MARITIME Series

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THE CANADIAN INSTITUTE FOR RESEARCH ON REGIONAL DEVELOPMENT

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# About the Monograph

We are living in an era marked by a changing economy, one in which knowledge-based industries are redefining traditional production processes and globalization is gradually eliminating trade barriers. One of the features of this "new" economy is that the fields of medicine and pharmaceuticals are being revolutionized by rapidly evolving biotechnologies. In the following study we attempt to define these changes and to determine their impact on the biopharmaceutical industry in Atlantic Canada. After examining some of the recent trends influencing the development of the industry throughout the world, and briefly outlining its structure in Canada, we review the main characteristics of Atlantic Canada's biopharmaceutical industry together with its organization and development. We begin by taking stock of the companies that form the core of the region's industry — companies directly involved in primary biopharmaceutical activities such as research, manufacturing, and distribution. To further our understanding of the industrial dynamics at work, we then turn our attention to a study of the regional infrastructure that supports the industry, from business services and universities to the growing importance of public and private sector interaction. As we shall see, clusters of biopharmaceutical activity are forming in various centres across the region. How we influence their development depends on the direction given to regional industrial strategies and other determining factors such as the regulatory framework, R & D, investment capital, and human resources. We conclude by outlining potential policy options for all levels of government, particularly in areas where they work in close collaboration with other stakeholders (regional, national, and international) — stakeholders that could buttress the development of biopharmaceutical clusters in Atlantic Canada.

# About the Author

Sébastien Breau joined the Canadian Institute for Research on Regional Development (CIRRD) as an economist/researcher in 1999. He has a Bachelor of Social Sciences (honours in economics) from the Université de Moncton and an M.A. in economics from the Université Laval. Prior to joining the CIRRD, he worked with a national, independent applied research institution where he gained extensive experience in economic analysis and forecasting, particularly in the area of provincial economies. His primary research interests are regional economics and the knowledge-based economy. Most recently, his work has focused on the changing structure of economic activity in Atlantic Canada, the dynamics of regional labour markets, interprovincial migration trends, and the phenomenon of convergence between Canadian provinces.

# Contents

# Foreword and Methodology

In November of 1997, the Canadian Institute for Research on Regional Development (CIRRD) published one of the first comprehensive studies on industrial biotechnologies in Atlantic Canada.[1] The present monograph, which was inspired by this document, explores in greater depth the integration of biotechnologies in the pharmaceutical industry and its economic impact in Atlantic Canada.

This study is part of a shared project between the CIRRD and the Atlantic Canada Opportunities Agency (ACOA). It is exploratory in nature in that it investigates some of the principal developments taking place in the biopharmaceutical industry, emphasizing the industry's recent expansion in Atlantic Canada and its characteristics as well as examining various strategies to further promote its growth.

Because of the rapid growth in the industry, conventional information sources such as Statistics Canada (currently in the process of revamping its databases) are not yet up to the task and can only partially reflect the changing industrial classifications. Therefore, several information sources were used to gather facts and figures at various levels of the study. For international data, IMS Health Canada provided detailed statistics on world markets. For general industry trends, I conducted a thorough review of the literature and consulted documents from international organizations (e.g., OECD, WHO, WIPO, WTO, etc.), private industry analysts (e.g., PricewaterhouseCoopers, KPMG, Ernst & Young, *Scrip Magazine*, etc.), industry associations (e.g., Pharmaceutical Research and Manufacturers of America, etc.), Internet information networks (e.g., PharmInfoNet, Pharmaceutical Online, etc.), as well as various government departments and agencies (e.g., U.S. Foreign Commercial Service and Department of State, Industry Canada, etc.). For national data, I relied on statistics drawn from IMS Health Canada databanks; however, the two primary

1. Fabrice Rigaux, *Industrial Biotechnology in the Atlantic Provinces: From Emergence to Development?* (Moncton, N.B.: The Canadian Institute for Research on Regional Development, 1997).

sources of quantitative information were accessed via Contact Canada and the Canadian Company Capabilities (CCC) guide (Strategis — Industry Canada). The former offered the most up-to-date and comprehensive data collection available for pharmaceutical and biopharmaceutical companies throughout Canada. It covered corporate data, such as sales figures, commercial and industrial partnerships and alliances, product profiles, employment levels, and other pertinent information. The CCC was used to complement the previous databank. Strategis was also helpful in providing detailed information on international trade flows. Finally, I carried out a series of interviews with both regional and national stakeholders — including experienced business executives, new entrepreneurs, academic researchers, and representatives of industry associations and governments — to gather additional qualitative information on industry developments.

Besides the many people who took the time to answer my questions, various others also helped me during my research. In particular, I would like to acknowledge the assistance of Éveline Landa (National Research Council of Canada's Biotechnology Research Institute), Patrick Lacroix (Canada's Research-Based Pharmaceutical Companies), Stephen Kunz (IMS Health Canada), and Malcolm MacBeath (ACOA). I would also like to thank Michel Belliveau for his research assistance, as well as Colette Allain, who helped me establish the databanks used in the analysis and Josette Thériault for retyping parts of the manuscript.

A first draft of the manuscript was presented at the Biotechnology Strategy Meeting held in St. John's, Newfoundland, in June of 2000 and benefited from the discussions that followed with several of the participants. In addition to the officials with ACOA who organized the meeting and took part in the discussions, I would like to thank John Argall (executive director of BioAtlantech in New Brunswick), David King (president and CEO of Seabright Corporation in Newfoundland), and Bill Mills (executive director of BioNova in Nova Scotia), who shared with me some of their many insights. Furthermore, several of the participants at the 29th Annual Conference of the Atlantic Canada Economics Association in October 2000, to which a working paper based on the manuscript was also presented, made numerous helpful observations, and the book has been improved as a result.

The study also benefited from the valuable comments of Steve Armstrong (director of Life Sciences at In*NOVA*corp) and Neil Ritchie (president and CEO of BioMed Management/Business Development

Office, Dalhousie University Medical School). Last but not least, I would like to express my gratitude to Maurice Beaudin and Donald J. Savoie, who provided me with many valuable suggestions which helped enhance the final version of the manuscript. Any errors that survived their scrutiny are the responsibility of the author.

# Introduction

If you skim through a business magazine or newspaper these days, chances are you will come across headlines such as "Decades of Research into Tissue Engineering Are About to Pay Off As Dozens of Startups Perfect Living Organs Grown in the Lab, Not the Body"[2] or "BioChem Pharma Announces $80 million Investment by the Government of Canada in Major Vaccine Development Project."[3] These are just two of the many breakthroughs made by biotechnologies in recent years.

Indeed, during the final quarter of the last century, biotechnologies were taking off and, without a doubt, pushing back the scientific boundaries of the medical and pharmaceutical fields. The union of more traditional knowledge with revolutionary biotechnological applications is resulting not only in new areas of research and development but also in novel methods of product design, manufacturing, and delivery. As new developments continue to transform the face of the pharmaceutical industry, the shockwaves will be felt throughout the world. In some nations where clusters of industrial pharmaceutical activity already exist, such as in the U.S. (e.g., the New Jersey, New York, Pennsylvania belt), the United Kingdom, Germany, France, and Switzerland, long-established industry giants are embracing this new science, replenishing their product pipeline, and, perhaps more importantly, bringing new products to market quicker and more efficiently.

The advent of biotechnologies also signals shifts in global industry dynamics, creating new opportunities for countries and regions with historically less sophisticated pharmaceutical industries than those just mentioned. For Canada, which has, over the years, fostered a strong research infrastructure and broadened its innovative capacity,

2. Catherine Arnst and John Carey, "Biotech Bodies: Decades of Research into Tissue Engineering Are About to Pay Off As Dozens of Startups Perfect Living Organs Grown in the Lab, Not the Body," *Business Week* no. 3588 (27 July 1998): 56.
3. Press release (Laval, Québec): "BioChem Pharma Announces $80 Millions Investment by the Government of Canada in Major Vaccine Development Project," *Canada NewsWire* (3 April 2000).

this means a chance to move up to the forefront of biopharmaceutical developments. So far it has risen to the challenge and is increasingly considered one of the hotspots for such companies. It is even viewed as a world leader in certain niche areas such as vaccines. Montreal-based BioChem Pharma, for example, has become, in just over a decade, one of the world's top forty R & D companies for the number of products in development. New companies are also springing up right across the country and taking advantage of new opportunities.

Yet, because biotechnologies are evolving at such a rapid pace and continually transforming the face of the pharmaceutical industry, the task of gauging the industry's impact on economic activity is made harder. For instance, traditional data sets recording pharmaceutical manufacturing activity are based on earlier industrial classification systems (i.e., 1980), when biotechnologies were only beginning to emerge in industrial processes. Hence, these sets can only partly reflect the changing nature of the industry.

The principal goal of this study is thus to explore the recent developments taking place in the biopharmaceutical industry and, from a more regional perspective, to review its characteristics in Atlantic Canada. More specifically, it is to identify the factors affecting the region's competitive position, as well as the challenges that lie ahead in creating opportunities for sustained regional industrial growth.

In Atlantic Canada, the biopharmaceutical industry is young but vibrant. Of the fifty or more regional firms that currently make up the sector, which represents just over 5 percent of Canadian biopharmaceutical companies, two-thirds of them were created between 1990 and 2000. Over the last five years alone, job creation in the industry has been growing at an average rate of approximately 7 percent annually; it currently employs over 1,250 people. Building on the strengths of an expanding biotechnological capacity and a considerable pool of specialized and highly trained scientific personnel, regional firms contribute to the manufacture of a wide array of therapeutic, vaccine, and diagnostic products. The industrial innovativeness of biopharmaceutical firms has also been encouraged by strong local private-public sector interaction. And by increasingly adopting export-based commercial strategies, they are well plugged into international trade currents.

On the downside, with the exception of a few pockets of concentrated activity, the industry remains somewhat fragmented and dispersed. The requirements for human resources are gradually changing, and the labour market for highly qualified staff is tightening, rendering the task of attracting and retaining entrepreneurs more difficult. Access to capital resources, despite significant improvements over the last few years, is still limited, often because of a company's lack of experience and an inability to commercialize products in a timely manner, which, as we will see, is a major concern of investors. Regulatory hurdles in provincial drug reimbursement programs affect the level of investment in R & D by larger multinational companies. Likewise, federal government funding for R & D is slated to increase significantly in the near future with the creation of the Canadian Institutes of Health Research. Making sure Atlantic Canadian research institutions secure their share of investments will require a new approach to interdisciplinary research teams; they must be capable of tackling the more complex biomedical problems using innovative technologies such as genomics technology and bioinformatics.

These are some of the challenges facing the regional biopharmaceutical industry. There is no doubt that the potential for regional biopharmaceutical development is great, but how governments and industry respond to the problems that lie ahead will be instrumental to its success. In the words of Allen Scott, "Regions that fail to make an early start in fostering the development of a particular industry, or that fall behind in some way, are susceptible to 'lock-out' in the sense that they are liable to find it increasingly difficult to catch up with – much less overtake – the leading contenders."[4]

The study includes three chapters. The first is devoted to establishing what constitutes the biopharmaceutical industry and studying some of the recent trends shaping its development. We also examine how the industry is structured, considering it from international, national, and Atlantic Canadian perspectives. In chapter two, we thoroughly review the formation of biopharmaceutical activity in Atlantic Canada. We start by examining the companies that make up the industry's core, i.e., their corporate profiles, sectors of intervention, and commercial strategies. To get an even broader picture of how the industry is organized, we then focus on its supporting infrastructure. Chapter three explores some of the factors affecting the

4. Allen J. Scott, *Regions and the World Economy: The Coming Shape of Global Production, Competition, and Political Order* (Oxford University Press, 1998), 98.

development of regional industrial activity. In particular, we look at the issues surrounding the regulatory environment, patent protection, research and development funding, access to venture capital, and human resources development. Finally, in our concluding remarks we explore possible future policy alternatives designed to encourage the growth of the biopharmaceutical cluster in Atlantic Canada.

# I

# The Recent Evolution of the Pharmaceutical Industry: International and Canadian Perspectives

The purpose of this chapter is twofold. First, it lays the groundwork for an analysis of the pharmaceutical industry by sorting out some of its main characteristics, such as identifying the players and their roles in the industry. Second, it examines some of the developments unfolding throughout the industry to help us understand what is happening at both the international and Canadian levels. This, in turn, will set the stage for the study in chapter 2 of the pharmaceutical industry in Atlantic Canada.

## The Pharmaceutical Industry: Who, What, and How?

Although at first glance defining the nature of the pharmaceutical industry seems fairly straightforward, the task is actually complex. The reason is that the industry cannot be narrowed down to one specific group of companies. It is made up of a number of stakeholders, each of which pursues its own interests in a market environment constrained by government regulations. Borrowing a sport's analogy first used by Gordon and Maule: "The drug game becomes complicated because of the number of players with differing and interacting interests, and because government plays the role of supplier, customer and insurer as well as referee, and has to change roles as circumstances dictate."[5]

In Canada, as in most industrialized countries, the major players are governments (federal and provincial), manufacturers and researchers (i.e., innovators), distributors (including wholesalers and retailers), hospitals, and finally the customer. Together with industry, government and consumer associations, regulatory bodies, and so forth, the pharmaceutical industry constitutes an extensive web indeed. Within this scheme, as we shall see, the team captain or pivotal player is the manufacturer/producer of pharmaceutical products. Consequently,

5. J. Gordon and C. Maule, "Who Are the Players?" *The Canadian Pharmaceutical Journal* (February 1989): 68–73.

the scope of this study will focus, for the most part, on the industrial production or manufacturing component of the pharmaceutical industry. However, since research and development is a vital part of the industry and given that manufacturers themselves often take on the roles of wholesalers/distributors, we will also review these two components.

What exactly is the pharmaceutical industry? The standard definition of the pharmaceutical and medicine industry, according to the North American Industry Classification System (NAICS), is the following: the industry comprises "establishments primarily engaged in manufacturing drugs, medicines and related products for human or animal use. These establishments may undertake one or more of several processes, including basic processes, such as chemical synthesis, fermentation, distillation and solvent extraction; grading, grinding and milling; and packaging in forms suitable for internal and external use, such as tablets, vials, ampoules and ointments."[6]

Although this definition encompasses a wider range of products than the outdated Standard Industrial Classification (SIC [1980]) system, it still remains too constraining for the purposes of this study since it is centreed exclusively on pharmaceutical manufacturing firms, too often ignoring the growing number of health-related biotechnology companies and products (which have become known as *biopharmaceuticals*). Furthermore, because of its significant knowledge-based component and in an effort to better grasp the economic weight of the pharmaceutical industry as a whole, we shall broaden the definition to include professional, scientific, and technical services along with some health care services. In particular, we look at research and development activities in the life sciences, which comprise establishments primarily engaged in conducting research and experimental development in the fields of medicine, health, biology, biotechnology, pharmacy, veterinary, and other allied subjects. We will also include medical and diagnostic laboratories mainly engaged in providing analytic or diagnostic services. These services are generally provided to the medical profession or to the patient on referral from a health practitioner.

