
- a need for mentors, role models and champions for CAHC/NHP research in CAHC/NHP educational institutions
- a need for more training of CAHC/NHP practitioners, educators and students in conducting research and using research findings
- a need for more funding for CAHC/NHP research, training and infrastructure

The workshop made many specific suggestions as to how to meet these needs and identified four strategies as high priority (Boon, 2):

- completion of a CAHC/NHP research needs assessment (under way)
- support for a network of CAHC/NHP researchers and clinician investigators
- development of CAHC/NHP research learning modules
- development of CAHC/NHP research training support programs for faculty

Roundtable on Information and Informed Choice

The dissemination and use of reliable information about CAHC/NHP, as well as the enabling of people to make informed choices about CAHC/NHP, is an ongoing theme in consultations about CAHC/NHP, including consultations among people with HIV/AIDS. A recent Health Canada roundtable on Information and Informed Choice dealt with four broad areas of concern (de Bruyn 2001a):

- sources and systems of expert information
- collecting, evaluating, selecting and presenting accessible information for practitioners and consumers

- public and professional education in receiving and using information
- improving connections, consistency and integration in providing information

Participants made a number of suggestions about how to generate information and knowledge that would address the needs of consumers and practitioners:

- funding for an infrastructure that would support the links between information gathering, clinical practice and community care (the infrastructure could support such activities as the gathering of case reports, pilot studies in preparation of research grant applications, development of methodologies, mentoring of CAHC/NHP researchers, training and personnel awards for CAHC/NHP practitioners/researchers)
- training, funding and support for complementary/alternative practitioners to write up case reports
- systematic reviews of literature relating to products and practices that have been in use in other countries
- controlled pilot studies in institutional settings to foster dialogue and collaboration between complementary/alternative and conventional practitioners
- use of dual-trained practitioners (conventional and complementary/alternative training) to build bridges, design research and interpret evidence

Roundtable on Health Law and Ethics

The use of health care and health products – whether conventional or complementary/alternative – involves

considerations relating to the ethical and legal conduct of health providers, health care facilities and health product manufacturers. These were the subject of a recent Health Canada roundtable on health law and ethics. Among other topics, the areas of discussion included (de Bruyn 2001b):

- the relationship between the practitioner and the person seeking care
- legal and ethical issues raised by the use of CAHC/NHP in diverse settings
- access to CAHC/NHPs
- research ethics boards for research projects involving CAHC/NHPs

The discussion about the relationship between practitioners and people who use CAHC/NHPs is of particular relevance to research on best practices in health care service delivery. Participants noted the need for practitioners who are practiced in (de Bruyn 2001b, 8):

- ongoing learning and modification of clinical practice
- understanding and respecting people's approaches to their health and well-being
- supporting people in making informed choices
- communicating the boundaries of the practitioner's responsibilities
- conveying disagreement or contra-indication

Also relevant to CAHC/NHP research are the participants' concerns about ethics review for research involving CAHC/NHPs (de Bruyn 2001b, 16). Participants noted that the knowledge and judgement required to assess clinical trial protocols for NHPs are significantly different from those in trials of allopathic products. Some participants feared that members of research ethics boards may not be sufficiently knowledgeable about NHPs and may be too conservative when assessing innovative research methodologies. Participants suggested that it would

be challenging for research ethics boards to recruit people with the appropriate expertise in NHPs.

Advancing research priorities

Research Priority-Setting Conference

The 1999 Research Priority-Setting Conference laid out an initial direction for research on NHPs for Health Canada (Priority-Setting Conference, 1). It recommended that research supported by Health Canada:

- be of a seed nature
- give priority to cross-cutting research across disciplines
- be delivered within a framework of an NHP research network
- support research relevant to industry and health care practitioners

The conference also identified five research priorities (Priority Setting Conference, 12):

- a credible and complete database which will allow assessment of knowledge to date
- research on the safety (toxicities, NHP-drug interactions), efficacy and mechanism of action of NHPs (basic, pre-clinical animal studies, clinical studies and long-term follow-up research)
- research to aid in the development of quality control methodologies and the development of standards
- research on consumer usage and health economics
- development of methodologies that can demonstrate the efficacy of NHPs in the contexts in which they are used, which do not lend themselves to the randomized controlled clinical trial (individualized

treatment in relation to multiple aspects of health and lifestyle, unique preparations, incremental dosing)

Research Priorities in NHP-Drug Interactions

The issue of NHP-drug interactions has come up repeatedly in consultations about CAHC/NHP research. The NHPD recently held a conference to identify research priorities in this area (de Bruyn 2002).

In general, participants suggested that priority should be given to research dealing with:

- NHPs that are in high use
- populations that are at risk of NHP-drug interactions (e.g., populations defined by age, gender, diseases or conditions, genetic factors, etc.)
- interactions with drugs that have critical dose requirements
- interactions with potential or known severe outcomes

In the area of biomedical, clinical, and epidemiological research, the four top priorities were:

- to develop methodologies and conduct research to characterize NHPs in use (in their natural form and in prepared formulations), develop standards for NHPs used in research and practice and publish monographs providing a complete characterization of NHPs used in research and practice
- to identify the mechanisms of action of NHPs
- to determine the clinical relevance of potential or theoretical NHP-drug interactions
- to determine the use of NHPs in the population in order to determine the priority to be given to research on a particular NHP,

assess the relative significance of demonstrated NHP-drug interactions and determine the priority to be given to research on potential NHP-drug interactions

In the area of research related to reporting, dissemination and use of information about interactions, the four top priorities were:

- research into early warning systems for NHP-drug interactions (systems and strategies that can be used or developed to provide early indications of potential NHP-drug interactions, including population-based and product-based monitoring)
- assessment of the needs of stakeholders (consumers, practitioners, regulators, distributors, delivery systems) regarding information on NHPs and NHP-drug interactions
- using a focused, population-based approach to determine areas of greatest risk for NHP-drug interactions and mechanisms for collecting information about NHP-drug interactions
- identifying ways to make it easier for stakeholders to report information about adverse drug reactions/drug interactions, to make stakeholders more willing to report information, and to make stakeholders more capable in providing information

Next Steps

As the above summary of recent activities indicates, there is growing momentum in Canada to build research capacity and to advance the research agenda with regard to CAHC and NHPs. Researchers, practitioners, consumers, information providers, industry, government and research funders are actively

looking at specific and concrete ways to move forward.

In this context, there is a potential for synergy between the HIV/AIDS field and the broader CAHC/NHP field. With their long experience in the use of CAHC/NHPs, in research (biomedical, clinical, epidemiological, sociocultural, community-based), in community organization, industry relations, and in consultation and lobbying, people and organizations in the HIV/AIDS field have much to contribute to CAHC/NHP research.

At the same time, the momentum in the broader CAHC/NHP field may help to strengthen the capacity of the HIV/AIDS field to identify, to participate in and to advance research on CAHC and NHPs, particularly research of special relevance to people with HIV/AIDS.

