The Canadian Natural Health Product Regulatory Landscape – Opportunity for the Modernization and Globalization of Chinese Medicine and Health Products

加拿大新天然健康药品法規剖析與中醫藥現代化和國際化的機遇

ICMCM 2009

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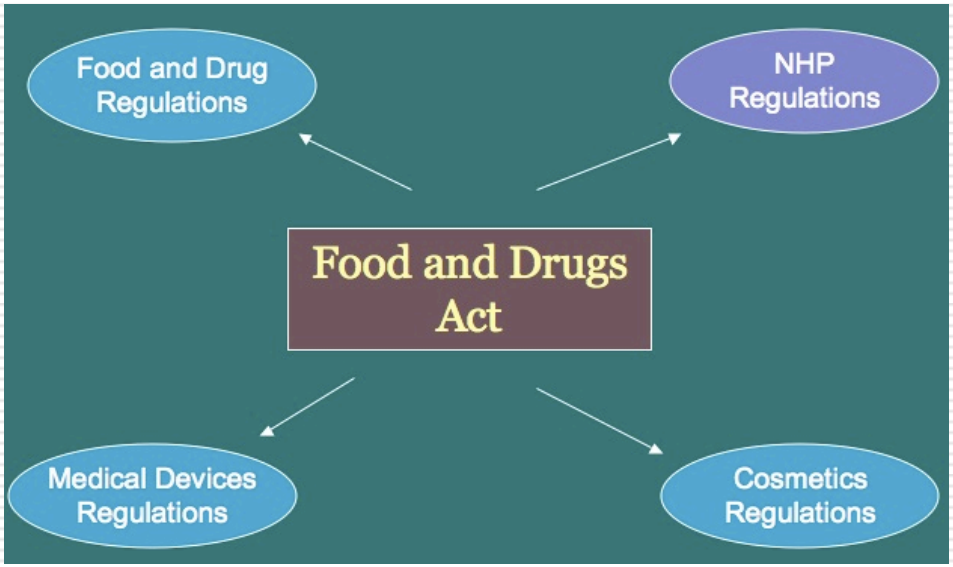
Presentation Outline 讲座提要

A. Canada Market/Industry at a Glance 加拿大市场行业概况
B. Canadian NHP Regulations 加拿大天然健康药品法规
C. Challenge & Opportunity 挑战与机遇
D. Strategy 策略
E. Case Studies 案例
F. Wellgenex Brief Introduction 公司简介
G. Q & A 问答

A. Canada Market & Industry at a Glance 加拿大市场行业概况

- 70% of Canadian use NHPs
- 42,000 products in Canada
- $4.3 billion annual sales
  - 50% vitamins and minerals
  - 30 % herbs and botanicals
- Canada is net importer of NHP
  - $217 million import Vs. $174 million export (in 2004)
    - > 50% from the US
    - 12% from China

B. Regulations - Overview 法规简述



- Used to be either food or drug before 2004
- NHP regulations introduced in 01/01/2004 by Health Canada
- Regulated as subset of drugs. Pre-market approval required.
- NHP regulations: **Product licensing, site licensing/GMP, clinical trials**, labeling, adverse reaction reporting

B. Regulations - NHP Definition 天然健康药品定义

Substance:

1. A plant, an alga, a bacterium, a fungus or a non-human animal material
2. An extract or isolate of the above
3. Vitamins (selected)
4. Amino acids
5. Essential fatty acids
6. Synthetic duplicates of any of 2 to 5

o Minerals

1. Probiotics (益生素)

Function/Claim:

2. Therapeutic - diagnosis, treatment, mitigation, or prevention (except Schedule A diseases)
3. Risk reduction
4. Structure/function

B. Regulations - Product Licensing (PL) 产品注册认证

- Types of product license application (PLA)
  - Compendial
  - Traditional claim
  - Non-traditional claim
  - Homeopathic
  - Transitional DIN
- Required supporting evidence in PLA
  - Efficacy
  - Safety
  - Quality
- PL open to foreign applicants with Canadian representatives
- PL issued as Natural Product Number (NPN)

B. Regulations - PL Cont'd 现有产品注册时限优先

Existing NHP PLA deadline:

Product Category Priority Approach	
Priority 1 - NHP substances currently on TPD's NewDrug List	June 1, 2004
Priority 2 - Isolates, amino acids, fatty acids, concentrated volatile (essential) oils indicated for internal use, and extracts other than those prepared by traditional methods	Jan 1, 2005
Priority 3 - Algal, bacterial, fungal, probiotics and non-human animal materials	June 1, 2005
Priority 4 - Plants, plant materials, extracts prepared by traditional methods, and volatile (essential) oils other than those that are concentrated and indicated for internal use	June 1, 2006
Priority 5 - Vitamins and Minerals	Jan 1, 2007
Priority 6 - Homeopathic Medicines	June 1, 2007

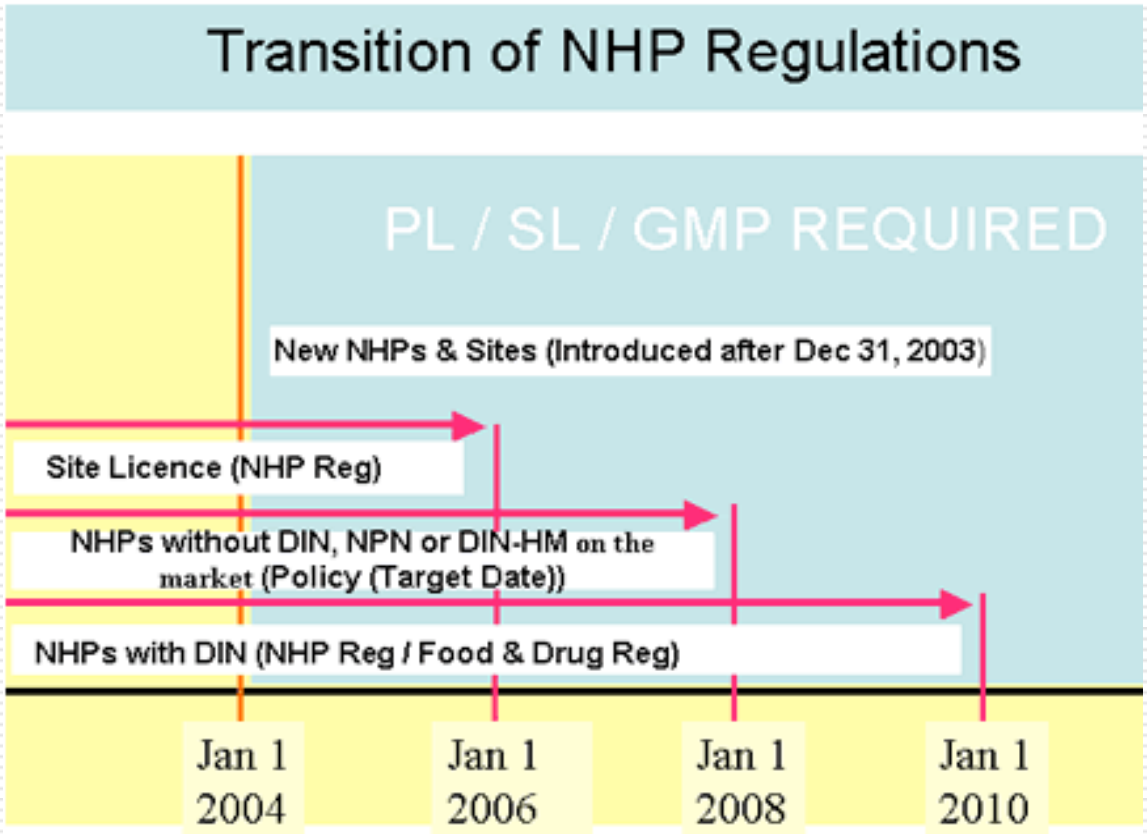
B. Regulations - GMP & Site Licensing (SL) 场地认证

- GMP required to ensure product safety and quality. SL required for all manufacturers, packagers, labelers and importers in Canada
- Required submission
  - Application form
  - Quality assurance report (QAR), or
  - GMP inspection report by Health Canada
- Foreign sites - SL NOT issued to foreign manufacturers
  - For NHP manufactured outside of Canada, Canadian importer to add the foreign site to its SL by providing one of the following evidence to support that the products meet Canadian GMP requirements
    - A QAR
    - A audit inspection report
    - A license from the accepted regulatory authority (e.g. GMP certificate)
  - Countries with Mutual Recognition Agreement (MRA)- The European Community, Switzerland, Australia