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6. In keeping with the North American Industry Classification System (NAICS), products manufactured include anesthetics, antibiotics (including veterinary), antiseptics (medicinal), blood derivatives (for human or veterinary use), botanical products (medicinal, ground, grade, and milled), contact lens solutions, contraceptive preparations, cough medicines, diagnostic agents, endocrine products, feed additives, herbs (grinding, grading, and milling), hormones and derivatives, vaccines, veterinary products, vitamins, and water decontamination or purification tablets (Statistics Canada, Ottawa, 1997).

Taking a closer look at the production process also helps to draw a clearer picture of who is involved in the pharmaceutical industry, what is produced, and how. Generally speaking, we can break down the process through which a pharmaceutical product flows into four basic steps: research, primary production, secondary production, and distribution and commercialization (see figure 1). Following is a brief description of each of those steps.

Research is at the source of the industrial process. As stated by Harry C. Eastman in his pioneering Report of the Commission of Inquiry on the Pharmaceutical Industry, research activity is made up of fundamental (or basic), applied, and clinical research (including preclinical research).[7]

The goal of basic research is the advancement of scientific knowledge, with no thought being given to a specific application; typically, it involves the synthesis of chemical compounds, the discovery of new biological/biotechnological processes, as well as animal experimentation.[8] This type of research is generally carried out by in-house researchers and is concentrated in the U.S., Germany, Switzerland, the U.K., and France, which are where most pharmaceutical multinationals have their head offices. In some instances, however, and one could argue that this is becoming increasingly the case, basic research takes place in specialized institutes, universities, or hospitals renowned for the high quality of their research.

Applied research, as the name implies, is aimed at the advancement of scientific knowledge with a specific practical application. For example, one could study production processes to better the quality of products or reduce their production costs. For that reason, it is conducted at a centre of manufacturing activity, which more often than not is at company headquarters.

As for clinical research, it consists of screening new products and testing them on humans with a view to winning regulatory approval. This research is conducted through private contract research organizations and/or clinical trials networks/laboratories (universities and hospitals) in each market country in order to meet domestic regulatory requirements.

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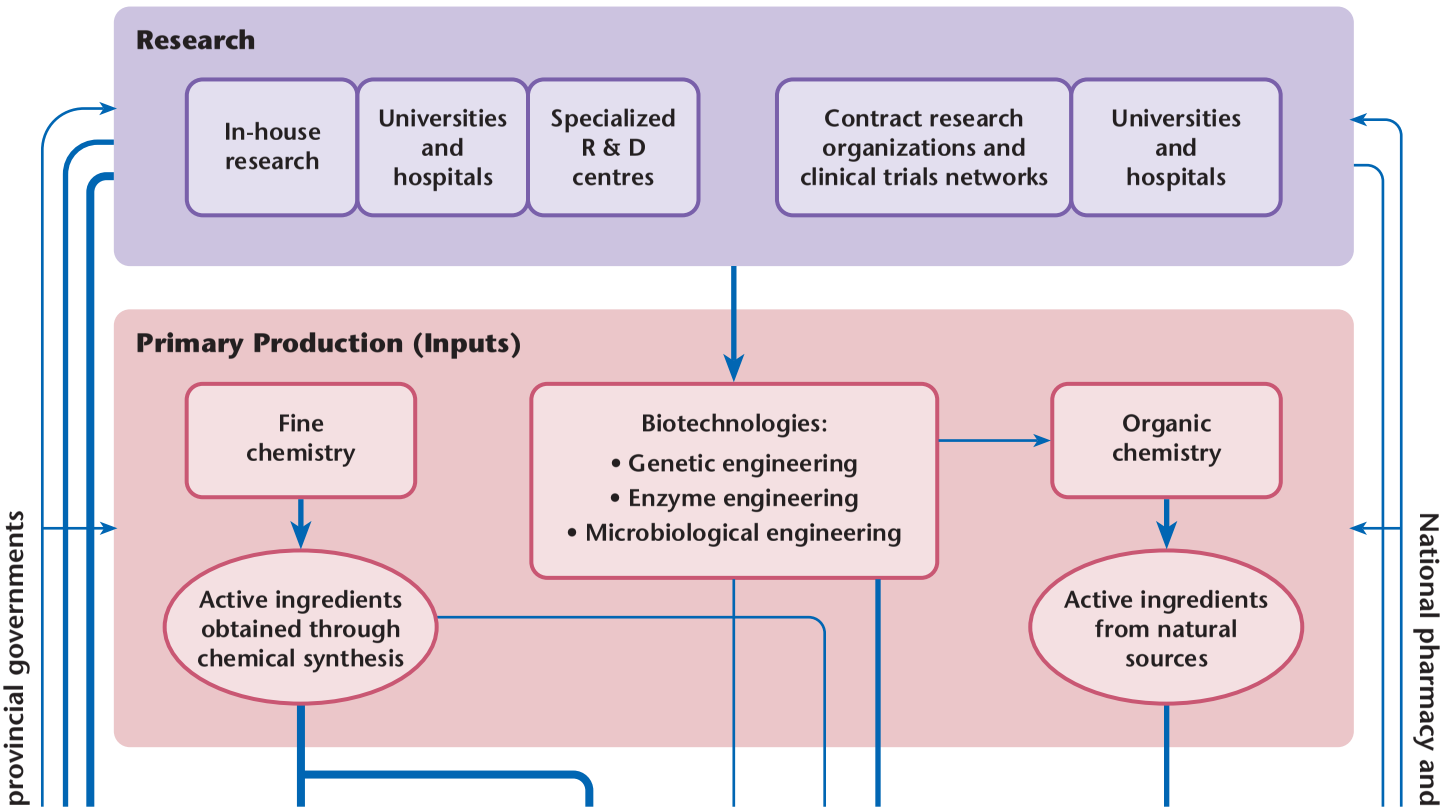
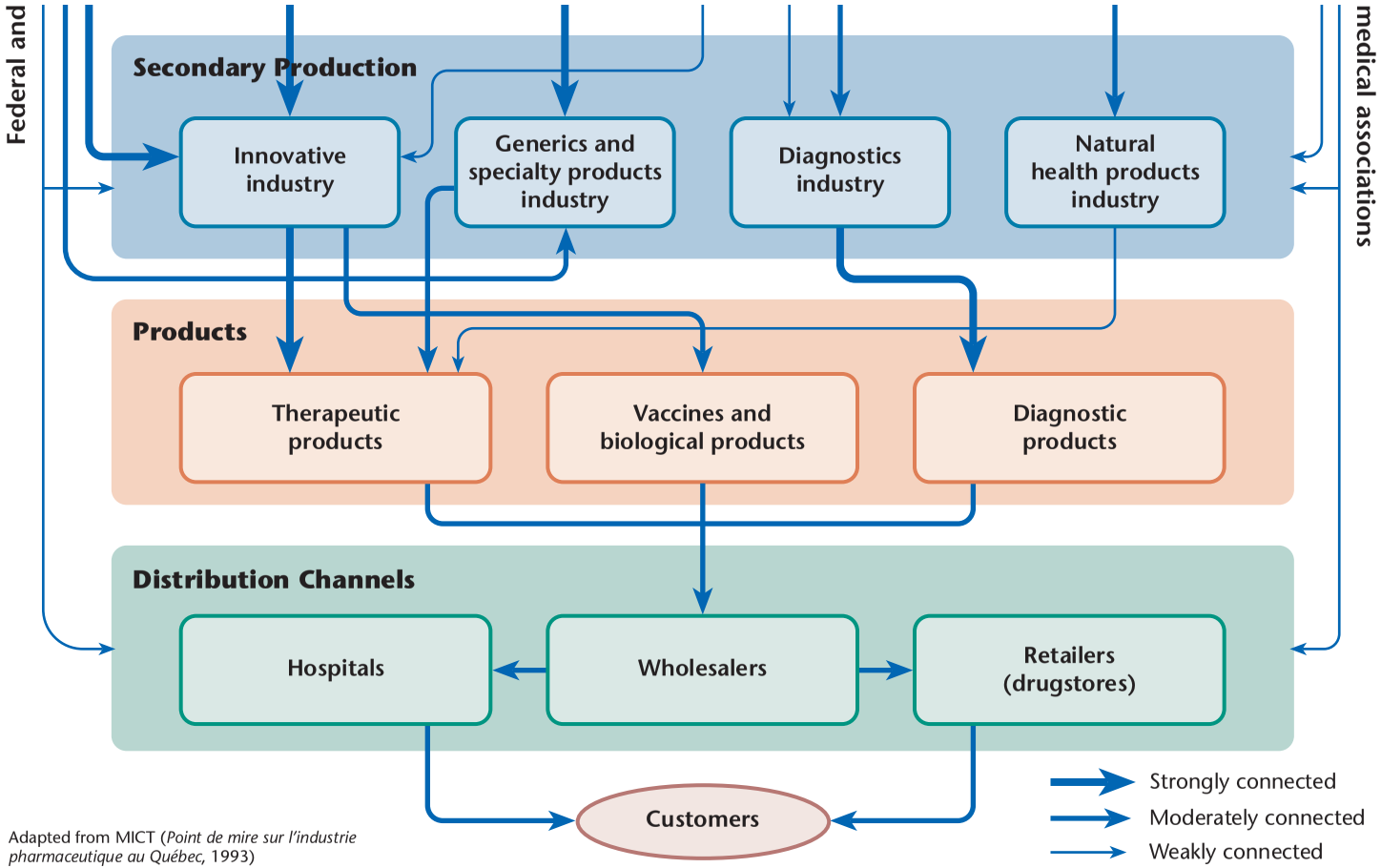
7. H. C. Eastman, *Report of the Commission of Inquiry on the Pharmaceutical Industry* (Ottawa, 1985), 450.
8. Patented Medicine Prices Review Board (PMPRB), *Eleventh Annual Report* (31 December 1998), 45.

Figure 1

The Pharmaceutical Production Process






Adapted from MICT (*Point de mire sur l'industrie pharmaceutique au Québec*, 1993)

The next step in the supply chain is primary production.[9] The primary production of active ingredients (i.e., the chemical substance responsible for the claimed pharmacological effect of a drug)[10] has its roots in fine chemistry, organic chemistry (these are the two traditional sectors), and, increasingly, biotechnologies. This process is usually based on economies of scale (i.e., high volumes of production at the least possible cost) and requires large amounts of capital, sophisticated equipment, and highly qualified personnel. Piggybacking off research and development, this production phase is considered an input to the actual pharmaceutical transformation process, which occurs in the following stage.

Indeed, secondary production (or formulation) takes place when active ingredients are formulated or manufactured into pharmaceutical products in their final dosage form. This process is far less intricate than primary production, and as a result it is usually much more decentralized to domestic market countries in order to meet specific requirements (i.e., packaging, labeling, etc.). Finally, distribution of the products is also decentralized to domestic market countries. From wholesalers to hospitals and retailers (pharmacies), the funneling of drug products to consumers is the last important component in the production process.

All things considered, pharmaceutical products can be categorized according to their intended purpose — that is, diagnostic (to aid in the detection of a disease), therapeutic (treatment), and vaccines and other biological products (prevention). Products included in the diagnostics category are instruments and reagents used for the screening, diagnosis, and monitoring of diseases. They consist, for the most part, of immunoassays (tests for hormones, allergies, HIV, etc.), clinical chemistry (enzymatic, electrochemical, and chromatographic techniques), hematology testing (blood counts), diabetes (omnipresent on the home-testing market), and microbiology tests (supplies of bacterial cultures and various probe tests for specific microorganisms).

From the industry's standpoint, therapeutic drugs are typically labeled according to their patent status. For instance, patented drugs (also known as innovative or brand-name drugs) provide a manufacturer with the exclusive right to make and sell a drug for a certain period of time. Nonpatented drugs, in contrast, refer to generic copies

9. Québec, ministère de l'Industrie, du Commerce et de la Technologie, *Point de mire sur l'industrie pharmaceutique au Québec* (Québec, 1993).

10. As labeled by the Patented Medicine Prices Review Board.

of existing patented drugs and other specialty products that were previously subject to patent protection.[11] For the average consumer, on the other hand, drugs are most often referred to as either prescription or nonprescription medicines. In the first case, prescription medicines are usually prescribed by physicians and dispensed by pharmacists, both in hospitals and in the community via drugstores. As for nonprescription medicines, or over-the-counter (OTC) drugs, they consist of self-medication drugs available without a prescription at assorted retail outlets. Among the more familiar OTCs are remedies for headaches, colds, and upset stomachs.

But therapeutics also include *natural health* remedies, the functional foods and nutraceuticals technology. Their emergence into the sphere of pharmaceuticals can be attributed, among other things, to the increasing use of traditional medicines derived from plants, herbs, and other natural sources as alternatives to modern medicine and pharmaceuticals. In the chapters that follow, when exploring some of the promising segments of Atlantic Canada's pharmaceutical industry, we will take a closer look at functional foods and nutraceuticals.

Finally, the emergence of biotechnologies has also injected new life into vaccines and other biological products. Combined with the fact that vaccination is no longer limited to infants, a growing number of companies are focusing their resources on the development of new and improved vaccines. Advances in vaccines against sexually transmitted diseases, flu vaccines, adjuvants (i.e., substances pooled with antigens to enhance the immune response), and high-tech vaccines such as naked DNA vaccines (which involve genes instead of proteins) are expanding the boundaries of this field. In addition to vaccines, this group of products contains other biological materials such as plasma and blood products, insulin (a hormone produced by the beta cells of the pancreas that helps to regulate the amount of glucose in the blood), as well as scores of other hormones, serums, and enzymes.

In short, the pharmaceutical industry is made up of a wide variety of players, each of which engages in one or more functions in the production process. To understand the industry's dynamic evolution, however, we need to look at some of the leading trends in pharmaceuticals over the last few years.

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11. A note to the reader: most *innovative* companies in Canada are regrouped under the Rx & D Association, or Canada's Research-Based Pharmaceutical Companies (formerly the Pharmaceutical Manufacturers Association of Canada), while *generic* companies are represented by the Canadian Drug Manufacturers Association (CDMA).

## Industry Trends: From Scientific Revolution to Corporate Restructuring

Perhaps nowhere is the impact of biotechnologies greater than in the pharmaceutical industry. What is often called one of the cornerstones of the third industrial revolution, biotechnology has become an integral part of the pharmaceutical industry.[12] In fact, the explosion of biotechnological science in medical and pharmaceutical research and development continues to transform the industry.