The roundtable on March 10-11, 2002 is intended to explore the potential for synergy – mutual strengthening and collaboration – in several specific areas. These have been selected because they have been identified as areas for action in HIV/AIDS consultations and/or in CAHC/NHP consultations:

- building research capacity
- methodological development
- NHP research
- health services research
- knowledge dissemination and uptake
- building and strengthening liaisons

Brief summaries of these areas follow. These summaries are not meant to be definitive, but are rather meant to identify some recurring themes with regard to the area. The overall objective of the roundtable is, in each of these areas:

- to identify priorities/opportunities
- to select three top priorities/opportunities

- to identify strategies to advance these top priorities/opportunities

Building research capacity

Building research capacity refers to efforts to increase the ability and readiness of individuals and organizations to identify, develop and conduct research on CAHC/NHPs. Some of the needs identified in recent consultations include:

- funding for CAHC/NHP training awards, research projects and research infrastructure
- mentors, role models and champions for CAHC/NHP research
- training in conducting research and using research findings for CAHC practitioners, educators and students
- training and funding for CAHC practitioners to write up case reports
- networks of researchers and practitioners to develop and implement research agendas
- research funding panels with appropriate expertise to review CAHC/NHP research projects
- research ethics boards with appropriate expertise to review CAHC/NHP research projects

Methodological development

CAHC/NHP researchers have emphasized the need to use or develop research methodologies that are appropriate to the therapy under investigation. This can be challenging. For example, what research methods are appropriate when studying practices based on the mind-body dynamic? Or, what research methods are appropriate when dealing with non-standardized therapies (e.g., individualized treatment regimens, incremental dosing of products, use of non-standard products or unique product

preparations, etc.)? While randomized controlled clinical trials may be used or modified in some circumstances, in other circumstances other research methods such as individual case reports, case series, case-control studies, etc. may be needed.

Researchers are asking for meetings and mechanisms by which they can address methodological issues and build bridges between different methodological schools (e.g., with conventional medical researchers). Among the issues to be addressed are types of evidence (What counts as evidence? What evidence is appropriate?) and measures of outcomes (What is being measured? Is the measure appropriate?).

Natural health products research

There have been recurring priorities in consultations about research on NHPs. These have included:

- review and evaluation of existing research
- product standards and quality control methodologies
- methods to characterize NHPs
- safety, efficacy, risks, dosage, indications and counter-indications of NHPs
- mechanisms of action for NHPs
- NHP-drug interactions (biomedical and clinical research)
- utilization of NHPs (widely-used NHPs, specific populations)
- the role of NHPs in managing HIV/AIDS and/or HIV antiretroviral therapy
- the role of NHPs in managing hepatitis C

Health practices/services research

Health practices research includes research to understand complementary/alternative modalities of practices and care, research to document their health outcomes, research to determine their efficacy and

research to establish their cost-effectiveness, etc. Health services research includes research into the ways in which CAHC is provided, research into different types of combinations of CAHC and conventional health care, and research into the costs of CAHC, etc. Suggested areas of activity have included:

- research on the utilization of complementary/alternative practices and practitioners
- the review and evaluation of existing research
- case reports and case series
- controlled pilot studies to build bridges between complementary/alternative and conventional practitioners
- research on models of ‘integrated’ (complementary/alternative and conventional) health care
- research on therapeutic relationships that promote disclosure, informed consent and shared decision-making (particularly with conventional practitioners about CAHC/NHPs)
- research on the efficacy and cost-effectiveness of complementary/alternative practices or care
- The role of complementary/alternative practices or care in managing HIV/AIDS and/or HIV antiretroviral therapy
- the role of complementary/alternative practices or care in managing hepatitis C

Research dissemination and uptake

Consumers of CAHC/NHPs are looking for reliable, accessible and easy-to-understand information about CAHC/NHPs. Consequently, health intermediaries and information providers are working to evaluate and select information, to present information in ways that will be accessible to consumers, and to increase the skills of practitioners and consumers in working with information about CAHC/NHPs. Suggested ways to facilitate the dissemination and uptake of research have included:

- systematic reviews of research
- development of standardized concepts and terminology across CAHC modalities
- directories and networks that facilitate access to experts
- training for health intermediaries in understanding and evaluating research findings (critical appraisal skills, knowledge of research methods, knowledge of statistics and knowledge of the therapy under consideration)
- education of conventional practitioners about CAHC/NHP
- education of CAHC practitioners about conventional health care and health research

Building or strengthening liaisons

The effort to promote research on CAHC/NHPs is gathering momentum in Canada. People with HIV/AIDS, their national and community organizations and their practitioners have contributed to this momentum. However, other parties and stakeholders – other health communities and organizations, CAHC practitioners, industry and Health Canada – have also contributed. What are some specific ways to build or strengthen liaisons between the HIV/AIDS field and the broader CAHC/NHPs field?

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Natural Health Products Research in Children and Youth: A Priority-Setting Conference

Toronto, Ontario. March 17 – 18, 2002

sponsored by

*Natural Health Products Directorate and
The Hospital for Sick Children Foundation*

*report prepared by
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The views expressed in this document are those of the conference participants and do not necessarily represent those of Health Canada.

Executive Summary

As part of its mandate to facilitate the research of natural health products (NHPs), and in keeping with its objective to foster collaboration and partnership building, the Natural Health Products Directorate (NHPD) at Health Canada continued its relationship with The Hospital for Sick Children Foundation by co-hosting a second conference on NHP research in children and youth on March 17-18, 2002. The participants included academics, researchers, paediatricians, practitioners of complementary and alternative health care (CAHC), parents and hospital administrators, as well as representatives from the NHP industry and various government agencies.

The conference participants were asked:

- to identify the current state of NHP-based research relative to children and youth;
- to facilitate dialogue and promote networking within and between the conventional and complementary and alternative health care communities; and
- to establish a research agenda and identify priorities that will assist in the development of the evidence base that will both provide Canadians with the information required to make informed decisions about NHPs and their use with children, and that will also support the regulatory framework proposed by the NHPD.

Through group and plenary discussions, the participants identified four research priorities to address these objectives.

1. **Create a usage database and evaluate current data on NHPs relative to children.** It would be helpful to identify the NHPs that are most commonly used by Canadian children and the conditions for which NHPs are most frequently

used in the treatment of children, as well as to determine what research has already been done in this area.

- a. **Undertake a national survey** to determine who is using what products to treat which conditions, and to determine when and why they are using these products.
- b. **Piggyback the national survey onto existing surveys** such as the national census, the National Longitudinal Survey of Children and Youth (supported by Human Resources Development Canada) and similar existing surveys.
- c. **Identify, synthesize and evaluate existing data on NHPs.** Existing databases on NHPs should be evaluated to ascertain if they can provide useful information on NHP use by children. This evaluation might involve the use of systematic reviews and meta-analyses.
- d. **Work with the Cochrane Collaboration,** an international organization that prepares and maintains

systematic reviews that the general populace can use to make more informed decisions about various health care therapies and products. The Cochrane Collaboration may be helpful since it already has fields or networks that pay particular attention to complementary medicine and child health.

