The University of Toronto

Pharmaceutical Research & Manufacturing in Ontario
Sector Analysis

IMPACT CONSULTING GROUP
Presentation Overview

1. Industry Overview
   - Introduction
   - Scope / Size / Growth
   - Emerging Markets
   - Industry Trends
2. Companies
   - Sector Profile
   - Cluster
   - Top Industry Players
3. Factors
   - Labour Force
   - Future Plans
4. Intellectual Property Measures
   - Patents
   - R&D Funding
5. Taxes
6. Challenges
Pharmaceutical Industry Overview

Introduction
The pharmaceutical sector is one of the most innovative and profitable industries in Canada

**Strong Economy**
- The Canadian pharmaceutical sector is composed of companies developing and manufacturing innovative medicines and generic pharmaceuticals as well as over the counter drug products.
- Canada has the ninth largest pharmaceutical industry largest in the world, accounting for about 3% of the world market by sales.
- Brand-name companies undertake R&D to develop new or improved patented therapies while the generic firms develop bio-equivalent copies of innovative drugs once patents expire.

**Strong R&D infrastructure**
- Seventeen of Canada’s top 50 research universities are located in Ontario, seven of which (led by the University of Toronto) attract more than $100 million in sponsored research funding annually.
- Ontario has 25 research and academic hospitals employing 10,000 scientists, clinical investigators and other researchers conducting $850 million in research annually.

<table>
<thead>
<tr>
<th>SECTOR</th>
<th>COMPANIES</th>
<th>FACTORS</th>
<th>INTELLECTUAL PROPERTY</th>
<th>INTERNATIONAL COMPARISON</th>
</tr>
</thead>
</table>

Source: Invest in Canada: Clinical Trials in Ontario, 2009
Pharmaceutical Industry
Scope, Size, & Growth
Pharmaceutical research and manufacturing in Canada

- Canadian pharmaceuticals market grew by 9.5% in 2010 to reach a value of $21.6 billion
- Compound annual growth rate (CAGR) of 7.2% for the period 2006-2010
- Largest player is Pfizer with a market share of 14.4% in Mississauga, Ontario
- Canadian pharmaceuticals market is forecast to decelerate, reaching a CAGR of 4.1% (2010-2015)
- This will drive the market for 2015 to reach $26,386 million, an increase of 22.4% since 2010
- The generics market represents 57.1% of total pharma market, had total revenues of $4.9 billion in 2010, representing a CAGR of 14.3% between 2006 and 2010
- The performance of the market is forecast to decelerate, with an anticipated CAGR of 6.4% for the five year period 2010 - 2015

Ontario is the hub for many pharmaceutical giants in Canada, both research based and generics.

- Canada’s pharmaceutical industry is the 9th largest globally, with revenues of over $8B from more than 25 Ontario companies, close to 60% of Canadian revenues.
- Ontario is a major North American life sciences hub.
- Strong history of medical breakthroughs – includes discovery of insulin, development of the pacemaker, world’s first hospital-to-hospital telerobotic-assisted surgery.
- The province’s pharmaceutical industry employs more than 15,500 workers.
- Home to 50% of Canada’s pharmaceutical and biotech companies, including global giants AstraZeneca, Bayer, GlaxoSmithKline, Eli Lilly, Johnson & Johnson.
- Most of the pharmaceutical manufacturing capacity in Canada is generic, and the majority are located in Ontario.

The Canadian generic drug industry is very export focused, with most output coming from Ontario.

- Canada’s generic drug industry generates 40% of its sales volume from exporting made-in-Canada pharmaceuticals, primarily to the United States.
- Generic pharmaceutical companies export more than $1B annually from Ontario.
- At its Toronto R&D and production facilities, Apotex has developed a triple combination HIV/AIDS drug for export to developing countries under Canada’s Access to Medicines Regime (CAMR) and offered to sell it at cost.