B. Regulations - Clinical Trials 临床试验

- Clinical trial not mandatory for PLA
- NHP clinical trials (Phase I-III) allowed for:
  - New condition(s) of use
  - Additional evidence to support PL application and approval
  - NHP with no prior history of use in humans
  - Comparative bioavailability studies on two NHP
  - NHP used to treat side effects of a conventional drug
  - NHP used to enhance efficacy of a conventional drug
- Full clinical trial application (CTA) required to be filed with Health Canada to obtain Notice of Authorization (NOA) prior to the commencement of the trial
- Health Canada only authorizes trials to be conducted in Canada
- Usual cost of a NHP clinical trial ranges $100,000 to $300,000

B. Regulations - Implementation Timeline 法规实施时限



B. Regulations - License Application Cost & Timeline
注册认证费用与时间

- Currently no application fees
- Timeline: PL - 60 days to over 2 years; SL - 2 to 6 months.
- Cost recovery scheme proposed (see table below). April 2008 implementation postponed

Application Type	Fee	Timeline (in days)
Compendial PL	$1,500	60
Compendial-like PL	$1,700	150
Non-compendial (single ingredient) PL	$1,810	150
Non-compendial (multi-ingredient) PL	$3,610	150
SL	$2,110	60

B. Regulations - License Application/Submission Status
注册认证审批进度

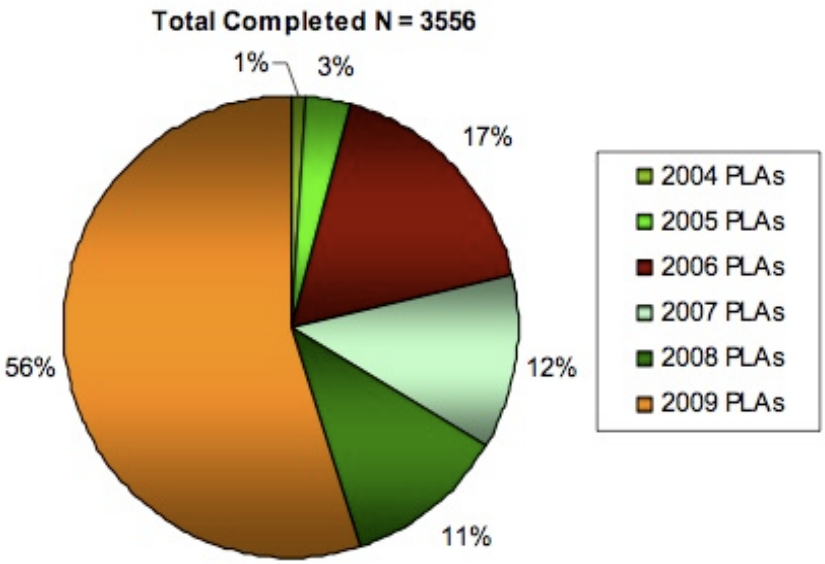
PL & SL processed since 2004

	PL*	SL**
Application received	38,255	1,244
License issued	13,143	808
Refused/ Withdrawn	12,604	364
Outstanding	12,508	72

* As of June 30, 2009, Health Canada

** As of November 20, 2008, Health Canada

PL processed 4/01-6/30/2009



C. Challenge & Opportunity 挑战与机遇

- Historic Challenge
  - Classified as food with no claims allowed for traditional Chinese medicine (TCM)/Chinese Medicine (CM)
  - Primarily marketed within overseas Chinese. Limited market access to mainstream consumers
  - Low price finished formulated TCM/CM due to limited demand
  - Low value added high energy cost raw materials
  - Adulteration and contamination (heavy metal, pesticide etc.)
  - Endangered species used in TCM/CM