- e. **Establish a National Centre of Excellence (NCE)** for NHPs and CAHC, with nodes established by geography and expertise. Local geographical needs and sensitivities would be considered, as would the expertise of various specialities and practices. Paediatrics would be one of the top three priorities for this NCE.
2. **Explore both basic and clinical science issues.** There are broad gaps in our knowledge of NHPs and their use by children and youth that can only be bridged by basic science and clinical research.
 - a. **Identify areas of high need and/or high prevalence of use.** The health conditions that are most commonly encountered in paediatric care and the NHPs that are used most frequently by children should be the primary focus of preliminary research. Possible areas of investigation could include the pharmacokinetics of NHPs as well as drug-NHP interactions and NHP-NHP interactions.
 - b. **Build a basic science knowledge base.** After identifying the diseases that should be the focus of research, the studies will seek answers to similar questions about the use of NHPs to treat specific diseases so that a matrix of information can be constructed.
 - c. **Collaborate, co-operate and communicate with existing networks, practitioners and NHP experts.** Researchers studying NHPs and children should work with existing networks (e. g., the Canadian Paediatric Clinical

Conference Objectives

- Identify the current state of NHP based research relative to children and youth.
- Facilitate dialogue and promote networking within and between the conventional and CAHC communities
- Establish a research agenda and identify priorities that will assist in the development of the evidence base that will both provide Canadians with the information the need to make informed decisions about NHPs and their use by children, as well as support the regulatory framework proposed by the Natural Health Product Directorate.

Pharmacology Network) or partner with the Canadian Institutes of Health Research (CIHR) where research into NHPs and their use by children could fit into existing programs.

3. Set priorities for knowledge translation and transfer to consumers. Consumers want accurate and intelligible information on NHPs, especially when using these products with their children. They want to have confidence in both the products they take (with respect to efficacy, safety and quality) and in the information they receive (about product claims and content).

- a. Identify quality information on the Internet.** Websites that provide monographs informed by the most recent evidence-based medical research on the more commonly used NHPs could appear on a list of approved sources of information. This could be part of an initiative, facilitated by the NHPD, to establish a central clearing house for information dissemination.
- b. Identify professionals who are knowledgeable about NHPs.** While many people offer information and advice about NHPs, there is a wide range of expertise and competence. Only those who are knowledgeable should be dispensing and providing advice about NHPs.
- c. Accredite pharmacies and health food stores.** Pharmacies and health food stores that have properly trained personnel onsite can be accredited as centres that provide quality information on NHPs. However, the impression must not be fostered that the NHPD is trying to regulate in an area of provincial jurisdiction.

d. Educate the end consumer. To provide consumers with more and accurate information about NHPs, pamphlets and posters could be available in pharmacies, health food stores and the offices of health care professionals; curricula in high schools could be expanded; and public forums could be hosted.

4. Research ethical questions related to the health care of children and research methodologies for the study of NHP use in children. Policies that guide ethical research involving children need to be better developed. There is also a need to establish guidelines for NHP research that respect both accepted scientific methods and the various paradigms of NHP use.

- a. Review the Tri-Council Policy statement.** After a review of the Tri-Council Policy statement governing the conduct of ethical research in humans, a companion document could be developed that would specifically address ethical concerns about research involving children.
- b. Review international law and policy.** Since other jurisdictions may have already undertaken the task described above, a review of international law and policy could avoid unnecessary duplication and identify uniquely Canadian needs.
- c. Determine potential barriers to NHP research in children.** Through consultation and surveys of paediatric research ethics boards (REBs) and various research councils (such as CIHR), potential barriers to NHP research with children could be identified. Having identified possible barriers, it would be possible to design strategies to resolve them.
- d. Start with the research methodologies that are known.** There are accepted scientific research methodologies that could be applied to the research of NHP use in children, including randomized clinical

trials. In addition, observational studies and epidemiological studies are both accepted methods and are adaptable to NHP research.

e. Establish clinical trial research guidelines for children and youth.

NHPs are often used in a specific cultural or paradigm context, and/or as part of individualized treatments that are not always easily adapted to randomized trials. The levels of evidence that have traditionally been accepted in CAHC research are often not the same as those for conventional medicine.

During the working and plenary sessions, the participants shared their expertise, experiences and opinions with considerable enthusiasm and goodwill. It was noted that research on NHP use in paediatric populations should also include the fetus, since the NHPs that a mother may take could also affect the unborn child. Several participants stressed that children and youth populations are often ‘forgotten populations’ in health care research. Too often, results from research completed on adults are simply extrapolated to this younger population.

Introduction

As part of its mandate to facilitate the research of natural health products (NHPs), and in keeping with its objective to foster collaboration and partnership building, the Natural Health Products Directorate (NHPD) at Health Canada continued its relationship with The Hospital for Sick Children Foundation (HSCF) by co-hosting a second conference on NHP research in children and youth on March 17-18, 2002. The first collaborative conference took place on November 30 – December 1, 2001 in Toronto and considered funding priorities for NHP research in children and youth.

The March 2002 conference was held at the Metropolitan Hotel in Toronto, Ontario. The participants included academics, researchers, paediatricians, practitioners of complementary and alternative health care (CAHC), parents and hospital administrators, as well as representatives from the NHP industry and from various government agencies, including the National Research Council of Canada (NRC), the Therapeutic Products Directorate and the NHPD. The conference was co-chaired by Michael J. Smith, Senior Advisor at the NHPD, and Sunita Vohra, a paediatrician and researcher at the HSCF in Toronto.

The objectives for the conference were threefold. The conference participants were asked:

- to identify the current state of NHP-based research relative to children and youth;
- to facilitate dialogue and promote networking within and between the conventional and complementary and alternative health care communities; and
- to establish a research agenda and identify priorities that will assist in the development of the evidence base that will both provide Canadians with the information required to make informed decisions about NHPs and their use with children, and that will also support the regulatory framework proposed by the NHPD.

Following welcoming remarks by Michael J. Smith of the NHPD and Gwen Burrows of the HSCF, the participants introduced themselves. To provide background information for the working sessions that would follow, a variety of speakers gave talks on the use of NHPs by children and youth, drawing on their particular expertise or experience. Allison McCutcheon of the Department of Botany at the University of British Columbia spoke on “Quality Control and Product Standard Research for NHPs,” while Sunita Vohra offered insights from both her work as a paediatrician and as a clinical researcher. Christine Harrison, a bioethicist at The Hospital for

Sick Children, spoke on “Natural Health Products and Children: The Ethics of Care and Research.” Sydney MacInnis gave a parent’s perspective, while Maureen Horne-Paul, a naturopathic doctor, provided the point of view of a CAHC practitioner. Each participant was provided with a hard copy of the presentations of the various speakers as well as a summary document. A brief summary of these presentations follows.

Key Issues in Paediatric Research

- There are differences in paediatric vs. adult absorption/distribution/metabolism/excretion.
- There is the potential for different adverse reactions than those documented in adult populations.
- There are concerns about the potential long-term effects of exposure during times of peak growth and development.
- The paediatric population is a more vulnerable population.
- Working with a paediatric population raises issues of autonomy, informed consent/assent and patient compliance.

Key Issues for Natural Health Products Research

- Similar products can vary widely from brand to brand with respect to quality, constituents, concentration, standardization, dosage form or units, markers/marker content, plant species and parts used.
- ‘Quality’ tends to mean different things to different people, including the amount of the active ingredient present in the product; that the product is safe, efficacious and consistently manufactured; that the correct

plants/parts were used; and/or that the product is pure.