### Trade Balances: Pharmaceutical and Medicine Manufacturing

<table>
<thead>
<tr>
<th>Year</th>
<th>Export</th>
<th>Import</th>
<th>Balance</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>1,853</td>
<td>5,962</td>
<td>(4,109)</td>
</tr>
<tr>
<td>2001</td>
<td>2,307</td>
<td>7,044</td>
<td>(4,737)</td>
</tr>
<tr>
<td>2002</td>
<td>2,552</td>
<td>8,071</td>
<td>(5,519)</td>
</tr>
<tr>
<td>2003</td>
<td>3,401</td>
<td>9,044</td>
<td>(5,643)</td>
</tr>
<tr>
<td>2004</td>
<td>4,011</td>
<td>9,563</td>
<td>(5,551)</td>
</tr>
<tr>
<td>2005</td>
<td>4,337</td>
<td>10,030</td>
<td>(5,693)</td>
</tr>
<tr>
<td>2006</td>
<td>5,443</td>
<td>11,370</td>
<td>(5,927)</td>
</tr>
<tr>
<td>2007</td>
<td>6,802</td>
<td>12,334</td>
<td>(5,533)</td>
</tr>
<tr>
<td>2008</td>
<td>6,768</td>
<td>12,661</td>
<td>(5,893)</td>
</tr>
<tr>
<td>2009</td>
<td>7,569</td>
<td>14,511</td>
<td>(6,942)</td>
</tr>
</tbody>
</table>

Source: Statistics Canada. Value in Millions of Canadian Dollars.
Overall, Toronto is highly economical for companies seeking to conduct clinical trials

- Toronto is extremely cost competitive relative to other major cities for conducting clinical trials
- Generous R&D tax incentives
- Internationally recognized expertise with well-established clinical trial networks, contract research organizations
- Streamlined access to population that is demographically and ethnically diverse

Source: Invest in Canada: Clinical Trials in Ontario, 2009
Pharmaceutical Industry
Emerging Markets
Many opportunities for chronic diseases treatment

- Two-thirds of total deaths in Canada are from chronic diseases
- Three out of five Canadians older than 20 years of age have a chronic disease and four out of five people are at risk
- Cardiovascular disease, cancer, chronic obstructive pulmonary disease (COPD) and diabetes are the leading causes of morbidity and mortality
- Cardiovascular disease is the number one killer in Canada and also the most costly disease in Canada
- Sales of prescription cardiovascular drugs were worth more than C$3 billion, while total number of cardiovascular drugs prescribed in 2010 was 77.13 million, an increase of 3.6% compared with 2009
- Lipitor was Canada’s most dispensed drug in Canada, with 12.3 million prescriptions
- In total, chronic diseases cost the Canadian economy at least C$190 billion (US$187.2 million) a year, according to the Public Health Agency of Canada

Source: Mergent Online - Pharmaceuticals Sectors North America, Dec 2011
Emerging market in the manufacture and development of generic drugs

- Generics accounted for 57.3% of prescriptions, and approximately 26% of the total pharma market in Canada
- Growth boosted by patent expiration of branded drugs, rapidly aging population, and government support through cost reduction measures
- The generics market is expected to reach $9.4 billion in 2013
- This represents a CAGR growth of over 14% between 2009-2013
- However, generic drug prices are considerably higher than the US
- Canadian prices on 64 generic prescription drugs available in both Canada and the US were 90% higher on average than American prices for the same drugs
- Retail prices for generic drugs in Canada were 73% of the price of their brand-name equivalents, compared with just 17% of the price of their brand-name equivalents in the US
Therapeutic areas of focus for generic drugs

- Cardiovascular drugs are #1 in terms of total prescription
- Oncology at top in terms of hospital sales, $808.1 million revenue
- Diabetes, hypertension expected to drive generics market in the future
- The regenerative medicine market has the potential to emerge as one of the largest growth drivers of the global economy, and experience explosive growth to reach US$15-US$20 billion in the next 15 years

Source: Mergent Online - Pharmaceuticals Sectors North America Dec 2011
Pharmaceutical Industry
Industry Trends
Generic drug uptake is still slow due to disparity between patented and generic drug regulations

- The level of generic drug uptake in Canada is significantly lower than the uptake of patented medicines

Several factors may be holding back this trend:
- The price of generic drugs is not significantly cheaper than their patented counterparts
- Patented drugs have a regulatory approval board that has some influence over pricing; however, there is no equivalent in place for generics
- Drug pricing is generally allocated by province or territory, which can cause further discrepancies between medicines in difference areas

Source: Mergent Online - Pharmaceuticals Sectors North America Dec 2011
Decline in the early half of 2011 in pharmaceutical & medicine manufacturing

- Ontario faced a decline in the major indicators of the pharmaceutical and medicine manufacturing industry

- National output from Ontario is over 60%

Source: Ontario Economic Overview, Jan 2012
Pharmaceutical companies are actively looking for ways to offset generic competition on out of patent drugs

- Large pharmaceutical companies are focusing on the long neglected rare disease market as a potential growth area.

