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Biopharmaceutics in Canada



Benchmarking of
Canadian Biopharmaceutical
Science and Technology

Prepared for Industry Canada
Life Science Branch

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Executive Summary

- This report provides a quantitative analysis of the Canadian biopharmaceutical sector using the Medline biomedical scientific articles database and the United States Patents and Trademark Office (USPTO) database.
- Using time series (1990-2001), the report outlines the evolution of biopharmaceutics at the world and Canadian levels. It uses stationary distributions (1996-2001) to compare Canada to other countries as well as Canadian provinces, Census Metropolitan Areas and institutions among themselves.
- The biopharmaceutical sector has been categorized into fifteen therapeutic and nine technology clusters. In-depth analyses were performed for scientific output as well as for invention output using the clusters independently and in pairs (therapy-technology).

PART I SCIENTIFIC PUBLICATIONS IN BIOPHARMACEUTICS

Biopharmaceutical Science at the International Level

- Between 1990 and 2001, the number of papers published in the field of biopharmaceutics at the world level increased by 33%, that is, from 48,000 to 64,000 papers per year.
- Between 1996 and 2001, Canada published 13,076 papers, which represents 3.5% of the world output in the field.
- Close to 16% of Canadian papers in the biomedical and clinical research sector belong to the field of biopharmaceutics compared to 14% at the world level.
- The indicators used here show that, globally, Canada is an important producer of scientific output in biopharmaceutics, and its production is of a high standard.
- Between 1996 and 2001, papers published in Canadian therapeutic research concentrated particularly in hormone therapies (2,958 papers), psychotherapeutics (2,313) and cardiovascular therapies (1,957). Despite their predominant presence in the literature, the annual growth of papers in hormone therapies at the Canadian and world levels has been relatively low compared to that of other therapies.
- Vaccines and other types of immunization, the fastest growing therapeutics in Canada, grew by over 130% between 1990 and 2001. This trend follows the annual growth observed worldwide. Anti-virals is the second most growing therapy in Canada, but the Canadian world share does not seem to follow the pace of world growth in recent years.
- Among technological platforms associated with biopharmaceutics, the genomics, proteomics and genetic engineering platform leads in Canada in terms of total scientific output and annual growth of papers.

Biopharmaceutical Science in Canada

- At the provincial level, Ontario has the largest number of papers, followed by Quebec, Alberta and British Columbia.
- When a variety of indicators are taken into account, Quebec ranks first in biopharmaceutical science, followed by Alberta, Ontario, Manitoba and British Columbia.
- Montreal is the leading CMA in absolute number of papers and is followed by Toronto and Vancouver. When population is taken into account, Saskatoon and Sherbrooke are the leading CMAs in biopharmaceutical science.
- Scientists from Canadian universities authored approximately 60% of the papers in biopharmaceutics. Health sector institutions authored about 37%, while government bodies and corporations are responsible for 2% each.
- Leading universities are the University of Alberta, the University of British Columbia, the University of Toronto, McGill University, the University of Calgary and McMaster University.

- Leading health sector institutions are the University Health Network, the Hospital for Sick Children, the Centre Hospitalier Universitaire de Québec (CHUQ), Toronto Public Health and the Royal Victoria Hospital.
- The leading government institutions are the National Research Council of Canada (NRC), Health Canada and Agriculture and Agri-Food Canada.
- The leading corporations are Merck Frosst, Boehringer-Ingelheim, Aventis and BioChem Pharma.

PART II TECHNOLOGICAL INVENTIONS IN BIOPHARMACEUTICS

Biopharmaceutical Inventions at the International Level

- Between 1990 and 2001, the number of patents granted by the USPTO in the field of biopharmaceutics has grown sixfold, increasing from 391 to 2,492 patents per year.
- At the world level, using a multicriteria analysis, Canada ranks third overall in biopharmaceutical inventions (ex equo with Denmark). Canadian inventors are wholly or partly responsible for 702 inventions in biopharmaceutics.
- 531 patents in biopharmaceutics are wholly or partly owned by Canada, and 89% of these patents are owned by institutions. The net outflow of IP is about 5% (fraction of intellectual property by Canada/fraction of invention by Canada).
- As with scientific output, the genomics, proteomics and genetic engineering platform is the leading technological platform in patents. Cancer therapeutics is the most important therapeutics patent cluster, while it was only 3rd in terms of scientific papers.

Biopharmaceutical Inventions in Canada

- Although Ontario and Quebec hold considerably more patents than other Canadian provinces, Alberta and Saskatchewan have a better performance when population, specialization in biopharmaceutics and citations per patent are factored in.
- Saskatchewan is the only province with a positive flow of IP and Ontario has a very small outflow. Other provinces have an outflow of IP varying from 14% to 100%.
- Toronto is the leading Canadian Census Metropolitan Area (CMA) in terms of the absolute number of patents and is followed by Montreal, Edmonton, Vancouver, Saskatoon and Ottawa–Hull. Each of these CMAs is responsible for more than 30 inventions in biopharmaceutics.
- When population is factored in, the Saskatoon CMA is the clear leader in biopharmaceutics, followed by Edmonton, Toronto, London, Montreal and Ottawa-Hull.
- There are about 131 Canadian institutions with at least one patent in biopharmaceutics.
- Twenty-two leading institutions received on average at least one patent every two years. They own about 64% of the Canadian IP held by institutions involved in biopharmaceutics. Eight of these institutions are corporations, eight are from the university sector, four are from the government or non-government sector, and two are from the hospital sector.
- Not surprisingly, leading companies come mainly from the pharmaceutical sector (e.g. Aventis, Boehringer Ingelheim and NPS Allelix).
- The leading universities are the University of Saskatchewan, the University of British Columbia and McGill University.
- The leading government departments or agencies are the NRC and the Alberta Research Council.

Contents

LΧθ	ecutive	Summary	i
_			
vie	เทอดร.		V
Intr	oducti	on	1
PA	RT I	SCIENTIFIC PUBLICATIONS IN BIOPHARMACEUTICS	2
1	Biop	narmaceutical Science at the International Level	3
	1.1	Global trends in biopharmaceutical science	3
	1.2	Benchmarking Canada in biopharmaceutical science	
2	Biop	narmaceutical Science in Canada	
	2.1	Biopharmaceutical papers by province	12
	2.2	Biopharmaceutical papers by Canadian CMAs	
	2.3	Biopharmaceutical papers by Canadian institutions	18
PA	RT II	TECHNOLOGICAL INVENTIONS IN BIOPHARMACEUTICS	21
3	Biop	narmaceutical Inventions at the International Level	22
	3.1	Global rate of patenting	22
	3.2	Distribution of biopharmaceutical inventions by cluster	
	3.3	Leading countries in biopharmaceutical inventions	25
4	Biop	narmaceutical Inventions in Canada	28
	4.1	Biopharmaceutical patents by province	28
	4.2	Biopharmaceutical Patents by Canadian CMAs	30
	4.3	Biopharmaceutical Patents by Canadian Institutions	31
Co	nclusio	n	33
Anı	nex 1	Scientific output of the world and Canada - Time series 1990-2001	35
	nex 2	Scientific output of Canadian provinces - Time series 1990-2001	
Δηι	10v 3	Scientific outputs of Canadian institutions - 1996-2001	

Figures

Figure i	Papers in biopharmaceutics in Mediine, 1990-2001	3
Figure 2	Percentage of biopharmaceutical papers by Canada, 1990-2001	4
Figure 3	Canadian scientific output by therapeutics, 1990-2001	8
Figure 4	Canadian scientific output by technology, 1990-2001	9
Figure 5	Map of Canada's strengths and weaknesses by cluster, 1996-2001	10
Figure 6	Map of Canada's strengths and weaknesses by cluster pair, 1996-2001	
Figure 7	Biopharmaceutical papers by province, 1996-2001	
Figure 8	Map of Canadian provinces' strengths and weaknesses by therapeutics, 1996-2001	
Figure 9	Map of Canadian provinces' strengths and weaknesses by technology, 1996-2001	
Figure 10	Biopharmaceutical papers by leading CMAs, 1996-2001	
Figure 11	Patents in biopharmaceutics granted by the USPTO, 1990-2001	
Figure 12	Percentage of biopharmaceutical patents by Canada, 1990-2001	
Figure 13	Biopharmaceutical patents by province, 1990-2001	
Figure 14	Number of inventions by leading CMAs, 1990-2001	
Tables		
Table I	Comparison of Canada to similar countries in biopharmaceutical science, 1996-2001	5
Table II	Distribution of papers at the world level by therapeutic and technological cluster, 1996-2001	6
Table III	Distribution of papers at the Canadian level by therapeutics and technology, 1996-2001	7
Table IV	Papers in biopharmaceutics by Canadian provinces, 1996-2001	13
Table V	Papers and average impact factor of leading Canadian institutions by sector, 1996-2001	19
Table VI	World patents in biopharmaceutics by cluster pair, 1990-2001	25
Table VII	Leading countries in biopharmaceutical patents, 1990-2001	26
Table VIII	IP of leading countries in biopharmaceutical patents, 1990-2001	27
Table IX	Patents of Canadian provinces in biopharmaceutics, 1990-2001	29
Table X	IP of Canadian provinces in biopharmaceutics, 1990-2001	
Table XI	IP of leading Canadian institutions by sector, 1990-2001	32
Table XII	World's papers in biopharmaceutics by therapeutics, 1990-2001	35
Table XIII	Canadian papers in biopharmaceutics by therapeutics, 1990-2001	
Table XIV	World's papers in biopharmaceutics by technology, 1990-2001	
Table XV	Canadian papers in biopharmaceutics by technology, 1990-2001	
Table XVI	Canadian provinces' papers in biopharmaceutics by therapeutics, 1996-2001	
Table XVII	Canadian provinces' specialization index by therapeutics, 1996-2001	
Table XVIII	Canadian provinces' relative impact factor by therapeutics, 1996-2001	
Table XIX	Canadian provinces' specialization index by technology, 1996-2001	
Table XX	Canadian provinces' relative impact factor by technology, 1996-2001	
Table XXI	Leading Canadian institutions' papers by therapeutics, 1996-2001	
Table XXII	Leading Canadian institutions' specialization index by therapeutics, 1996-2001	
Table XXIII	Leading Canadian institutions' papers by technology, 1996-2001	
Table XXIV	Leading Canadian institutions' specialization index by technology, 1996-2001	
·	5	



Scientometric analysis

The scientometric analysis is based on the use of the Medline database produced by the US National Library of Medicine (NLM). The database was conditioned by Science-Metrix with a view to producing statistics on the scientific publications in the biomedical and clinical medicine sector. The database has one limitation: it comprises only the affiliation of the first author of a paper. This means that it is difficult to perform studies on collaborations although one could foresee the development of methods to associate most authors with specific affiliations and, thus, provide a walk-around way to compute statistics on collaboration. Nevertheless, this limitation is more than made up for by the power of the keywords used in Medline - the Medical Subject Headings or MeSH. These constitute a controlled vocabulary used for indexing articles in Medline.

The construction of the dataset for the scientometric analysis is essentially based on the use of MeSH Terms. A MeSH Term is composed of a "descriptor" and a "qualifier" that pinpoints a specific aspect of the concept represented by the descriptor. Biopharmaceutical papers were selected using descriptors related to biomolecules or the synthetic replacement of biomolecules, and described by the following qualifiers:

Pharmacokinetics - Used for the mechanism, dynamics and kinetics of exogenous chemical and drug absorption, biotransformation, distribution, release, transport, uptake and elimination as a function of dosage, extent and rate of metabolic processes.

Pharmacology - Used with drugs and exogenously administered chemical substances for their effects on living tissues and organisms. It includes the acceleration and inhibition of physiological and biochemical processes and other pharmacologic mechanisms of action.

Therapeutic use - Used with drugs, biological preparations and physical agents for their use in the prophylaxis and treatment of disease. It includes veterinary use.

These are examples of MeSH Terms used in the query that selected the papers for the biopharmaceutical dataset:

- Protein, recombinant/therapeutic use
- DNA/pharmaceuticals
- Antibodies, Monoclonal/therapeutic use

In addition, the descriptors "gene therapy" and "vaccine" were used on their own. Time series cover the 1990-2001 period, and in-depth studies were performed on a dataset comprising the last six years (1996-2001).

Using the MeSH Terms, the dataset was further divided along two sets of clusters, one related to therapeutic uses and one related to technological platforms. Fifteen relevant clusters were kept for therapeutics:

- Antiarthritics
- Anti-infectives
- Antispasmodics & Antisecretives
- Anti-virals
- Bronchial & Other Respiratory Therapies
- Cancer & Other Neoplasms
- Cardiovascular Therapies
- Cholesterol

- Contraceptives
- Dermatologicals
- Diabetes
- Hemostatic Modifiers
- Hormones
- Psychotherapeutics and Neurological Disorders
- Vaccins & Other Immunizations

Similarly, nine technological clusters were retained to represent the most important technological platforms:

- Antibodies Technology (i.e. Monoclonal Antibodies, Recombinant Antibodies);
- Bioinformatics (i.e. Bioinformatics, In Silico Biology, Molecular Informatics, Data Mining);
- Biophotonics (i.e. Bioimaging, Imaging Agent, Photodynamic Therapy);
- Combinatorial Chemistry & Drug Screening (i.e. High Throughput Screening, Rational Drug Design);
- Genomics, Proteomics & DNA Technologies (i.e. Genomics, Genetics, Proteomics, DNA, RNA robes, Oligonucleotide Array, Biochips, Antisense Drugs, etc.);
- Mass Spectrometry;
- Mimetics:
- Nanotechnology (i.e. Biosensors, DNA, RNA Probes, Oligonucleotide Array, Biochips, BioMems);
- Regenerative Medicine (i.e. Stem Cell Technologies, Gene Therapy, Cloning Technologies).