- Product purity can be adversely affected by contamination (such as by microorganisms, heavy metals or pesticides) or by adulteration (i.e., the intentional addition of undeclared substances).
- Most adverse drug reactions are due to poor quality – e.g., when an incorrect plant is unintentionally substituted for the correct plant due to misidentification; or when the product contains contaminants or adulterants
- Product potency is a complex issue when dealing with botanical medicines and other multi-ingredient products.
- Standardized products are products that have a consistent marker content, ensuring product consistency from batch to batch. However, markers are not necessarily the active ingredient(s) that give that product its therapeutic benefit. Different manufacturers might use different markers for the same product and, even when they use the same marker, they might standardize the product to different concentrations of the marker. Therefore, even with standardization procedures in place, the potency of products is not assured from brand to brand.
- Active ingredients are not identified for the majority of botanical medicines.
- Relevant biological activity assays are required to obtain meaningful measurements of potency.
- While the interaction between drugs and NHPs (particularly botanical medicines) is increasingly receiving attention, much more research needs to be completed.

Ethical Considerations

- The National Council on Ethics in Human Research (NCEHR) states that research involving children seeks knowledge that may

protect children from harm, benefit individual children and/or benefit children as a group.

- Ethical values and principles at stake:
 - informed choice;
 - respect of various perspectives;
 - trust;
 - safety; and
 - justice.
- Ethical research includes the selection and achievement of morally acceptable ends, and the morally acceptable means to those ends.
- Guiding ethical principles:
 - respect for human dignity;
 - free and informed consent;
 - vulnerable persons;
 - privacy and confidentiality;
 - justice and inclusiveness; and
 - the balancing of harms and benefits.

Parent's Perspective

- Parents are often drawn to the use of NHPs for the care of their children because of a curiosity with natural healing and gaps in the care that conventional medicine can provide.
- Both forms of care have their successes and failures.
- The use of CAHC does not supplant or replace the use of conventional medicine; instead, CAHC complements conventional medicine.
- Parents are often left with the task of integrating conventional and CAHC therapies and products.
- Parents must often rely on other parents as well as on their own initiative and skill as they seek information on CAHC therapies

and products, and must adapt their lifestyle to the new demands of alternative diets and practices.

Possible Research Priorities

- NHPs are used as much for health promotion as for the treatment of illness.
- Which NHPs are being used by whom to treat which conditions?
- There is a need for information on NHPs and children relative to use, access, costs and how NHP use affects the health of children.
- Which NHPs pose the greatest risk or potential for harm and the greatest potential for benefits?
- What are appropriate standards for quality and safety in NHPs, and how do these standards compare with those set for pharmaceutical products and drugs? Are the two sets of standards comparable?
- Do NHP research trials need the same scientific standards as those used for pharmaceuticals? What research methodology is appropriate?
- Do we have good endpoints for clinical trials in children: are they valid, reliable and sensitive to change?
- Should we continue to do systematic reviews and meta-analyses of CAHC therapies and products?
- What role should patient/consumer preferences play in setting research priorities?
- Why do consumers use NHPs with children? Are they well informed? How did they become informed? Were their sources of information of high quality?

After a morning of presentations followed by lunch, the facilitator reviewed the conference objectives and the steps by which the discussions would

proceed. He noted that while the NHPD might not be able to act on every recommendation proposed by the participants, it was nevertheless important for each working group to provide clear and detailed advice for each of their proposals. The participants (including the presenters) then assembled into four pre-selected working groups. Each working group concurrently met for 90 minutes to consider a variety of priorities and options that would address the objectives that had been set for the conference. They eventually narrowed their proposals to a list of not more than five priorities. (The priorities suggested by each working group are recorded in Appendix D) During the plenary session that followed, a reporter from each group provided an overview of that group's priorities to the other participants. Through consultations with the participants, these priorities were consolidated into the following preliminary list of priorities.

Preliminary List of Priorities

1. Develop a usage database – what is being done by whom to treat what.
2. Evaluate the existing data on NHPs relative to children.
3. Determine the standardizations that need to be set for NHPs to enhance their quality.
4. Explore the basic science issues related to the use of NHPs with children, particularly with respect to:
 - a. NHPs and drug interactions; and
 - b. NHPs and pharmacokinetics.
5. Explore the clinical science issues related to the use of NHPs with children, particularly with respect to:
 - a. clinical trials involving NHPs when there are no other recognized or accepted treatment for a particular condition;

- b. observational research at sentinel sites; and
 - c. drug interactions and pharmacokinetics.
6. Set priorities for knowledge translation and transfer to consumers.
7. Research ethical questions related to the health care of children.
8. Monitor outcomes of initiatives to improve the quality, efficacy and safety of NHPs as well as the translation and transfer of information to enhance consumers' informed choice.
9. Research methodologies for the study of NHP use in children.
10. Research dosage considerations – i.e., the safe and therapeutic dosages for NHP use in children.

Final List of Priorities

On the second day of the conference, the participants voted to further consolidate and narrow their focus to four research priorities. These priorities were:

1. Create a usage database and evaluate current data on NHPs relative to children.
2. Explore both basic and clinical science issues pertaining to:
 - a. drug interactions and pharmacokinetics;
 - b. clinical trials involving NHPs when there are no other recognized or accepted treatment for a particular condition; and
 - c. observational research at sentinel sites.
3. Set priorities for knowledge translation and transfer to consumers.
4. Research ethical questions related to the care of children, and research methodologies for the study of NHP use in children.

Working groups for each of these four research priorities were formed by participant self-selection. During the working session that followed, each working group devised strategies that would advance their particular priority. The opportunities and

challenges that may be encountered in the implementation of each strategy were considered and discussed. A reporter from each group once again presented their work to the other participants during the subsequent plenary session.

In the third and final working session, the working groups discussed the ‘next steps’ that could be taken to implement each strategy that they had identified during the previous session. The working groups provided concrete and practical steps to guide the implementation of the various strategies that were chosen for the research priority that had been the focus of their attention. The ‘next steps’ were to provide a map that would describe who would be doing what, and when they would be doing it. Possible sources of funding (if applicable) were also to be identified.

The results of these deliberations are described in the remainder of this report. In the discussion that follows, each priority is introduced by background information describing the relevance of that priority. Strategies and possible next steps for advancing the proposal are then presented, sometimes in separate sections and sometimes blended into one discussion.

Research Priorities, Strategies and Next Steps

Create a Usage Database and Evaluate Current Data on NHPs Relative to Children

Background

Prior to studying the efficacy, safety and quality of NHPs, it would be helpful to direct this research toward those NHPs that are most commonly used by Canadian children. It would also be helpful to know which conditions are most frequently treated with NHPs, either in conjunction with conventional therapies and

products or with NHPs alone. Similarly, it would be prudent to review existing data on NHPs to determine what research has already been done, to avoid duplication of efforts. Has that research been sufficiently rigorous? Have adverse reactions occurred when particular NHPs are taken or used in certain ways?

Strategies

- 1. Undertake a national survey** to determine who is using what products to treat which conditions, and to determine when and why they are using these products. Initially, pilot surveys could be taken in physicians’ offices (both general practitioners and paediatricians) and perhaps through the practices of midwives and obstetricians, and in selected paediatric hospitals. Once the survey has been piloted and validated, a national survey could be undertaken at selected sentinel sites (such as clinics in paediatric hospitals and public health clinics where larger numbers of children are treated), at pharmacies (using touch screen info kiosks) and in commercial establishments where end-users are purchasing products. This surveying could be extended to include CAHC practitioners, specialty magazines (e.g., parenting magazines) and trade shows.