- Doing so could help overcome their thinning drug pipelines, profit margins and partially offset the impact of generic competition on the rest of their drug portfolios.

- Drugs worth more than US$30 billion will go out of patent in 2012.

- Companies such as Pfizer, Eli Lilly and AstraZeneca are expected to see a severe hit to bottom line figures in the near future.

Source: Mergent Online - Pharmaceuticals Sectors North America, Dec 2011
Open innovation is a new model that pharmaceutical companies are looking to adopt to enhance pipelines and increase overall productivity.

- Only 4 of the top 10 pharmaceutical companies have pipelines that contain products valuable enough to offset the losses, assuming the molecules make it all the way through to successful commercialization.

- On average, of every dollar in revenue lost from established products by the largest pharmaceutical companies, new products are only expected to replace 26 cents.

- Open innovation provides the opportunity for organizations to look beyond their own walls to address the “innovation deficit” at a reduced cost.

“At Pfizer Canada, over the last two to five years, open innovation has become a significant platform in our strategy.” – Mark Lundie, Director, R&D at Pfizer Canada Inc.

<table>
<thead>
<tr>
<th>SECTOR</th>
<th>COMPANIES</th>
<th>FACTORS</th>
<th>INTELLECTUAL PROPERTY</th>
<th>INTERNATIONAL COMPARISON</th>
</tr>
</thead>
</table>

Source: MaRs White Paper: New Models of Innovation in Life Sciences, April 2011
Open innovation is a new model that pharma companies are looking to adopt to enhancing pipelines and increase overall productivity.

**Collaboration is at the core of the open innovation approach:**
- Open innovation can have a number of different definitions
  - Definition is the free flow of IP
  - Open source with no IP
  - Semi-open with public-private partnership
  - Pre-competitive innovation - early stage research where competitors and partners would share resources for the benefit of all
  - IP position would come into play only at a later pre-determined, still pre-competitive stage

**Some models in progress:**
- Ontario Institute of Cancer Research, keeps the IP as part of the arrangement
- Collaborations with the Centres of Excellence in Commercialization and Research (CECR) are already seeing some commercial success
- More recently, Pfizer Canada supported Pfizer Inc’s partnership with one of the world’s pre-eminent pre-competitive research initiatives: Toronto-based Structural Genomics Consortium (SGC)

Source: MaRs White Paper: New Models of Innovation in Life Sciences, April 2011
Closed innovation model vs. open innovation model

Source: MaRS White Paper: New Models of Innovation in Life Sciences, April 2011
Differences between the traditional pharma blockbuster models and the open innovation model under consideration by many firms

Source: MaRS White Paper: New Models of Innovation in Life Sciences, April 2011
A shift towards active development in Ontario

In the recent years, Ontario has made significant investment in the health technologies industry:

- Ontario supports five Ontario Centers for Excellence, a program established to strengthen research linkages between academia and industry.
- Ontario launched the Life Sciences Commercialization Strategy in 2010.
- The province is investing over $161 million as part of the strategy.
- Ontario possesses a network of research parks and incubators which includes:
  - The MaRS Discovery District in Toronto: dedicated to accelerating the rate of successful commercialization of new discoveries.
  - The Stiller Center for Technology Commercialization: designed for start-up technology-based companies to help them bring their innovation to the market place.
  - The Ottawa Biotechnology Incubation Center: involved in the growth sectors of telecommunications, photonics, microelectronics, software and life sciences.

Source: Life Sciences Ontario and Ontario Canada websites.
Ontario Life Sciences Commercialization Strategy was launched in 2010 to further the life sciences sector.