These datasets were used to produce detailed statistics based on the following indicators:

Number of papers - Number of scientific papers written by authors located in a given geographical, geopolitical or organizational entity (e.g. countries, cities or institutions).

Percentage of papers relative to total output, index of specialization - This is an indicator of the intensity of research in a given geographic or organizational entity relative to the overall output for a given reference. For example, if the percentage of Canadian papers (the geographic entity) in the field of biopharmaceutics is greater than the percentage of papers in this field at the world level (the reference), then Canada is said to be specializing in this field.

Impact factor - This indicator is a proxy for the quality of the journals in which papers are published. It is based on a calculation of citations received by journals. An average is calculated through the assignment of a journal impact factor to each paper belonging to a given geographic or organizational entity.

Technometric analysis

Patents are often used as a measure of invention despite several well-known disadvantages associated with their use:

- **incompleteness**: many inventions are not patented since patenting is only one way of protecting an invention;
- **inconsistency in quality**: the importance and value of patented inventions vary considerably;
- **inconsistency across industries and fields**: industries and fields vary considerably in their propensity to patent inventions;
- **inconsistency across countries**: inventors from different countries have a different propensity to patent inventions, and countries have different patent laws.

Despite these limits, patents are widely used to compare the level of technological development of different geographic and organizational entities. This report uses the United States Patents and Trademark Office (USPTO) database. Its data are widely used to measure invention, since the USPTO is one of the largest repertories of patented inventions in the world. Because the USA is the largest market in the world, the most important inventions tend to be patented there. Although the USPTO database presents an obvious bias towards the USA, it is still a potent tool for comparing other countries.

The delineation of the field of biopharmaceutics was performed by thoroughly analyzing the entire list of US patent classes (see www.uspto.gov/go/classification for more details on US patent classes). This showed that the relevant classes were classes 424 and 514, both falling under the heading *Drug, bio-affecting, and body treating compositions*. The two classes were then analysed at length to determine the relevant sub-classes for the biopharmaceutical sector. Only subclasses associated exclusively with pharmaceutical uses of biomolecules were selected. These are the subclasses that were selected:

For **Class 424**: 1.17, 1.41, 1.45, 1.49, 1.69, 9.34, 85.1, 85.2, 85.4, 85.5, 85.6, 85.7, 93, 94, 130-194, 195.11, 196-233, 235, 278-283, 533, 534, 800-810, 821, 822, 830.

For **Class 514**: 2-21, 44, 800-809.

As for papers, patents were categorized along two variables, the therapeutic uses and the technological group. Since there is no equivalent for MeSH Terms in the USPTO database, the selection of patents for each cluster was made using two different approaches. Entities for technological groups were retained using classes and subclasses, while therapeutics were selected using chosen keywords in patent abstracts.

As the number of patents is quite small, the entire 12-year period between 1990 and 2001 was used to compute all the statistics. This methodological decision was made to guarantee that a large enough dataset was available for desegregated statistics (e.g. inventions by province). Due to the

important growth in the number of patents granted, the last years impact more on statistics than the earlier years. This goes a long way in meeting the requirement to have an up-to-date view of biopharmaceutics. Importantly, despite using the whole 1990-2001 time-period, the number of patents granted in biopharmaceutics is relatively small, and because the patent classes are not as precise as MeSH Terms, it was determined that only aggregated numbers (world level) were significant enough to be presented at the cluster level.

Unlike scientific publications, patents possess two fields that contain bibliographic information relevant to the calculation of where the patent originates: the inventor field and the assignee field. An inventor is necessarily a physical person, whereas an assignee can be a physical person and/or an institution. These fields are used to compute statistics on two different indicators, namely, invention and intellectual property (IP).

The inventor field contains data on the name of the inventor(s) and where he or she resides. The assignee field contains the name of the entity that owns the IP of the patent. When this field is empty, the inventor is the owner of the intellectual property, and, in this case, the addresses contained in the inventor field are used to compute where the IP is owned. In some cases, where an individual is the owner of the IP, the address of this owner is used to compute the location of the IP. The majority of patents are owned by corporations, and their addresses, which appear in the assignee field, are used to compute the geographical location of ownership of IP.

This report presents data on invention and IP and also distinguishes institutional IP from total IP. The location of inventors provides a proxy for the creativity of regions, whereas the location of ownership of IP, particularly of institutional IP, provides an indicator of the potential economic impact of inventions.

Citations received for each patent were counted for the year that they were granted and the two years that followed. For patents granted in 1990, for example, citations received in 1990, 1991 and 1992 were counted.

The net flow of IP was calculated on the basis of the proportion of invention by region versus the proportion of IP owned by each region. In the calculation of provincial net flow of IP, the part of invention and IP whose origin is unknown was redistributed at the *pro rata* of known inventions and IP for each province.

Otherwise, proportions were used, which explains why some totals (n) are lower than the arithmetic sum by region. This is due to collaboration between, for example, provinces (when an inventor in B.C. collaborates with an inventor in Newfoundland, then each province is given one patent; when this is calculated at the level of Canada, the patent is counted only once (n)).

Data that is weighted per capita at the level of countries uses population statistics made by the US census bureau. These statistics present annual data for every country estimated at mid-year. Data from Statistics Canada was also used to compute the number of patents per capita of Canadian provinces and Canadian Census Metropolitan Areas.

I ntroduction

This report was produced by Science-Metrix for Industry Canada's Life Sciences Branch. The latter plays an instrumental role in the development of a Biopharmaceuticals Technology Roadmap that aims to:

- Forecast future markets and identify unmet needs;
- Identify present and emerging science and technology that have the greatest economic and social impact for Canada;
- Identify the domestic business environment required to build on domestic strengths;
- Develop a strategic and relevant action plan for industry, academia and government.

All these aims rely on the provision of accurate data on Canada's strengths. This study benchmarks Canada in biopharmaceutics against the world scientific and technological frontier with the aim to characterizing Canada's strengths and comparative advantages. It also aims to characterize the geographical dynamics of Canadian biopharmaceutical science and technology and identify key players.

The report is divided into two main parts: the first part covers biopharmaceutical science and the second biopharmaceutical technology. Each part analyzes the dynamics of the field, Canada's position at the world level, the geographical dynamics at the provincial and metropolitan level and, lastly, the distribution of outputs at the institutional level.

PART I SCIENTIFIC PUBLICATIONS IN BIOPHARMACEUTICS

1 Biopharmaceutical Science at the International Level

This section presents data on the global rate of growth of scientific papers written in the field of biopharmaceutics at the world level (Section 1.1). It subsequently benchmarks Canadian scientific output against that of countries with an advanced life science and pharmaceutical sector as well as roughly comparable populations and gross domestic product: Denmark, France, Germany, the Netherlands, Switzerland and the United Kingdom (Section 1.2).

1.1 Global trends in biopharmaceutical science

Figure 1 shows that the number of papers in biopharmaceutics grew steadily during the 1990s. The number of scientific papers grew from about 48,000 in 1990 to 64,000 in 2001, an increase of one third over the twelve-year period. In terms of the percentage of total papers in the Medline database, the growth has been somewhat slower, that is, from 12.5% to 13.7% (10% growth). The growth in the number of papers in biopharmaceutics has not been steady when measured against the total number of papers in Medline, since it reached a peak in 1996. It is possible, nevertheless, that this growth is going to fall back on a "baseline", which would be consistent with the growth observed in the early 1990s (see the imaginary line drawn in Figure 1). When the data for 2002 and 2003 will be available, it will be possible to verify this hypothesis. These data show that biopharmaceutics represent a very important sector that is of rising scientific interest to the biomedical and clinical research communities.

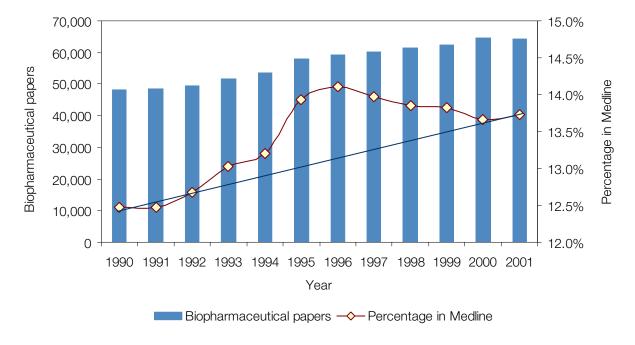


Figure 1 Papers in biopharmaceutics in Medline, 1990-2001 Source: Compiled by Science-Metrix from Medline.

1.2 Benchmarking Canada in biopharmaceutical science

Figure 2 shows that Canada's output of papers in biopharmaceutics is stable. The percentage of biopharmaceutical papers versus total Canadian papers in Medline was exactly the same in 2001 as it was in 1990: 15.2%. Similarly, the share of the total number of papers in biopharmaceutics that were written by Canadian authors was the same in 2002 as it was in 1990: 3.5%. This share is slightly higher than the percentage of Canadian papers in Medline regardless of fields, that is, 3%, which means that Canada specializes in the field of biopharmaceutics.

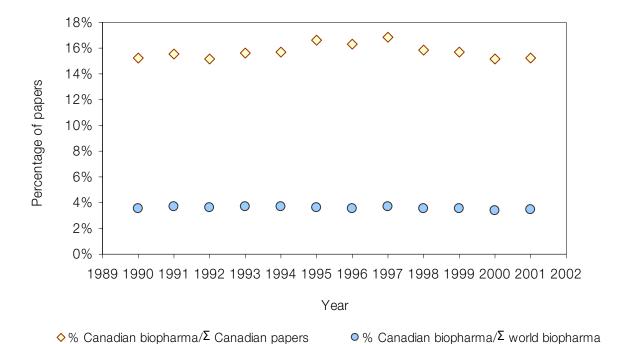


Figure 2 Percentage of biopharmaceutical papers by Canada, 1990-2001 Source: Compiled by Science-Metrix from Medline.

Table I shows that Canada published 13,076 papers between 1996 and 2001, which represents 3.5% of the world output in this field. One can see that Canada performs very well in this field since its scientific output is not so far off from that of much larger countries such as France, Germany and, to a lesser extent, the United Kingdom. This fact is reflected in the number of papers per million inhabitants: 71 in Canada against 48 in France, 42 in Germany and 65 in the United Kingdom. However, in papers per capita, Canada is easily surpassed by even smaller countries. For example, Switzerland has 107 papers per million inhabitants, Denmark 93 and the Netherlands 79.

Compared to other countries, Canada specializes in biopharmaceutics: 15.8 % of its papers in the biomedical sector are in biopharmaceutics compared to 13.9% at the world level. Within the list of comparable countries, the only country that has a larger percentage of its papers written in the field of biopharmaceutics is France. Similarly, the average impact factor is second only to that of

Switzerland, which means that Canadians scientists in biopharmaceutics tend to publish papers in highly cited journals.

Table I Comparison of Canada to similar countries in biopharmaceutical science, 1996-2001

Country	Biopharma papers Biopha	arma papers per year/ on habitants	Biopharma/ Σ Papers	Average impact factor
Canada	13,076	71	15.8%	3.6
Denmark	2,975	93	14.0%	3.0
France	17,078	48	16.7%	3.3
Germany	20,651	42	14.2%	3.3
Netherlands	7,443	79	14.7%	3.4
Switzerland	4,655	107	15.0%	3.9
United Kingdom	23,034	65	13.1%	3.5
World (n)	372,524	10	13.9%	3.4

Source:

Compiled by Science-Metrix from Medline.

Table II presents the distribution of papers at the world level according to two types of clusters: therapies and technologies. The therapeutics clusters comprise the most relevant targets of the biopharmaceutical industry. The technological clusters are the platforms that are most commonly used to develop biopharmaceuticals.

The most important target in biopharmaceuticals at the world level is associated with the use and the regulation of hormones. The second most common scientific interest is in the treatment of neurological and psychiatric disorders. Other important therapeutics includes cancer, cardiovascular diseases and anti-infective targets.

The most important technologies are those related to the genomics, proteomics and genetic engineering platform. Other important technological platforms include imaging and biophotonics as well antibodies.

Table II Distribution of papers at the world level by therapeutic and technological cluster, 1996-2001

Therapeutics	Antibodies Technology	Bioinformatics	Combinatorial & Drug Screening	Genomics, Proteomics & Genetic Engineering	Imaging & Biophotonics	Mass Spectrometry	Mimetics	Nanotechnology	Regenerative Medicine	n
Antiarthritics	781	n.s.	n.s.	632	362	n.s.	222	75	248	3,701
Anti-infective	2,311	200	530	5,950	4,304	276	600	1,716	532	43,132
Antispasmodics & Antisecretives	276	n.s.	n.s.	549	839	n.s.	405	173	77	7,929
Anti-virals	834	63	343	3,770	685	80	126	478	475	11,975
Bronchial & Other Resp. Therapies	3,085	89	138	4,539	2,588	41	1,380	681	1,151	28,420
Cancer & Other Neoplasms	5,588	199	611	18,494	6,114	171	1,045	1,718	6,410	51,362
Cardiovascular Therapies	2,990	247	216	6,032	5,774	68	1,206	1,381	1,840	51,296
Cholesterol	329	n.s.	73	1,584	732	n.s.	123	265	265	8,025
Contraceptives	74	n.s.	n.s.	231	203	n.s.	990	45	n.s.	1,886
Dermatologicals	1,672	47	55	2,050	1,797	n.s.	678	420	516	13,562
Diabetes	633	80	67	3,004	924	32	262	390	362	15,922
Hemostatic Modifiers	2,347	95	305	3,529	2,831	64	456	802	1,018	22,174
Hormones	3,271	327	401	18,415	6,674	181	6,557	2,428	1,977	75,275
Psychotherap. & Neuro. Disorders	3,232	368	400	10,482	6,074	128	1,211	5,330	2,340	60,965
Vaccines & Other Immunizations	7,917	101	344	6,018	827	37	2,489	565	782	25,031
n	31,573	1,933	5,009	89,310	36,512	1,600	9,613	16,884	18,736	372,524

n.s.: Non significant - Data with less than 30 papers are not presented and were not used in

the analysis

Source: Compiled by Science-Metrix from Medline.