The first signs of biotechnology's impact on the pharmaceutical industry can be traced back to the nineteenth century, to a time when the pharmaceutical industry was still nascent under Louis Pasteur's pioneering research into the fermentation process. With the study of living microbes as active ingredients or agents of fermentation came a better understanding of the chemical reactions and interconversions that make up the metabolism of microbial, animal, and plant cells. In time, this led to the discovery of penicillin (the world's first naturally occurring antibiotic) by Alexander Fleming in 1928. World War II was another important stepping stone, as the need to combat the plague of bacterial infections among wounded soldiers paved the way for process engineering (i.e., large-scale manufacturing of products obtained through primary fermentation).[13]

Today, biotechnology has leapt far beyond the realm of standard immunoproducts, producing vitamins, steroid hormones, viral vaccines (i.e., vaccines to prevent human and animal diseases), etc. As we head into the twenty-first century, "It now appears evident that the current and potential applications of the new biotechnologies in medicine amount to essentially a new approach to drug discovery, design, production and delivery."[14]

Most of the new developments in pharmaceutical biotechnology rest upon forays into two principal scientific methods or processes: genetic engineering and hybridoma technology. The term *genetic engineering*, otherwise known as recombinant DNA technology, first appeared in the mid-1970s to describe the process whereby enzymes cut DNA at specific locations. Essentially, it is a technique that

12. Lester C. Thurow, *Building Wealth: The New Rules for Individuals, Companies, and Nations in a Knowledge-Based Economy* (New York: Harper Business, 1999).

13. For a more detailed treatment of the historical aspects of biopharmaceuticals, see M. Beekman and G. Turnock, *Biotechnological Innovations in Health Care* (1991), 4–6.

14. Elettra Ronchi, *Biotechnology and the New Revolution in Health Care and Pharmaceuticals: The Science and the Technology*, Paris: OECD Biotechnology Unit, 1997, 33–52.

consists of "slicing" DNA molecules from different sources and transferring them from one organism to another or rejoining them to obtain new combinations of material. Genetic engineering led to the large-scale production of protein drugs, such as human insulin for patients suffering from diabetes, as well as to genomics, which studies the relationship between genes and cell function under conditions of both health and disease in order to design new drugs (at the heart of genomics also lies the Human Genome Project) (see box 1).

It is said that genomics "is now the engine driving target discovery, validation and compound development in the pharmaceutical and biotechnology industries. Traditional approaches, in particular classical pharmacology, are being integrated into the newer techniques to produce a more rational approach to developing drugs more economically."[15]

The other groundbreaking scientific advances in pharmaceutical biotechnology are rooted in hybridoma technology. A hybridoma is a new cell created by the fusion of an established cancer cell line with the cells of the immune system. As a result, these cells have the ability to make a specific antibody and can reproduce themselves over long periods of time. Because of such features, hybridoma technology (i.e., monoclonal antibody technology) is now commonly used in new diagnostic tests to detect a variety of diseases, including venereal diseases and hepatitis.

Besides offering novel and breakthrough treatments, biotechnologies have not only greatly reduced the time required to bring new drugs to market, but they have increased their efficiency and continue to accelerate the process of pharmaceutical discoveries. Technologies such as combinatorial chemistry (this is a new trend in chemical research which consists of a technology for creating diverse libraries of molecules and testing them rapidly for desired properties), the study of proteomes, and photodynamic therapy all show great promise for new-product development.

As an example of the lightning speed at which biotechnologies are flourishing in the pharmaceutical industry, *Pharmaprojects* Annual Review (for the year ending in May 1999) reported that on a therapeutic basis, the most significant increases in new R & D projects were in genomics and other biotechnologies. Together with recombinants,

15. Rebecca Currie and Ian Lloyd, "Research Still Healthy – But is the Revolution Imminent?" *Scrip Magazine* (January 1998): 63–65.

**Box 1**

## The Human Genome Project: Helping to Chart New Frontiers in Pharmaceutical R & D

The Human Genome Project (HGP) is an international endeavour led by the U.S. Department of Energy and the National Institutes of Health whose goal is to identify all of the approximately one hundred thousand genes in human DNA and subsequently to sequence its three billion DNA subunits. The HGP first got off the ground in the early 1990s and was expected to last some fifteen years, but with rapid technological progress, it is expected to be completed by 2003 at the latest.

What are genes? Genes, which are part of the genome, may be described as the blueprint for living organisms. They carry the information for making all the proteins required by organisms. In short, the benefits of understanding genes and the information they contain are quite remarkable, even revolutionary, and the applications of that understanding are widespread, ranging from areas such as medicine to the environment, energy, forensics, agriculture, bioprocessing, etc. For the pharmaceutical industry, mapping genes and using the catalogue of information that it provides can lead to earlier detection and improved diagnosis of diseases, rational drug design, and the discovery of new drugs and therapeutic treatments, and it can significantly shorten the time it takes to make new biological discoveries. Already, genetic research breakthroughs have extended our understanding of pharmaceutical R & D, opening up pathways to new vaccines to treat diseases such as AIDS and tuberculosis, as well as drugs to fight cancer. Eventually, that knowledge of genes might be used not only to diagnose and treat diseases but also to prevent them.[16]

16. For more information on the HGP, visit the Web sites of the US Department of Energy at www.er.doe.gov/production/ober/hug_top.html and the Oak Ridge National Laboratory at www.ornl.gov/TechResources/Human_Genome/home.html.

the number of drugs in development shot up 40.9 percent in one year alone: from 362 projects in 1998 to 510 in 1999. In the fight against cancer, the second-leading cause of death in North America, a survey by the Pharmaceutical Research and Manufacturers of America (PhRMA)[17] reveals that some 150 biotechnological drugs are in the development stage, including treatments for various types of cancers (i.e., pancreatic, lung, prostate, breast, liver, kidney, colon, and ovarian cancers). Already, bioengineered drugs against hairy cell leukaemia have been approved, as well as medicines for heart attacks (thrombolytic agents), Crohn's disease, and rheumatoid arthritis (TNF-α antibody) and numerous vaccines against infectious agents (hepatitis B virus, HIV, etc.). So far, approximately sixty-three biotechnology products have been approved and are available on the market.

More than ever, the influx of biotechnologies is breathing new life into the pharmaceutical industry, increasing the efficiency of drug development, and suggesting innovative avenues of research. This is a very welcome sign for companies that are increasingly feeling the pressures of bottom-line financial performances and rising cost-containment measures. All told, it is safe to say that the prognosis for biotechnological research and development in the health care sector is good.

Another emerging and dominant trend in the pharmaceutical industry is the metamorphosis undergone by the industry's value chain and the growing recourse to outsourcing, or subcontracting, of specific operations. Up until the late 1970s (and one could argue well into the 1980s) operations of a typical major multinational pharmaceutical company were fully vertically integrated — that is, a company had all production components and capabilities under one roof. Today, with corporate streamlining a top priority, outsourcing is in vogue, and the new kid on the block is the contract research organization (CRO).

CROs first emerged as ad hoc subcontractors to the industry, providing expertise in the area of clinical trials — that is, the evaluation or assessment of the effects of a new drug or medicine on humans. But the trend towards outsourcing has developed both upstream and downstream. For example, more and more big pharmaceutical companies are contracting out primary-manufacturing functions,

17. Pharmaceutical Research and Manufacturers of America (PhRMA), *Pharmaceutical Industry Profile – 1999*, 7–10.

including such activities as drug production process development, full-scale production of bulk substances, etc. Secondary operations also mirror this trend, albeit to a lesser extent, with formulation development and dosage-form manufacturing increasingly being performed by a third party.[18] Finally, at the end of the assembly line, even packaging services have become big business for independent contractors.

There is no denying that the "opening up" of big pharmaceutical businesses, combined with the introduction of new technologies, is changing the face of the industry. This phenomenon, in turn, is creating a plethora of potential niches for smaller drug firms: "Companies specializing in individual stages of the research and development process — from designing libraries to applying for regulatory approval – are springing up like midnight mushrooms."[19] The traditional drug firms are thus able to outsource any part of the research and development process, and are increasingly doing so. Again, one of the most noticeable examples of this has been the explosion, or proliferation, of health-related biotechnology companies.

At the same time as big companies are boosting their profit levels by rationalizing their operations with the increasing use of subcontractors, more and more firms are seeking partnerships, or alliances, within the pharmaceutical industry — *consolidation* is the latest buzzword in the industry. Indeed, in an effort to secure a successful future in a global environment faced with mounting cost-containment pressures and shorter product life-cycles, a new wave of mergers, acquisitions, and alliances has rocked the corporate boat of the big players. As reported in an article in the *Wall Street Journal*: "The prevailing mantra among the biggest players is that drug development and worldwide marketing have become so expensive that only the Goliaths can succeed. The future may well bring a global drug industry with only a half dozen giants."[20] In Europe, for example, Swedish giant Astra AB recently joined forces with Britain's Zeneca Group PLC to form one of the world's leading pharmaceutical companies. In the United States, Pfizer Inc. and Warner-Lambert Co. (with its blockbuster cholesterol-lowering drug Lipitor) have just completed one

18. Enrico Palastro and Sonia Tulcinsky, "Making Sense of a Supply Chain in Flux," *Scrip Magazine* (November 1998): 55–58.

19. "The Pharmaceutical Industry," *Economist* 346, no. 8056 (21 February 1998): S5.

20. Michael Waldholz, Elyse Tanouye, and Gardiner Harris, "Rx for Drug Companies: Get Hitched, Stat! — With Executives Aging and Patents Expiring, Industry Is Ripe for Megamergers," *Wall Street Journal* (4 November 1999).

of the largest mergers in business history. Closer to home, one of Canada's largest generic-drug makers, Novopharm Ltd., has been acquired by Israel's Teva Pharmaceutical Industries Ltd. In a nutshell, large multinationals are looking for ways to reduce the rising costs of bringing new drugs onto market, meet the demands of governments' health care cost-containment policies, and increase R & D productivity. In its 1997 Pharmaceutical sector market and deal survey, PricewaterhouseCoopers estimates that for the period 1989–97, the total value of the thirty largest deals around the globe exceeded U.S. $200 billion; the deals representing about three-quarters of that total took place over the last four years (i.e., between 1994 and 1997).[21]

Although often overshadowed by headlines of megamergers, acquisitions and strategic alliances are also reshaping the landscape of small- and medium-sized firms in the industry. For instance, smaller biotechnology companies are increasingly seeking partnerships or collaborations with larger well-established pharmaceutical companies in order to gain access to venture capital and commercialization or marketing expertise. In return for allowing them to tap into their resources, big pharmaceuticals acquire new technologies and scientific know-how that would otherwise be too expensive or simply impossible to finance in-house. Another study by PricewaterhouseCoopers shows that in the first six months of 1999, as big pharmaceutical companies continued to search for higher margins, biotech deals worldwide were worth more than U.S. $15 billion.[22]

What's more, the vacuum created by the mergers and acquisitions of major companies has left behind a flurry of potentially profitable niches for other small firms using innovative technologies; hence, alliances between numerous smaller-sized start-up firms, university researchers and institutes, and domestic and foreign companies are also blossoming. In all, the number of mergers, acquisitions, and strategic alliances has risen from 121 in 1986 to 627 in 1998. This phenomenal growth in alliances is also the end result of the changing nature of the industry's supply chain. As we shall see in the next section, this has helped change the face of the pharmaceutical industry throughout the world.

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21. PricewaterhouseCoopers, *Higher Performing Strategic Alliances in the Pharmaceutical, Biotechnology and Medical Device and Diagnostic Industries* (August 1999).

22. PricewaterhouseCoopers, *Pharmaceutical Sector Insights: Analysis and Opinions on Merger and Acquisition Activity* (1999).

## The International Context and the Two Faces of the Pharmaceutical Industry

In the wake of these trends and changes sweeping the pharmaceutical industry, a cursory look at what is happening on the international scene reveals two things. The first is that consolidation in the upper echelons of the industry continues to concentrate market and product shares in the hands of a few, very powerful multinationals. Beneath the giants, however, there exists a different reality: a very fragmented industry, a sort of bazaar in which the quick burst of new scientific and technological discoveries can propel companies from tiny start-up firms to big-dollar operations.

The chessboard of the international pharmaceutical industry has for some time been dominated by large multinational enterprises. Historically, this could be associated with the primary production of active ingredients, which, as is well known, requires substantial manufacturing facilities; these facilities are often found only at company headquarters. Today, despite some investments made in non-traditional, pharmaceutical-friendly countries (such as Ireland, Puerto Rico, and potentially China and Brazil), the recent increase in mergers and acquisitions has accentuated this clustering. A look at the top fifteen pharmaceutical companies in 1997–98 reveals that their geographical roots are limited to five countries: the United States, the United Kingdom, Switzerland, Germany, and France (see table 1).

Collectively, these fifteen multinationals represented just over 44 percent of total global pharmaceutical sales (i.e., retail plus hospital sales) in 1997–98. This concentration of market share has increased over the years, particularly in the 1990s as the takeover campaign has accelerated, reflecting to a large degree the desire to maintain and even increase the high profit margins in an already lucrative industry. To get an idea of just how lucrative this segment of the business actually is, the operating profit margin (before interest and taxes) of the ten leading pharmaceutical companies in 1997 averaged approximately 30.4 percent. In comparison, the average for the telecommunications and electronics industry hovers around the 15 to 20 percent range.

None the less, despite the concentration of sales in the upper echelons of the industry, it is interesting to note that taken individually none of these huge multinationals had a market share greater than roughly 5 percent. As for the remaining 56 percent of the sales market, much of it is spread out among companies concerned with

**Table 1**

**The World's Top Fifteen Parmaceutical Companies, 1997–98**

| Country | Company (Worldwide Ranking[a]) |
|---|---|
| **United States** | Merck & Co. (1) |
| | Bristol-Myers Squibb (5) |
| | Pfizer (7) |
| | American Home Products (8) |
| | Johnson & Johnson (9) |
| | Lilly (10) |
| | Abbott (12) |
| | Schering-Plough (14) |
| **United Kingdom** | Glaxo Wellcome (3) |
| | AstraZeneca (4)[b] |
| | SmithKline Beecham (11) |
| **Switzerland** | Novartis (6) |
| | Roche (13) |
| **Germany** | Aventis (2)[c] |
| **France** | Sanofi-Synthélabo (15) |

*Source: Scrip Magazine*, January 1999.

[a] Rankings are based on 1997–98 prescription sales;

[b] AstraZeneca is also partly Swedish;

[c] Aventis is a new life sciences company resulting from the proposed merger of Hoechst (Germany) and Rhône-Poulenc, which also owns Pasteur Mérieux (France).

secondary manufacturing and research activities. This segment of the industry is much more decentralized and fragmented — in line with specific market requirements.

Needless to say, there exists a high degree of geographical correlation between pharmaceutical production and usage. And, as one could expect, with more than half of the fifteen biggest pharmaceutical companies in the world headquartered within its boarders, the United States is a global powerhouse in pharmaceutical production. Overall, the U.S. accounted for about 37 percent of the worldwide pharmaceutical sales market with total factory-gate sales of U.S. $113 billion in 1998 (see table 2).