- Ontario aims to be the best place in the world to take innovative bio-medical discoveries and turn them into new products and services that meet unmet patient needs.
- Through capitalizing on local talent and research capacity, the province seeks to accomplish this by executing a Life Sciences Commercialization Strategy, which consists of three objectives:
  - promote even greater collaboration among government, academia and industry
  - position Ontario as the “go-to” place for innovative multinational pharmaceutical and advanced health technologies firms looking to source new technologies and test promising new therapies
  - grow the Ontario biotech industry, already the largest in Canada, to the point where it rivals those of leading centres in the U.S. and abroad

Source: Health Technology Exchange – Life Sciences Commercialization Strategy, April 2010
Pharmaceutical Industry Sector Profile
Ontario has the infrastructure, people, and expertise to conduct top quality clinical trials

- Centrally managed public healthcare system helps streamline patient characterization, recruitment, and tracking
- There are many contract research organizations who are well experienced in managing clinical trials across Canada as well as internationally
- Data from Ontario clinical trials is recognized by Canadian, US, and EU medical authorities
- Health Canada’s regulatory review process is highly efficient:
  - 7 days for Phase I studies
  - 30 days for other Phases

Source: Invest in Canada, Clinical Trials in Ontario 2009
Ontario has advanced pharma manufacturing capabilities

- Ontario is a manufacturing powerhouse, with people, resources, the location and infrastructure essential for success in today’s competitive economy – which is why 11 of the world’s 20 largest multinational advanced health technology companies have operations in here.

- The use of strategic outsourcing is becoming an accepted practice to spread the risk of development and lower fixed costs.

- Ontario has world-class capacity in terms of contract manufacturing services, both for small-molecule and protein-based therapies.

Source: Health Technology Exchange – Life Sciences Commercialization Strategy, April 2010
Pharmaceutical Industry Clusters
Toronto is the largest pharmaceutical cluster in Ontario, and Canada

- Toronto is home to 55% of Canada's pharmaceutical companies, making the Toronto region the largest pharmaceutical cluster in the nation
- Of the 17,000 pharmaceutical jobs in Canada, 11,000 are based in the Toronto area

**Recent Investments**

- Sanofi Pasteur invested $350 million over 10 years for a worldwide Cancer Vaccine Program, anchored at a $25 million corporate research campus located at Sunnybrook and Women's College Health Sciences Centre
- Eli Lilly's 65,000 ft² research facility at Sunnybrook and Women's College Health Sciences Centre has a global mandate to improve the effectiveness of developing drugs for osteoporosis, health disease, cancer, mental health, and infectious diseases
- Apotex's new $150 million R&D facility will be the largest of its kind in Canada.

Source: InvestInToronto.ca
Mississauga is the third largest life sciences cluster in Canada

Mississauga Life Sciences cluster
- Mississauga is home to the third largest life sciences cluster in Canada with more than 375 companies employing approximately 24,800 people
- The industry is attracting highly-skilled scientific and technical personnel with post-secondary education from in and around Mississauga
- The industry also requires experienced management to lead the production and drive the marketing of products and services

Companies in the area include
- Alcon Canada Inc.
- Allied Research International
- Amgen Canada Inc.
- AstraZeneca Canada Inc.
- Baxter Corp.
- Cobalt Pharmaceuticals Inc.
- Contract Pharmaceuticals Ltd.
- GlaxoSmithKline Inc.
- Hoffmann-La Roche Ltd.
- Maxxam Analytics Inc.
- MDS Pharma Services
- Patheon Inc.
- Pharma Medica
- Valeant Pharmaceuticals

Source: A Profile of Mississauga’s Life Sciences Cluster, 2008
Pharmaceutical companies are significant R&D investors in both academic and small companies.

- The pharmaceutical industry re-invests over $1.1 billion annually in R&D in Canada, of which Ontario is the largest recipient, receiving more than $500 million.
- Pharmaceutical companies are significant investors both in academic research and in small biotech companies.
- Pharmaceutical companies have invested more than $1.1 billion in local R&D over the past decade.
- AstraZeneca invested $250 million over 10 years to facilitate the expansion and the creation of 700 new jobs.
- The Structural Genomics Consortium at the University of Toronto for research on over 350 proteins will be made available to scientists worldwide. This project is funded by a $70 million grant from the Welcome Trust in the UK and support from GlaxoSmithKline.