Between 1996 and 2001, the most prolific areas in Canadian therapeutic research in terms of papers were hormones (2,958 papers), psychotherapeutics (2,313) and cardiovascular therapies (1,957) (see Table III). The most productive technology platforms were genomics, proteomics & genetic engineering (3,353 papers), imaging & biophotonics (1,245 papers) and antibodies technology (1,049 papers).

Table III Distribution of papers at the Canadian level by therapeutic and technological cluster, 1996-2001

Therapeutic	Antibodies Technology	Bioinformatics	Combinatorial & Drug Screening	Genomics, Proteomics & Genetic Engineering	Imaging & Biophotonics	Mass Spectrometry	Mimetics	Nanotechnology	Regenerative Medicine	n
Antiarthritics	n.s.	n.s.	n.s.	31	n.s.	n.s.	n.s.	n.s.	n.s.	129
Anti-infectives	83	n.s.	n.s.	213	107	n.s.	30	49	n.s.	1,183
Antispasmodics & Antisecretives	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	257
Anti-virals	n.s.	n.s.	n.s.	108	n.s.	n.s.	n.s.	n.s.	n.s.	283
Bronchial & Other Respiratory Therapies	123	n.s.	n.s.	187	93	n.s.	80	n.s.	53	1,089
Cancer & Other Neoplasms	146	n.s.	n.s.	582	173	n.s.	n.s.	37	159	1,389
Cardiovascular Therapies	102	n.s.	n.s.	239	169	n.s.	n.s.	52	40	1,957
Cholesterol	n.s.	n.s.	n.s.	53	39	n.s.	n.s.	n.s.	n.s.	312
Contraceptives	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	31	n.s.	n.s.	48
Dermatologicals	43	n.s.	n.s.	53	48	n.s.	n.s.	n.s.	n.s.	321
Diabetes	34	n.s.	n.s.	152	36	n.s.	n.s.	n.s.	n.s.	687
Hemostatic Modifiers	77	n.s.	n.s.	117	81	n.s.	n.s.	30	n.s.	779
Hormones	127	n.s.	n.s.	874	228	n.s.	257	101	100	2,958
Psychotherap. and Neuro. Disorders	108	n.s.	n.s.	418	238	n.s.	33	201	71	2,313
Vaccines & Other Immunizations	263	n.s.	n.s.	215	n.s.	n.s.	74	n.s.	n.s.	681
n	1,049	66	166	3,353	1,245	51	345	590	577	13,076

n.s.: Non significant - Data with less than 30 papers are not presented and were not used in

the analysis

Source: Compiled by Science-Metrix from Medline.

Figure 3 presents annual scientific production trends according to therapeutics between 1990 and 2001. In terms of annual scientific output, therapeutic vaccines and other immunizations grew by over 130% between 1990 and 2001. This trend follows that observed worldwide. Anti-virals come in second in terms of annual growth during this period (almost 105%). This area of therapeutics is growing at the same rate at the world level but the Canadian share does not seem to have followed the pace in recent years. Hence, the coming years might show some deficiencies compared to the world frontier in the Canadian biopharmaceutical sector in anti-viral therapeutics research.

In the last decade, hormone therapies reached an upper limit at the Canadian and world levels in terms of their annual growth. Even if this area of therapeutics has a relatively strong presence in the literature compared to other platforms, data reveal that its growth has levelled off or dropped slightly in biopharmaceutical research compared to that of other therapeutics.

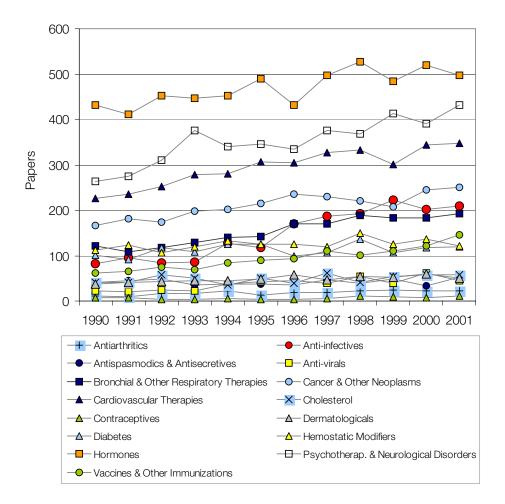


Figure 3 Canadian scientific output by therapeutics, 1990-2001 Source: Compiled by Science-Metrix from Medline.

The use of genomics, proteomics & genetic engineering techniques experienced the strongest growth in Canadian biopharmaceutical science during the last decade (see Figure 4), and this pattern is also observed at the world level. Canada's average share of 3.5 % of the world papers in genomics, proteomics & genetic engineering is fairly constant over the 1990-2001 period.

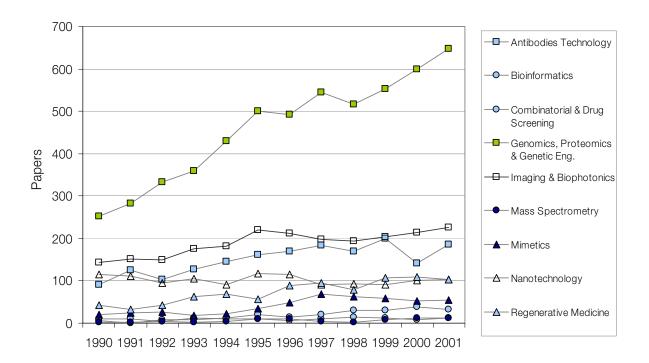


Figure 4 Canadian scientific output by technology, 1990-2001 Source: Compiled by Science-Metrix from Medline.

Figure 5 examines the strengths and weaknesses of Canada in biopharmaceutical therapies and technologies. In this figure and the following ones, Canada's position is determined by two variables: the index of specialization, which indicates whether Canada puts more emphasis on the publication of papers in a given cluster, and the relative impact factor, which determines whether Canada's papers in a given cluster are published in journals that are cited more frequently than the world average in the given cluster. The upper right quadrant represents Canada's greatest strengths, whereas the lower left quadrant represents Canada's greatest weaknesses. The upper left quadrant is where there is an upside potential in publishing more in a given cluster, whereas the lower right-hand side quadrant presents an upside potential by publishing in journals that are more frequently cited.

Canada clearly excels in the targeting of diabetes and to a lesser extent the use and regulation of hormones in therapies. Canada specializes in therapies related to cholesterol, but it would improve its position in the world community by publishing in more highly cited journals in this field. In terms of technological clusters, Canada is strongest in mimetics. Canada publishes in highly cited journals (high relative impact factor) in mass spectroscopy, but it needs to publish more in this area to be considered a specialist. Conversely, it specializes in genomics, proteomics and genetic engineering, but there is room for improvement in terms of publishing in more highly cited journals. Canada's clearest weaknesses are in vaccines and other immunizations, and to a lesser extent, contraceptives and anti-viral therapies.

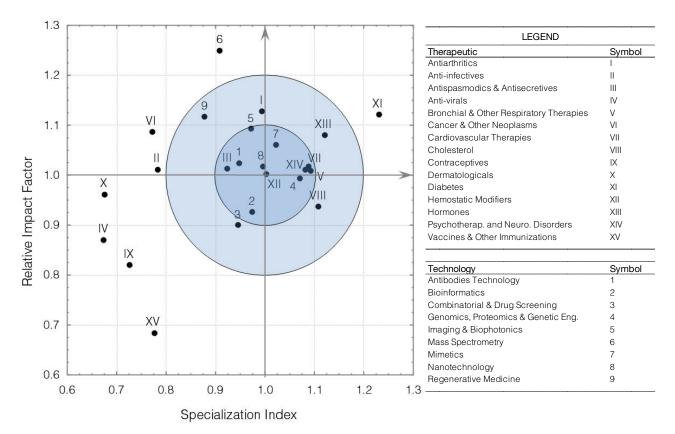
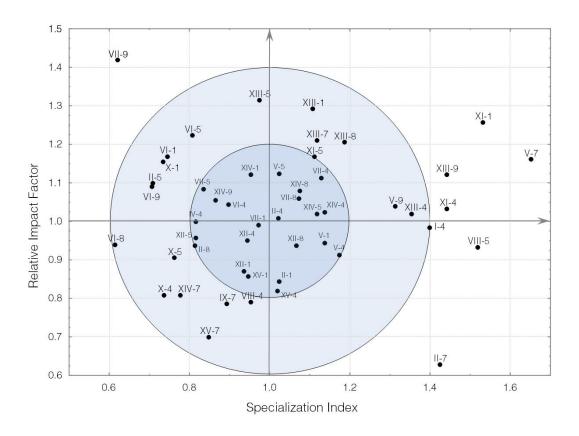


Figure 5 Map of Canada's strengths and weaknesses by cluster, 1996-2001

Source: Compiled by Science-Metrix from Medline.

Figure 6 reveals Canada's strengths and weaknesses when therapies and technologies are considered in pairs. As one can see, Canada is very strong in the application of antibodies, genomic technologies and biophotonics and imaging to cure diabetes. Canada is also strong in the use of mimetics and regenerative medicine for bronchial and other respiratory therapies. The combined use of many technological platforms such as regenerative medicine, antibodies technology, genomics, mimetics and nanotechnologies with hormone therapies is also an area in which Canada excels. The use of regenerative medicine in cardiovascular therapies is the research and development cluster pair where Canada has the strongest impact on the world scientific community. Cancer therapies combined with regenerative medicine, antibodies and imaging and biophotonics are also relatively high impact fields but which are showing no true specialization at the country level.

Canada's weaknesses includes the use of mimetics for vaccines, the use of genomics for dermatological therapies and the use of nanotechnology for cancer therapies. Figure 6 shows that there is an upside potential in the use of biophotonics for cholesterol therapies. There is little value in Canada's relatively numerous papers in the use of mimetics for anti-infectives considering that those papers are published in journals with little impact. In fact, the use of mimetic technologies for anti-infectives therapies has the lowest impact in the Canadian biopharmaceutical sector.



LEGEND							
Therapeutic	Symbol	Technology	Symbol				
Antiarthritics	I	Antibodies Technology	1				
Anti-infectives	II	Bioinformatics	2				
Antispasmodics & Antisecretives	Ш	Combinatorial & Drug Screening	3				
Anti-virals	IV	Genomics, Proteomics & Genetic Eng.	4				
Bronchial & Other Respiratory Therapies	V	Imaging & Biophotonics	5				
Cancer & Other Neoplasms	VI	Mass Spectrometry	6				
Cardiovascular Therapies	VII	Mimetics	7				
Cholesterol	VIII	Nanotechnology	8				
Contraceptives	IX	Regenerative Medicine	9				
Dermatologicals	Χ						
Diabetes	XI						
Hemostatic Modifiers	XII						
Hormones	XIII						
Psychotherap. and Neuro. Disorders	XIV						
Vaccines & Other Immunizations	XV						

Figure 6 Map of Canada's strengths and weaknesses by cluster pair, 1996-2001

Source: Compiled by Science-Metrix from Medline.

The data presented in this section reveal that, globally, Canada is an important producer of scientific output in biopharmaceutics at the world level and that its production is of a high standard.

2 Biopharmaceutical Science in Canada

Whereas the first section examined how Canada's performance in biopharmaceutics compared to that of the world level, this section examines the distribution of papers within Canada. Section 2.2 presents data desegregated by province, whereas section 2.3 presents biopharmaceutical papers by Canadian CMAs.

2.1 Biopharmaceutical papers by province

Figure 7 shows that Ontario has the largest number of papers, followed by Quebec, Alberta and British Columbia. Manitoba, Saskatchewan and the Atlantic provinces each have around 500 papers.

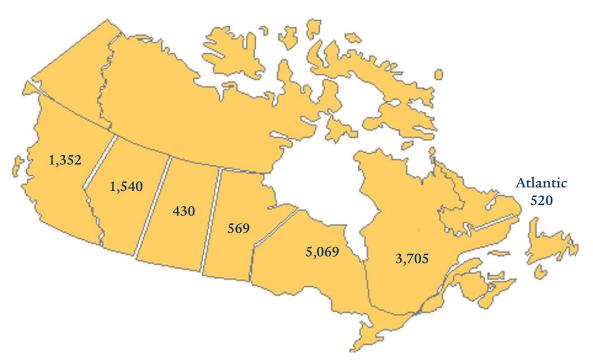


Figure 7 Biopharmaceutical papers by province, 1996-2001 Source: Compiled by Science-Metrix from Medline.

Table IV reveals that, when a variety of indicators are taken into account, Quebec ranks first among Canadian provinces in terms of scientific production in biopharmaceutics. The province is followed by Alberta, Ontario, Manitoba and British Columbia. Alberta is the leader in terms of papers per capita, followed closely by Quebec and Manitoba. Quebec leads in terms of the percentage of its biomedical literature in biopharmaceutics (19% versus 16% in Canada), and its papers are published in journals that have, on average, the highest impact factor (see Table IV).