The survey would involve various stakeholders in the process of NHP research. It would help to raise public awareness of NHPs, and the purpose and results of the survey could be publicized through both scientific and popular media. To achieve results that are as representative of the Canadian population as possible, the researchers must be careful to ensure that the selection of participating sites does not inadvertently pre-select the data (i.e., avoid selection bias). They must verify that respondents are willing to disclose information on the survey, especially when the surveys are administered in practitioners’ offices, since many users of NHPs do not routinely divulge this information to their physicians. The

surveys would need to be constructed in a way that is culturally sensitive, and their administration and collection would require close coordination. The cost of such a national survey could be considerable.

2. **Piggyback the national survey onto existing surveys** such as the national census, the National Longitudinal Survey of Children and Youth (supported by Human Resources Development Canada) and similar existing surveys. By employing these already well-established surveys, it would be possible to collect information on a continuous and reliable basis. It would also be possible to study phases in NHP use and to focus on specific topics of interest. As is often the case, gaining funding for such an initiative might prove challenging.
3. **Identify, synthesize and evaluate existing data on NHPs.** Databases on NHPs that already exist should be evaluated to ascertain if they can provide useful information on NHP use by children and youth. Databases such as the Pharmacist's Letter and NAPRALERT (NAtural PRoducts ALERT) could be assessed, since they are well referenced; are updated daily; consider dosage range, efficacy and contraindications; and translate research published from other languages. Other databases that might be reviewed include the Lawrence Review of Natural Products.

Since an enormous amount of information would need to be evaluated and synthesized, this might require people who are particularly skilled in information technology as well as the use of systematic reviews and meta-analyses. A virtual network and/or coordinating centre could harness the skills and efforts of many experts in these fields. It might also be

possible to partner with similarly interested groups, particularly scientific journals that occasionally seek review articles.

However, since these databases can only be fully accessed by subscription, there would be certain costs involved. Some databases and reviews are more user-friendly than others and it would require varying degrees of skill and expertise to successfully navigate them for our purposes. Public access to databases on NHPs and their use in the health care of children could help Canadians to make more informed choices. As just mentioned, these databases are often accessible through subscription only and are usually written in highly technical language that is intelligible only to experts. Consequently, these factors would normally place the databases beyond the grasp of most consumers. These concerns are discussed later in this report in the section on information translation and transfer.

A further concern involves the ownership of the data. There may be proprietary rights and/or licensing concerns that prevent data, once retrieved, from being published or used in the desired way. It is noted that in Europe and the USA, these matters are being addressed through legislation that governs disclosure.

4. **Possible collaboration with the Cochrane Collaboration** merits particular comment. The Cochrane Collaboration is an international organization that prepares and maintains systematic reviews that the general populace can use to make more informed decisions about various health care therapies and products. It has fields or networks that pay particular attention to complementary medicine (under the direction of Dr. Brian Berman at the University of Maryland School of Medicine) and child health (coordinated by Dr. Terry Klassen, Chair of the Department of Paediatrics at the University of Alberta in Edmonton). Since these fields or networks of the Cochrane Collaboration would support collaborative review groups, it may be possible to forge a partnership with

them. Such an undertaking would increase positive interactions between members of the Cochrane Collaboration and CAHC practitioners and researchers. It would permit the systematic review and evaluation, by an existing network of experts, of current data on NHP use by children and youth. Where appropriate, additional systematic reviews and meta-analyses could be undertaken.

Next Steps

1. **Establish a National Centre of Excellence (NCE) for NHPs and CAHC**, with nodes established by geography and expertise. Local geographical needs and sensitivities would be considered, as would the expertise of various specialities and practices. Paediatrics would be one of the top three priorities for this NCE. This recommendation would be directed at networks of practitioners, funding agencies, universities, hospitals, industry and the general public. By working with a broad base of stakeholders – viz., researchers, practitioners and consumers – and by forming links with national organizations (e.g., the Canadian Paediatric Society), awareness of the work and goals of this NCE would be increased. The NCE would establish review criteria for its database, enhance research capacity via training and education, and contribute to knowledge transfer.

It is envisioned that seed money might be derived from the NHPD with ongoing funding coming from CIHR. Matching funding might be accessed from local foundations. The NCE should be structured in such a fashion that corporations can make tax-deductible donations to its work.

Establishing this NCE within six months to one year would be the first priority. It is

hoped that a database could be functional within one year.

2. **Do an environmental scan** to identify existing databases. This task could be undertaken by the NHPD and Health Canada. The scan would identify existing data on NHPs as well as interested and qualified individuals. By completing such an environmental scan, it would be possible to avoid duplicating previous efforts and to identify when these efforts have not sufficiently encompassed the unique needs of Canadians.

This undertaking could be one of the first projects of the NCE described above. For the data gleaned by this scan to remain current and comprehensive, ongoing review and monitoring would be necessary.

Explore Both Basic and Clinical Science Issues

Background

There are broad gaps in our knowledge of NHPs and their use by children and youth, which can only be bridged by basic science and clinical research. Some of these gaps relate to the pharmacokinetics of NHPs in general, but particularly when they are used by children. Other knowledge gaps include the interactions between NHPs and drugs, and even between NHPs and other NHPs, since these are not well studied or understood. Basic science and clinical research needs to be undertaken in a systematic fashion to set priorities and close the gaps.

Strategies

1. **Identify areas of high need and/or high prevalence of use** – i.e., areas of paediatric health care that have particularly high needs, and NHPs that are used most frequently. The health conditions that are most commonly encountered in child and youth health care

should be a primary focus of preliminary research. This initial research can lead to more exacting clinical trials that will be more rigorous. Possible areas of investigation could include the pharmacokinetics of NHPs as well as drug-NHP and NHP-NHP interactions.

Next Steps: Establish the criteria for deciding key areas of research. The following criteria might be considered. The more criteria that are met by a particular area of high need or high prevalence, the higher priority that area of research merits.

- prevalence of condition
- NHP utilization
- burden of illness (individual, familial, socioeconomic, etc.)
- efficacy of current therapy
- existing interest / research capacity / funding potential

The development of research criteria also aids funders to identify priorities when requests for proposals are made.

Based on these criteria, four areas of clinical concern were suggested as the focus of preliminary research: inflammatory diseases, infectious and immune diseases, respiratory diseases and mental illnesses.

2. **Build a basic science knowledge base.** After choosing to focus on four highly prevalent conditions – i.e., inflammatory diseases, infectious/immune diseases, respiratory diseases and mental illnesses – it would be possible to create a matrix showing information that would be sought through research. For each of these conditions, the following questions or areas of research could be the focus of

efforts, thereby creating the matrix of information that is constructed in the following figure.

- What is the quality of the NHPs used to treat the condition?
- What formulations are used and which are more effective?
- What is the most efficacious dosage?
- Are there safety and toxicological issues; are there harmful interactions that must be considered; can too large a dosage be toxic?
- What are the pharmacokinetics of the product?
- How does the product affect the metabolism of the patient with the disease?
- What is the mechanism of action of the product?
- Who is using the product and for what conditions; how effective is it?
- Have clinical trials tested this product for this condition?
- How is the product being utilized? Is information on the product available to consumers? Has there been a synthesis of data concerning this product relative to this condition, and if so, where?
- Does the use of this product for the treatment of this condition raise any ethical questions?