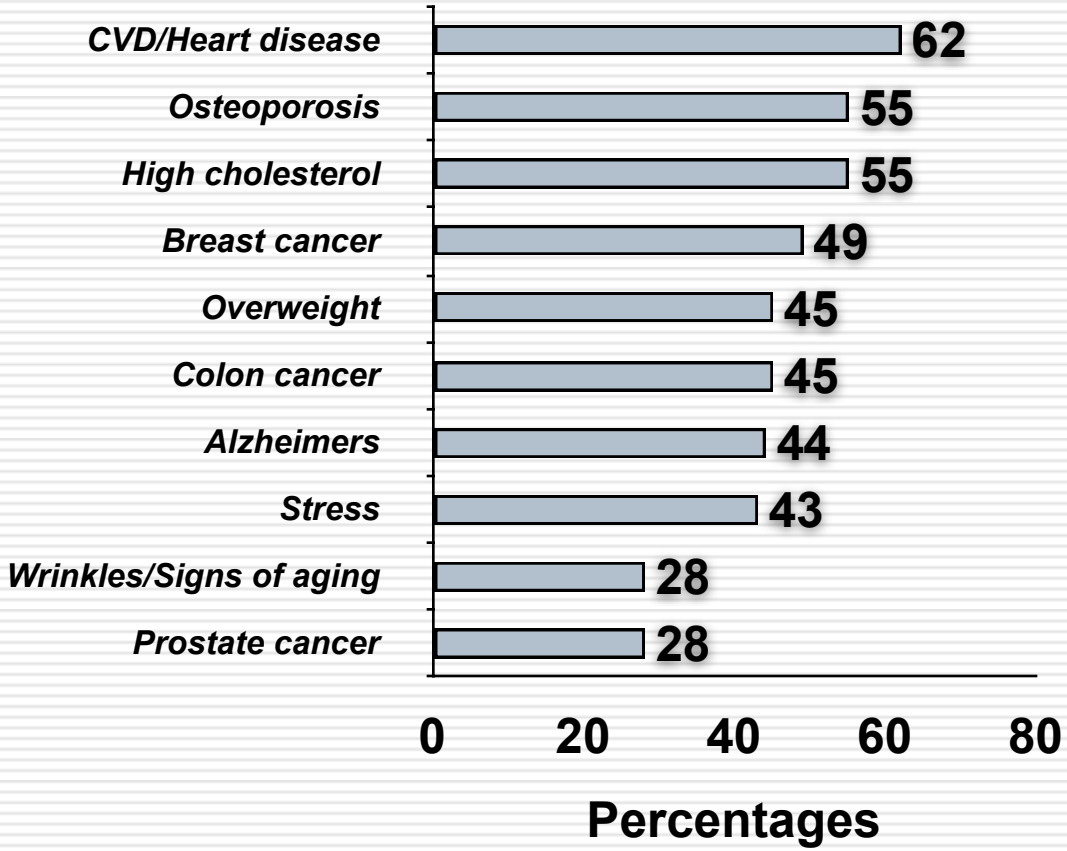
C. Challenge & Opportunity 挑战与机遇

- New Opportunity
  - Increasing popularity of personalized medicine
  - Market conversion from single-ingredient to formulated products
  - Demonstrated safety and efficacy of TCM/CM especially for wellness maintenance and chronic health conditions
  - TCM/CM regulated as subset of drugs under NHP regulations of which claims are allowed
    - Traditional claims
    - **Non-traditional claims (treatment, risk reduction, structure/function**)
  - Health Canada product license opened to foreign applicants
  - Greater access to mainstream market domestically and globally
  - Gateway to the US market