It is estimated that the number of firms strictly involved in the manufacturing of pharmaceuticals in the U.S. is close to eight hundred (the data include products manufactured for human use only, and excludes wholesalers, retail or dispensing units, and specialized

**Table 2**
**The Global Pharmaceutical Sales Market**

| Region | 1994 Sales (Billions of $ U.S.) | 1998 Sales (Billions of $ U.S.) | 2002 Sales (Billions of $ U.S.) | AACG* (%) 1994–98 | AACG* (%) 1998–2002 |
|---|---|---|---|---|---|
| North America | 79.1 | 118.4 | 164.0 | 10.6 | 8.5 |
| Europe | 72.0 | 79.3 | 99.6 | 2.5 | 5.9 |
| Japan | — | 40.2 | 48.8 | — | 4.9 |
| Latin America | 17.5 | 23.2 | 32.0 | 7.3 | 8.4 |
| SE Asia+China | — | 13.2 | 20.1 | — | 11.1 |
| *China* | *4.8* | *5.6* | *9.0* | *3.9* | *12.6* |
| Eastern Europe | 4.1 | 5.3 | 7.4 | 6.6 | 8.7 |
| Middle East | — | 7.0 | 10.5 | — | 10.7 |
| Africa | — | 4.7 | 5.3 | — | 3.1 |
| Indian Sub-Continent | — | 5.2 | 7.2 | — | 8.5 |
| Australasia | 2.5 | 3.7 | 5.3 | 10.3 | 9.4 |
| CIS | 2.1 | 2.7 | 3.2 | 6.5 | 4.3 |
| **Total** | **256.2** | **302.9** | **403.4** | **4.3** | **7.4** |

*Sources:* IMS Health's *Global Pharma Forecasts 1998–2002* (as reported in *Scrip Magazine*, January 1999), IMS and PMSI data; special compilation by Sébastien Breau.

**Note:* Average Annual Compound Growth.

research-only companies), and they employ just under 210,000 people.[23] The structure of the industry is broadly based, profiting from the manufacturing of active ingredients and innovative new medicines, OTC drugs, the growing production of generics, well-established multinationals, and burgeoning small- and medium-sized enterprises, along with solidly implemented distribution channels and world class research facilities, which have helped make the U.S. a global leader in pharmaceutical R & D. A survey carried out by the Pharmaceutical Research and Manufacturers of America (PhRMA) revealed that 25 percent of the industry's total employment is directly related to R & D activities, while 36 percent of worldwide company-financed R & D is conducted in the U.S.[24] These efforts appear to be bearing fruit. Indeed, the same review showed that of the 152 major drugs developed in the world from 1975 to 1994, 45 percent were of American origin.

23. Earl-Slater, as reported in *The Queen's Health Policy Team, International Pharmaceutical Industry Study* (March 1994), 116.

24. PhRMA, *Parmaceutical Industry Profile*, 1999.

If anything, the upsurge of biotechnologies into the pharmaceutical arena might just reinforce the global industrial dominance of U.S. companies, since the U.S. is already the bastion of thriving biotechnology firms. One example of the pre-eminence of the U.S. in this field can be observed in the advancements made in genetics. A 1996 study by the PhRMA identified 150 genetically engineered pharmaceutical and health care patents issued by the U.S. Patent and Trademark Office in 1995. Of the applicants who received patents, 122 (more than 81 percent) were from the U.S.[25]

Because of different domestic policies and regulations, the pharmaceutical industry in Europe is much more fragmented than it is in the U.S. Taken together, there are approximately thirty-five hundred firms churning out pharmaceutical products in the European Community (with total industry sales valued at U.S. $80 billion in 1998).

An article in the *Economist*, entitled "Europe's Ailing Drug Makers,"[26] draws attention to what has become a growing problem. Using Germany and France as an example, which together represent more than half of the European market, it shows how in many cases small companies have managed to survive only because of advantageous government policies. Now, however, smaller European firms are feeling the strain of mounting government-spending cuts and the opening up of national markets, changes that are exposing them to stiffening competition from foreign companies. Some are turning to exports and others to niche markets. Italy, for example, is maintaining its reputation as a leading provider of active ingredients by focusing on its fine-chemistry expertise. Still, it is clear that the winds of change are blowing for Europe's pharmaceutical industry.

Evidence of the changing European pharmaceutical landscape can also be found in the trend towards consolidation that is gradually developing in the industry. In some countries, this rationalization is already well underway. The United Kingdom, for example, has gone from six major multinationals in the early nineties to just three in 1998. Mergers and takeovers at the level of small- and medium-sized enterprises (SME) have also helped to restructure the industry, bringing together biotechnologies and pharmaceutical R & D. Furthermore, the health and life sciences sector in the U.K. is part of the Technology Foresight program (Foresight). Initiated in 1995, the program is part of a national reorientation of industrial policy and seeks to bring

25. PhRMA, *Patent Survey*, 1996.

26. "Europe's Ailing Drug Makers," *Economist*, vol. 351 no. 8114 (10 April 1999): 59–60.

together various actors in targeted industries to identify structural weaknesses and create new development strategies.[27] Although it is still too early to measure the success of such a program, it has helped foster the growth of some of the most dynamic research centres in the world. Using a slightly different approach, Ireland has also built up a healthy pharmaceutical industry. In that case, the government of Ireland provided various tax incentives and concessions in order to lure several multinational manufacturing plants.

In Asia, Japan remains the dominant player. In 1996, there were 1,424 pharmaceutical firms belonging to the Japan Pharmaceutical Manufacturers Association, and they provided work for 193,000 people. With sales of U.S. $40.2 billion in 1998, Japan is the second-largest national market after the U.S. Although it is firmly committed to R & D and has a strong manufacturing base, with large multinationals such as Takeda and Sankyo (ranked seventeenth and nineteenth respectively on a global scale), Japan imports a large quantity of pharmaceutical products. In 1997, total pharmaceutical imports accounted for 8.5 percent of Japan's production.

Along with other countries in Southeast Asia, China displays evidence of having enormous market potential over the next few years. Since 1990, the Chinese pharmaceutical industry has been growing steadily, and according to the IMS Health's *Global Pharma Forecasts*, the Chinese market is expected to expand at an annual average compound growth rate of 12.6 percent from 1998 to 2002 (see table 2). Such a promising outlook has attracted a flood of international investment in what was once a relatively untapped market. A report by the U.S. Department of State (Foreign Commercial Service) reveals that there are currently more than eighteen hundred foreign-invested pharmaceutical ventures in China as compared to less than a dozen or so such enterprises in the late 1980s.

Another rapidly expanding pharmaceutical market is Latin America, led by Brazil, Argentina, and Mexico. Brazil, ranked in 1998 as the globe's seventh-largest pharmaceutical market (representing roughly 3 percent of total worldwide sales), is of particular interest to Canadian businesses because its economy is heavily dependent on imports. In fact, despite a recent slowdown in sales, imports continue to rise as foreign products claim a larger share of the Brazilian market.

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27. A. Lagendijk and D. Charles, "Clustering as a New Growth Strategy for Regional Economies?: A Discussion of New Forms of Regional Industrial Policy in the United Kingdom", in *Boosting Innovation: The Cluster Approach* (OECD Proceedings, 1999), 127–153.

For instance, in 1994, Canadian exports of pharmaceutical products to Brazil added up to roughly Cdn. $1.2 million, placing it thirty-fifth on the list of countries of destination. Five years later, that figure jumped to over Cdn. $11.3 million. Brazil has become one of the top-ten destinations for Canadian pharmaceutical exports. As we shall see in the following section, this reflects a slowly improving trade picture for Canada on the whole, a result of the increased international competitiveness of Canadian-based pharmaceutical companies.

## A Glance at Canada's Pharmaceutical, Biotechnology, and Diagnostics Industry

The roots of Canada's pharmaceutical history can be traced back to the beginning of the twentieth century, although it was not until World War I that major industrial developments took place. In light of a shortage in the supply of medications experienced by Canadian troops on the battlefields (at that time, medical supplies originated mostly from European countries), Canada began manufacturing its own medicine.[28] Building on scientific breakthroughs, the 1920s and 1930s witnessed a flurry of domestic pharmaceutical company start-ups (e.g., Frosst, Mowatt-Moore, Connaught) as well as the creation of large multinationals (e.g., Roche and Abbott). Following World War II, Canada's entrepreneurial spirit fuelled the growth of small- and medium-sized pharmaceutical companies, while the big multinationals continued to consolidate their position at the top.

Today, even though Canada is not considered a heavyweight in the global pharmaceutical industry as are the United States, the United Kingdom, Switzerland, Germany, France, and Japan, this country's international profile is gaining from a recognition for its innovative research capacities and world-class industrial biotechnologies. Indeed, with the explosive growth in health-related biotechnology and diagnostics companies, combined with their integration into pharmaceuticals, just over 750 firms make up Canada's industrial pharmaceutical fabric. These companies produce a wide range of goods: as an example, the PMPRB reported that more than twenty-one thousand drug products were available in Canada in 1998.

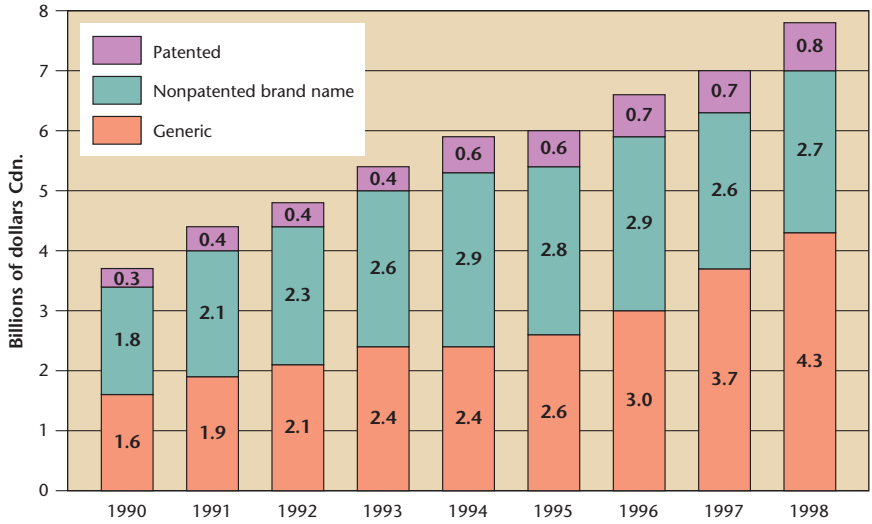
In sales, Canada currently ranks eighth in the world with approximately 2 percent of the international pharmaceutical market. Throughout the 1990s, annual factory drug sales in Canada soared

28. Michel Trépanier, *L'industrie pharmaceutique,* INRS-Urbanisation (September 1992), 13–14.

to virtually double-digit growth rates. Averaging 9.8 percent growth per year, manufacturers' sales of patented and nonpatented drugs in Canada have more than doubled over the last nine years, rising from Cdn. $3.7 billion in 1990 to Cdn. $7.8 billion in 1998 (see figure 2).

**Figure 2**

**Manufacturers' Sales of Patented and Nonpatented Drugs in Canada, 1990–98**




*Sources*: PMPRB, Statistics Canada, and IMS Canada.

Sales of patented drugs have increased significantly over the past few years, boosted by drug products which act on the blood and blood-forming organs (i.e., anticoagulant agents and blood factors), nervous system (i.e., antidepressants and antiepileptics), and musculoskeletal system (i.e., anti-inflammatories) and by drugs affecting the sensory organs (i.e.; decongestants and anti-infectives). Generics, although relatively smaller in absolute terms, have also experienced solid growth in sales, driven in large part by new health care cost-containment policies, the patent expiry of leading products, and an overall improvement in the image of generic products.

Another way of looking at the trend in sales is from the retailers' perspective. In a recent study on Canadians' health expenditures by use of funds, the Canadian Institute for Health Information reported that in 1997, for the first time since 1975, nationwide total retail sales of drugs surpassed spending on physicians' services. While total

outlays on hospitals still account for the lion's share of total health expenditures (32.9 percent), spending on drugs now ranks second with 14.8 percent of payouts.[29] This is the result of the aging of the population and other shifts in demographics and changes in disease treatment, prices, and prescribing habits of physicians.

Despite the fact that most firms established in Canada are domestic-independent firms (approximately 79 percent), more than two-thirds of total sales in 1997 accrued to large subsidiaries of foreign groups (roughly 21 percent of firms). Moreover, by themselves, the ten-largest pharmaceutical companies in the country accounted for 45 percent of total sales in 1998 (based on figures from IMS Health Canada's report *State of the Pharmaceutical Industry, 1998*). All except one, Apotex Inc., were subsidiaries of foreign companies. One of the benefits of big multinationals, however, is that they generate a lot of jobs. In all, estimates pegged total industry employment in 1997 at almost forty-six thousand, with 48 percent of jobs stemming from foreign subsidiaries. A similar report by the Coalition for Biomedical & Health Research estimated that the Canadian biopharmaceutical industry employed forty-three thousand people in 1996, of which twenty thousand worked for manufacturers of patented products (i.e., mostly multinationals), six thousand for producers of generics, twelve thousand in health biotechnology companies, and another five thousand in related services.[30] Also, in the same year, the Medical Research Council of Canada reported that more than fifteen thousand academic researchers were involved in health-related fields.

On average, a foreign subsidiary operating in Canada employs about 230 people. A review of the breakdown of firms by number of employees indicates that this is much higher than the number for the typical national firm. Indeed, 48 percent of firms in Canada have less than 20 employees, 32 percent between 20 and 99 employees, and 16 percent between 100 and 499 employees; only 4 percent of pharmaceutical companies in Canada have more than 500 employees.

In terms of international trade, the fact that pharmaceutical sales in Canada are dominated by foreign multinationals would suggest that imports are likely to be high. And in fact, Canada does report a huge trade deficit. Over the course of 1998 alone, imports valued at

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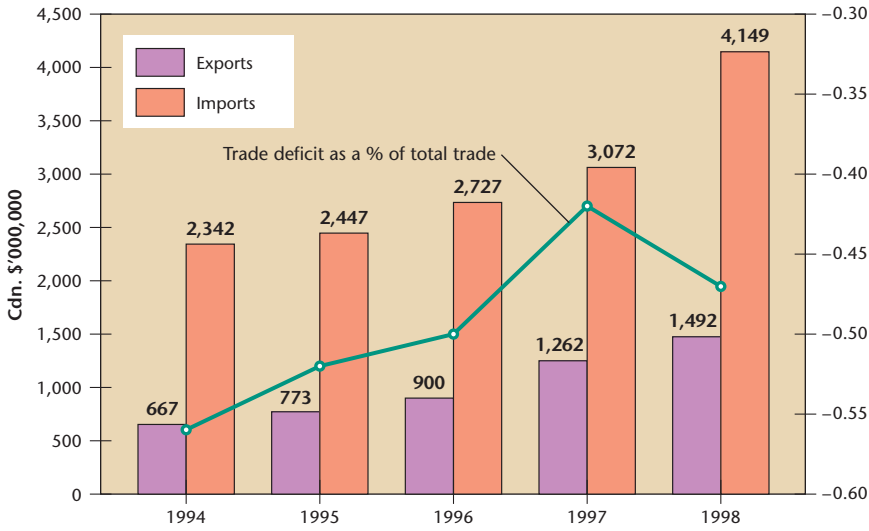
29. Canadian Institute for Health Information, *National Health Expenditure Trends, 1975–2000*, 2000.