Source: InvestInToronto.ca
Pharmaceutical Companies
Top Industry Players
Many global giants in the pharma industry are present in Ontario

<table>
<thead>
<tr>
<th>Company</th>
<th>Specialty</th>
<th>Employees in Canada</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apotex</td>
<td>Generic drugs</td>
<td>5,800 people</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>Oncology, cardiovascular, central nervous system disorders, gastrointestinal, respiratory care</td>
<td>1,050 people</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>Diabetes, neuroscience</td>
<td>500 people</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>Vaccines, respiratory care, central nervous system disorders</td>
<td>3300 people</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>Consumer healthcare</td>
<td>N/A</td>
</tr>
<tr>
<td>Pfizer Canada</td>
<td>Consumer Healthcare</td>
<td>2000 people</td>
</tr>
<tr>
<td>Roche</td>
<td>Cancer drugs, viral infections, metabolic, central nervous system disorders and inflammatory diseases</td>
<td></td>
</tr>
<tr>
<td>Sanofi-Pasteur</td>
<td>Vaccines</td>
<td>1100 people</td>
</tr>
</tbody>
</table>
Factors
Labour Force
The concentration of R&D in Canada is the highest in Ontario

• With almost 90,000 full-time equivalent employment in R&D, Ontario is home to 45 per cent of Canada's total R&D personnel

• Ontario is the home of world-renowned research centres such as University of Toronto Banting & Best Dept of Medical Research; Ottawa Heart Institute, London Health Sciences Centre

Talent programs have been implemented by the province to encourage research & development

**Research Talent Programs**

- The Early Researcher Award (ERA) program provides funding to help promising, recently-appointed Ontario researchers build their research teams
- The Post-Doctoral Fellowship (PDF) program provides outstanding scientists with two-year fellowships at Ontario universities
- The Premier’s Discovery Awards (PDA) celebrate Ontario’s most accomplished researchers by recognizing excellence in research for either a single discovery or a body of work on both domestic and international fronts
- The Premier’s Catalyst Awards (PCA) help build a culture of innovation and entrepreneurship in Ontario by recognizing excellence and leadership in innovation
The pharmaceutical manufacturing labour market is still feeling the effects from the recession

- Ontario has an extensive apprenticeship program and co-op training network that produces industry ready workers

- Canada lost more than 3,600 pharmaceutical jobs in the second half of 2010 as domestic and export sales slowed

- Pharmaceutical manufacturing in Canada, and other established markets, was hit by the recession, emerging market competition and industry-specific challenges

- Layoffs and closures followed and, although there was some market improvement, recovery was slow

Source: Mergent Online – Pharmaceutical Sectors North America, June 2011
Pharmaceutical Manufacturing Employment in Ontario

- Employment in the pharmaceutical and medicine manufacturing sector has shown an overall decline from 2008-2010.
- Slight improvement in Q1 of 2011, remains to be seen if the change in trend will be sustained.

Source: Industry Canada Ontario Economic Overview, Jan 2012
Factors
Future Plans
Highlights from recent developments in Ontario

Ontario’s research and development footprint has been given a boost, resulting in the creation of an estimated 300 new research jobs over the next five years.

**Key Developments**

- **Roche Canada** is developing a new $200M research centre for clinical trials at its Mississauga plant, which will create 200 highly specialized research jobs. With this new venture, Roche will have more than 650 employees in Ontario.

- **Novartis Pharmaceuticals Canada** announced a $40M investment towards a global clinical study led from Hamilton for the drug Rasilez.

- **Teva Canada** is investing $56M to expand its production plant in Stouffville, while GlaxoSmithKline has announced it will invest $30M to expand its manufacturing facility in Mississauga.

Source: Industry Canada Ontario Economic Overview, Jan 2012;
Highlights from recent developments in Ontario

- Sanofi Pasteur established a $101M vaccine research and development facility in Toronto in June
  - The company spends nearly C$200 million dollars on R&D in the country, making it the number one investor in the country’s pharmaceutical industry
- Chinese drugmaker, Beijing SL Pharmaceutical (SSE: 002038) announced in August that it would invest C$20 million (US$19.7 million) in Ontario to form a joint venture with local Canadian partner, PnuVax Inc
  - The JV startup, called PnuVax SL Biopharmaceuticals, will specialize on the R&D, production, and sales of vaccines and antibodies
  - SL Pharmaceutical will hold an 85% stake in the joint venture while PnuVax, which specializes in vaccine manufacturing processes, will own the rest