Next Steps: Use the matrix and the aforementioned research criteria to identify high burden / high prevalence areas.

3. **Collaborate, co-operate and communicate with existing networks, practitioners and NHP experts.** Researchers who are studying NHPs and children should work with existing networks – e.g., the HIV/AIDS clinical trials network and the Canadian Paediatric Clinical Pharmacology Network (CPCPN). The CPCPN was recently established as a network linking six universities across Canada (UBC, Manitoba,

Western, McMaster, Toronto and Montreal). It is comprised of experts in drug research involving children.

Attempts to forge such collaborations may raise issues concerning the credibility of NHP research and the role of NHPs in patient care, and may expose the tensions that can exist when different therapeutic cultures, agendas and paradigms come into contact with each other. However, because consumers/patients are using NHPs in increasing numbers, there is a need to study the safety and efficacy of these products. Even if some practitioners are uncomfortable with or are uncertain about the use of NHPs, it was the view of the conference participants that this reticence could not preclude the study of these products.

It will be challenging to build the research teams that can properly advance all three strategies listed above. Moreover, as before,

acquiring sufficient funding could also be problematic. Nevertheless, the opportunities to conduct more comprehensive and advanced research, to foster greater co-operation and communication, and to improve our knowledge of NHPs significantly outweigh these concerns. There is tremendous public interest and support for research in this area, including support from some high profile champions. And there is an increasing willingness in many funding agencies and foundations (such as The Hospital for Sick Children Foundation) to fund and/or support NHP research.

Next Steps: Immediately undertake collaborative ventures. The CPCPN is meeting in April, 2002. A participant from this conference will be attending,

Next Steps: Partner with CIHR institutes where research into NHPs and their use with children and youths can fit into existing programs.

Figure 1: Basic Science and Clinical Research Matrix

Condition \ Focus	Inflammatory diseases	Infectious/ immune diseases	Respiratory diseases	Mental Illness
Quality				
Formulation				
Dosage				
Safety / toxicology				
Pharmacokinetics				
Metabolism				
Mechanism				
Usage / outcomes				
Clinical trials				
Utilization				
Knowledge transfer				
Data synthesis				
Bioethics				

Next Steps: Consider the establishment of a National Centre of Excellence. To assist this endeavour, a workshop should be held that would assist its participants:

- to frame a NCE proposal;
- to identify appropriate themes (NHP, CAHC, Paediatrics); and
- to identify groups that could be partners in the application.

Set Priorities for Knowledge Translation and Transfer to Consumers

Background

Consumers want accurate and intelligible information on NHPs, especially when it comes to the use of these products with their children. They want to have confidence in both the products that they take (with respect to efficacy, safety and quality) and in the information that they receive (about product claims and content). There is concern that sources of credible information are scarce or difficult to access or understand, while some easily accessed sources may provide inaccurate information. The needs of the consumer – the end user – must be considered when products are designed.

Strategies

1. **Identify quality information on the Internet.** The Internet has the potential to be a source of reliable and credible information in user-friendly language that the general public can understand. Some websites provide monographs, informed by the most recent evidence-based medical research, on the more commonly used NHPs. Sites that provide this level of quality service could appear on a list of

approved sources of information. This would distinguish these sites from those that provide less credible information or use technical language that is difficult for the average consumer to understand.

2. **Identify professionals who are knowledgeable about NHPs.** While many people offer information and advice about NHPs, there is a wide range of expertise and competence. Only those who are knowledgeable should be dispensing and providing advice about NHPs. This is particularly true when concerns exist about interactions between prescription drugs and NHPs, or between over-the-counter drugs and NHPs. Continuing education courses should be available for professionals, such as pharmacists, to keep them abreast of current data on NHPs. Information from current research should be ‘translated’ into readily understood language and disseminated to professionals, consumers and manufacturers alike. This process should be information-driven rather than market-driven. Admittedly, such a proposal would have to overcome financial challenges and obstacles to information transfer.
3. **Accredit pharmacies and health food stores.** Pharmacies and health food stores that have properly trained onsite personnel can be accredited as centres that provide quality information on NHPs. Existing initiatives by the Canadian Pharmacist’s Association and the Canadian Health Food Association (CHFA) to educate their memberships concerning NHPs should be encouraged to continue.

Several challenges could arise with this strategy. A curriculum would need to be developed to ensure that personnel (whether in pharmacies or health food stores) are properly trained, and such accreditation would need to win the acceptance of both providers and consumers. Furthermore, the impression must not be fostered that the NHPD is trying to regulate in an area of provincial jurisdiction. Finally, such an

undertaking could be costly, and it is not clear where funds would be obtained.

4. **Educate the end consumer.** To provide consumers with more and accurate information about NHPs, a number of venues could be used to disseminate quality information. Pamphlets and posters could be available in pharmacies, health food stores and the offices of health care professionals. Curricula in high schools that teach students about health could be expanded to include the potential benefits and risks of NHPs. Community forums could also be a venue where information could be provided to the public.

Finding sites that are both appropriate and willing to participate could be challenging. Such a program could be costly, and would not likely have ready and obvious benefits. The literature must be written in such a way that generic products are discussed rather than specific brands or lines.

Next Steps

1. **Establish a central clearing house for information dissemination.** Information endorsed by Health Canada would be made available to consumers via an Internet site and via brochures and information sheets that would be distributed to health care professionals, health food stores, pharmacies, community health centres, etc. The creation of a central clearing house would be facilitated by the government, in partnership with industry, the CHFA, professional associations (pharmacists, CAHC professionals, etc.) and professional societies. Advertisements in the media would alert the public to the existence of a central clearing house that is providing credible, accurate and intelligible information on NHPs. Within the next six months, partners for this

project could be identified and the infrastructure necessary for its activation could be created. Information that would be disseminated to the public could be organized during the next year.

2. **Actively promote accreditation process.** While the creation of a central clearing house of information is a more passive process, the accreditation of individuals who are knowledgeable in information concerning NHPs would require active outreach. By attending and speaking at professional conferences, tradeshow and public events about the benefits of accrediting certain individuals who are knowledgeable in NHPs, it would be possible to stimulate interest in this type of certification. Consumers would prefer to consult properly trained and certified personnel, and providers such as pharmacists and health store employees would recognize an opportunity to promote their services. Such accreditation would be completely voluntary, and could become part of professional continuing education requirements. It is expected that it would take approximately one year to design and implement such an accreditation process.

Research Ethical Questions Related to the Health Care of Children, and Research Methodologies for the Study of NHP Use in Children

Two groups of participants came together to discuss two separate topics. Consequently, strategies one, two and three focus on ethics, while strategies four and five focus on research methodologies.

Background

The Tri-Council Policy statement for ethical research in humans already exists and must be taken into account when NHP research involving humans is proposed. However, the section of that policy that deals with ethical research involving children is

not well developed. Helping to improve and expand this section would be a worthwhile endeavour, with specific attention being paid to the issues relevant to CAHC.