30. Pharmaceutical Manufacturers Association of Canada (PMAC), Canadian Drug Manufacturers Association (CDMA), Industry Canada, Medical Research Council of Canada (MRC), and Ernst & Young.

Cdn. $4.2 billion towered over exports of Cdn. $1.5 billion (see figure 3).[31] In most cases, the subsidiaries of large multinationals import active ingredients for secondary manufacturing of pharmaceutical products in their final dosage form, which are then distributed within national boundaries. To meet the growing demand for drug products, imports increased considerably over the last few years, more than doubling since 1990.

**Figure 3**

**Canada's Pharmaceutical Trade Deficit, 1994–98**




*Sources:* Industry Canada – Strategis.

On the other hand, exports have also picked up the pace, and over the last five years, with the exception of 1998, growth in exports outpaced import growth. As a result, the trade deficit as a percentage of total trade has been gradually declining. The strength in exports is attributable, in part, to increased production of Canadian generics and the emergence of its biopharmaceutical companies, which have made huge strides based on steady R & D progress.

A key to success in the pharmaceutical industry is innovation, and the only way to achieve it is through R & D. In this regard, Canada

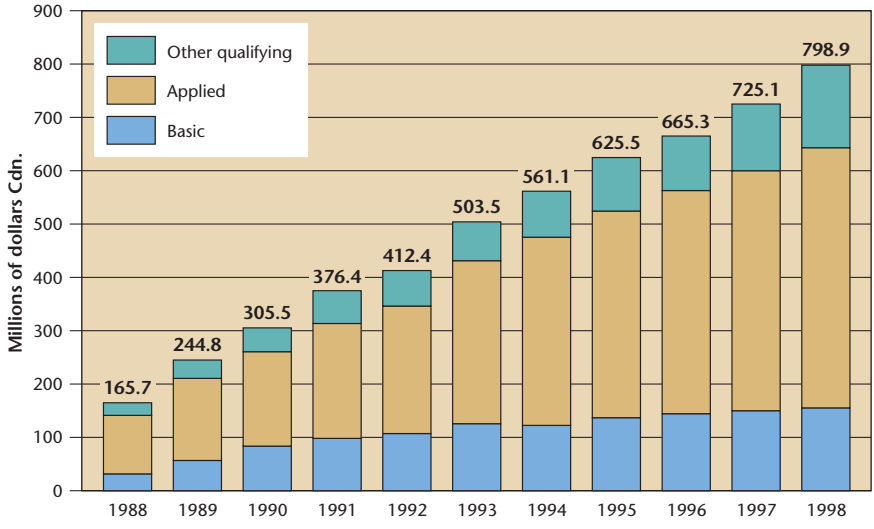
31. In other words, the export-import ratio for the pharmaceutical industry in Canada was approximately 0.35 in 1998. As a measure of comparison, the typical export-import ratio for countries such as France, Germany, the U.K., and the U.S. hovers in the 1.2 to 1.6 range.

has come a long way. Until 1987, Canada's international competitive position in terms of attracting pharmaceutical investment dollars was undermined by weak patent protection laws. This changed, however, with the introduction of Bill C-22 in November of 1988, which was later reinforced by Bill C-91 in 1993. In effect, these legislative provisions extended patent protection from seventeen to twenty years, giving manufacturers seven to ten years of product exclusivity. By the same token, they encouraged large multinationals to spend more on R & D in Canada. The PMPRB reports that total R & D expenditures in 1998 reached just under Cdn. $800 million, nearly five times greater than its level ten years earlier, when it stood at Cdn. $166 million. In Canada, most R & D spending is directed at applied and clinical research, followed by basic and other types of research (see figure 4).

Yet, these figures tend to underestimate the total value of R & D expenditures in Canada, given that only companies reporting sales of patented medicines are required to file R & D data. Hence, many firms actively engaged in R & D are not accounted for. This is the case, for example, with health-related biotechnology and diagnostic companies. Adding up these segments (data were obtained from the *Canadian Biotechnology Directory*, 1999; *Diagnostics Canada Directory*, 1999; and *Pharma, Biopharma & Nutraceuticals Canada Directory*, 1999)

**Figure 4**

**Total R & D Expenditures in Canada by Type of Research, 1988–98**




*Source:* PMPRB.

total R & D expenditures in 1997 were in the neighbourhood of Cdn. $1.5 billion.[32] As for its economic significance, this represents roughly 12 percent of overall R & D spending in the Canadian manufacturing sector, an impressive figure since biopharmaceutical jobs, for example, only account for about 2 percent of total manufacturing employment. Furthermore, drawing on a highly qualified workforce, approximately 13,900 Canadians are directly employed in R & D activities, and they earn, on average, wages of $52,000 per year (nearly 33 percent more than the average manufacturing salary).

The structure of the industry, from a sector-based perspective, reveals a number of facts. As mentioned earlier, more than 750 companies form the biopharmaceutical industry in Canada (these are companies directly involved in all stages of the production process). However, categorizing theses companies based on their respective industrial sectors is complicated by the fact that to a large extent they are not confined to one industry segment but are rather multidisciplinary. None the less, after cross-referencing the database using a sectorial approach (i.e., pharmaceutical/health-related biotechnology/diagnostic), it is possible to obtain a breakdown of companies according to industrial activity (see figure 5A).

Almost half of Canadian firms focus their efforts on pharmaceutical products only. They include some well-established prescription-drug makers, manufacturers of OTC drugs, contract research organizations, contract manufacturing organizations, and firms specializing in clinical trials research. Bit by bit, however, firms have been diversifying their resources by taking advantage of and combining new scientific know-how, processes, and methods. These multifaceted firms constitute the other half of the Canadian biopharmaceutical industry. For instance, at the same time biotech firms provide a whole new platform for therapeutic products, their versatility also allows them to take on new endeavours in diagnostics and genomics as well as nutraceuticals, vaccines, and other health-related products. As Canada continues to develop its biotechnology expertise, these segments of the industry show signs of tremendous potential for Canadian pharmaceuticals.

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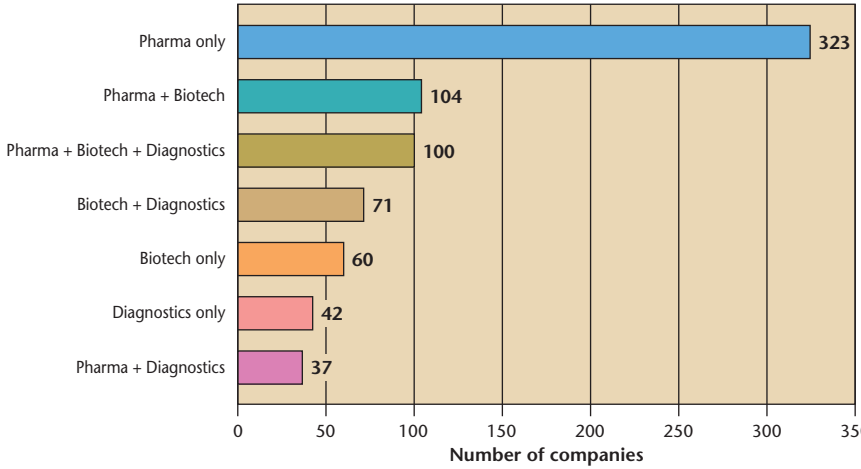
32. It should be noted that on top of the positive impact of a more competitive intellectual-property-rights regime, the importance of R & D tax incentives in attracting and stimulating private sector research dollars is also a significant element of a government's technology and innovation policy. In this regard, using a B-index methodology to compare tax systems for R & D in eleven countries (including the G7), a recent report from the Conference Board of Canada ranked Canada first in terms of providing the most favourable tax treatment for R & D.

**Figure 5A**

**Breakdown of Pharmaceutical, Health-Related Biothechnology, and Diagnostic Firms in Canada according to Industrial Activity, 1997–98**




*Sources:* *Pharma, Biopharma & Nutraceuticals Canada Directory* (1999), *Canadian Biotechnology Directory* (1999), *Diagnostics Canada Directory* (1999), Strategis – *Canadian Companies Capabilities* (1999), Pharmaceutical Manufacturers Association of Canada (1999) and Canadian Pharmacists Association (1999); compilation by Sébastien Breau.

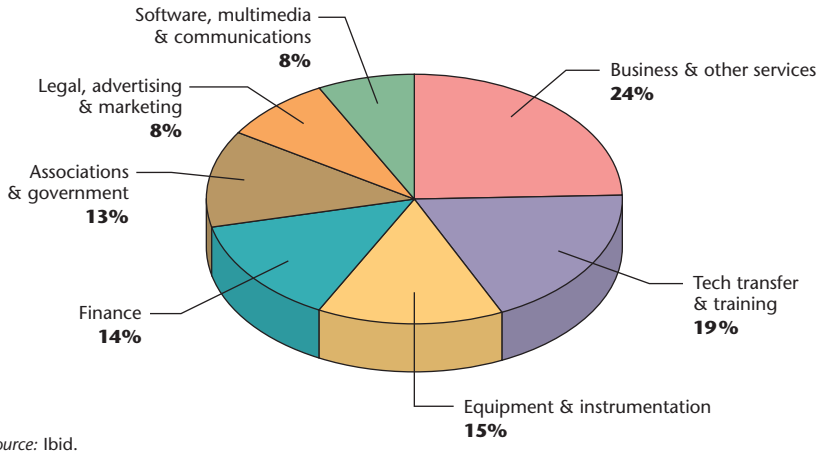
The industrial firms are serviced by a second group of companies (see figure 5B). They provide business services (i.e., marketing and management consulting and recruitment services), technology transfer and training services, various equipment and instrumentation supplies, financial services, legal services, and advertising and multimedia (software) support services. They also include government services (economic development agencies, etc.) as well as various associations linked to the industry. When all is said and done, the biopharmaceutical industry in Canada consists of over sixteen hundred enterprises.

## Provincial Distribution of Biopharmaceutical Companies

A quick roundup of the provincial distribution of biopharmaceutical firms in Canada helps depict some of the regional dynamics at work in the industry — its structural differences and common characteristics. In a 1985 study on the localization of the pharmaceutical industry in Canada, Fernand Martin wrote: “In Canada, the pattern of localization is similar to the one found in the United States in the sense that it is spatially concentrated. Indeed, Ontario and

**Figure 5B**

**Breakdown of Companies Providing Services to the Biopharmaceutical Industry in Canada according to Service Activity, 1997–98**



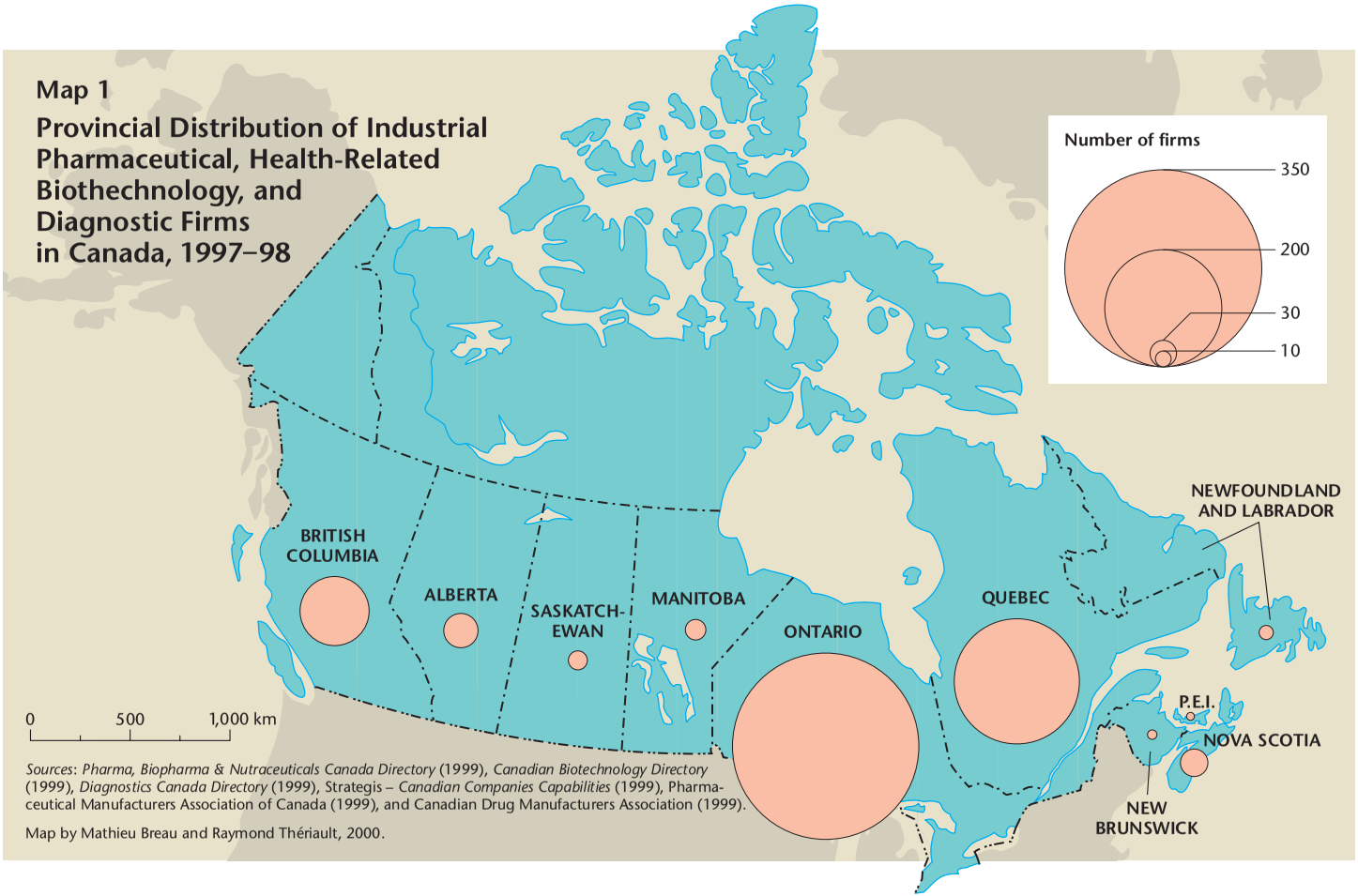

*Source:* Ibid.

Quebec monopolize the industry…."[33] That was fifteen years ago, and although there have been some changes in the Canadian pharmaceutical landscape, it is still much the same today.