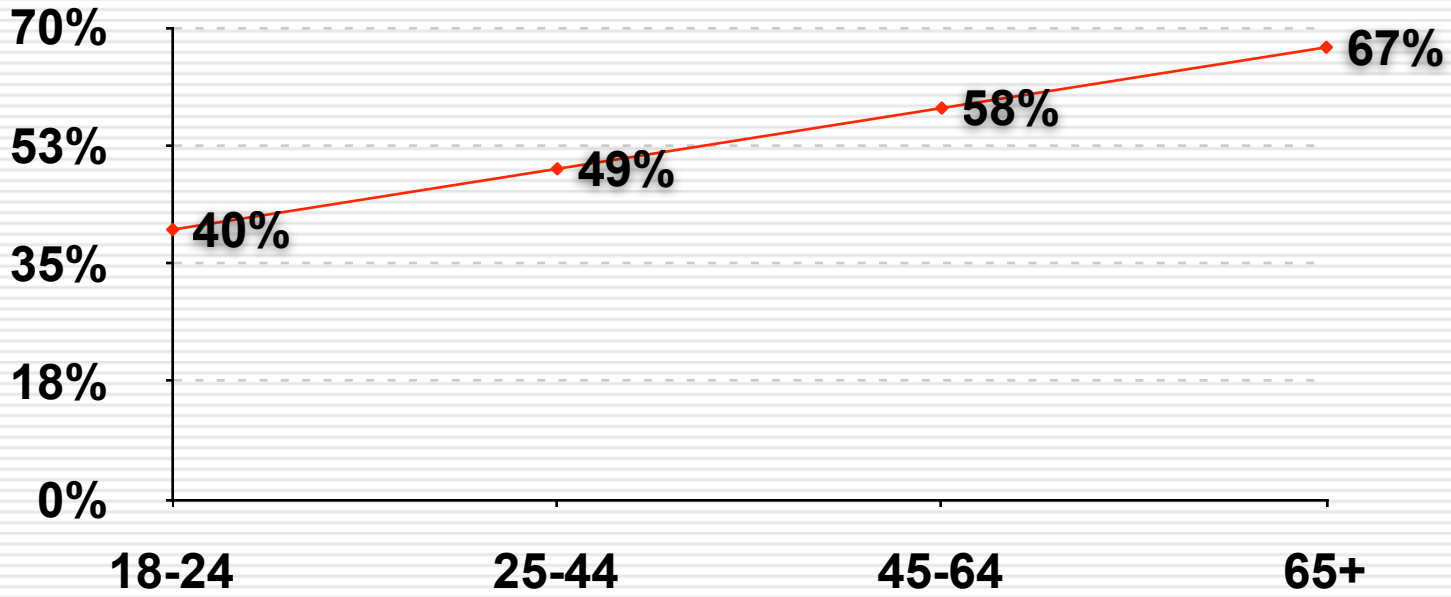
D. Strategy 策略

- Adapt to culture sensitivity, philosophy difference, consumer behaviour and market demand
- Leverage on the convergence of TCM and conventional medicine towards modern science (phytomedicine, botanical drug, CM Vs. TCM)
- Focus on 1) the baby boomer consumers that are in need the most and spend the most on NHP; 2) areas that conventional medicine has limited success (e.g. osteoporosis, arthritis, diabetes, cancer, heart heath, Alzheimer's disease, etc.)
- Select TCM/CM products with simple key benefits supported by modern scientific evidence (i.e. clinical trials in China) or can be easily validated through clinical trials
- Conduct NHP clinical trial in Canada for validation when required
- Apply for product license to secure pre-market approval
- Establish R&D collaboration and investment in Canada for value chain integration

Top Health Concerns of 50+
50岁以上的消费者的主要健康问题分析



NHP Usage Increases With Age
天然健康药品的使用随年龄的增长而增加



Source: AH & H Consumer Survey 1999

E. Case Studies - Alive Vitamins, Canada 案例

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Canada

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Drugs and Health Products

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Product Information

User Guide | Terminology Guide | Compendium of Monographs

New Search

Natural Product Number:	80002123
Current Status:	Active
Brand Name(s):	Glucosamine Sulfate 500 Mg Osteoarthritic Joint Pain Relief
Name of Licensee:	Alive Vitamins
Dosage Form:	Capsule
Recommended Route of Administration:	Oral

Recommended Dose:

Sub Population (Sub Pop.)					Amount				Frequency (Freq.)			
Sub Pop.	Age	Min.	Max.	UoM* Age	Quantity (Qty)	Min.	Max.	UoM* Qty	Freq.	Min.	Max.	UoM* Freq.
Adults				daily	3.0			capsule	3			daily

* UoM: Unit of Measure

Recommended Use or Purpose:
Helps to relieve joint pain associated with osteoarthritis. Protects against the deterioration of cartilage. Factor in the building of health cartilage.