Source: Industry Canada Ontario Economic Overview, Jan 2012;
Ontario is partnering with Quebec to form a formidable cluster

- Ontario and Quebec have partnered to create the Québec-Ontario Life Sciences Corridor, a key initiative of the Ontario-Québec Trade and Cooperation Agreement

- The corridor will contain 1139 life sciences companies and over 65,000 employees, making it one of the largest bioclusters in the world
Intellectual Property Measures
Patents
Ontario is trying to improve the flow of Intellectual Property from researchers to companies in order to improve commercialization

- The Northern Ontario Heritage Fund Corporation’s Emerging Technology Program encourages IP development and commercialization of new technologies
  - Non-repayable contributions of up to $100,000 may be provided on a cost-shared basis for research and pre-competitive development technical projects.
  - Repayable loans of up to $1 million or 50 per cent of eligible project costs, whichever is less, may be provided to capital projects.
  - Up to one-half of the NOHFC funding may be in the form of a conditional grant with the remainder in the form of a repayable loan.

Source: Northern Ontario Heritage Fund Corporation
The environment for IP protection in Canada needs to be improved to encourage further R&D

- World class IP regime will help attract more jobs and more investment in pharmaceutical industry
- Although Canada already has strong governance, research institutions and educated workforce, improvements to IP would increase our competitive advantage
  - Right to appeal an adverse court decision on a patent challenge
  - Currently, generic manufacturers have this advantage but research based companies do not
  - Additional scope and duration of IP protection is needed to be consistent with other industrialized countries
  - Patent term restoration to offset regulatory delays in approval of a medicine should be implemented, a protection which other G7 countries have
The environment for IP protection in Canada needs to be improved to encourage further R&D.

**Comparison of Canadian and Non-Canadian Bio/pharmaceutical IP Regimes**

<table>
<thead>
<tr>
<th>Sector</th>
<th>Companies</th>
<th>Factors</th>
<th>Intellectual Property</th>
<th>Taxes</th>
<th>Challenges</th>
</tr>
</thead>
<tbody>
<tr>
<td>SECTOR</td>
<td>COMPANIES</td>
<td>FACTORS</td>
<td>INTELLECTUAL PROPERTY</td>
<td>TAXES</td>
<td>CHALLENGES</td>
</tr>
<tr>
<td>Right of Appeal</td>
<td>European Union (27 Member States)</td>
<td>Canada</td>
<td>United States</td>
<td>Other Countries</td>
<td></td>
</tr>
<tr>
<td>Data Exclusivity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No ‘linkage’ regimes like in Canada or in US.</td>
<td>PM (NOC) Regulations that link market approval to patent validity.</td>
<td>Linkage regime similar to Canada’s (the “Hatch-Waxman” system)</td>
<td>Canada and US are only major countries with “linkage” regimes.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>However, provisional measures (e.g. interlocutory relief) are also available in EU to prevent patent infringement.</td>
<td>No provisional measures available. Inequities in “linkage regime” (e.g. no right of appeal for innovators) favor generic manufacturers over innovators.</td>
<td>Absence of problematic inequities: e.g. innovators have a right of appeal. Provisional measures available.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Source:** Rx&D Reality Check: Analysis of the CGPA’s Economic Impact Assessment of Proposed Pharmaceutical IP Provisions, 2011
The environment for IP protection in Canada needs to be improved to encourage further R&D.

### Comparison of Canadian and Non-Canadian Bio/pharmaceutical IP Regimes

<table>
<thead>
<tr>
<th>Patent Term Restoration</th>
<th>European Union</th>
<th>Canada</th>
<th>United States</th>
<th>Other Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Maximum 5 years additional market exclusivity.</td>
<td>Maximum 5 years additional market exclusivity.</td>
<td>Maximum combined post-approval market exclusivity 14 years.</td>
<td>Like EU, combined 5 year / 15 year max.</td>
</tr>
<tr>
<td></td>
<td>Maximum combined patent/ Supplemental Protection Certificates (SPC) post-approval market exclusivity of 15 years.</td>
<td>None</td>
<td>Max combined post-approval market exclusivity 14 years.</td>
<td>Japan: Like EU, combined 5 year / 15 year max.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>South Korea: Max 5 year additional market exclusivity.</td>
<td>Switzerland: Max 10 years additional market exclusivity.</td>
</tr>
</tbody>
</table>