Together, Ontario and Quebec account for almost 71 percent of all pharmaceutical and biopharmaceutical companies in Canada, and more than 87 percent of total employment in the industry. The greater concentration of jobs in Central Canada is not surprising given that these provinces serve as the home bases of the country's pharmaceutical giants. For example, of the forty largest companies (in terms of sales volume) in the country, thirty-six (or 90 percent) are located within a 50-km radius of either Toronto or Montreal. What has changed, however, is the fact that the explosion of biotechnologies has given rise to a whole host of new biotech-based pharmaceutical companies, creating something of a two-tone industry: big pharmaceuticals (mostly multinational corporations) on one side and small- and medium-sized biopharmaceuticals on the other. Across Canada, this added dimension has sparked new life in the industry.

On a provincial basis, Ontario remains the industry's stronghold as it is home to more than 41 percent of all pharmaceutical or related companies (see map 1). The Greater Toronto Metropolitan

33. Fernand Martin, *Localisation de l'industrie pharmaceutique au Canada*. Background study prepared for the Commission of Inquiry on the Pharmaceutical Industry (Ottawa, January 1985): 20–21.


Map 1
Provincial Distribution of Industrial Pharmaceutical, Health-Related Biothechnology, and Diagnostic Firms in Canada, 1997–98
Number of firms
350
200
30
10
BRITISH COLUMBIA
ALBERTA
SASKATCH-EWAN
MANITOBA
ONTARIO
QUEBEC
NEWFOUNDLAND AND LABRADOR
P.E.I.
NOVA SCOTIA
NEW BRUNSWICK
0
500
1,000 km
Sources: Pharma, Biopharma & Nutraceuticals Canada Directory (1999), Canadian Biotechnology Directory (1999), Diagnostics Canada Directory (1999), Strategis – Canadian Companies Capabilities (1999), Pharmaceutical Manufacturers Association of Canada (1999), and Canadian Drug Manufacturers Association (1999).
Map by Mathieu Breau and Raymond Thériault, 2000.

Area (GTMA) is a magnet for corporate (national) head offices of big multinationals: it is here that they can tap into Canada's largest pool of consumers and where access to financial resources as well as marketing and other market consultants is greatest.[34] Among some of the industry leaders established in the GTMA are Glaxo Wellcome Inc, Astra Pharma Inc., Eli Lilly Canada Inc., Warner-Lambert Canada Inc., Hoffman-La Roche Ltd., and Pasteur Mérieux Connaught Canada Inc, as well as Canada's top manufacturers of generic products: Novopharm Ltd. and Apotex Inc. Besides administrative functions, these headquarters also regroup most of the R & D and manufacturing activity (especially secondary manufacturing or the mixing of ingredients). Advances in biotechnological applications, while buttressing the growth of larger companies, are also spearheading the creation of smaller biopharmaceutical firms across the province. For instance, London has established itself as a broad-based biotech cluster, Ottawa is becoming a preferred location for genomics research, and Guelph is solidly positioned in the field of veterinary pharmaceuticals.

The number of biopharmaceutical companies in Quebec amounts to nearly 30 percent of the national total. Although this proportion is lower than its western neighbour's, the industry here is no less vibrant; in fact at present, there is tremendous momentum in Quebec's biopharmaceutical industry.[35] Like the GTMA, Montreal's peripheral communities (i.e., Kirkland, Saint-Laurent, and Laval) are home to several big players in the industry. They include Merck Frosst Canada Inc., Bristol-Myers Squibb Pharma Group, Wyeth-Ayerst Canada Inc., Pfizer Canada Inc., Hoechst Marion Roussel Canada Inc., Medis Health and Pharmaceuticals (Canada's largest distributor of pharmacy-related products), and BioChem Pharma Inc. (perhaps Canada's foremost biotechnology-based pharmaceutical company).

It is increasingly recognized that the biotechnology sector is at the source of the industry's revitalization in Quebec.[36] Numerous factors have converged to explain the dynamism of the province's biopharmaceutical industry. For one, both the federal and provincial governments, foreseeing the industrial potential of biotechnologies, invested

34. It is interesting to note that approximately 73 percent of marketing agencies and market consultants dealing with biopharmaceuticals are located in Ontario, with Toronto accounting for just about half of those firms.

35. A 1990 study of the Quebec pharmaceutical industry suggests that the Ontario-Quebec ratio of companies is approximately 1.8 (Gilles Breton, February 1990). Our research, based on 1997–98 data, suggests that the ratio is more in the area of 1.5.

36. On this subject, see, for example, Mulder Management Associates.

heavily in the region's scientific infrastructure by establishing the National Research Council's Biotechnology Research Institute and the Institut Armand-Frappier. Furthermore, the provincial government's industrial policy made it one of the first governments (early in the 1980s) to target the biopharmaceutical industry as a key cluster to develop. Accordingly, Quebec offers a wide variety of programs and incentives to encourage the establishment and expansion of biopharmaceutical manufacturing facilities, human resources development, etc. The provincial government is also firmly committed to creating a prosperous research environment by allocating a variety of tax credits for R & D activity (for example, scientific researchers in Quebec receive a 20 percent supplementary income tax credit, and international researchers actively conducting R & D in Quebec get a five-year provincial income tax exemption). These measures have contributed to making Quebec one of the most generous fiscal environments for R & D activity in the world.

For its part, Western Canada accounts for almost 24 percent of industrial biopharmaceutical activity in Canada. Although British Columbia is home to a few large companies (such as Stanley Pharmaceuticals), the pharmaceutical industry in this region is mostly developing around smaller firms focusing on biotechnologies. Companies such as QLT Phototherapeutics of Vancouver and StressGen Biotechnologies of Victoria are but a few examples of biopharmaceuticals enjoying remarkable growth. The province's infrastructure boasts several research facilities centered around the University of British Columbia and Simon Fraser University. Alberta is also rapidly emerging as a biopharmaceutical hotbed with internationally recognized research centres and strong provincial research funding. The Alberta Heritage Foundation for Medical Research has alone contributed more than Cdn. $540 million to basic biomedical research over the past twenty years. Saskatchewan has solid foundations in nutraceuticals (mostly derived from the agri-food biotechnology sector) and several biopharmaceutical companies specializing in veterinary products. As for Manitoba, which is rather like the Atlantic provinces, its biopharmaceutical industry was practically non-existent up until the 1990s (roughly two out of three biopharmaceutical companies in Manitoba were established after 1990). Since then, however, the industry has burgeoned. Founded in 1991, Novopharm Biotech Inc. (its parent company is Novopharm Ltd., one of Canada's largest manufacturers of prescription pharmaceuticals) carries out R & D in both innovative and generic products at its facilities in Winnipeg.

The provincial capital is also now the site of the NRC's Institute for Biodiagnostics, a world-class R & D centre focusing on therapeutic applications (for cancer and heart disease) and informatics.

Although modest in the national context, the four Atlantic provinces account for in excess of 5 percent of Canadian biopharmaceutical companies. More than 1,250 people are directly employed in the industry, and they are involved at all stages of the production process. Concentrated in Nova Scotia (with approximately thirty industrial firms engaged in R & D activity, which places Nova Scotia fifth in the nation), particularly in and around the Halifax-Dartmouth area, the region's biopharmaceutical cluster is still growing and developing, but at a rapid pace and in all fields. In fact, throughout Atlantic Canada, two out of three biopharmaceutical businesses were founded within the last ten years. The engine of growth driving this entrepreneurial spirit has been fuelled by the many advances in biotechnology applications, which have created industry segments propitious to new innovative companies.

With the shift to a knowledge-based economy and the globalization of markets, it is imperative that we enhance our understanding of the biopharmaceutical industry and its role and potential within the Atlantic Canadian framework. To do so requires an in-depth analysis of the business organizations that make up the industrial fabric of the biopharmaceutical sector. The following chapter is devoted to this task and also explores some of the characteristics of the supporting infrastructure and other services. Chapter 3, for its part, examines some of the issues faced by regional entrepreneurs, such as R & D funding, the availability and skills of local human resources, regulatory hurdles, access to start-up financing, and other government initiatives to further the expansion of the industry.

# II

# Taking Stock of the Biopharmaceutical Industry in Atlantic Canada

Structural changes in, and the convergence of, the pharmaceutical industry and biotechnologies have led to shifts in industry dynamics, creating new opportunities for business development. But exactly how is the biopharmaceutical industry shaping up in Atlantic Canada? Are regional entrepreneurs capitalizing on these new opportunities, and if so, in what fields? Is the regional infrastructure conducive to the creation of biopharmaceutical enterprises? In an attempt to answer these questions and shed some light on the formation of the industry in Atlantic Canada, we begin by examining some of the characteristics of companies directly involved in primary biopharmaceutical activities, such as research, manufacturing, and distribution services. To get a more complete view of the industrial dynamics at work, we then look at the supporting business activities and infrastructure that revolve around the industry's primary activities.

## At the Core of the Industry

The dual structure of the biopharmaceutical industry at the national level (examined above, especially in Quebec and Ontario), where small- and medium-sized companies live side by side with large multinationals, does not exist in the Atlantic provinces. It will be recalled that in Central Canada, the industry is anchored by big multinational pharmaceutical firms (including both innovative and generic companies with roots that can be traced back to developments in fine chemistry), which produce a broad range of products and are involved in every step of the production process, from basic research to manufacturing and product distribution. Alongside these industry leaders, smaller biopharmaceutical firms have sprung up, focusing their activities on particular industry segments. These companies have emerged from the biotechnological revolution.

In Atlantic Canada, the predominance of large multinationals is much less significant. Certainly they finance pharmaceutical research activity — although as we shall see in chapter 3, it is mostly applied

rather than basic research, which is mainly conducted at company headquarters. Even so, their chief commitment is to the other end of the spectrum, where regional offices assure marketing and distribution functions. Indeed, big multinationals, most of which are member companies of the Pharmaceutical Manufacturers Association of Canada (now known as Canada's Research-Based Pharmaceutical Companies), employ more than four hundred sales representatives, who are active throughout the Atlantic provinces increasing the market exposure for their companies' products and promoting their distribution to hospitals and pharmacies.[37] These same companies are *virtually absent* from the production process as they take no part in any local primary or secondary manufacturing activity. In this regard, the industry's workhorse in Atlantic Canada is the small biopharmaceutical firm; what follows is a description of some of its main characteristics.

### *Corporate profiles*

Overall, some fifty companies make up the core of the biopharmaceutical industrial fabric in Atlantic Canada (table 3 lists most of these firms).

These companies participate at all stages of the production system and are also strongly connected to the upsurge of biotechnologies. A breakdown of these firms according to industrial activity reveals that 62 percent of them rely on biotechnology-based activities. A closer look at the corporate profile of the firms involved in the sector, again from an industrial perspective, also reveals two prevailing characteristics that go hand in hand: the industry is still at the embryonic stage, and it is highly fragmented.

The first indication that the industry in the Atlantic provinces is nascent can be found in the fact that only a handful of the region's companies were created prior to the 1980s. Taken together, this group represents a meagre 13 percent of all companies (compared to a national distribution of 27 percent, as shown in figure 6). As one would expect, they are among the region's well-established companies, having integrated both R & D and manufacturing activities as well as a number of marketing and distribution functions. Roughly another 22 percent of companies were established between 1980 and 1990, when biotechnologies were beginning to flourish and research-

37. See Canada's Research-Based Pharmaceutical Companies (Rx & D), *Provincial Profiles* (Ottawa: Rx & D, 1999).

**Table 3**

**Biopharmaceutical Companies in Atlantic Canada Engaged in Industrial Activity**

| Nova Scotia |
|---|
| Armbro Pharmaceuticals Ltd. |
| Chitogenics Ltd. |
| Cytex Pharmaceuticals |
| Delex Therapeutics Ltd.* |
| Diazans Ltd. |
| Dominion Biologicals Ltd. |
| Efamol Canada (1998) Ltd. |
| Empyrean Bioscience Inc. |
| Epitome Pharmaceuticals Inc |
| Fusogenix Inc.* |
| H & R Liposomes Inc. |
| Hologene Genetic Technologies |
| Immunovaccine Technologies |
| Jellett Bioteck Ltd. |
| Kemic Bioresearch Laboratories Ltd |
| Medis Health and Pharmaceuticals (reg. off.) |
| MedMira Laboratories Inc. |
| Naturally NS Health Products |
| New Age Biomaterials Inc. |
| NovaNeuron Inc. |
| Novopharm Ltd. |
| Ocean Nutrition Canada Ltd. |
| Octopus Diagnostics Research (BioMedica) |
| Oligopharm Ltd.* |
| Oncodynamics Inc. |
| Performance Genomics Inc.† |
| Pharmatech Research Inc. |
| Precision Biologicals Inc. |
| Quantanova Canada |
| Sepracor Canada Ltd. |
| Straw House Herbals |

| New Brunswick |
|---|
| Food Research Centre* |
| L & D Manufacturing |
| Maritime MicroBiologicals |
| Clinical Trials Division |
| RPC–Aquaculture & Biotechnology† |
| Vaccinium Technologies |

| Newfoundland and Labrador |
|---|
| A/F Protein Canada Inc. |
| All Materials Products Inc. |
| Bio-ID Corp. Ltd.* |
| Gateway Maritime Inc. |
| Newfoundland Aqua Products Inc. |
| PA Pure Additions* |
| Pharmaceutical Supplies Ltd. |
| Terra Nova Biotechnology* |
| Wesleyville Hatchery |

| Prince Edward Island |
|---|
| Aqua Bounty Farms |
| Aqua Health Ltd. |
| Aquatic Diagnostic Services* |
| Atlantic Fish Health Inc. |
| Diagnostic Chemicals Ltd. |

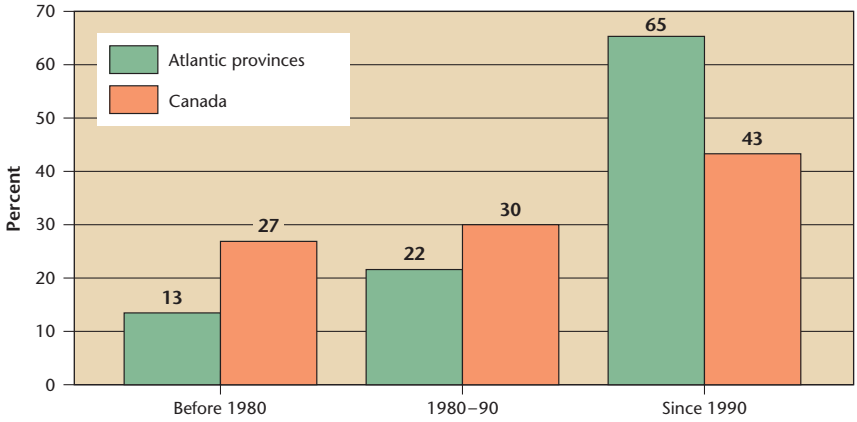
* University spinoff.

