

NutriNet Canada, Product Quality Initiative 2008 – 2009: Final Report

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1.0 Overview

NutriNet Canada in the interest of continuing the momentum of the work conducted in 07/08 to build a national product quality program for the FFNHP Sector, approved funding for the following three objectives;

Dissemination & Outreach: Communicate 2007/08 accomplishments at industry meetings, workshops and conferences and through preparation of peer-review publications.

NHP Prioritization: Convene the Expert Advisory Committee (Feb. 18, 2009) for the Lab proficiency Program to update the priority list for methods development and validation.

Industry Investment: Conduct stakeholder meetings to disseminate activities and gain interest and investment in moving forward with a plan to support the Product Quality Initiative in future.

2.0 Project Work plan Status

Dissemination & Outreach	Status
Finalizes manuscript for Ginseng SLV & ruggedness trial	Complete
Prepare Ginseng package for AOAC Official Methods Board	Complete
Finalizes manuscript for Echinacea extraction study & SLV	Complete
Evaluate/establish Echinacea Community under new AOAC model to support future collaborative study	Complete
Prepare manuscript from Microbial project for publication	Complete
Regulatory report: Synthesize & update HPRP documents for dissemination on NutriNet web-site.	Complete
NHP Prioritization	Status
Submit existing Canadian List from 2006 to AOAC for IRS inclusion	Complete
Attend ingredient ranking subcommittee meetings, Dec & Jan.	Complete
Synthesize current NHP priorities; government/industry/funders.	Complete
Conduct EAC meeting to re-prioritize NHPs for Canada.	Complete
Industry Investment in Quality	Status
Conduct strategic review of opportunities to finance PQI	Complete
Host stakeholder meeting on feasibility of PQI model	Complete

All activities outlined in the workplan were completed by within the requisite timeframe.

3.0 Project Details

For each specific objective a detailed account of the activities conducted to meet the objective is provided along with a discussion of research outcomes.

3.1 Dissemination & Outreach

The work conducted, under the Product Quality Initiative through 2007/2008, have far-reaching impact on both the NHP Industry but also the researchers studying these products. Given the extensive diversity of the research community, the interested government organizations and the industry itself, a concerted effort was made to have the project work be delivered in multiple formats, maximizing the program visibility.

3.1.1 Invited Lectures

The following is a list of invited lectures presented at scientific meetings and Industry events that included work conducted under the Nutrinet project. The list includes activities occurring from the completion of the Nutrinet 2007/2008 project and up till the conclusion of the Nutrinet 2008/2009 project. Nutrinet Canada and AAFC were acknowledged as providing funding in full or partial support of the research, as appropriate.

“Appropriate Method Selection & Use when Determining Constituents in NHPs” presented at the 7th Annual Oxford International Conference on the Science of Botanicals & 4th Annual American Society of Pharmacognosy Interim Meeting, Oxford Mississippi, April 12-16, 2008.

“Detecting Adulteration: Analytical Method Selection & Appropriate Use” presented at the Council for Responsible Nutrition (CRN) Day of Science, Penatgon City, Arlington, Virginia, May 8th, 2008.

“Bioscience Applied Research at BCIT” presented during the Research & Innovation in BC Showcase, BC-Canada-China Pavilion, Beijing, People Republic of China, May 26-29, 2008.

“The Role of Analytical Methods in Product Development, Quality Control & Regulatory Compliance” presented during the American-Indo Symposium on Integrative Indian Medicine and Botanical Science, New Delhi, India, October 13-17, 2008.

“Building Natural Health Product Quality Standards”, Canadian Standards Association, BC Consumer Advisory Group, Victoria, BC, October 27th, 2008.

“NHP Quality Standards & Regulations and the Implications for Clinical Trials” presented as part of the Clinical Research Professionals of British Columbia Seminar Series, Vancouver, BC, January 21st, 2009.

“The Importance of Analytical method Selection & Appropriate Use in Ensuring Product Integrity” presented at the 6th Annual NHP Research Conference & Tradeshow: gateway to Wellness, Vancouver, BC, February 18-21, 2009.

3.1.2 Poster Presentations

In addition to invited presentations a number of posters were presented at scientific meetings resulting from research conducted under the Product Quality Initiative.