Research based pharma companies require significantly longer time for drug development

- Comparison of drug development timeline for generic companies vs research based pharma companies

<table>
<thead>
<tr>
<th>Drug development phases</th>
<th>Innovative companies</th>
<th>Generic companies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research &amp; development</td>
<td>2-6.5 years (early stage development)</td>
<td>6 months-1 year (secure active ingredient and formulation)</td>
</tr>
<tr>
<td>Tests &amp; trials</td>
<td>7 years for 60% of total costs</td>
<td>3-6 months for 1 million</td>
</tr>
<tr>
<td>Time from laboratory to market</td>
<td>11-13 years</td>
<td>2.25-6.5 years</td>
</tr>
<tr>
<td>Estimated total costs</td>
<td>897 million</td>
<td>4 million</td>
</tr>
<tr>
<td>Time to recoup investments</td>
<td>7-9 years</td>
<td>No limit of time</td>
</tr>
</tbody>
</table>


- Research-based companies spend more than 200 times the amount spent on the development of a drug than do generic companies.
- The association wants a strong and predictable protection of their intellectual property

Source: Ontario Innovation for a Better Tomorrow, Jan 2011
Balance is needed between research based pharmaceutical firms and generic drug makers

**Comprehensive Economic and Trade Agreement (CETA)**

- Research-based pharmaceutical firms and generic drug makers in Canada have differing opinions over the Comprehensive Economic and Trade Agreement (CETA), which is now being negotiated between Canada and the EU

- The deal includes proposals from Europe that would, considerably lengthen the period of market exclusivity for brand-name drugs in Canada and provide more extensive structural protection for innovative drugs of any country in the world

- The agreement potentially creates new opportunities for economic growth in Canada through increased bilateral trade with the EU

Source: Mergent Online – Pharmaceutical Sectors North America, June 2011
The Canadian Generic Pharmaceutical Association (CGPA), reported in a study that Canadian payers, including federal and provincial governments, businesses and patients would face substantially higher drug costs as exclusivity is extended on top-selling prescription drugs, with the annual increase in costs likely to be approximately C $2.8 billion (US$2.7 billion) a year.

Canada’s Research-Based Pharmaceutical Companies (Rx&D) association, however, disagreed with the CGPA’s claims, and said it was based on flawed assumptions and should be ignored.

Rx&D further added that IP improvements over the past 25 years have generated an 800% increase in pharmaceutical R&D investment in Canada, a fact that the CGPA had ignored.

Source: Mergent Online – Pharmaceutical Sectors North America, June 2011
Intellectual Property Measures
R&D Funding
The current venture capital financing shortage is taxing the resource intensive nature of the pharma research industry

- It takes years and tremendous resources – up to $1 billion – to develop just one drug
- Tightening credit markets post recession, still recovering
- Recognized shortage of venture capital financing
- Significant financing gap between early and late-stage growth that needs to be closed

Source: Health Technology Exchange – Life Sciences Commercialization Strategy, April 2010
Ontario has several funding and support resources for companies commercializing technologies and products

- The $250 million Ontario Emerging Technologies Fund aims to drive start-up investment in high growth potential companies together with qualified venture capital funds and private sector investors.
- The $205-million Ontario Venture Capital Fund focuses on attracting investment in high growth companies with the goal of bringing exciting new discoveries to market faster.
- The $29-million Investment Accelerator Fund provides high-potential innovative companies in Ontario with early-stage financial support and management expertise to help make these businesses more attractive to follow-on investors.
- The Health Technology Exchange – htx.ca – accelerates innovation, commercialization and growth of Ontario’s medical and assistive technologies sector by providing Ontario scientists, engineers, and entrepreneurs with funding, market research and intelligence, and networking opportunities.
- The Ontario Research Fund (ORF) is a key component of Ontario’s plan to promote scientific excellence by supporting research that can be developed into innovative goods and services that will boost Ontario’s economy.