Table IV Papers in biopharmaceutics by Canadian provinces, 1996-2001

Province	Biopharma I papers	Biopharma papers per year/ million habitants	Biopharma/ Σ Papers	_	Average rank of provinces
Quebec	3,705	84	19%	3.8	1
Alberta	1,540	88	17%	3.6	2
Ontario	5,069	74	14%	3.6	3
Manitoba	569	83	17%	3.2	4
British Columbia	1,352	56	15%	3.7	5
Saskatchewan	430	70	17%	2.6	6
Nova Scotia	373	66	14%	2.8	7
Newfoundland	100	30	16%	2.9	8
Prince Edward Isl.	35	42	14%	1.6	9
New Brunswick	12	3	4%	2.1	10
Unknown	37	-	8%	2.9	
Canada (n)	13,076	71	16%	3.6	

Source:

Compiled by Science-Metrix from Medline.

Figure 8 examines the strength and weaknesses of Canadian provinces in biopharmaceutical therapies. Desegregated data for papers published by Canadian provinces in therapeutics (Table XV) and technology group (Table XVII) are presented in Annex 2. The specialization index of each province by cluster is also presented in Annex 2.

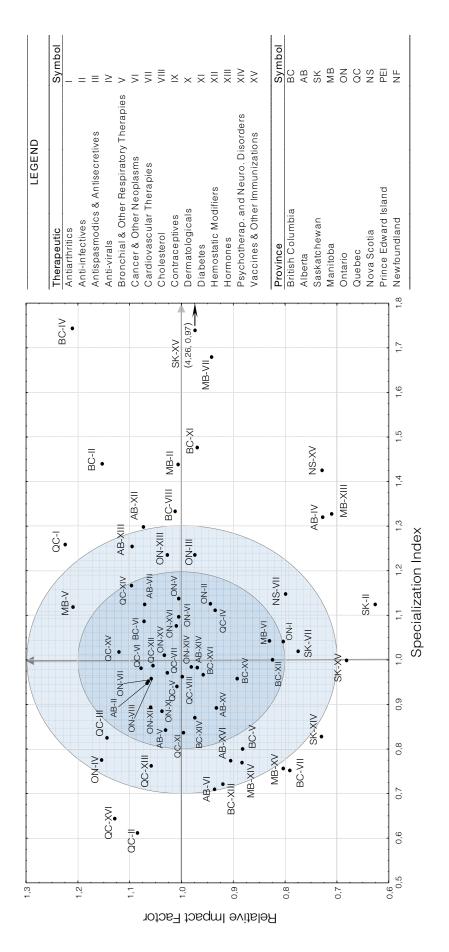
In Canada, Alberta leads in hormone therapy in terms of specialization and scientific impact, followed by Ontario. British Columbia is strong in anti-virals and anti-invectives: the province has many research activities on HIV/AIDS, which are carried out at the Centre for Excellence in HIV/AIDS at St. Paul's Hospital. The centre is a network for researchers from all around the province, but in particular from the University of British Columbia. Also, the Centre for Microbial Diseases and Immunity Research at the UBC is a focal point of research on anti-infectives. The province is also specialized in cholesterol and diabetes therapies, but has a lower impact than research performed in anti-virals and anti-infectives.

The leader in antiarthritic therapy is Quebec with a relatively high level of specialization (22% more specialized than other provinces) and the strongest scientific impact observed at the provincial level. The *Université de Montréal*, in collaboration with the *Centre hospitalier de l'Université de Montréal* (CHUM), inaugurated the *Université de Montréal* Chair in Osteoarthritis in 2000.

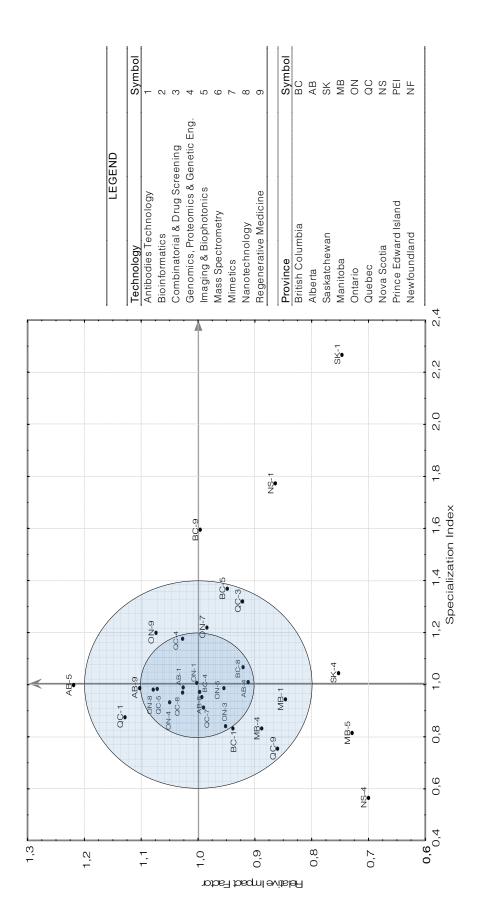
Manitoba specializes in cardiovascular and anti-infective therapies. The Institute of Cardiovascular Sciences (University of Manitoba) located at the St. Boniface Hospital Research Centre is highly active in cellular and molecular basic research and experimental cardiology. At a higher level of scientific impact, Manitoba performs well in bronchial and other respiratory therapies.

Saskatchewan is strongly specialized in vaccines with over 400% more papers than the Canadian average in this therapeutics cluster. The Veterinary Infectious Disease Organization (VIDO) at the University of Saskatchewan is a world leader in developing vaccines for infectious diseases in farm animals. VIDO has developed five innovative and very successful vaccines that are leading in the international market, including the first genetically engineered vaccine for animals. Saskatchewan's relative impact factor in vaccines is close to the Canadian average but this is probably associated with the relatively lower impact of agricultural and livestock research compared to that of biopharmaceutical research. This trend could evolve due to the fact that the VIDO is increasingly emphasising research on vaccines as a way of improving human health.

Figure 9 reveals that technology platforms at the provincial level are less differentiated than therapeutics clusters. British Columbia is more specialized in regenerative medicine and in imaging & biophotonics. Quebec specializes in combinatorial & drug screening, but has a relatively low impact factor in this area. With a similarly fairly low impact factor, Saskatchewan and Nova Scotia specialize in antibody technologies. Alberta has a strong impact factor in papers on imaging & biophotonics technologies, but it does not specialize in this cluster.



Map of Canadian provinces' strengths and weaknesses by therapeutics, 1996-2001 Compiled by Science-Metrix from Medline. Figure 8 Source:



Map of Canadian provinces' strengths and weaknesses by technology, 1996-2001 Compiled by Science-Metrix from Medline. Figure 9 Source:

2.2 Biopharmaceutical papers by Canadian CMAs

This section presents statistics on papers in biopharmaceutics written by scientists located in Canadian Census Metropolitan Areas (CMA). Data is presented for CMAs where scientists published at least one hundred papers during the 1996-2001 period.

Figure 10 presents the leading CMAs in terms of scientific output. Montreal is the leading Canadian CMA in terms of the absolute number of papers and is followed by Toronto and Vancouver. Each of these CMAs had more than 1,000 papers in biopharmaceutics published during the six-year period.

When population is taken into account, Saskatoon and Sherbrooke are the clear leaders in biopharmaceutical science. The two CMAs together with London, Hamilton, Halifax, Edmonton, Quebec City, Winnipeg and Montreal all publish more papers per capita than the Canadian average.

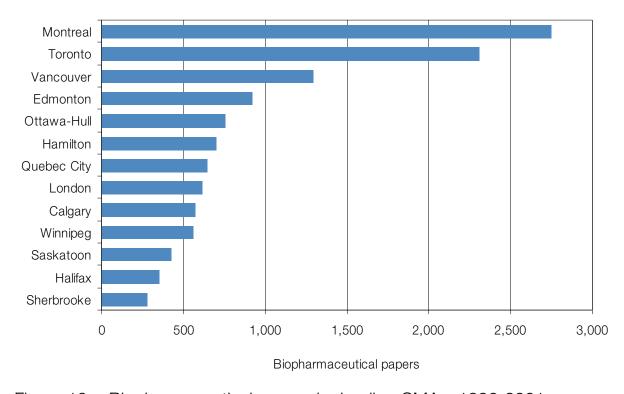


Figure 10 Biopharmaceutical papers by leading CMAs, 1996-2001 Source: Compiled by Science-Metrix from Medline.

2.3 Biopharmaceutical papers by Canadian institutions

Table V shows that scientists from Canadian universities authored approximately 60% of the papers in biopharmaceutics, health sector institutions 37% and government and corporations 2% each.

The leading universities are the University of Alberta and the University of British Columbia: they have the greatest number of papers, specialize in biopharmaceutics and have a greater impact factor than the average in their sector. They are followed by the University of Toronto, McGill University and the University of Calgary.

In general, the leading health sector institutions are the University Health Network, which excels by publishing in highly cited journals, the Hospital for Sick Children, the *Centre Hospitalier Universitaire de Québec* (CHUQ) which is highly specialized in biopharmaceutics, Toronto Public Health and the Royal Victoria Hospital, the latter also excelling by publishing in highly cited journals.

The leading government institution clearly is the National Research Council of Canada, while Health Canada and Agriculture and Agri-Food Canada are also among the leaders.

Leading corporations comprise Merck Frosst, which has an excellent scientific production in biopharmaceutics, Boehringer-Ingelheim and Aventis. All these firms are highly specialized in the field in terms of scientific publications.

The number of publications and the specialization index of leading Canadian institutions (more than 100 papers between 1996 and 2001) are presented by therapeutics and by technology group in Annex 2. As with the Canadian level data showed before, diabetes is clearly a Canadian strength. The institutions that are most specialized in diabetes therapy are the Hamilton Health Science Corporation (6.92) and St. Michael's Hospital in Toronto (4.80). The Hamilton Health Science Corporation manages the Diabetes Care and Research Program, and recently, Aventis Pharma gave a \$1 million donation to fund a Chair in Diabetes Research at McMaster University and McMaster University hospitals linked with the Hamilton Health Science Corporation network.

The leading universities in hormones are the University of Toronto (207 papers) and the University of Alberta (199 papers). In this therapeutic cluster, the health sector organization with the highest degree of specialization is the *Centre hospitalier universitaire de Québec* (CHUQ) (1.76), which rank fourth with 143 papers published during the period studied (1996-2001). The second most specialized university hospital is the Sir Mortimer B. Davis Jewish General Hospital (1.58) (see Table XX, Annex 3).

Psychotherapeutics research is led by the University of Toronto (167 papers), the University of British Columbia (155 papers) and McGill University (133 papers). The Montreal Neurological Hospital and Institute specializes highly (3.63) in this type of therapy with 72 papers. The University Health Network ranks first in cancer therapeutics with 117 papers and is the most specialized Canadian institution in the field (2.23).

Table V Papers and average impact factor of leading Canadian institutions by sector, 1996-2001

Sector	Papers	Index of specialization	Average impact factor
University (n=49)	7,803	1.0	3.4
University of Alberta	865	1.2	3.7
University of British Columbia	830	1.1	3.7
University of Toronto	783	0.8	4.0
McGill University	535	0.9	3.9
University of Calgary	521	1.2	3.7
McMaster University	512	1.1	3.4
Université de Montréal	454	1.1	3.4
University of Western Ontario	438	1.0	3.4
University of Manitoba	398	1.2	3.3
University of Saskatchewan	322	1.2	2.4
Queen's University	304	1.0	3.3
Dalhousie University	293	1.0	2.8
Université de Sherbrooke	261	2.0	2.9
University of Guelph	244	0.9	1.8
University of Ottawa	242	1.1	3.8
Université Laval	233	1.1	3.4
Health & Hospital (n=112)	4,847	1.0	4.0
University Health Network	484	0.9	4.8
Hospital for Sick Children	387	0.9	4.1
CHUQ	359	1.8	4.0
Toronto Public Health	287	0.6	4.1
Royal Victoria Hospital	259	1.5	4.3
Corporation (n=73)	281	1.5	3.2
Merck Frosst Canada Inc.	36	1.4	5.5
Boehringer Ingelheim Limited	25	3.2	2.5
Aventis	23	4.0	3.5
BioChem Pharma Inc.	21	3.6	2.5
Inex Pharmaceutical Corporation	15	3.6	3.6
Quadra Logic Technologies Inc. (QLT)	13	3.9	2.2
Government (n=17)	308	0.6	2.3
National Research Council Canada	110	0.9	3.1
Health Canada	59	0.5	1.9
Agriculture and Agri-Food Canada	58	0.7	1.4
National Defence	13	0.5	1.7
Fisheries and Oceans Canada	12	0.7	1.6
Others & Unknown (n=17)	158	1.4	2.3
Total (n=268)	13,076	1.0	3.6

Source: Compiled by Science-Metrix from Medline.

The most highly specialized institutions in cancer therapy are the British Columbia Cancer Agency (4.71) and the Sir Mortimer B. Davis Jewish General Hospital (3.26). Not surprisingly, the Montreal Heart Institute (5.90) highly specializes in cardiovascular therapeutics. The institute is constituted of 19 teams working in basic research, 22 in clinical research and 8 in technological research.