Brown PN, Roman M. *Determination of Hydrastine and Berberine in Goldenseal Raw Materials, Extracts and Dietary Supplements by HPLC-UV: Collaborative Study*, at AOAC Pacific North West Meeting, Tacoma, Washington, June 18-19, 2008.

Chan M, Brown PN, **Lister P**. *Single Laboratory Validation of HPLC Method for Determination of Phenolic Echinacea Constituents*, 122nd AOAC International Annual Meeting, Dallas, Texas, US, September 21-24, 2008.

Brown PN, Yu R, Roman M. *Determination of Ginsenoside Content in Panax Spp. Raw Materials and Finished Products by HPLC-UV: Collaborative Study*, 122nd AOAC International Annual Meeting, Dallas, Texas, US, September 21-24, 2008.

Finley J, Brown PN. *Microbial Load Criteria Limitations for Botanicals and Dietary Supplements*, 122nd AOAC International Annual Meeting, Dallas, Texas, US, September 21-24, 2008.

Chen A, Chan M, Brown PN. *A Study to Determine if Cichoric Acid Degradation Occurs During Extraction and Analysis of Echinacea Root Materials*, 6th Annual NHP research Conference & Tradeshow: Gateway to Wellness, Vancouver, British Columbia, February 18-21, 2009.

3.1.3 Publications

The research conducted by BCIT with both partial and full support from Nutrinet Canada has resulted in a number of peer-review scientific publications. Despite the focus of the work towards supporting industry, the importance of publication in scientific journals cannot be stressed enough. Without the credibility of being subjected through peer-review the methods will not be widely adopted by the greater NHP Community Internationally. The following is a list of publications and manuscripts submitted and prepared for review resulting from the Product Quality Initiative.

Brown PN, Paley LA, Roman MC, Chan M (**2008**) Single Laboratory Validation of a Method for Detection and/or Quantification of Select Alkaloids in Goldenseal Supplements and Raw Materials by Reversed-Phase High Performance Liquid Chromatography. *Pharmaceutical Biology*, 46(1): 135-144.

Brown PN, Roman M (**2008**). Determination of hydrastine and berberine in goldenseal materials, extracts and dietary supplements by high-performance liquid chromatography with UV: Collaborative Study. *Journal of AOAC International*, 91(4): 694-701.

Brown P.N., Betz J.M. (**2008**) Guidelines for Analytical Method Selection & Appropriate Use When Determining Chemical Constituents in Dietary Supplements. *Planta Medica*, 74:313.

Brown PN (**2009**). The Importance of Analytical Method Selection & Appropriate Use in Ensuring Dietary Supplement Integrity. *Pharmaceutical Biology* 47(S1): 24.

Chen A, Chan M, Brown PN (**2009**). A Study to Determine if Cichoric Acid Degradation Occurs During Extraction and Analysis of Echinacea Root Materials. *Pharmaceutical Biology* 47(S1):30.

Yu R, Brown PN. Determination of Ginsenoside Content in *Panax ginseng* C.A. Meyer and *Panax quinquefolius* L. Raw Materials and Finished Products by HPLC-UV: Single Laboratory Validation (SLV) Study. *Journal of AOAC International* (submitted).

Brown PN, Chan M. Optimization and Single Laboratory Validation Study of a High-Performance Liquid Chromatography (HPLC) Method for the Determination of Phenolic Echinacea Constituents. *Analytical and Bioanalytical Chemistry* (submitted).

Finley JP, Brown PN. A Review of Microbial Load Criteria Limitations for Botanicals. *Journal of AOAC International* (under review).

Yu R, Brown PN. Determination of Ginsenoside Content in *Panax ginseng* C.A. Meyer and *Panax quinquefolius* L. Raw Materials and Finished Products by HPLC-UV: Collaborative Study. *Journal of AOAC International* (under review).

3.1.4 Industry Outreach through Extension

Through our research and outreach initiatives we have been able to have a significant impact within the FFNHP sector as evidenced by the significant interest demonstrated by stakeholders. Through our efforts gaps between many tangentially related to the Stakeholders have been bridged. Examples of this include invited presentations to foreign countries (see Section 3.1.1) and to new stakeholders such as the Clinical Research Professionals of BC, and the creation of partnerships with the Department of Foreign Affairs & International Trade and Environment Canada whose interest focuses on the identification of botanicals and NHPs containing CITES listed plants.