Source: Health Technology Exchange – Life Sciences Commercialization Strategy, April 2010
Key initiatives through the Ontario Life Sciences Commercialization Strategy

- Direct $1 million to MaRS Innovation for proof-of-principle funding to accelerate the commercialization of Ontario-generated IP

- Invest up to $17 million in new infrastructure for clinical trials and investigational testing. This is an area of great potential for the life sciences industry, including the pharma sector

- The investments in new infrastructure include:
  - Ontario Clinical Trials Fellowship Program, aimed at recruiting new talent, which involves matching funds from industry
  - Expanding capacity at McMaster University’s world-class Population Health Research Institute to support the management of Phase IV clinical trials on a global scale
  - New province-wide coordinating infrastructure to streamline administrative processes and ethics reviews across multiple clinical sites in order to increase speed of patient recruitment

Source: Health Technology Exchange – Life Sciences Commercialization Strategy, April 2010
The Next Generation of Jobs Fund aims to accelerate projects to help establish the province as a global leader.

- The Next Generation of Jobs Fund is a five year $1.15 billion strategy that aims to help innovative companies lead worldwide, particularly in markets with long term growth potential.

- The fund is aimed at projects that can create knowledge based jobs in Ontario, such as pharmaceutical research & manufacturing.

- Goal is to create synergies among researchers, industry and entrepreneurs.

- Having a high impact, large scale projects is part of the requirements (over $25 million, or at least 100 jobs).

- Modelled after the province’s $500 million Automotive Strategy.

Source: Ontario’s Next Generation of Jobs Fund, 2008
Taxes
Canada’s Scientific Research and Experimental Development (SR&ED) tax program provides tax credits

Scientific Research and Experimental Development (SR&ED) Tax Incentive Program

- The first $3 million of current expenditures is refundable up to $1.3 million per year (35% federally and 10% provincially) in Ontario for Canadian-Controlled Private Corporations (CCPC), provided taxable income under $700,000 and taxable capitalization under $50 million.
- For those qualifying CCPCs, there are federal tax credits of 20% on research and expenditures above $3 million, of which 40% of such credits are refundable.
- Non-CCPCs can receive a 20% non-refundable federal credit on current and capital expenditures and a 10% certain refundable credit on the first $3 million, subject to income and capital limits.
- Banks will advance loans based on estimated refundable Scientific Research and Experimental Development (SR&ED).

Source: Invest Toronto – Life Sciences Sector
Many provincial initiatives are in place to provide tax credits to encourage innovation and research.

**Ontario Business Research Institute (OBRI) Refundable Tax Credit**
- Up to $4 million (20% of up to $20 million of pre-clinical research expenditures) of refundable tax credit for pre-clinical work at approved academic institutions in Ontario
- Available to for-profit companies that have a permanent establishment in Ontario
- Advance ruling no longer required

**Ontario Innovation Demonstration Fund**
- Up to $4 million per company over 2 years provided to select early-stage companies

Source: Invest Toronto – Life Sciences Sector
Ontario offers even more credits and incentives for R&D specifically

**Ontario Research and Development Tax Credit (ORDTC)**

- It is a non-refundable tax credit that provides a 4.5 per cent tax credit based on eligible SR&ED expenses carried out in Ontario.
- One of the most generous R&D tax credit programs in the world.
- Among G7 countries, only Italy has a more generous tax benefit for R&D.
- When tax credits are factored in, $100 in R&D expenditures can be reduced to less than $44 – and less than $37 for small businesses.
- The credits can be carried back for 3 years, or forward for 20 years.
- New corporations that commercialize intellectual property developed by Canadian universities, college or research institutions can take advantage of the Ontario Tax Exemption for Commercialization (OTECE).
- OTEC refunds provincial income tax and corporate minimum tax for each of a corporation’s first ten taxation years.
- Companies are offered the opportunity to acquire the rights to the IP developed at public research centres in Ontario.

Challenges
Challenges for the pharmaceutical industry are driven by expiration of patents and capital requirements

- The sector continues to face a dynamic business environment driven by expiring patents, reduced R&D spending, and potential intellectual property (IP) regulatory reform

- Among smaller players, raising capital continues to be the biggest challenge

- Funding sources being sought out are strategic partners for amounts over $10 million

- Due to the up-front, capital intensive nature of the industry, many smaller companies believe it will take over 5 years for companies to earn revenue

Source: Industry Canada Ontario Economic Overview, Jan 2012; PwC Canadian Life Sciences Industry Forecast 2011