In terms of technological platform, the Sir Mortimer B. Davis Jewish General Hospital and the CHUQ are the most specialized Canadian institutions in genomics & proteomics (see Table XXI, Annex 3). The University of Saskatchewan has the greatest specialization (2.25) in antibodies technology. Other institutions that stand out in terms of specialization are in the regenerative medicine technology group: McMaster University (2.70) and the University Health Network (2.39). The McMaster University Faculty of Medicine performs work on regenerative technology applications in cancer research and degenerative cell biology. Furthermore, a research centre dedicated to regenerative medicine funded by a private donation will soon be established at the University Health Network.

Combined with its high score in terms of papers on cancer therapy, the British Columbia Cancer Agency specializes in regenerative medicine technology (9.81). The Agency's Cancer Research Centre is home to eight research laboratories.

PART II TECHNOLOGICAL INVENTIONS IN BIOPHARMACEUTICS

3 Biopharmaceutical Inventions at the International Level

This section examines the distribution of patents granted by the United States Patent and Trademark Office (USPTO) at the international level. In particular, Section 3.1 examines the rate of growth of patents in biopharmaceuticals, Section 3.2 examines the distribution of patents by country while Section 3.3 examines the distribution of patents by cluster.

3.1 Global rate of patenting

Between 1990 and 2001, the number of patents granted by the USPTO in biopharmaceutics has grown more than sixfold, increasing from 391 to 2,492. The percentage of biopharmaceutical patents granted has also grew considerably, increasing from 0.4% to 1.4%. Although one can see in Figure 11 that the number of patents granted went down in 2000 and 2001 in comparison to the two previous years, it is also clear that the number of patents granted in 2000 and 2001 fell back to a "baseline" established in the early 1990s.

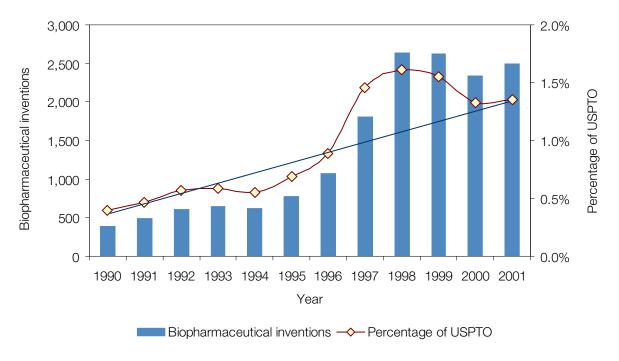


Figure 11 Patents in biopharmaceutics granted by the USPTO, 1990-2001 Source: Compiled by Science-Metrix from USPTO data.

It is possible that there was an increase in the application for patents during the early years of the late 1990s stock market rally (see 1996 to 1999 on Figure 11). However, the reason that the number of granted patents decreased can hardly be attributed to the difficulties that have plagued the stock market from 2000 onward, as patents are granted on average two years after filing. Thus the stock

market slowdown of 2000 presumably slowed applications that year, and, if this is so, the lower number of patents granted would have shown up only in 2002.

Another potential cause for the lower number of patents granted in 2000 could be the cautious stance of the US and UK governments towards patents concerning the genome. Because the Blair and Clinton administrations were already actively discussing this matter in 1999, it is highly likely that patent examiners in the USPTO adopted a prudent stance and did not grant patents whose legitimacy could be contested afterwards. Finally, a third and more likely potential cause was a technical problem plaguing the patent office, that is, the outstanding number of filings for patents covering expressed sequence tags in the late 1990s:

The number of patents issued or being applied for by genomics companies is mind-boggling. Over 2,000 patents on full-length genes have already been granted by the U.S. Patent and Trademark Office (USPTO). But the number of patent applications runs into the millions. The USPTO confesses that they have no idea how many patents applications are pending on expressed sequence tags (EST's) which are "signatures" or parts specific to each gene - since they "quit tracking them" about four years ago, at which time they had about half a million. In the past 200 years, the USPTO has processed six million patent applications. Based on company disclosures, there are currently over three million patent applications on ESTs alone. (http://www.biotech-info.net/geno-types.html).

Hence, the burst observed in 1997 to 1999 is likely due to an artefact induced by the race to patent expressed sequence tags. In any case, despite a momentary repose following this burst in the number of patents granted, patents granted in the field of biotechnology appear to be set to continue increasing, considering that the data from 2000 and 2001 follow the same trend as those from 1990 to 1996.

Figure 12 shows that there has been an important growth in the proportion of patents by Canada in the field of biopharmaceutics. Whereas in 1990, only 0.6% of patents granted were in the field of biopharmaceutics, in 2001 the proportion had grown to 2.8%. In fact, although this is not a long time series and one should be careful in interpreting trends, biopharmaceutical patents appear to have reached a stable level around the 2.8% mark. The share of total biopharmaceutical patents that where granted by the USPTO to Canada also grew steadily from 1993 onwards – from 2.8% of total biopharmaceutical patents in 1993 to 5.1% in 2001.

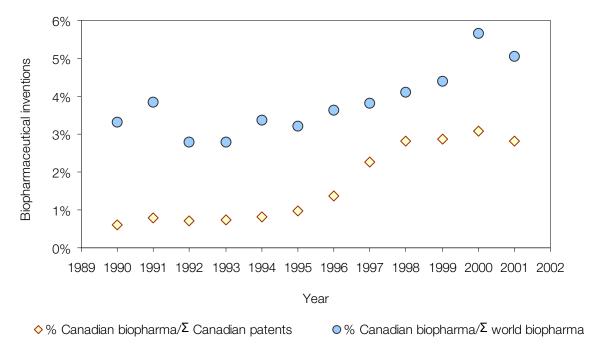


Figure 12 Percentage of biopharmaceutical patents by Canada, 1990-2001 Source: Compiled by Science-Metrix from USPTO data.

3.2 Distribution of biopharmaceutical inventions by cluster

A cluster analysis of world biopharmaceutical patents shows that genomics, proteomics and genetic engineering is the leading technology platform (see Table VI). Moreover, the technology of this platform is highly used in cancer and vaccine therapeutics. This platform, which combines cancer therapies and vaccines with the robustness of high-throughput genomic technologies, enables the discovery and clinical validation of cancer and DNA-based immunization at unprecedented speed.

Overall, therapeutics for the treatment of cancer and other neoplasms is the platform that receives the most patents for the period. With an expected increase of 50% in world global cancer rates to 15 million cancer cases per year by 2020 (World Cancer Report 2003, World Health Organization), the biopharmaceutical patenting related to cancer treatment could be the most promising avenue of intellectual property protection. As cancer has become one of the most devastating diseases worldwide, the biopharmaceutical sector follows this trend by patenting an increasing number of inventions in this field.

Psychotherapeutic and neurological disorders are another highly patented therapeutics. A paired cluster analysis of inventions shows that genomics and proteomics is the prevailing technology cluster in this area.

Table VI World patents in biopharmaceutics by cluster pair, 1990-2001

	Technology							
Therapeutic	Antibodies Technology	Genomics, proteomics & genetic engineering	Imaging & Biophotonics	Nanotechnology	Regenerative Medicine	n		
Antiarthritics	25	74	n.s.	n.s.	n.s.	189		
Anti-Infective	11	86	n.s.	n.s.	n.s.	331		
Antispasmodics & Antisecretives	n.s.	n.s.	n.s.	n.s.	n.s.	19		
Anti-Virals	90	316	n.s.	34	37	604		
Bronchial & Other Respiratory Therapies	68	311	11	23	28	667		
Cancer & Other Neoplasms	437	943	158	132	239	2,162		
Cardiovascular Therapies	124	506	70	41	68	1,245		
Cholesterol	n.s.	26	n.s.	n.s.	n.s.	78		
Contraceptives	10	31	n.s.	n.s.	n.s.	64		
Dermatologicals	25	175	n.s.	16	20	559		
Diabetes	24	118	n.s.	n.s.	30	424		
Hemostatic Modifiers	66	293	21	n.s.	38	754		
Hormones	121	563	43	22	110	1,672		
Psychotherap. & Neuro. Disorders	168	718	36	50	112	1,698		
Vaccines & Other Immunizations	168	863	15	29	108	1,613		
n	1,798	6,688	589	671	1,209	16,510		

n.s.: Non significant - Data with less than 10 patents are not presented and were not used in

the analysis

Source: Compiled by Science-Metrix from USPTO data.

3.3 Leading countries in biopharmaceutical inventions

At the world level, and in a tie with Denmark, Canada ranks 3rd overall in the field of biopharmaceutics, when the following indicators are considered: number of patents, patents by inhabitants, percentage of biopharmaceutical patents to total patents by country and average citations per patent (Table VII).

With 702 inventions in biopharmaceutics, Canada ranks 5th at the world level, following the US, Japan, Germany and the UK. Canada's performance is excellent considering that it has more or less the same number of patents as countries that are much larger in terms of population, that is, Germany, the UK and France. Canada ranks 6th in terms of patents per capita. Israel is the country with the largest average number of patents per capita per year – 3.5 per year per million inhabitants versus 1.9 in Canada. Other countries that fare well when population size is taken into account are the USA, Switzerland, Denmark and Sweden.

With 1.9% of its patents in biopharmaceutics, Canada is more specialized in this field than the world average (1%). In fact, Canada is 6th in terms of the percentage of its patents in the field of biopharmaceutics. Canada is more specialized than other leading countries, such as the USA, Switzerland and Sweden, but less specialized than Demark and Israel.

Citations received for each patent were counted for the year that they were granted and for the two years that followed (e.g. for patents granted in 1990, citations received in 1990, 1991 and 1992 were counted). At the world level, Canada ranks 8th and each of its patents is cited 0.39 times on average. This figure is below the world average (0.47 cites per patent). The countries whose biopharmaceutical patents are often cited include Switzerland, the USA, Sweden, Austria, the Netherlands, Belgium and Denmark.

Table VII Leading countries in biopharmaceutical patents, 1990-2001

Country	Biopharma inventions	Biopharma patents per year/ million habitants	Biopharma/ Σ Inventions	Average citations per patent	Average rank of leading countries
United States	11,458	3.5	1.3%	0.52	1
Switzerland	272	3.1	1.5%	0.53	2
Canada	702	1.9	1.9%	0.39	3
Denmark	183	2.9	3.6%	0.39	3
Sweden	252	2.4	1.8%	0.46	5
Israel	232	3.5	3.0%	0.31	6
Austria	137	1.4	2.4%	0.45	7
Belgium	177	1.4	2.2%	0.40	8
United Kingdom	781	1.1	1.8%	0.37	8
Netherlands	240	1.3	1.6%	0.42	10
Australia	270	1.2	3.2%	0.29	11
Germany	841	0.9	0.8%	0.38	12
France	668	0.9	1.5%	0.34	13
Japan	1,211	0.8	0.4%	0.34	14
Italy	281	0.4	1.4%	0.35	15
World (n)	16,510	0.2	1.0%	0.47	

Source:

Compiled by Science-Metrix from USPTO data.

Since patents contain data on inventors and assignees, it is possible to produce statistics not only on inventions but also on intellectual property. Table VIII shows that there are 598 patents that are partly or fully owned by Canada (4th rank). Globally, 93% of biopharmaceutical IP is owned by institutions (companies, governments, universities, foundations, etc.) and, therefore, only 7% by individuals. In Canada, this figure is slightly lower, since 89% of patents are owned by institutions. Table VII also presents data on the net flow of IP (invention/IP calculated fractionally) of leading countries. Most leading countries have a net deficit in IP: their inventors make a larger contribution than the actual portion owned by these countries. The USA, the Netherlands and Switzerland have a positive inflow, whereas Canada has a slight outflow of IP – 4.9% of Canadian

inventions are owned by foreign countries. This outflow is lower than that observed in biotechnology (8.8%) and generally in Canada (8%). This suggests that the Canadian biopharmaceutical industry has a slightly greater propensity to be locally owned than is the case in biotechnology.

Table VIII IP of leading countries in biopharmaceutical patents, 1990-2001

Country	Institutional IP	Total IP	% of IP owned by institutions	Estimated net flow of IP
United States	10,602	11,331	94%	+2.7%
Japan	1,058	1,107	96%	-2.1%
Germany	610	683	89%	-3.1%
Canada	531	598	89%	-4.9%
France	517	550	94%	-3.6%
United Kingdom	512	540	95%	-15.8%
Netherlands	256	260	98%	+31.9%
Switzerland	205	224	92%	+12.8%
Italy	200	216	93%	-9.8%
Australia	196	209	94%	-12.2%
Sweden	150	178	84%	-10.1%
Israel	138	154	90%	-19.8%
Denmark	130	149	87%	-5.3%
Austria	75	86	87%	-27.5%
Belgium	75	81	93%	-42.4%
World (n)	15,411	16,510	93%	100%

Source: Compiled by Science-Metrix from USPTO data.

4 Biopharmaceutical Inventions in Canada

This last section examines the distribution of patents within Canada. Section 4.1 examines the growth of biopharmaceutical inventions by province, whereas section 4.2 presents data desegregated by CMAs.

4.1 Biopharmaceutical patents by province

Figure 13 shows that Ontario has the largest number of patents by far (318), whereas Quebec has less than two thirds as many. Alberta has about a third of the inventions of Ontario; Saskatchewan has a sixth.