† Government.

ers ventured to commercialize their discoveries. However, the majority of business start-ups, some 65 percent, took place subsequent to 1990. The fact that such a large proportion of businesses originated in the last decade of the millennium coincides with the ever-increasing proliferation of biotechnologies in the pharmaceutical sphere. It also ties in with the recognition of the potential economic benefits of fostering such a knowledge-based industry in Atlantic Canada and the mobilization of resources to promote its growth. As we will see, this is especially true for Nova Scotia.

**Figure 6**

**Distribution of Firms in the Industrial Biopharmaceutical Sector by Date of Establishment, Atlantic Canada**



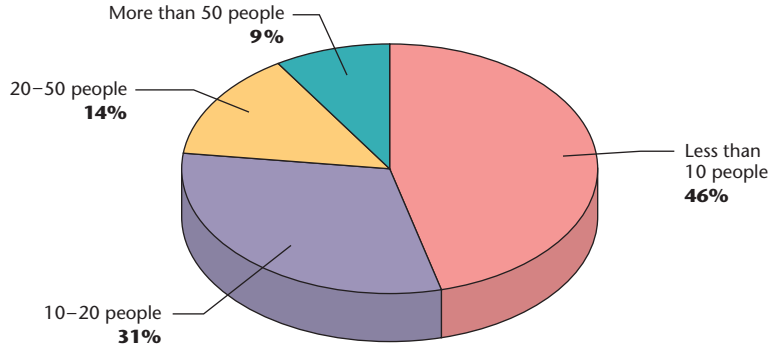

*Sources:* *Pharma, Biopharma & Nutraceuticals Canada Directory* (1999), *Canadian Biotechnology Directory* (1999), *Diagnostics Canada Directory* (1999), Strategis – *Canadian Companies Capabilities* (1999), Pharmaceutical Manufacturers Association of Canada (1999), and Canadian Pharmacists Association (1999); compilation by Sébastien Breau.

With more than half of the companies engaged in biopharmaceutical activities in the Atlantic provinces having been established in the 1990s, it is not surprising to see that most of them are relatively small (see figure 7). In fact, the significant number of small producers — approximately 77 percent of them employ less than twenty people, and just 23 percent more than twenty — is not only suggestive of a nascent industry but also of a very fragmented one in which companies are striving to break through into individual niche markets. The capacity of small firms to innovate and develop new ideas for products for specific markets, niches that are all too often impossible for large firms to target because of the extensive diversity of pharmaceutical research areas and the huge costs associated with backing a broad research base, has indeed been an industry catalyst.[38] But the ability of a small firm concentrating on only one or a few products to compete effectively with larger factories turning out a wider range of products also has the effect of distorting the region's industry. The focus on specialized R & D has, if not isolated certain companies,

38. In Atlantic Canada, the focus of corporate activity is undoubtedly on the R & D component of the production process. Research shows that while 54 percent of companies actually manufacture a pharmaceutical-related product, 84 percent of firms have in-house laboratories actively conducting research.

**Figure 7**

**Distribution of Biopharmaceutical Firms by Size, Atlantic Canada, 1997–98**




*Source:* Ibid.

fragmented the industry into pockets of expertise plagued by a lack of qualified management personnel and appropriate financing (chapter 3 deals with these topics in more detail).

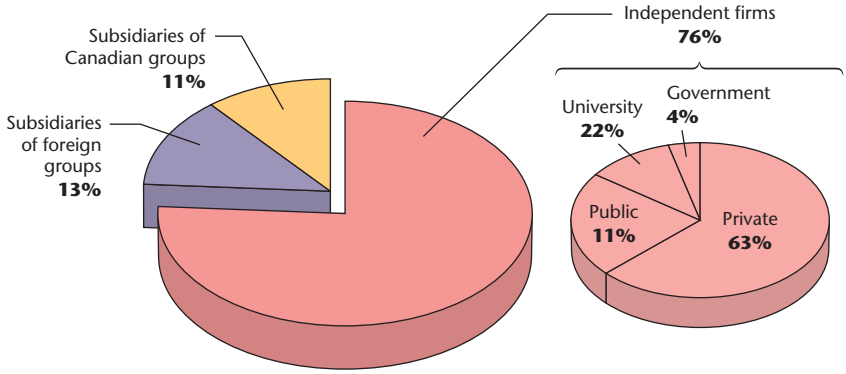
The apparent relationship between age and company size is also reflected in the ownership patterns of companies. In this regard, just over three-quarters of the firms are owned by local interests, 11 percent are subsidiaries of Canadian groups with a presence in the Atlantic provinces (i.e., through R & D or production facilities), and the remaining 13 percent are controlled by foreign groups or corporations (see figure 8). An examination of the breakdown of locally owned firms is also revealing.

For example, 63 percent of companies are owned by private stakeholders (or have majority independent ownership), while a notable 22 percent are affiliated with universities (i.e., university spinoffs). This factor is evidence of an important mutual interaction between the public and private sectors in pharmaceutical and biopharmaceutical R & D. We will explore this subject in greater detail later in the chapter.

Finally, an analysis of sales figures reported by the companies also sheds some light on the structure of the industry. Almost half of the firms disclosed sales of less than Cdn. $1 million, while those with sales between Cdn. $1 million and $5 million accounted for another

**Figure 8**

**Distribution of Biopharmaceutical Companies by "Ownership" Status in Atlantic Canada, 1997–98**




*Source:* Ibid.

19 percent of companies (see figure 9).[39] Altogether, they represent no more than 25 percent of overall sales, but in relation to employment they are the backbone of the industry, generating approximately 76 percent of total jobs. The remainder, in this case the bulk of the sales, are controlled by a mere 16 percent of companies, which collectively are responsible for 24 percent of industry employment.

### *Sectors of intervention*

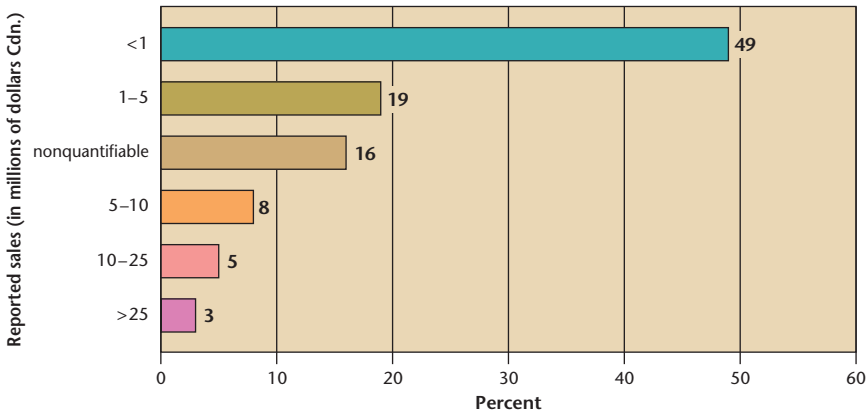
One of the most striking and distinctive features of the biopharmaceutical industry is the extensive variety of products it brings to market. And with the growing convergence between the pharmaceutical industry and biotechnologies, a development that is reshaping the boundaries of scientific and industrial R & D, the potential for product specialization is enormous. As expected, this trend is clearly reflected in Atlantic Canada, where approximately 48 percent of firms concentrate their efforts on a single component of the biopharmaceutical industry (mainly therapeutics), while 43 percent report working in two distinct sectors and only 9 percent in all three.

It is also interesting to note that the bulk of firms simultaneously take up various functions, namely, R & D, manufacturing, marketing of products, and other types of activities (see figure 10). One-third

39. It is important to remind the reader that the statistics recorded in this figure are for information purposes only. They inevitably contain inaccuracies related to the confidentiality or partial disclosure of some sales data, thus limiting the already relatively small sample size.

**Figure 9**

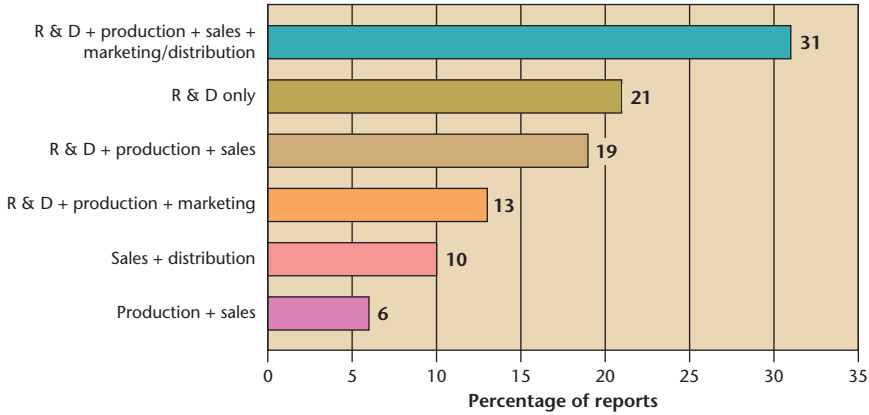
**Breakdown of the Industrial Biopharmaceutical Sector in Atlantic Canada according to Level of Sales, 1997–98**




*Source:* Ibid.

**Figure 10**

**Breakdown of Firms Functions according to Type of Activity, 1997–98**



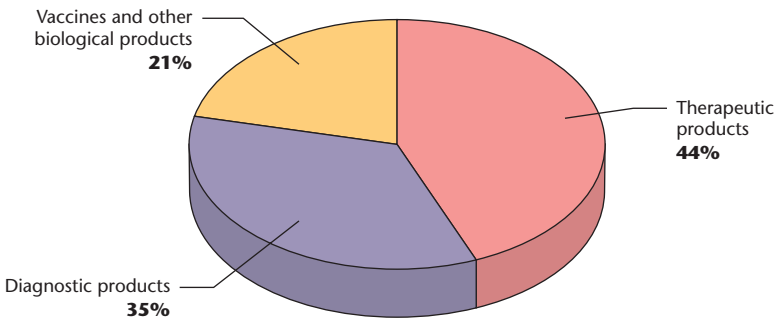

*Source:* Ibid.

of biopharmaceuticals have actually integrated all activities under a single roof, while a further 48 percent of companies maintain two or three production functions. The remaining 21 percent of firms are those specializing in the R & D of new products or services. They include several contract research organizations (such as Aquatic Diagnostic Services in Prince Edward Island) and firms dedicated to research on clinical trials.

Seen from another angle that uses a simple weighted average to measure the share of reported activities in each field allows us to break down industrial activity according to the types of products manufactured — that is, therapeutics, vaccines and other biological products, and diagnostic products (see figure 11 and ff.).

**Figure 11**

**Distribution of Industrial Activity by Types of Products, 1997–98**




*Source:* Ibid.

*Note:* This figure presents the breakdown of biopharmaceutical industrial activity in Atlantic Canada when large foreign-owned wholesalers/distributors with branches in the region are excluded from the production system. This is done in order to get a better understanding of the regional industrial organization.

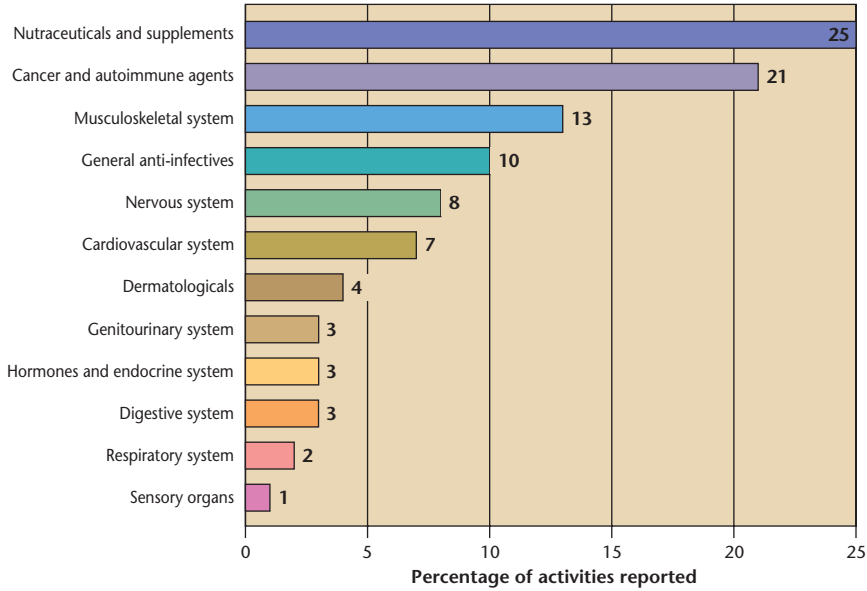
Almost half of all biopharmaceutical activity is dedicated to the development of therapeutic products. Amid all of the different fields of expertise (see figure 11 A), one of the major driving forces behind the significance of this segment is the recent surge in nutraceuticals and functional foods (pharma-foods). Hence, it is important to explore this subject in more detail. Nutraceuticals are products isolated or purified from foods; they are generally sold in medicinal forms not usually associated with food and are demonstrated to have a physiological benefit or to provide protection against chronic disease.[40] Functional foods, which are similar in appearance to or may in fact be conventional foods, are consumed as part of a normal diet and are demonstrated to have physiological benefits and/or to reduce the risk of chronic disease because of properties other than those connected with their basic nutritional functions. A report by BioAtlantech illustrates the difference between the two using cranberry as an example: "The cranberry is recognized to provide healthful benefits in the mitigation of urinary tract infections. Drinking cranberry juice

40. As defined by the Bureau of Nutritional Sciences of the Food Directorate — Health Canada.

## Breakdown of Findings in Figure 11

### Figure 11 A

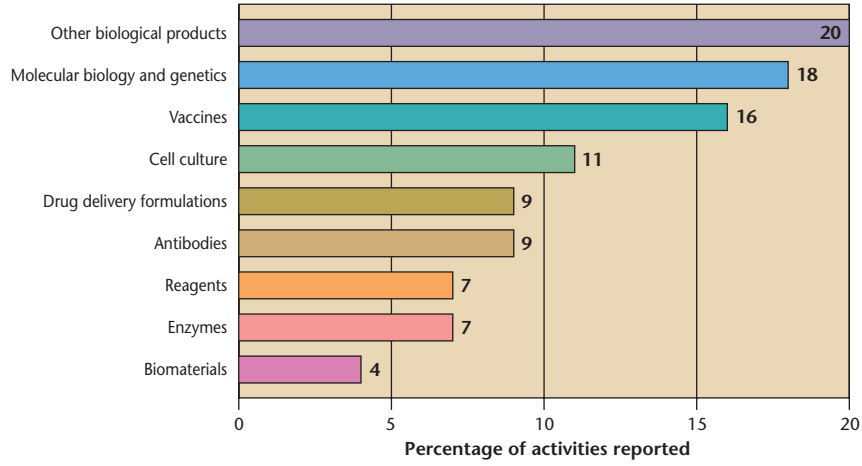
### Therapeutic Products




*Source:* Ibid.