Risk Information:

Cautions and Warnings
Consult a health care practitioner if symptoms worsen

Contra-Indications
Do not use if you are pregnant or breastfeeding

Medicinal Ingredients	Quantity per Dosage Unit	Extract	Potency
2-amino-2-deoxy-D-glucose sulfate	500.0 mg		

Non-Medicinal Ingredients
Gelatin
Magnesium Stearate
Rice flour

Issued: 2006-09-20

E. Case Studies - Foods For Beauty, Hong Kong 案例

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Product Information

User Guide | Terminology Guide | Compendium of Monographs

New Search

Natural Product Number: 80011513

Current Status: Active

Brand Name(s): Skin Vitamins And Minerals

Name of Licensee: Foods for Beauty Enterprise Limited

Dosage Form: Tablet

Recommended Route of Administration: Oral

Recommended Dose:

Sub Population (Sub Pop.)					Amount				Frequency (Freq.)			
Sub Pop.	Age	Min.	Max.	UoM* Age	Quantity (Qty)	Min.	Max.	UoM* Qty	Freq.	Min.	Max.	UoM* Freq.
Adults					1.0			tablet	3			daily

* UoM: Unit of Measure

Recommended Use or Purpose:
Helps to maintain healthy skin. Helps in tissue formation. Helps to produce and repair connective tissue. Helps to maintain eyesight, skin, membranes and immune function. A factor for the maintenance of good health. Provides antioxidants for maintenance of good health. Helps the body to metabolize carbohydrates, fats and proteins.

Risk Information:

Medicinal Ingredients	Quantity per Dosage Unit	Extract	Potency
Biotin	100.0 µg		
Calcium	165.0 mg		
Chromium	20.0 µg		
Copper	1.0 mg		
Folate	100.0 µg		
Iron	2.0 mg		
Lutein	2.0 mg		
Lycopene	1.5 mg		
Magnesium	65.0 mg		
Manganese	1.0 mg		
Molybdenum	20.0 µg		
Niacinamide	20.0 mg		
Pantothenic acid	20.0 mg		
Riboflavin	20.0 mg		
Selenium	50.0 µg		
Thiamine	20.0 mg		
Vitamin A	1000.0 µg RAE		
Vitamin B12	20.0 µg		
Vitamin B6	20.0 mg		
Vitamin C	200.0 mg		
Vitamin D	2.5 µg		
Vitamin E	50.0 mg AT		
Zinc	5.0 mg		

Non-Medicinal Ingredients
Croscarmellose
Magnesium Stearate
Microcrystalline cellulose
Stearic Acid

Issued: 2009-07-08

E. Case Studies - Changxing Pharmaceutical, China 案例

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Drugs and Health Products

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Product Information

User Guide | Terminology Guide | Compendium of Monographs

New Search

Natural Product Number: 80011476

Current Status: Active

Brand Name(s): Zhiling Capsule

Name of Licensee: Changxing Pharmaceutical Co. Ltd

Dosage Form: Capsule

Recommended Route of Administration: Oral

Recommended Dose:

Sub Population (Sub Pop.)					Amount				Frequency (Freq.)			
Sub Pop.	Age	Min.	Max.	UoM* Age	Quantity (Qty)	Min.	Max.	UoM* Qty	Freq.	Min.	Max.	UoM* Freq.
Adults						2.0	3.0	capsule		2	3	daily

* UoM: Unit of Measure

Recommended Use or Purpose:
Used in Traditional Chinese Medicine to tonify the lung and the kidney.

Risk Information:

Cautions and Warnings
Do not use if pregnant or breastfeeding.

Contra-Indications
Discontinue use if allergic reaction occurs. Do not use or use with caution if you have autoimmune diseases such as multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis. If symptoms persist, consult a health care practitioner.

Medicinal Ingredients	Quantity per Dosage Unit	Extract	Potency
Cordyceps sinensis	250.0 mg		

Non-Medicinal Ingredients
Gelatin

Issued: 2009-07-08

E. Case Studies - Site License (Wellgenex) 案例

Health Canada / Santé Canada

SITE LICENCE

Site Licence Number:
Numéro de la licence :
300493

LICENCE D'EXPLOITATION

This Licence is issued by the Minister of Health under the Authority of section 29 of the Natural Health Products Regulations
Cette licence est délivrée par le ministre de la Santé conformément à l'article 29 du Règlement sur les produits de santé naturels

Issued to:
Délivré à:

Name of Licensee:
Nom du titulaire : **WELLGENEX SCIENCES INC.**

Address:
Adresse :
150 – 10451 SHELLBRIDGE WAY
RICHMOND
BRITISH COLUMBIA
CANADA
V6X 2W8

to perform the following activities at authorized buildings listed on the Domestic Site Annex and Foreign Site Annex:
pour exécuter les activités suivantes dans les bâtiments autorisés lister sur Annexe des sites Canadiens et Annexe des sites étrangers :