There is a need to establish guidelines for NHP research that both respect accepted scientific methods and the various paradigms of NHP use. It is often stated that the manner in which NHPs are sometimes used in older, more traditional therapies makes it difficult (if not impossible) to evaluate NHPs by the current gold standards of recognized scientific research (although this concern is not unique to NHPs). Consequently, those who hold this view suggest that new methods for the study of NHPs must be developed. Presumably, similar concerns would be raised for the study of NHP use in children.

Strategies

1. **Review the Tri-Council Policy statement.** After a review of the Tri-Council Policy statement governing the conduct of ethical research in humans, a companion document could be developed that would specifically address ethical concerns pertaining to research involving children. The companion document would focus on the ‘best interests of the child,’ although such interests can, admittedly, be difficult to define.
2. **Review international law and policy.** Other jurisdictions may have already undertaken the task described in the first strategy. Accordingly, a review of international law and policy could avoid unnecessary duplication. However, it would be necessary to evaluate any international laws and policies in terms of the unique needs of Canadians.

Next Steps for strategies 1 and 2: The Hospital for Sick Children Foundation and the NHPD could facilitate the creation of a working group and a larger advisory group of relevant stakeholders (including conventional and CAHC practitioners, and representation from the National Council on Ethics in Human Research and the Canadian Paediatric Society). The HSCF would fund this project, including the costs of hiring a research assistant and a consultant to write the document, and the costs of meetings of the group members. The project would require at least one year to complete.

3. **Determine potential barriers to NHP research in children.** Through consultation and surveys of paediatric research ethics boards (REBs) and various research councils (such as CIHR), potential barriers to NHP research with children could be identified. Having identified possible barriers, it would be possible to design strategies to resolve them.

Next Steps: The NHPD would encourage academic researchers to develop a team of experts in NHPs, research with children, and survey research to develop and submit a grant application to CIHR.

4. **Start with known research methodologies.** There are accepted, scientific research methodologies that could be applied to the research of NHP use in children, including randomized clinical trials. In addition, observational studies and epidemiological studies are both accepted methods and are adaptable to NHP research. Existing research methodologies, including international sources, should be reviewed for appropriate strategies. As always, research methods must place patient safety first and must use valid and reliable outcome measures.
5. **Establish clinical trial research guidelines for children and youth.** Through consultation with paediatric REBs, CIHR, and the Tri-Council, methods to access information could be

developed. There are a number of challenges that would need to be considered when research methods and guidelines are designed. Like some conventional health care research, treatments involving NHPs are often part of a multi-treatment therapeutic approach. NHPs are often used in a specific cultural or paradigm context, and/or are part of individualized treatments that are not easily adapted to randomized trials. There is ongoing debate/discussion concerning the levels of evidence that have traditionally been accepted in CAHC research, since these are often not the same as those for conventional medicine.

Conclusion

During the working and plenary sessions, the participants shared their expertise, experiences and opinions with considerable enthusiasm and goodwill. It was noted that research on NHP use in paediatric populations should also include the fetus since the NHPs that a mother is taking could also affect the unborn child. Several participants stressed that children and youth populations are often ‘forgotten populations’ in health care research. Too often, results from research completed on adults are simply extrapolated to this younger population.

At the end of the second day, Michael J. Smith from the NHPD and co-chair of the conference, thanked the participants for their hard work and useful contributions. He welcomed the many recommendations that had been made during the two days of discussions, while acknowledging that not all of them fell within the jurisdiction of the NHPD. Nevertheless, he reassured the participants that the information and ideas generated during the conference would be reviewed with great interest, would be disseminated to the appropriate parties and would form the basis for further endeavours by the NHPD.

Gwen Burrows of The Hospital for Sick Children Foundation – a co-sponsor of the conference – also expressed her gratitude to the participants and noted that the HSCF appreciates the contribution that this conference will make to the foundation’s goals of supporting paediatric care, research and education.

Appendix A Participants List

Walid Aldoori Whitehall-Robins Mississauga, Ontario	Maureen Horne-Paul Naturopath Kingston, Ontario	Nancy Morse Nutricia Canada Inc Kentville, Nova Scotia
Susan Baker American Academy of Paediatrics Children's Hospital of Buffalo Buffalo, New York	Melissa Johnson Health Canada Ottawa, Ontario	Doug Richardson Parent Aurora, Ontario
Lola Baydala Misericordia Child Health Clinic Edmonton, Alberta	Francois Jooste Natural Health Clinic Smithville, Ontario	Michael Rieder Children's Hospital of Western Ontario London, Ontario
John Burgess Rockingham Pharmasave Halifax, Nova Scotia	Bonnie Kaplan University of Calgary Calgary, Alberta	Paul Saunders Canadian College of Naturopathic Medicine North York, Ontario
Peter Chan Health Canada Ottawa, Ontario	Sid Katz University of British Columbia Vancouver, British Columbia	Jackie Shan CV Technologies Inc Edmonton, Alberta
Lawrence Cheng Chamber of Chinese Herbal Medicine of Canada Toronto, Ontario	Valérie Lanctot-Bedard Guilde des Herboristes Canadian Coalition of Herbal Associations South Stukely, Quebec	Planning Team
Michael Cheng-Che Chung Amber TCM Healing Centre West Vancouver, British Columbia	Sydney MacInnis Parent Toronto, Ontario	Irma Boyle Health Canada Ottawa, Ontario
Tammy Clifford CHEO Research Institute Ottawa, Ontario	Robin Marles Brandon University Brandon, Manitoba	Gwen Burrows The Hospital for Sick Children Foundation Toronto, Ontario
Joan Gilmore Osgoode Hall Law School Toronto, Ontario	Doreen Matsui Canadian Paediatric Society Children's Hospital of Western Ontario London, Ontario	Allison McCutcheon University of British Columbia Vancouver, British Columbia
Tutti Gould Hylands Homeopathic Canada Sutton, Quebec	Siddika Mithani Health Canada Ottawa, Ontario	Michael J. Smith Health Canada Ottawa, Ontario
Christine Harrison The Hospital for Sick Children Toronto, Ontario	David Moher Children's Hospital of Eastern Ontario Research Institute Ottawa, Ontario	Sunita Vohra The Hospital for Sick Children Toronto, Ontario
		Facilitator
		Dennis O'Hara Toronto, Ontario

Appendix B Conference Agenda

Sunday, March 17

9:00 a.m. Welcome from the Natural Health Products Directorate —*Michael J. Smith*
Welcome from the Hospital for Sick Children Foundation—*Gwen Burrows*

9:20 a.m. Introductions (all participants) — *Facilitator assisted*

Keynote Presentations

10:00 a.m. Quality Control & Product Standard Research for NHPs —*Allison McCutcheon*

10:30 a.m. Break

10:50 a.m. Conventional Health care Provider & Researcher perspectives —*Sunita Vohra*

Views from the field....

11:20 a.m. Bioethics Perspective—*Christine Harrison*
Parent Perspective —*Sydney MacInnis*
CAHC Practitioner Perspective —*Maureen Horne-Paul*

12:30 p.m. Lunch

1:30 p.m. First Working Group Session – Establishing the Priorities
Each group will identify priorities for developing a research agenda for the study of the use of NHPs by children and youth. See the Group List to determine which group you are in. Also, see Instructions for 1st Working Session.

3:00 p.m. Break

3:20 p.m. **First Plenary Session**—*Facilitator*
Each group reports. The goal will be to construct a single list of 4 to 6 priorities derived with the consensus of all participants.