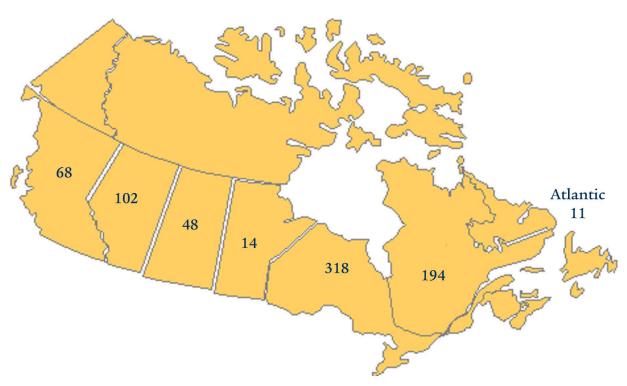


Figure 13 Biopharmaceutical patents by province, 1990-2001 Source: Compiled by Science-Metrix from USPTO data.

Table IX reveals that when multiple indicators are taken into account, Alberta ranks first among the leading provinces in Canada, that is, provinces with at least four patents per year on average in the field of biopharmaceutics. The province is followed by Saskatchewan, Ontario, Quebec and British Columbia. Other provinces are not really in the race, neither in terms of the absolute number of patents nor in terms of patents per capita.

Saskatchewan is the leader in terms of biopharmaceutical inventions per capita, followed by Alberta. Saskatchewan is also the most specialized province in biopharmaceutics, since 6.2% of its

patents are in this field. On average, Alberta and Saskatchewan receive significantly more citations per patent than other leading provinces.

Table IX Patents of Canadian provinces in biopharmaceutics, 1990-2001

Province	Biopharma inventions	Biopharma patents per year/ million habitants	Biopharma/ Σ Inventions	Average citations per patent	Average rank of leading provinces
Alberta	102	2.9	2.9%	0.57	1
Saskatchewan	48	3.9	6.2%	0.50	2
Ontario	318	2.3	1.6%	0.35	3
Quebec	194	2.2	2.7%	0.32	4
British Columbia	68	1.4	1.4%	0.35	5
Manitoba	14	1.0	1.3%	0.21	
Nova Scotia	9	0.8	1.4%	0.33	
New Brunswick	2	0.2	2.8%	0.50	
Unknown	18		0.5%	0.17	
Canada (n)	702	1.9	1.9%	0.39	

Source:

Compiled by Science-Metrix from USPTO data.

Using IP as an indicator, Table X confirms Ontario's leadership in terms of the absolute number of biopharmaceutical patents. The proportion of IP of the leading provinces is, by and large, the same as for inventions. The percentage of IP owned by institutions varies a little among leading provinces, that is, between 86% and 95%, but the net flow of IP varies considerably. Saskatchewan has a minute gain (0.1%) and Ontario a very small loss (0.6%). Leading provinces such as Alberta, Quebec and British Columbia incur substantial losses of IP – respectively -25%, -18% and -14%.

Table X IP of Canadian provinces in biopharmaceutics, 1990-2001

Country	Institutional IP	Total IP	% of IP owned by institutions	Estimated net flow of IP
Ontario	231	268	86%	-0.6%
Quebec	113	129	88%	-18.3%
Alberta	58	63	92%	-25.3%
British Columbia	44	49	90%	-13.7%
Saskatchewan	39	41	95%	+0,1%
Manitoba	8	10	80%	-18.6%
Nova Scotia	2	2	100%	-68.3%
New Brunswick	-	-	0%	-100.0%
Unknown	40	42	95%	
Canada (n)	531	598	89%	-4.9%

Source:

Compiled by Science-Metrix from USPTO data.

Although Ontario and Quebec have considerably more patents than other Canadian provinces, Alberta and Saskatchewan perform better when population, specialization in biopharmaceutics and citations per patent are taken into account.

4.2 Biopharmaceutical Patents by Canadian CMAs

This section presents statistics on US patents granted to inventors located in Canadian CMAs. Data is presented for CMAs where inventors have obtained at least one patent per year during the 1990-2001 period.

Toronto is clearly the leading Canadian CMA in terms of the absolute number of patents. The city is followed by Montreal, Vancouver, Ottawa–Hull and Edmonton (Figure 14). Each of these CMAs patented more than 100 inventions during the period. When population is factored in, Saskatoon is the clear leader in biopharmaceutics, followed by Edmonton, which has about a third as many inventions per capita than Saskatoon. Toronto ranks 3rd, London 4th, Montreal 5th and Ottawa-Hull 6th.

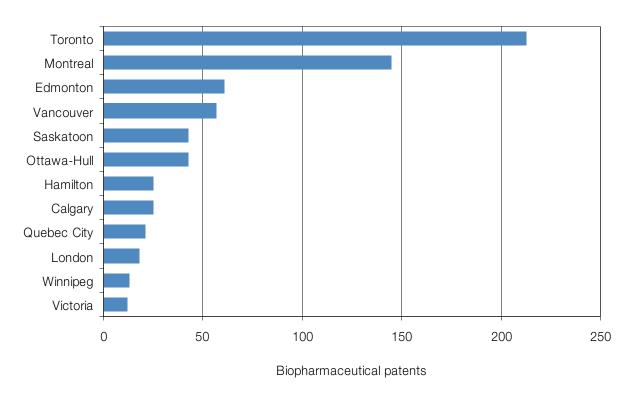


Figure 14 Number of inventions by leading CMAs, 1990-2001 Source: Compiled by Science-Metrix from USPTO data.

4.3 Biopharmaceutical Patents by Canadian Institutions

This section presents statistics on US patents owned by Canadian institutions that had at least one patent per year on average during the period examined (1990-2001).

There are 131 Canadian institutions with at least one patent in biopharmaceuticals. Table XI presents the leading institutions as well as the sectorial distribution of IP in biopharmaceutical patents in Canada. There are five times as many corporations (n=91) than university-sector (n=17) institutions with patents in biopharmaceutics. However, the gap is not as large in terms of patents, since corporations were granted 314 patents and universities 145 over the same time period. About 10% of the patents are owned by governmental institutions and less than 6% by health sector institutions.

During the 1990-2001 period, the leading corporations in biopharmaceutical IP were Aventis, Boehringer Ingelheim and NPS Allelix. Leading universities were the University of Saskatchewan, the University of British Columbia and McGill University. Leading governmental sector organizations were the National Research Council of Canada and the Alberta Research Council. Together, the 22 leading organizations in Canadian biopharmaceuticals account for 64% of the IP owned by institutions.

Table XI IP of leading Canadian institutions by sector, 1990-2001

Sector	Patents owned
Corporation (n=91)	314
Aventis	69
Boehringer Ingelheim Ltd.	24
NPS Allelix Corp.	23
Generex Pharmaceuticals Inc.	9
Resolution Pharmaceuticals Inc.	9
1149336 Ontario Inc.	8
Inex Pharmaceuticals Corp.	7
Theratechnologies Inc.	6
University (n=17)	145
University of Saskatchewan	32
University of British Columbia	21
McGill University	19
University Technologies International Inc.	13
Queen's University at Kingston	12
University of Alberta	10
Université Laval	9
Université de Montréal	7
Government (n=8)	<i>55</i>
National Research Council of Canada	19
Alberta Research Council	17
Agriculture and Agri-Food Canada	6
Natural Resources Canada	6
Health & Hospital (n=8)	30
Hospital for Sick Children	7
Mount Sinai Hospital Corporation	7
Unknown (n=2)	2
Total (n=131)	531

Source: Compiled by Science-Metrix from USPTO data.

C onclusion

This report shows that the field of biopharmaceutics is growing rapidly both at the world level and in Canada. Between 1990 and 2001, the number of scientific papers per year increased by 33%, while the number of technological inventions grew sixfold at the world level. Biopharmaceutics account for 14% of the scientific literature in Medline, and 1% of the patents granted by the USPTO between 1990 and 2001 were also in this field.

The share of the scientific output published by Canada is 3.5% of the world output in the field. In absolute terms, the number of papers by Canada is growing at the same rate as the world's total number. Canada's scientific production is not only considerable; it is also of high quality. Within Canada, Ontario has the largest number of papers, followed by Quebec, Alberta and British Columbia. However, when a variety of indicators are taken into account, Quebec ranks first in biopharmaceutical science, followed by Alberta, Ontario, Manitoba and British Columbia. Similarly, although Ontario and Quebec hold considerably more patents than other Canadian provinces, Alberta and Saskatchewan have a better performance when population, specialization in biopharmaceutics and citations per patent are factored in.

Montreal is the leading CMA in terms of the absolute number of scientific papers, followed by Toronto and Vancouver. When population is taken into account, Saskatoon and Sherbrooke are the leading CMAs in biopharmaceutical science. Toronto is the leading CMA in terms of the absolute number of patents and is followed by Montreal, Edmonton, Vancouver, Saskatoon and Ottawa-Hull. When population is factored in, the Saskatoon CMA is the clear leader in biopharmaceutics, followed by Edmonton, Toronto, London, Montreal and Ottawa-Hull.

Scientists from Canadian universities authored approximately 60% of the papers in biopharmaceutics, health sector institutions 37% and government and corporations 2% each. The pattern is quite different for inventions where corporations hold 60% of IP, universities 27%, government 10% and health sector institution a mere 6%. When the number of papers and the number of patents are considered, the two leading universities are the University of British Columbia and McGill University. The leading government institution clearly is the National Research Council, whereas the leading corporations are Boehringer-Ingelheim and Aventis.

Anti-virals form the therapeutics cluster that has grown at the fastest rate at the world level, but it is also the cluster in which Canada specializes the least and in which it has the third lowest relative impact factor. By contrast, Canada is strong in hormones and diabetes clusters for which the growth rate is low at the international level. In terms of technology clusters, combinatorial and drug screening grows fastest at the world level, but Canada is neither specialized in this field nor does it have a strong impact there. Regenerative medicine is also growing rapidly at the world level but slowly in Canada. Mimetics is one of the technological clusters that present a good opportunity for Canada: it specializes in the field, has a high impact factor and the cluster is growing at the

world level. Canada is particularly strong in using mimetics for the treatment of respiratory diseases.

Canada has both a strong science base as well as many technologically advanced institutions. Although Ontario dominates the picture due to its sheer size, Saskatchewan, Alberta, British Columbia and Quebec all play an important role in the shaping of the Canadian biopharmaceutical landscape. However, there is a certain mismatch between Canada's scientific strengths and the clusters that are growing rapidly at the world level.

Scientific output of the world and Canada - Time series 1990-2001 A nnex 1

Table XII World's papers in biopharmaceutics by therapeutics, 1990-2001

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	Total
Antiarthritics	410	403	448	472	438	445	488	579	588	999	672	708	6,317
Anti-infectives	4,107	4,217	4,210	4,233	4,449	5,595	6,651	6,828	7,477	7,145	7,408	7,623	69,943
Antispasmodics & Antisecretives	1,258	1,163	1,188	1,197	1,220	1,332	1,368	1,363	1,398	1,347	1,233	1,220	15,287
Anti-virals	296	981	1,054	1,007	1,095	1,492	1,649	1,736	2,043	2,170	2,224	2,153	18,571
Bronchial & Other Respiratory Therapies	2,823	2,960	3,200	3,392	3,643	4,117	4,500	4,548	4,754	4,803	4,873	4,942	48,555
Cancer & Other Neoplasms	6,144	6,042	6,286	6,707	7,111	7,689	8,152	7,911	8,194	8,353	9,259	9,493	91,341
Cardiovascular Therapies	6,036	6,421	6,449	6,848	7,043	7,656	8,019	8,356	8,364	8,544	8,979	9,034	91,749
Cholesterol	938	948	993	1,042	1,047	1,311	1,180	1,274	1,242	1,341	1,424	1,564	14,304
Contraceptives	243	241	209	238	223	253	325	297	289	315	353	307	3,293
Dermatologicals	1,619	1,545	1,604	1,619	1,641	1,939	2,041	2,063	2,242	2,287	2,371	2,558	23,529
Diabetes	2,389	2,333	2,357	2,612	2,518	2,601	2,515	2,686	2,748	2,662	2,620	2,691	30,732
Hemostatic Modifiers	3,126	3,439	3,353	3,498	3,482	3,748	3,724	3,631	3,668	3,694	3,903	3,554	42,820
Hormones	11,171	10,783	11,104	11,576	11,495	11,970	12,256	12,651	12,621	12,512	12,783	12,452	143,374
Psychotherap. & Neurological Disorders	6,349	6,591	7,035	7,778	8,014	8,364	8,833	9,522	9,934	10,435	11,059	11,182	105,096
Vaccines & Other Immunizations	2,670	2,682	2,902	3,029	3,104	3,487	3,536	3,682	3,815	4,507	4,647	4,844	42,905
Total World	48,384	48,474	8,474 49,594	51,772	53,646	57,947	59,401	60,133	61,463	53,646 57,947 59,401 60,133 61,463 62,423	64,732	64,372	747,816

Table XIII Canadian papers in biopharmaceutics by therapeutics, 1990-2001

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	Total
Antiarthritics	1	10	17	16	22	14	19	19	23	24	22	22	219
Anti-infectives	82	96	84	86	127	117	170	187	193	223	201	209	1,775
Antispasmodics & Antisecretives	42	44	49	35	38	37	35	47	40	49	33	53	502
Anti-virals	22	20	24	22	38	43	45	39	54	39	61	45	452
Bronchial & Other Respiratory Therapies	122	109	118	129	141	142	171	170	189	183	184	192	1,850
Cancer & Other Neoplasms	167	182	174	198	202	215	235	230	221	207	245	251	2,527
Cardiovascular Therapies	227	235	252	278	280	306	305	327	332	301	344	348	3,535
Cholesterol	41	42	28	51	36	20	39	61	41	22	28	28	290
Contraceptives	7	7	4	4	9	4	က	9	12	6	7	-	80
Dermatologicals	37	42	43	45	45	48	28	47	54	53	29	20	581
Diabetes	101	92	117	109	125	125	66	107	137	107	117	120	1,356
Hemostatic Modifiers	112	123	106	120	132	125	126	120	149	126	136	122	1,497
Hormones	431	412	452	447	453	489	432	498	528	484	519	497	5,642
Psychotherap. & Neurological Disorders	264	275	311	375	340	346	334	376	368	413	390	432	4,224
Vaccines & Other Immunizations	61	65	74	69	85	88	93	110	101	110	122	145	1,124
Total Canada	1,717	1,772	1,807	1,904	1,976	2,096	2,088	2,203	2,153	2,208	2,199	2,225	25,954
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Table XIV World's papers in biopharmaceutics by technology, 1990-2001