Activities/ *Activités*	Authorized Activities/ *Activités autorisées*	Specific Authorization/ *Autorisation spécifique*	
		Sterile Dosage Form/ *Forme posologique stérile*	Homeopathic Medicine/ *Remède homéopathique*
Manufacturing/*Fabrication*	NO/*NON*	NO/*NON*	NO/*NON*
Packaging/*Emballage*	NO/*NON*	NO/*NON*	NO/*NON*
Labelling/*Étiquetage*	NO/*NON*	NO/*NON*	NO/*NON*
Importing/*Importation*	YES/*OUI*	NO/*NON*	NO/*NON*

This licence is renewable pursuant to section 36 of the Natural Health Products Regulations. Any changes to the activities authorized by this licence are subject to sections 32 and 33 of the Regulations.
Cette licence est renouvelable annuellement en vertu de l'article 36 du Règlement sur les produits de santé naturels. Tout changement aux activités autorisées par cette licence est régi par les articles 32 et 33 du Règlement.

Issued/ *Délivrée :*	Amended/ *Modifiée :*	Expiry/ *Expiration :*
January 25, 2009	N/A	January 25, 2010

Annex Attached/ ***Annexes jointes:***

P.P. Director General, Natural Health Product Directorate
Directeur général, Direction des produits de santé naturels

E. Case Studies - Foreign Site Annex [Phartech (Hong Kong)]案例

Health Canada / Santé Canada

SITE LICENCE

Site Licence Number:
Numéro de la licence :
300493

LICENCE D'EXPLOITATION

Foreign Site Annex/*Annexe des sites étrangers*

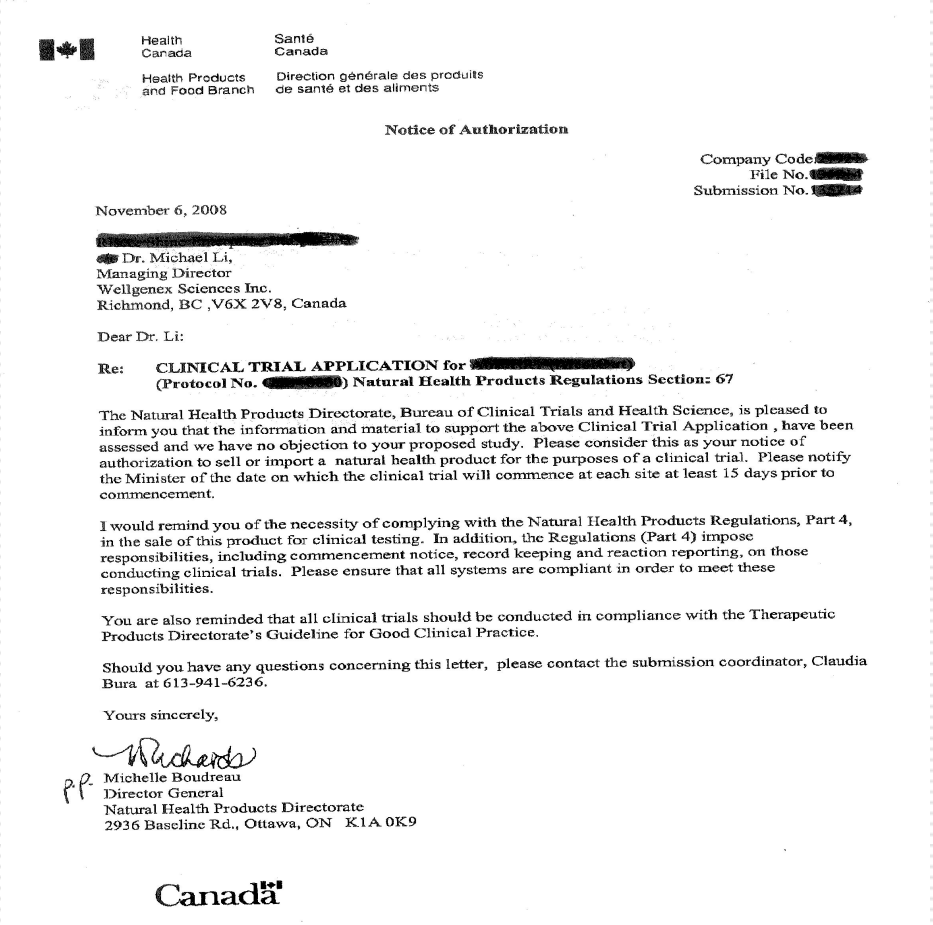
The following sites are considered to be in compliance with GMP requirements outlined in PART 3 of the Natural Health Products Regulations.