4:30 p.m. **Invitation to Reception** —*Gwen Burrows*
First day questionnaire—*Facilitator*
Each participant is asked to complete a quick questionnaire before attending the reception. The questionnaire should only take a minute or two to finish.

Appendix B **Conference Agenda** *(cont'd)*

Monday, March 18

- 9:00 a.m. **Re-cap of first day** — *Sunita Vohra*
- 9:15 a.m. **Second Working Group Session – Establishing the Strategies**
Participants self-select into the priority of their interest. Each group will propose strategies for addressing their priority. See Instructions for 2nd Working Group
- 10:45 a.m. **Break**
- 11:00 a.m. **Second Plenary Session** — *Facilitator*
Each group reports. The goal will be to construct a short list of preferred strategies for each research priority.
- 12:30 p.m. **Lunch**
- 1:30 p.m. **Re-cap of where we're at** — *Facilitator*
- 1:40 p.m. **Third Working Group Session – Identifying the Next Steps**
Participants self-select into the strategy of their interest to determine the next steps to take to implement that strategy. See Instructions for 3rd Working Group Session.
- 2:45 p.m. **Break**
- 3:00 p.m. **Third Plenary Session** — *Facilitator*
Each group will have 7 minutes to report on the next steps it has identified.
- 4:00 p.m. **Concluding Remarks** — *Michael J. Smith and Sunita Vohra*
Conference Adjourns *participants complete short questionnaire*

Appendix C Summary of Presentations

Key Issues in Paediatric Research

- Differences in absorption/distribution/metabolism/excretion
- Potential for different adverse reactions than those documented in adult populations
- Concerns about potential long-term effects of exposure during time of peak growth and development
- Vulnerable population
- Autonomy
- Informed consent/assent
- Compliance

Key Issues for Natural Health Products

Similar products can vary widely with respect to quality, constituents, concentration, standardization, dosage form or units, markers/marker content, plant species and parts used.

- Quality can mean the amount of the active ingredient; that the product is safe, efficacious and consistently manufactured; that the correct plants/parts were used; that the product is pure.
- Most adverse drug reactions are due to poor quality – i.e., when the wrong substitution is made, or when the product contains contaminants or adulterants.
- Product potency is a complex issue when dealing with botanicals and other multi-ingredient products.

- Standardized products are products that have a consistent marker content, ensuring product consistency from batch to batch.
- Potency is the amount of active ingredient required to obtain the desired therapeutic effect.
- Active ingredients are not identified for the majority of herbs.
- Relevant biological activity assays are required to obtain meaningful measurements of potency.

Ethical Considerations

- National Council on Bioethics in Human Research (NCBHR): research involving children seeks knowledge that may protect children from harm, benefit individual children, and/or benefit children as a group.
- Ethical values and principles at stake:
 - informed choice;
 - respect of various perspectives;
 - trust;
 - safety; and
 - justice.
- Ethical research includes the selection and achievement of morally acceptable ends, and the morally acceptable means to those ends
- Guiding ethical principles:
 - respect for human dignity
 - free and informed consent
 - vulnerable persons privacy and confidentiality
 - justice and inclusiveness
 - the balancing of harms and benefits

Possible Research Priorities

- NHPs are used as much for health promotion as the treatment of illness.
- What is being used; by whom; for what?
- Need for info re: use, access, costs, how NHPs affect quality of health in children.
- Which NHPs pose the greatest risk or potential for harm?
- What are appropriate standards for quality and safety in NHPs and how do these compare with the standards set for pharmaceuticals; are the two sets of standards comparable?
- Do NHP research trials need the same scientific standards as used for pharmaceuticals?
- Do we have good endpoints for clinical trials in children; are they valid, reliable and sensitive to change?
- Should we continue to do systematic reviews and meta-analyses?
- What role should patient/consumer preferences play in setting research priorities?
- Why do consumers use NHPs with children; are they well informed; how did they become informed; were their sources of information of high quality?

Appendix D Research Priorities of Working Groups

Group 1 – Red Group

1. Clinical Research
 - a. focus on NHPs being used now to set priorities
 - b. pilot projects for key areas to begin research
 - c. where there is no other identified treatment and the illness is severe
 - d. quality of NHPs used in clinical research
 - e. need to build research capacity too – clinical research skills and understanding of issues involved with NHP research
2. Knowledge Transfer and Information (Informed Choice)
 - a. labelling = selection of NHPD role in informed choice
 - b. where people get information
 - c. why people use what they use
 - d. allowing people to use info appropriately
 - e. database
3. Interactions
 - a. drug – NHP
 - b. NHP – NHP
 - c. food – NHP
 - d. communication/reporting of adverse reactions or interactions
4. Dosage Considerations
 - a. determining safe dosages
 - b. determining therapeutic dosages

- c. determining dosage used in clinical practice
5. Research Methodology
 - a. multi-approach treatments
 - b. cultural context
 - c. individualized treatments
 - d. role/challenges of conventional research paradigm and NHP use
 - e. comparison of diagnosis from various healing paradigms different levels of evidence between paradigms

Group 2 – Blue Group

1. Do Clinical Research
 - a. dosage spread
 - what is the safe range for children and youths
 - how do we or can we extrapolate from adults to kids
 - b. do observational research on a global to form the basis for future clinical trials
 - c. Research Ethics Boards
 - what do they know/believe
 - how do they assess protocols that don't 'fit' their ideas of 'best research methods'
 - d. collect information from some key sites where many children are treated
2. What are the standardization needs:
 - a. Markers
 - b. how reliable are international standards and studies?
3. Identify and assess existing data and create a database:

- a. synthesize current knowledge
 - b. create database of expertise, info about plant materials, existing research, etc.
 - c. develop a concise compendium of key research ideas
 - d. what can we learn from what others have already done?
 - e. develop good usage data – what is being used by Canadian children?
4. Knowledge transfer:
 - a. where do consumers get their information?
 - b. how reliable is that information?
 - c. what do we mean by informed choice?
 - d. what do conventional practitioners know; how effectively are they informing and communicating?
 - e. review of labelling in paediatrics
 5. Do Basic Science Research:
 - a. pharmokinetics, especially with respect to children and NHPs

Group 3 – Green Group

1. Efficacy and effectiveness – What are people doing/using?
2. How to evaluate the quality of existing evidence:
 - a. can evidence be extrapolated from adults to children?
 - b. does the required evidence/data already exist?
 - c. issues of quality, assessment and transparency must be resolved.
3. stimulate research if it is warranted
4. Transfer information to youth, parents and practitioners

5. Work with an open, expanded mind-set

Group 4 – Yellow Group

1. Identify and assess extant data
2. Do an environmental scan – What products are being used? What conditions are being treated? etc.
3. Do qualitative studies: decision making, information needs (all stakeholders)
4. Do scientific evaluation of the quality, safety and efficacy:
 - a. clinical Studies
 - level of evidence required to approve a clinical trial
 - quality
 - standards for quality
 - tests and standards for identity, purity and potency
 - safety
 - must have full toxicology data, unless adequate safety data in adults and no reason to believe different effects in children
 - efficacy
 - b. basic science
 - mechanisms of action
 - NHP-drug interactions,
 - NHP-NHP interactions, etc.
5. Monitor outcomes