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	Total
Antibodies Technology	3,887	4,029	3,787	4,381	4,438		4,823	5,007	4,996	5,435	5,587	5,725	56,985
Bioinformatics	156	173	174	222	273		294	295	305	335	326	378	3,227
Combinatorial & Drug Screening	157	177	210	248	387	450	532	618	790	843	1,025	1,198	6,638
Genomics, Proteomics & Genetic Eng.	6,945	7,325	8,506	9,677	11,445	13,299	13,301		14,051	14,806	16,616	17,017	146,507
Imaging & Biophotonics	3,837	4,067	4,046	4,461	4,756	5,425	5,458		5,788	6,089	6,704	6,865	63,104
Mass Spectrometry	92	74	66	112	149	174	212		185	269	334	378	2,284
Mimetics	717	791	740	694	716	1,047	1,523		1,521	1,700	1,626	1,521	14,318
Nanotechnology	2,242	2,278	2,261	2,476	2,487	2,910	2,797	2,676	2,640	2,747	3,013	3,011	31,538
Regenerative Medicine	1,028	1,073	1,197	1,531	1,860	8	2,511	2,701	2,763	3,156	3,798	3,807	27,648
Total World	48,384	48,474	49,594	51,772	53,646	57,947	59,401	60,133	61,463		64,732	64,372	682,341

Canadian papers in biopharmaceutics by technology, 1990-2001 Table XV

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	Total
Antibodies Technology	06	126	102	127	145	162	170	184	169	200	141	185	1,801
Bioinformatics	10	1	2	13	=======================================	10	9	-	15	13	6	12	126
Combinatorial & Drug Screening	9	-	∞	6	12	20	15	20	31	30	38	32	222
Genomics, Proteomics & Genetic Eng.	253	282	333	359	429	200	492	545	516	553	009	647	5,509
Imaging & Biophotonics	143	151	149	176	181	220	211	198	193	204	213	226	2,265
Mass Spectrometry	လ	2	2	က	4	1	10	2	2	∞	13	13	79
Mimetics	20	24	27	19	22	34	48	69	63	29	52	54	491
Nanotechnology	115	111	92	105	91	117	114	06	92	06	101	103	1,224
Regenerative Medicine	42	32	43	63	69	22	88	94	78	106	108	103	883
Total Canada	1,717	1,772	1,807	1,904	1,976	2,096	2,088	2,203	2,153	2,208	2,199	2,225	24,348

Scientific output of Canadian provinces - Time series 1990-2001 A nnex 2

Table XVI Canadian provinces' papers in biopharmaceutics by therapeutics, 1996-2001

					**************************************					001						
Province	Antiarthritics	səvitəəlui-inf	Antispasmodics & Antisecretives	Anti-virals	Bronchial & Other Respiratory Therapies	Cancer & Other Neoplasms	Cardiovascular Therapies	Cholesterol	Contraceptives	Dermatologicals	sətədsiQ	Hemostatic Modifiers	Hormones	Psychotherapeutics and Meurological Disorders	Vaccines & Other Immunizations	c
British Columbia	n.s.	176	n.s.	51	06	156	152	43	n.s.	49	71	58	266	229	89	1,352
Alberta	Π.S.	132	П.S.	44	108	116	259	35	η. S.	37	105	115	342	243	62	1,540
Saskatchewan	Π.S.	38	η.8.	n.s.	32	31	22	η. S.	n.s.	n.s.	η.8.	n.s.	70	99	83	374
Manitoba	Π.S.	70	n.s.	n.s.	48	62	139	n.s.	n.s.	n.s.	38	38	26	74	n.s.	532
Ontario	52	516	123	85	480	290	726	115	n.s.	110	238	373	1,127	906	284	5,069
Quebec	46	205	09	89	290	386	538	85	n.s.	92	192	168	977	299	124	3,705
Nova Scotia	n.s.	33	n.s.	n.s.	36	35	64	n.s.	n.s.	n.s.	n.s.	n.s.	44	94	n.s.	373
Prince Edward Island	n.s.	n.s.	η.8.	n.s.	η.8.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	35
Newfoundland	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	Π.S.	31	n.s.	100
Canada	129	1,183	257	283	1,089 1	1,389 1,957	1,957	312	48	321	687	779	2,958	2,313	681	13,076

Table XVII Canadian provinces' specialization index by therapeutics, 1996-2001 (Canadian basis)

С	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Vaccines & Other Immunizations	0.97	0.77	4.26	n.s.	1.08	0.64	n.s.	n.s.	n.s.	1.00
Psychotherapeutics and Meurological Disorders	96.0	0.89	1.00	0.79	1.01	1.02	1.42	n.s.	1.75	1.00
Hormones	0.87	0.98	0.83	0.81	0.98	1.17	0.52	n.s.	Π.S.	1.00
Hemostatic Modifiers	0.72	1.25	n.s.	1.20	1.24	0.76	n.s.	n.s.	n.s.	1.00
Setedsi	1.00	1.30	n.s.	1.36	0.89	0.99	n.s.	n.s.	n.s.	1.00
Dermatologicals	1.48	0.98	n.s.	n.s.	0.88	0.84	η. S.	n.s.	n.s.	1.00
Contraceptives	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	Ŋ.S.	1.00
Cholesterol	1.33	0.95	n.s.	n.s.	0.95	96.0	n.s.	n.s.	n.s.	1.00
Cardiovascular Therapies	0.75	1.12	1.02	1.75	96.0	0.97	1.15	n.s.	n.s.	1.00
Cancer & Other Neoplasms	1.09	0.71	0.78	1.10	1.10	0.98	0.88	Π.S.	n.s.	1.00
Bronchial & Other Respiratory Therapies	08.0	0.84	1.03	1.08	1.14	0.94	1.16	n.s.	n.s.	1.00
alsriv-ifnA	1.74	1.32	η. S.	η. S.	0.77	1.11	n.s.	n.s.	n.s.	1.00
Antispasmodics & Antisecretives	n.s.	n.s.	n.s.	n.s.	1.23	0.82	n.s.	n.s.	n.s.	1.00
səvitəəfini-inA	1.44	0.95	1.12	1.45	1.13	0.61	0.98	n.s.	n.s.	1.00
Antiarthritics	n.s.	n.s.	n.s.	n.s.	1.04	1.26	n.s.	n.s.	n.s.	1.00
Province	British Columbia	Alberta	Saskatchewan	Manitoba	Ontario	Quebec	Nova Scotia	Prince Edward Island	Newfoundland	Canada

Compiled by Science-Metrix from Medline.

Table XVIII Canadian provinces' relative impact factor by therapeutics, 1996-2001 (Canadian basis)

Source: Compiled by Science-Metrix from Medline.

Table XIX Canadian provinces' specialization index by technology, 1996-2001 (Canadian basis)

	<u> </u>		_							
Province	Antibodies Technology	Bioinformatics	Combinatorial & Drug Screening	Genomics, Proteomics & Genetic Engineering	soinotohqoiB & gnigsml	Mass Spectrometry	soifemiM	Иапоtесhnology	Regenerative Medicine	
British Columbia	0.83	n.s.	n.s.	0.97	1.37	n.s.	n.s.	1.07	1.59	1.00
Alberta	0.99	n.s.	n.s.	1.01	1.00	n.s.	0.74	0.95	0.99	1.00
Saskatchewan	2.27	n.s.	n.s.	1.04	Π.S.	η.8.	Π.S.	η. S.	n.s.	1.00
Manitoba	0.89	n.s.	Π.S.	0.86	0.83	n.s.	Π.S.	1.42	n.s.	1.00
Ontario	1.01	n.s.	0.84	0.93	0.98	Π.S.	1.22	0.98	1.20	1.00
Quebec	0.87	n.s.	1.32	1.17	0.98	η.8.	0.91	0.97	0.75	1.00
Nova Scotia	1.77	n.s.	Π.S.	0.56	n.s.	n.s.	Π.S.	n.s.	n.s.	1.00
Prince Edward Island	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Newfoundland	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Canada	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00

Compiled by Science-Metrix from Medline.

Table XX Canadian provinces' relative impact factor by technology, 1996-2001 (Canadian basis)

Province	γgolondɔəΤ səiboditnA	Bioinformatics	Combinatorial & Drug Screening	Genetic Engineering	soinotohqoid & gaigsanl	Mass Spectrometry	SolitemiM	Иапотесhnology	Regenerative Medicine	_
British Columbia	6.0	n.s.	n.s.	1.0	6.0	n.s.	n.s.	6.0	1.0	1.0
Alberta	1.0	n.s.	n.s.	6.0	1.2	n.s.	n.s.	1.0	1.1	1.0
Saskatchewan	0.7	n.s.	n.s.	0.8	0.0	n.s.	n.s.	n.s.	n.s.	0.7
Manitoba	0.8	Π.S.	n.s.	6.0	0.7	n.s.	n.s.	n.s.	Π.S.	6.0
Ontario	1.0	Π.S.	1.0	1.1	1.0	n.s.	1.0	1.1	1.1	1.0
Quebec	1.1	Π.S.	0.9	1.0	1.1	n.s.	1.0	1.0	6.0	1.1
Nova Scotia	6.0	Π.S.	n.s.	0.7	n.s.	n.s.	n.s.	n.s.	Π.S.	8.0
Prince Edward Island	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	0.4
Newfoundland	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	0.8
Canada	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
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Compiled by Science-Metrix from Medline.

Scientific outputs of Canadian institutions - 1996-2001 A nnex 3

Table XXI Leading Canadian institutions' papers by therapeutics, 1996-2001

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Vaccines & Other Immunizations	40	28	48	8	4	24	19	4	17	48	∞	6	74	7	15	12	7	∞	35	7	ო	59	က	4	4 (つ に	Ω τ	- ,	- c	N Ç	⊇ т	- 0	י מי	- <	681
Psychotherapeutics and Meurological Disorders	107	155	167	133	101	75	29	8	72	99	23	24	24	82	9/	82	28	21	က	51	37	32	45	16	0 7	- 0	Z3 7	1 -	N	0 6	2 0	2) c	<u>n</u>	2,313
Hormones	199	172	207	119	117	103	79	123	103	75	106	143	92	24	36	22	80	86	61	48	79	43	31	22	51	ე (4 0	9 5	- c	0 0	9 9	2 ;	<u> </u>	2,958
Hemostatic Modifiers	40	34	35	16	22	92	24	=	6	33	26	15	6	18	00	14	25	6	14	16	9	Ξ	15	2	~ ∟	ი ი	1 (C	- 1	- L	0 0	N C	9	N Ç	4 c	779
Diabetes	63	57	52	28	39	10	16	32	16	29	20	<u></u>	59	Ξ	4	7	Ξ	15	00	6	32	17	-	4	4 (1 0	<u>_</u> u	0 1	– c	0 0	N	1 -	- (n c	687
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Contraceptives	2	2	∞	_	0	0	_	က	2	0	_	4	_	0	0	N	0	Ø	4	2	0	0	-	_	- 1	- (0 0	> 0	0 0	0 0	0 0	> 0	0 0	0 0	48
Cholesterol	24	34	20	10	∞	က	4	16	24	7	0	7	တ	2	0	N	2	2	9	4	4	N	0	CV ·	, (V T	- c	o 0	> 5	1 (⊃ c	0 0	N ·	4 1	312
Cardiovascular Therapies	117	97	69	43	113	92	72	92	75	74	43	31	46	4	51	4	37	32	18	30	19	25	36	4	53	4 4 D 0	Σ 0	n (ρ	1 9	- 6	9 0	n (900	1,957
Cancer & Other Neoplasms	83	09	85	92	10	42	117	17	41	54	34	43	16	36	29	49	30	40	17	31	20	9	42	22	24	n (7 20	7	φ	2 5	2 ç	<u> </u>	25	- +	1,389
Bronchial & Other Respiratory Therapies	72	47	25	23	24	64	53	21	32	33	72	41	26	34	26	28	32	28	23	19	4	7	9	9	<u>ი</u>) c	∞ τ	= 0) (1 C	~ c	n 0	n ;	4 5	1,089
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Antispasmodics & Antisecretives	15	ω	20	12	0	21	7	တ	17	Ξ	2	-	4	Ξ	00	က	ო	တ	2	∞	0	N	က	N	cv c) c	N T	- 0	nc	V C) c	V () ç	2 ₹	257
Anti-infectives	73	112	99	8	34	22	99	35	27	20	45	18	58	23	23	34	6	ω	20	58	78	19	23	o	7	<u>,</u>	۲ ۵	n 0	N 5	† r	0 (0 0	ກ ;	4 ⊂	1,183
Antiarthritics	5	0	2	Ø	4	4	10	2	2	-	2	2	_	_	2	2	2	_	0	7	-	_	-	0	ഗ	> 1	- 0	> 0	⊃ g	0 0	⊃ c	o 0	> 1	- <	129
Institution	University of Alberta	University of British Columbia	University of Toronto	McGill University	University of Calgary	McMaster University	University Health Network	Université de Montréal	University of Westem Ontario	University of Manitoba	Hospital for Sick Children	CHUQ	University of Saskatchewan	Queen's University	Dalhousie University	Toronto Public Health	Université de Sherbrooke	Royal Victoria Hospital	University of Guelph	University of Ottawa	Université Laval		Sunnybrook & Women's College Health Sci. Ctre	Sir Mortimer B. Davis Jewish General Hospital	Mount Sinai Hospital		Vancouver Hospital and Health Science Centre		Montreal Neurological Hospital and Institute	Hopital Motie-Dallie du Onoin	National Research Council Canada	ot. Michael s nospital	British Columbia Cancer Agency	namilton nealth Sciences Corporation hetitut de cardiologie de Montréal	Canada

Compiled by Science-Metrix from Medline.