Results of the research conducted BCIT have also been reported on by other organizations via scientific presentations, web-sites, newsletters and member reports; including the following:

- American Herbal Products Association
- AOAC International – Inter-laboratory Management (publication)
- United Natural Products Alliance
- Office of Dietary Supplements (ODS), NIH

In fact, the ODS Dietary Supplement Reference Materials and Methods Program has referred to and/or referenced BCIT's Nutrinet activities in numerous publications including invited lectures and posters at following venues: CRN "Day of Science" Arlington, VA, 5/8/2008; Annual Meeting Pacific Northwest Section, AOAC International, Tacoma, WA, 6/17/2008; Natural Products Marketplace International Exhibition and Trade Show, Las Vegas, NV, 7/18/2008; 122nd Annual Meeting of AOAC International, Dallas, TX, 9/23/2008; 6th Annual Food Symposium "Relevant Regulatory and Analytical Challenges for Food and Dietary Supplements" Madison, WI, 8/26/2008; United States Pharmacopeia's Annual Scientific meeting, Kansas City, MO, 9/26/2008; 2008 Shanghai International Conference on Traditional Chinese Medicine, Shanghai, China, 10/12/2008; Indo-US Symposium on Botanicals", New Delhi, India, 10/16/2008; Natural

Products Marketplace International Exhibition and Trade Show, Las Vegas, NV, 7/17/2008.

Overall the efforts to disseminate work conducted under the Product Quality Initiative of Nutrinet Canada have been very successful reaching numerous Canadian and foreign government agencies, industry sectors and scientific community.

3.2 NHP Prioritization

To actively ensure research relevance to Industry BCIT maintains memberships with many professional societies and Industry associations including the BC Herb Grower's Association, Western Canadian Functional Food & Nutraceutical Network, NHP Research Society of Canada, Chemical Institute of Canada, American Botanical Council, American Society of Pharmacognosy, and AOAC International. It is through these memberships and active Industry Committee participation, such as AHPA's Botanical Standards and Lab Committee, NSF Joint Committee for Dietary Supplements, and AOAC Dietary Supplement Task Force, that BCIT is able to remain current and connected to the FFNHP sector.

The process by which NHPs are prioritized and selected for scientific study has a huge impact on the success, usefulness and overall impact of the research. Being a polytechnic means that BCIT conducts research that addresses commercial needs, and solves problems. Applied Research activities at BCIT are meant to **advance the state of practice**, not the frontiers of knowledge; to that end dating back to the first incarnation of BCIT's Lab Proficiency Program the NHP industry played a key role in selection of target NHPs and directing research.

The Expert Advisory Committee (EAC) for BCIT's Lab Proficiency Program was first established as an *ad hoc* committee in 2000 to provide guidance and support to first pilot projects entitled the BC Laboratory Standardization Program and funded by the BC Ministry of Agriculture, Food & Fisheries. When the project continued in 2004 with funding from the BC Science Council and Health Canada, the EAC was formally established. The primary purpose of the EAC was to establish a priority list of NHPs that would fit the criteria of BCIT's NHP Analytical Laboratory Proficiency Program. All EAC members made a commitment to the following terms;

Members of the EAC will

- a. guide and direct the project to ensure that the project achieves its objectives.
- b. assist in the dissemination of information and the approval of any necessary directional changes that have been submitted by the program director.
- c. review the prioritization listing to ensure that it is relevant with industry needs.

The EAC for the Lab Proficiency Program met in both 2004 and 2006 to meet the objectives of the research program. With funding from Nutrinet Canada, BCIT hosted the third meeting of the EAC on February 18th, 2009 at the Four Seasons Hotel in

Vancouver, BC. The meeting objectives were to 1. Provide an overview of the Product Quality Initiative, 2. Re-prioritize FFNHP's for future program activity and 3. Discuss opportunities for partnership and funding.