Les sites suivants sont considérés conforme avec les normes des bonnes pratiques de fabrication tel que stipulé dans la partie 3 du Règlement sur les produits de santé naturels.

Foreign Company Name: *Nom de la compagnie étrangère :* **Phartech (Hong Kong) Limited**			
Building Name: *Nom du bâtiment :* **Phartech (Hong Kong) Limited**			
Address: *Adresse :* **Unit 1C, 6/F, Cheung Fung Industrial Bldg, 23-39 Pak Tim Par St.**	City: *Ville :* **Tsuen Wan**	Province/State/*État:*: **Hong Kong**	
Postal Code: *Code postal :* **N/A**	Country: Pays : **P. R. of China**		

Activities/ *Activités*	Authorized Activities/ *Activités authorisées*	Specific Authorization/ *Autorisation spécifique*	
		Sterile Dosage Form/ *Forme posologique stérile*	Homeopathic Medicine/ *Remède homéopathique*
Manufacturing/*Fabrication*	YES/*OUI*	NO/*NON*	NO/*NON*
Packaging/*Emballage*	YES/*OUI*	NO/*NON*	NO/*NON*
Labelling/*Étiquetage*	YES/*OUI*	NO/*NON*	NO/*NON*

E. Case Studies - Clinical Trial NOA (Wellgenex) 案例



Health Canada / Santé Canada
Health Products and Food Branch / Direction générale des produits de santé et des aliments

Notice of Authorization

Company Code [redacted]
File No. [redacted]
Submission No. [redacted]

November 6, 2008

[redacted]
Dr. Michael Li,
Managing Director
Wellgenex Sciences Inc.
Richmond, BC ,V6X 2V8, Canada

Dear Dr. Li:

Re: CLINICAL TRIAL APPLICATION for [redacted]
(Protocol No. [redacted]) Natural Health Products Regulations Section: 67

The Natural Health Products Directorate, Bureau of Clinical Trials and Health Science, is pleased to inform you that the information and material to support the above Clinical Trial Application , have been assessed and we have no objection to your proposed study. Please consider this as your notice of authorization to sell or import a natural health product for the purposes of a clinical trial. Please notify the Minister of the date on which the clinical trial will commence at each site at least 15 days prior to commencement.

I would remind you of the necessity of complying with the Natural Health Products Regulations, Part 4, in the sale of this product for clinical testing. In addition, the Regulations (Part 4) impose responsibilities, including commencement notice, record keeping and reaction reporting, on those conducting clinical trials. Please ensure that all systems are compliant in order to meet these responsibilities.

You are also reminded that all clinical trials should be conducted in compliance with the Therapeutic Products Directorate's Guideline for Good Clinical Practice.

Should you have any questions concerning this letter, please contact the submission coordinator, Claudia Bura at 613-941-6236.

Yours sincerely,

p.p. Michelle Boudreau
Director General
Natural Health Products Directorate
2936 Baseline Rd., Ottawa, ON K1A 0K9

Canada

F. Wellgenex 公司简介

- Corporate highlight:
  - A Canadian professional firm focusing on life sciences, nutrition and natural health in North America (Canada, US) and Asia Pacific (China)
  - Experts with extensive expertise in academia, industry and government bridging the gap between science and business
  - Currently serving clients from Canada, US, China, India, Hong Kong, Taiwan, Japan, Singapore, Korea and Switzerland
- Area of specialty:
  - New market entry, due diligence, strategic alliance
  - R&D, product development and commercialization
  - Scientific & regulatory affairs

Wellgenex是一家专注于生命科学包括天然药物和营养健康品的加拿大专业服务公司

- 新市场拓展与开发, 投资评估, 战略伙伴建立
- 产品研发, 商业化及临床试验
- 科学法规事务, 认证与注册

Helping you create product excellence and connect to market success

G. Q & A 问答

谢谢！