Table XXII Leading Canadian institutions' specialization index by therapeutics, 1996-2001 (Canadian basis)

Institution	Antiarthritics	Anti-infectives	Antispasamodics & Antispassives	slsiiv-ifnA	Bronchial & Other Respiratory Therapies	Cancer & Other Neoplasms	Cardiovascular Therapies	Cholesterol	Contraceptives	Dermatologicals	Diabetes	Hemostatic Modifiers	Hormones	Psychotherapeutics & Meurological Disorders	Vaccines & Other Immunizations	E
University of Alberta	n.s.	0.93	n.s.	1.98	1.00	06.0	06.0	n.s.	n.s.	D. S.	1.39	0.78	1.02	0.70	0.89	1.00
University of British Columbia	n.s.	1.49	n.s.	n.s.	0.68	0.68	0.78	1.72	n.s.	n.s.	1.31	0.69	0.92	1.06	⊓.s.	1.00
University of Toronto	n.s.	0.79	n.s.	n.s.	n.s.	1.02	0.59	n.s.	n.s.	n.s.	1.26	0.75	1.17	1.21	n.s.	1.00
McGill University	n.s.	0.62	n.s.	n.s.	n.s.	1.14	0.54	n.s.	n.s.	n.s.	n.s.	n.s.	0.98	1.41	n.s.	1.00
University of Calgary	n.s.	0.72	n.s.	n.s.	n.s.	n.s.	1.45	n.s.	n.s.	n.s.	1.42	1.84	0.99	1.10	n.s.	1.00
McMaster University	n.s.	1.19	n.s.	n.s.	1.50	0.77	0.99	n.s.	n.s.	n.s.	n.s.	2.49	0.89	0.83	n.s.	1.00
University Health Network	n.s.	1.51	n.s.	n.s.	1.31	2.28	0.99	n.s.	n.s.	n.s.	n.s.	n.s.	0.72	0.78	n.s.	1.00
Université de Montréal	n.s.	0.78	n.s.	n.s.	n.s.	n.s.	1.40	n.s.	n.s.	n.s.	1.34	n.s.	1.20	1.01	n.s.	1.00
University of Western Ontario	n.s.	n.s.	n.s.	n.s.	0.88	0.88	1.14	n.s.	n.s.	n.s.	n.s.	n.s.	1.04	0.93	n.s.	1.00
University of Manitoba	n.s.	1.40	n.s.	n.s.	1.01	1.29	1.25	n.s.	n.s.	n.s.	n.s.	1.41	0.84	0.95	n.s.	1.00
Hospital for Sick Children	n.s.	1.29	n.s.	n.s.	2.23	0.83	0.74	n.s.	n.s.	n.s.	2.46	n.s.	1.21	0.77	n.s.	1.00
CHUQ	n.s.	n.s.	n.s.	n.s.	1.37	1.13	0.58	n.s.	n.s.	n.s.	n.s.	n.s.	1.76	0.85	n.s.	1.00
University of Saskatchewan	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	0.97	n.s.	n.s.	n.s.	n.s.	n.s.	0.91	0.97	4.50	1.00
Queen's University	n.s.	n.s.	n.s.	n.s.	1.34	1.1	0.90	n.s.	n.s.	n.s.	n.s.	n.s.	0.83	1.52	n.s.	1.00
Dalhousie University	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.16	n.s.	n.s.	n.s.	n.s.	n.s.	0.54	1.47	n.s.	1.00
Toronto Public Health	n.s.	1.31	n.s.	n.s.	n.s.	1.61	0.95	n.s.	n.s.	n.s.	n.s.	n.s.	0.88	1.62	n.s.	1.00
Université de Sherbrooke	n.s.	n.s.	n.s.	n.s.	1.47	1.08	0.95	n.s.	n.s.	n.s.	n.s.	n.s.	1.35	n.s.	n.s.	1.00
Royal Victoria Hospital	n.s.	n.s.	n.s.	n.s.	2.69	1.45	0.83	n.s.	n.s.	n.s.	n.s.	n.s.	1.47	n.s.	n.s.	1.00
University of Guelph	n.s.	2.27	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.1	n.s.	2.52	1.00
University of Ottawa	n.s.	n.s.	n.s.	n.s.	n.s.	1.21	0.83	n.s.	n.s.	n.s.	n.s.	n.s.	0.88	1.19	n.s.	1.00
Université Laval	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	2.61	n.s.	1.50	0.90	n.s.	1.00
	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.06	1.1	n.s.	1.00
Sunnybrook & Women's College Health Sc. Ctre	n.s.	n.s.	n.s.	n.s.	n.s.	2.30	1.40	n.s.	n.s.	n.s.	n.s.	n.s.	0.80	1.48	n.s.	1.00
Jewish General Hosp	n.s.	n.s.	n.s.	n.s.	n.s.	3.26	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.58	n.s.	n.s.	1.00
Mount Sinai Hospital	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.46	n.s.	n.s.	1.00
Institut de recherches cliniques de Montréal (IRCM)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	2.34	n.s.	n.s.	n.s.	n.s.	n.s.	1.07	n.s.	n.s.	1.00
Vancouver Hospital and Health Science Centre	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.09	n.s.	n.s.	1.00
CHU Mère-enfant Hôpital Sainte-Justine	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Montreal Neurological Hospital and Institute	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	3.63	n.s.	1.00
Hôpital Notre-Dame du CHUM	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
National Research Council Canada	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.64	n.s.	1.00
St. Michael's Hospital	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	2.29	n.s.	n.s.	n.s.	n.s.	4.80	1.26	n.s.	n.s.	1.00
British Columbia Cancer Agency	n.s.	n.s.	n.s.	n.s.	n.s.	4.71	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Hamilton Health Sciences Corporation	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	2.36	n.s.	n.s.	n.s.	n.s.	6.91	n.s.	n.s.	n.s.	1.00
Institut de cardiologie de Montréal	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	5.90	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Canada	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00

Compiled by Science-Metrix from Medline.

Table XXIII Leading Canadian institutions' papers by technology, 1996-2001

Institution	Antibodies Technology	Bioinformatics	Combinatorial & Drug Screening	Genomics, Proteomics & Genetic Engineering	Imaging & Biophotonics	Mass Spectrometry	Mimetics	Nanotechnology	Regenerative Medicine	n
University of Alberta	71		19	255	83	4	15	35	29	865
University of British Columbia	53	5 1	12	192	03 104	10	16	43	41	830
University of Toronto	55 46	8	6	222	69	5	34	43 36	41	783
McGill University	41	3	8	170	51	2	7	26	30	535
University of Calgary	33	5 5	7	131	46	3	8	28	30	521
McMaster University	34	5	6	128	45	2	16	21	61	512
University Health Network	67	1	3	128	53	2	12	14	51	484
Université de Montréal	30	3	4	116	36	1	9	29	11	454
University of Western Ontario	37	4	5	101	44	1	11	22	16	438
University of Manitoba	33	1	1	88	25	•	4	30	8	394
Hospital for Sick Children	25	1	3	92	44	1	16	25	25	387
CHUQ	24	•	2	145	30	2	19	12	6	359
University of Saskatchewan	57	3	2	83	23	_	14	8	4	316
Queen's University	15	5	9	65	26	3	4	19	6	304
Dalhousie University	38		1	53	17		4	12	3	293
Toronto Public Health	18	1	2	70	28		8	13	22	287
Université de Sherbrooke	26	2	1	74	29		6	11	6	261
Royal Victoria Hospital	20	2		69	22		11	6	11	259
University of Guelph	24	1	2	44	17		9	8	2	244
University of Ottawa	15		2	73	25		7	8	11	242
Université Laval	14		3	64	26		2	5	4	233
Ottawa Hospital	22		1	65	10	1	6	17	10	179
Sunnybrook & Women's College Health Sc. Ctre	14		1	31	18		4	9	11	172
Sir Mortimer B. Davis Jewish General Hospital	11		6	78	12		4	5	5	159
Mount Sinai Hospital	13			43	9		2	8	9	154
Institut de recherches cliniques de Montréal (IRCM)	9		4	48	8	1	1	9	5	140
Vancouver Hospital and Health Science Centre	10			35	19		4	5	8	134
CHU Mère-enfant Hôpital Sainte-Justine	6	1	2	35	13		3	3	5	128
Montreal Neurological Hospital and Institute	8			42	21			5	14	112
National Research Council Canada	10	1	10	32	24	2	4	10	2	110
Hôpital Notre-Dame du CHUM	11			41	6	1	2	3	5	110
St. Michael's Hospital	13	1		24	14		2	1	4	105
British Columbia Cancer Agency	7			34	15		_	1	45	104
Hamilton Health Sciences Corporation	3	,		5	10		2	3	1	102
Institut de cardiologie de Montréal	5	1	400	11	9		1	1		102
Canada	1049	66	166	3353	1245	51	345	590	577	13076

Table XXIV Leading Canadian institutions' specialization index by technology, 1996-2001 (Canadian basis)

Institution	Antibodies Technology	Bioinformatics	Combinatorial & Drug Screening	Genomics, Proteomics & Genetic Engineering	Imaging & Biophotonics	Mass Spectrometry	Mimetics	Nanotechnology	Regenerative Medicine	n
University of Alberta	1.02	n.s.	n.s.	1.15	1.01	n.s.	n.s.	0.90	n.s.	1.00
University of British Columbia	0.80	n.s.	n.s.	0.90	1.32	n.s.	n.s.	1.15	1.12	1.00
University of Toronto	0.73	n.s.	n.s.	1.11	0.93	n.s.	1.65	1.02	1.27	1.00
McGill University	0.96	n.s.	n.s.	1.24	1.00	n.s.	n.s.	n.s.	1.27	1.00
University of Calgary	0.79	n.s.	n.s.	0.98	0.93	n.s.	n.s.	n.s.	1.30	1.00
McMaster University	0.83	n.s.	n.s.	0.97	0.92	n.s.	n.s.	n.s.	2.70	1.00
University Health Network	1.73	n.s.	n.s.	1.03	1.15	n.s.	n.s.	n.s.	2.39	1.00
Université de Montréal	0.82	n.s.	n.s.	1.00	0.83	n.s.	n.s.	n.s.	n.s.	1.00
University of Western Ontario	1.05	n.s.	n.s.	0.90	1.06	n.s.	n.s.	n.s.	n.s.	1.00
University of Manitoba	1.04	n.s.	n.s.	0.87	n.s.	n.s.	n.s.	1.69	n.s.	1.00
Hospital for Sick Children	n.s.	n.s.	n.s.	0.93	1.19	n.s.	n.s.	n.s.	n.s.	1.00
CHUQ	n.s.	n.s.	n.s.	1.58	0.88	n.s.	n.s.	n.s.	n.s.	1.00
University of Saskatchewan	2.25	n.s.	n.s.	1.02	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Queen's University	n.s.	n.s.	n.s.	0.83	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Dalhousie University	1.62	n.s.	n.s.	0.71	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Toronto Public Health	n.s.	n.s.	n.s.	0.95	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Université de Sherbrooke	n.s.	n.s.	n.s.	1.11	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Royal Victoria Hospital	n.s.	n.s.	n.s.	1.04	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
University of Guelph	n.s.	n.s.	n.s.	0.70	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
University of Ottawa	n.s.	n.s.	n.s.	1.18	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Université Laval	n.s.	n.s.	n.s.	1.07	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Ottawa Hospital	n.s.	n.s.	n.s.	1.42	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Sunnybrook & Women's College Health Sc. Ctre	n.s.	n.s.	n.s.	0.70	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Sir Mortimer B. Davis Jewish General Hospital	n.s.	n.s.	n.s.	1.91 1.09	n.s.	n.s.	n.s.	n.s.	n.s.	1.00 1.00
Mount Sinai Hospital	n.s.	n.s.	n.s.	1.09	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Institut de recherches cliniques de Montréal (IRCM) Vancouver Hospital and Health Science Centre	n.s. n.s.	n.s. n.s.	n.s. n.s.	1.02	n.s. n.s.	n.s. n.s.	n.s. n.s.	n.s. n.s.	n.s. n.s.	1.00
CHU Mère-enfant Hôpital Sainte-Justine	n.s.	n.s.	n.s.	1.02	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Montreal Neurological Hospital and Institute	n.s.	n.s.	n.s.	1.46	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
National Research Council Canada	n.s.	n.s.	n.s.	1.13	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Hôpital Notre-Dame du CHUM	n.s.	n.s.	n.s.	1.45	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
St. Michael's Hospital	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
British Columbia Cancer Agency	n.s.	n.s.	n.s.	1.27	n.s.	n.s.	n.s.	n.s.	9.81	1.00
Hamilton Health Sciences Corporation	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Institut de cardiologie de Montréal	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1.00
Canada	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00