Similarly, AOAC's Dietary Supplement Task Force (DSTF) is comprised of members of the DS community who are actively engaged in pursuing the development of analytical tools to support product quality standards. BCIT has maintained a voting position on the DSTF since 2004 and plays an active role within this international community in guiding and facilitating the AOAC methods validation process. It is a sub-group of the DSTF that is responsible for Ingredient ranking for the AOAC.

One of the specific activities conducted as part of the 2008/2009 Nutrinet Product Quality Initiative, involved gathering and synthesizing industry, government and research priorities. This activity supports both the DSTF and Nutrinet's Product Quality Initiative, and specifically BCIT's Lab Proficiency Program. All of the priority ingredients (FFNHPs) identified from industry lists, granting agencies, and various Canadian and foreign government agencies were collected incorporated into the Dietary Supplement Ingredient Ranking Subgroup (see 3.2.1) and EAC FFNHP prioritization process (see 3.2.2).

3.2.1 Dietary Supplement Ingredient Ranking Sub-group

At the request of the Dietary Supplement Task Force (DSTF), which was established by AOAC International to facilitate Industry input to their congressionally mandated FDA/NIH contract for methods validation, an Ingredient Ranking Sub-committee was established. The Committee is comprised of members of the Task Force representing Research, Industry and FDA. The 12 voting members are listed in the table below and separated by area of representation.

Industry	Research	FDA/NIH
Daniel Fabricant, NPA	Jim Harnly, USDA	Jeane Rader, CFSAN
Monica Howard, CHPA	Kathy Sharpless, NIST	Vasilios Frankos, CFSAN
Andrew Shao, CRN	Paula Brown, BCIT	Agnes Nguyen Pho, CDER
Steven Dentali, AHPA	Mark Roman, AOAC	Jinhui Dou, CDER

BCIT having representation on this committee is advantageous to the NutriNet in that the Product Quality Initiative receives recognition for our efforts in the area of methods validation and ensures work is not redundant or duplicated. As a member of this Sub-committee and the DSTF, BCIT reviewed the existing ingredient list, ensured all ingredients previously prioritized by the EAC were included and participated in three 1-day ingredient ranking meetings (December 4th, 2008, January 22nd, 2009 and February 9th, 2009). The results of these meetings were presented at the EAC meeting on February 18th, 2009 in Vancouver, BC and the AOAC Ingredient ranking process and final priorities discussed.

3.2.2 EAC Meeting Summary

There were 15 EAC members in attendance and 15 observers, which resulted in representation by industry (57%), government (17%) and research organizations/institutions (26%). Please refer to the table below for a more detailed description of the attendee demographics.

Category	Sub-Category	Detailed Demographic
Industry	5 Associations	2 Provincial, 1 Regional, 1 Canadian, 1 US
	6 Companies	3 Ingredient Suppliers, 3 Product Manufacturers
	6 Service providers	3 Contract Labs, 2 Standard Companies, 1 other
Research	3 Academia	1 BC, Canada; 1 Delhi, India; 1 Shanghai, China
	3 Government	1 AAFC, 2 NRC
	2 Societies	1 Canadian, 1 US
Government	2 Provincial	1 BC, 1 AB (Agriculture)
	2 Federal	1 Health Canada, 1 Environment Canada
	1 Foreign	1 US NIH (Office of Dietary Supplements)

A detailed meeting summary, including the list of attendees, has been prepared and included with this report as **Attachment 1**. The intended outcome of this prioritization process was to identify a list of candidate FFNHPs to consider for methods development & validation, reference material verification and laboratory proficiency activities in future. The meeting attendees were provided with the EAC Meeting Summary documents from the 2004 and 2006 meetings. They were provided the opportunity to suggest alternative ranking mechanisms and considerations but decided to continue along the guidelines established in these earlier meetings.

After four tiers of prioritization and ranking, 8 FFNHPs remained, including Cranberries, Echinacea, Bilberry, Black Cohosh, Flaxseed, Blueberries and Omega fatty acids in FFNHPs. Rather than eliminate any of the remaining 8 ingredients it was decided that until funding had been secured the list would remain intact. It is recognized that the source of the funding, whether from Industry, Provincial, Federal or even foreign will have an impact on how the remaining ingredients are considered. The Tier 5 (final) FFNHPs are listed in the table below along with the target analytes and a summary of the specific considerations discussed by the EAC.

FFNHP	Analyte	Considerations
Bilberry	anthocyanins	detect adulteration, QC, popular product
Black Cohosh	triterpene glycosides	detect adulteration, QC, safety considerations, identity concerns
Blueberry	anthocyanins	Canadian crop, detect adulteration, QC, emerging products
Cranberry	anthocyanins	Canadian crop, QC, ↑ research focus, SLV complete

Echinacea	phenolics	Canadian crop, popular product, SLV complete, collaborative protocol prepared.
Flaxseed	lignanans	Canadian crop, product differentiation, SLV complete
Green tea	catechins	Research Focus, popular product, currently SLV underway in US
Omega FAs	Unconjugated	Health interest, Canadian sources, ↑ impact for FF & NHPs, voluntary monograph has assay

After the completion of this NHP re-prioritization exercise, the group discussed potential opportunities for partnership and funding to further this initiative, please refer to Attachment 1 and section 3.3 for details.

3.3 Industry Investment in Quality

The final objective of the 2008/2009 NutriNet Product Quality Initiative was to gain Industry investment in the program. There were two opportunities to conduct stakeholder meetings including the scheduled EAC meeting on February 18th, 2009 in Vancouver, BC and on March 10th, 2009 in Calgary, Alberta. The meeting summaries have been included in this report as **Attachment 1** (EAC Summary) and **Attachment 2** (Stakeholder Meeting Summary).

In brief, during the February meeting the discussion focused on the need to identify funding with five potential options identified:

1. Leverage fees from contract laboratories
2. The Growing Forward Program, AAFC
3. Partnering with a standard's company
4. Developing & offering training courses
5. Creating a central repository of information

Each of these potential opportunities were explored by all the participants in a open session, facilitated discussion (see attachment 1). The meeting concluded on the following points:

- The EAC agreed on the need and value of such a program to the NHP sector;
- Members agreed to look into possible funding and partnership opportunities for the program and report back to the committee.

A formal review was conducted at the end of the meeting and the full results of the meeting evaluation can be found in Attachment 1. Of the 16 respondents 50 % represented Industry, 25% government and 25% research & development and 15/16 participants reported that the meeting was valuable.

During the Industry Stakeholder meeting, March 10th, 2009, participants (see Attachment 2, Appendix I) were provided with information packages (see Attachment 2, Appendix II), welcomed by the facilitator, advised that the meeting discussions would

be compiled into a brief report for Nutri-Net Canada, and the specific meeting objectives given. The meeting objective was stated as, “To present work to date on Product Quality for FFNHPs by BCIT and tap into the collective wisdom of the group to assess the feasibility of a Product Quality program in Canada/US.”

Participants were asked to give a brief introduction to themselves, followed by a round-table interactive discussion answering the following question, “*From a researcher/consumer/ industry perspective, my hopes for a Product Quality program are...*”. Categorized by perspective, the details of these discussions can be found in Attachment 2. The responses of participants largely focused on two points:

- Acknowledgement of the critical role of quality for scientifically rigorous research, building and maintaining consumer confidence, and survival of the industry
- The need for training and on-going education in FFNHPs for consumers, researchers and industry

The final component of the workshop attempted to identify the next steps for implementing the business plan for sustained Product Quality Initiative. Participants were asked to answer the following questions with respect to the current product quality initiatives, “What is working now?”, “What is not working?”, “What do we need to fix?” and “What do we need to start doing?”.

The responses were sorted into thematic areas and complete details are provided in Attachment 2. The Canadian regulatory framework was viewed as a positive influence on industry, contributing Canada’s reputation as for quality. The collaborative nature of the FFNHP sector throughout the value chain was seen as an opportunity but inadequate training and a lack of funding, regulatory enforcement and regulations for FF were seen as barriers to growth of this sector and to implementing a product quality program.

It was identified that long-term funding should be sought, communication improved and stronger partnerships created with the US. The key areas where investment should be made were identified as activities that support the development of **High qualified personal** (training & education), **Communication Strategies**, and a **Long-term funded quality program**.