### Figure 11 B

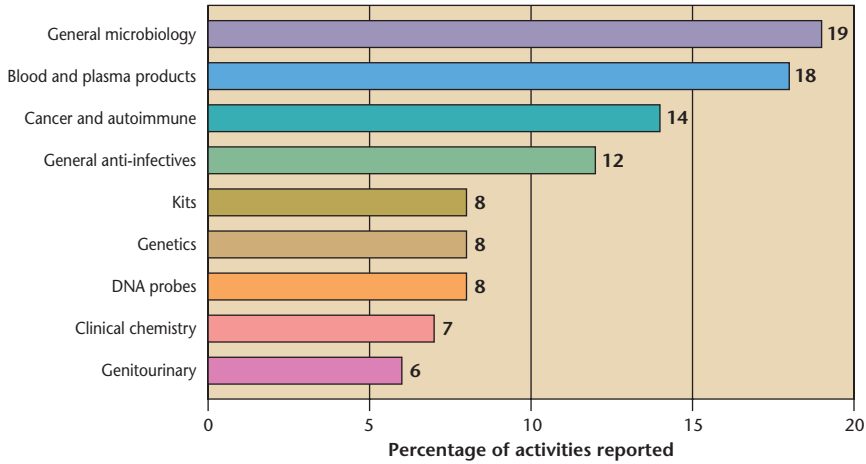
### Vaccines and Other Biological Products




*Source:* Ibid.

**Figure 11 C**

**Diagnostic Products**




*Source:* Ibid.

designed for this purpose would be to use its functional food application …. If the active ingredient(s) related to the mitigation of urinary tract infections were to be extracted and/or concentrated and consumed in tablet form, using claims substantiated by reasonable scientific evidence, that would represent a nutraceutical application of the fruit." [41]

In short, the rationale behind the thriving market for nutraceuticals can be divided in two. First, from the consumer's perspective, more and more people are making the diet-disease connection and are placing more emphasis on prevention than cure. This trend "gathers further pace as governments also have a keen interest in self-diagnosis and proactive prevention as a way of reducing health care costs."[42] Second, from the producer's point of view, because this is a relatively new concept and several wrinkles still need to be ironed out, particularly with respect to hard scientific evidence required to back up specific health claims, a number of big pharmaceutical companies are opting to stand by and assess some of the developments in the industry. This has had the effect of opening the door for smaller firms to move in and offer specialized products, which is what is happening in the Atlantic provinces. In addition to nutraceuticals, the

41. BioAtlantech, *Rendez-vous BioAtlantech 1999*, media fact sheet (BioAtlantech, April 1999), 1–6.

42. Gil Beyen and Eric Haliona, "Forging Alliances in Foods and Medicines," *Scrip Magazine* (May 1999): 31–33.

regional concentration of R & D activity in cancer and autoimmune agents as well as treatments for the musculoskeletal system (e.g., anti-inflammatories, antirheumatics) marks a departure from national sales trends, where the top three therapeutic groups focus on the cardiovascular system, the nervous system, and general anti-infectives respectively.[43]

The segment devoted to vaccines and other biological products is also a dynamic component of the industry. Together, more than one-third of companies in Atlantic Canada incorporate molecular sciences in their programs or use genomic-based approaches or other state-of-the-art scientific processes to discover new drugs. While vaccines account for only 16 percent of total activities in this category, it is interesting to note that approximately 71 percent of vaccines produced are intended for the veterinary and aquaculture markets. In fact, a number of companies in Atlantic Canada are among world leaders in the production of vaccines to control and prevent diseases in the veterinary, aquaculture, and shellfish industries.

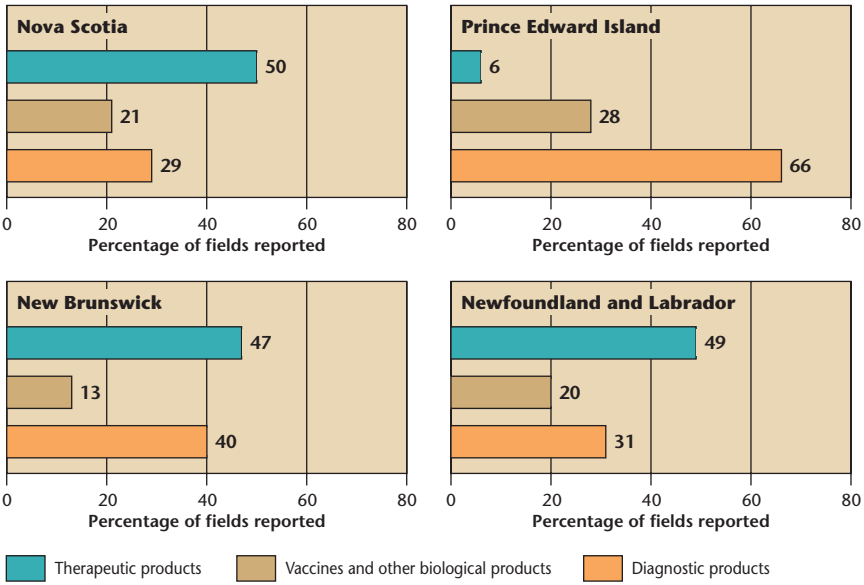
Finally, just over one-third of companies are engaged in producing or providing diagnostic services. As was the case with vaccines, 55 percent of diagnostic products and services are designed for veterinary and aquaculture purposes, leaving the other 45 percent of diagnostic technologies focused on human health care needs. Although the majority of firms provide in-house diagnostic-testing services, only 10 percent of them manufacture and sell user-friendly or diagnostic test kits.

Overall, from an intraregional standpoint, pharmaceutical and biotechnological health-related activity is dominated by Nova Scotia (which accounts for approximately 60 percent of the total), followed by Newfoundland and Labrador (18 percent), New Brunswick (12 percent), and Prince Edward Island (10 percent). Because of its size, Nova Scotia also has a strong presence in all fields of activity and a wide-ranging mix of companies (see figure 12). For example, those involved with therapeutic remedies range from well-known firms such as Efamol Canada Ltd. (established in 1977, Efamol produces essential fatty acids required for the normal structure and function of the body's tissues and organs at the cellular level) to new up-and-coming enterprises such as NovaNeuron Inc. (created in 1999, this company is developing validated drug targets for diseases of the central nervous system). Biotechnology firms producing diagnostic

43. PMPRB, *Eleventh Annual Report* (1998).

**Figure 12**

**Provincial Distribution of Biopharmaceutical Firms according to Types of Products, 1997–98**




*Sources:* *Pharma, Biopharma & Nutraceuticals Canada Directory* (1999), *Canadian Biotechnology Directory* (1999), *Diagnostics Canada Directory* (1999), Strategis – *Canadian Companies Capabilities* (1999), Pharmaceutical Manufacturers Association of Canada (1999), and Canadian Pharmacist Association (1999), compilation by Sébastien Breau.

products are also vital to the industry. One such company is Dominion Biological Limited, which concentrates its efforts on manufacturing several blood diagnostic devices. MedMira Laboratories Inc. is another illustration of the rapidly growing diagnostic sector; it recently opened a facility in Halifax that produces rapid-screening test kits designed to detect a variety of diseases, including HIV 1 and 2, hepatitis C, and prostate and breast cancer.

The focus on developing diagnostic products is even more evident in Prince Edward Island, where it accounts for two-thirds of all industrial biopharmaceutical activity. In fact in one way or another, all five companies on the Island are concerned with diagnostics. The province's most prominent firm, and perhaps Atlantic Canada's leading diagnostics company, is Diagnostic Chemicals Limited (DCL) of Charlottetown. Established in 1970, DCL has grown to employ more than two hundred people at its Prince Eward Island facility and U.S. and Mexican subsidiaries. It produces more than fifty different biochemical and diagnostic products, which are exported throughout

the world. Several Prince Edward Island companies are also benefiting from close ties to the aquaculture industry to produce vaccines against fish diseases. Over the last fifteen years, for instance, Aqua Health Ltd. has introduced more licensed vaccines to the aquaculture industry than any other company in the world. Nevertheless, in spite of making strong inroads into the diagnostics and vaccine segments, the development of therapeutic products is practically nil.

At first glance, the data for New Brunswick suggest that the province has a solid foundation in both the therapeutic and diagnostics sectors. However, a thorough examination of the facts reveals a less rosy picture. First, therapeutics revolve almost entirely around nutraceuticals, which represent 86 percent of total therapeutic products, leaving very little room for diversification into other therapeutic fields. In addition, the majority are small firms making use of a variety of biotechnologies with applications in fields other than pharmaceuticals, such as agriculture and food processing. Second, the diagnostics sector is bolstered by the presence of the government-owned Research and Productivity Council (RPC) in Fredericton and by its broadly based contract research, development, and technical services. For example, one arm of the organization, the Aquaculture and Biotechnology Program, by itself offers several diagnostic services: DNA-based techniques, molecular genetics, etc. Without the RPC, the capacity of the province's diagnostics sector would be seriously reduced. The traces of a biopharmaceutical industry in New Brunswick are far more subtle.

Newfoundland and Labrador, like Nova Scotia, has a more homogenous distribution of biopharmaceutical activity in all three fields, despite having many fewer companies. Research and development of nutraceuticals once again leads the field in therapeutics, but instead of focusing on fruit-derived products (as is the case in New Brunswick), technologies make use of marine sources. For example, Newfoundland Aqua Products Inc. produces nutraceuticals from seaweed/kelp, while PA Pure Additions, through the support of the Seabright Corporation Ltd. (i.e., the technology transfer agency of Memorial University), relies on seal blubber, sea urchins, and other marine resources to develop biomedical and pharmaceutical applications. The Seabright Corporation Ltd. also played a fundamental role in the commercialization of several diagnostic techniques developed by university researchers, creating several university spinoff companies. One such company is Terra Nova Biotechnology. It produces and markets monoclonal antibodies for in vitro diagnostic use, mainly in blood test kits.

Within each province, the infrastructure of universities and government laboratories form the focal points of biopharmaceutical activity. The best illustration of this can be found in Nova Scotia, where the Halifax-Dartmouth area, which accounts for roughly 65 percent of the province's firms (and over 40 percent of all firms in Atlantic Canada), is rapidly establishing itself as an attractive harbour for the life sciences. The cluster of enterprises is structured around the urban region's fertile R & D grounds such as Dalhousie University and the NRC's Institute for Marine Biosciences, as well as In*NOVA*corp's newly opened Bioscience Enterprise Centre, a business incubator that is helping to start up and develop biopharmaceutical companies. On the manufacturing side, a survey conducted by KPMG (financed in part by the Atlantic Canada Opportunities Agency) ranked Halifax as the most cost-competitive business location for the life sciences sector out of twenty-four selected cities across North America, Europe, and Japan.[44] In an effort to attract more businesses to the area, Halifax is also actively promoting its lifestyle, educational amenities for children, and all round good reputation for quality of life — increasingly influential factors when a company is choosing where to set up shop. But the cluster also stretches beyond municipal limits creating a biopharmaceutical corridor that extends to the province's Annapolis Valley, home to Acadia University and the Atlantic Food and Horticulture Research Centre in Kentville (which is active on the nutraceuticals front).

To a lesser extent, a similar pattern is emerging in other Atlantic provinces. In St. John's, Memorial University is the lifeline of creative biopharmaceutical entrepreneurs. Although manufacturing activity has been slow to develop here, it has a strong R & D background and technology transfer capabilities. Charlottetown is dominated by the presence of DCL and a few other diagnostic CROs linked to UPEI. The industrial framework in New Brunswick, however, is far more dispersed. Here, the biopharmaceutical triangle consists of Fredericton (and the firms located in and around the RPC, UNB, and BioAtlantech), Moncton (home to the Université de Moncton), and Saint John (where the regional teaching hospital is situated).

44. KPMG, *The Competitive Alternatives: A Comparison of Business Costs in North America, Europe and Japan*, (March 1999).

### *Patterns of industrial organization*

Given the essential role played by scientific breakthroughs in the biopharmaceutical industry (and remembering that 84 percent of biopharmaceutical firms in Atlantic Canada are actively involved in R & D), it is not surprising to find that more than half of all companies in Atlantic Canada can trace their origins to a university environment. Typically, these companies originate from university or federal research institutes and start off as technical consultancies in which scientists produce a variety of academic and expert reports incorporating a high degree of intellectual analysis. The expertise is usually based on the scientist's academic know-how and initially focuses on a specific problem. There follows a gradual process of development during which the preliminary product becomes a more routine analytical package and then a design technique before emerging as a distinct product. In its simplified form, the final product embodies the original expertise but is better suited to larger-scale manufacturing.

Although these steps outline the general process of scientific discoveries and technological advances in most university spinoffs, biopharmaceutical firms in Atlantic Canada with roots in academia exhibit two distinctive features, both of which depend on the course of action taken during the diffusion process. Indeed, the actual transfer of technology and commercialization of products, from public organizations to private sector initiatives, usually follows two different scenarios: either successful university researchers leave their laboratories (taking with them their valuable discoveries), or through various types of agreements, such as joint ventures, they develop and promote their products within a university framework.

In the first case, firms were founded by young entrepreneurial academics independently of their universities or other public institutions. Altogether, nearly twenty companies fall into this group, of which the majority date back to the 1980s, some as early as the 1970s. It is important to remember that for the most part, these companies are based on techniques, ideas, and discoveries that coincide with the early years of the biotechnology revolution and that at the time, the star (i.e., the most productive) bioscientists setting up these firms, aside from being very protective of the still scarce knowledge, were charting entirely new waters. Too often because of the lack of university–private sector ties, and especially since no other biopharmaceutical firms existed in the region, the only way these top-level scientists could push their discoveries through the somewhat lengthy and risky process of commercialization was by moving out

and creating new enterprises (despite the fact that the scientific innovations were developed in university laboratories). In doing so, they crossed the crucial line separating the university and the world of commerce, so that instead of technology transfer, what transpired was "people transfer."[45] By virtue of their actions, these academics can be credited with being the pioneers of the biopharmaceutical industry in Atlantic Canada. Today, they are also among the most promising entrepreneurs in the region and are breaking ground in therapeutics, diagnostics, and biological products. On average, each firm employs roughly 24 people, although the size of firms varies, ranging from 4 to 140 employees. Without exception, they all maintain in-house laboratory facilities and are involved in various research and development projects (generating roughly 150 R & D jobs in the region). As well, 70 percent of these firms are completely vertically integrated, not only conducting R & D but also producing, marketing, and distributing their products themselves, thus necessitating a high level of organization. Several of the firms are involved in financial, technical, and marketing/sales alliances with both domestic and foreign firms. Overall, about two-thirds export their products in order to bolster their sales figures (which are among the highest).

The second group of university spinoffs concerns researchers characterized by their on-going connection with academic institutions. In contrast to the previous scenario, universities, having recognized the potential economic benefits of commercializing research breakthroughs stemming from internal R & D programs, have set up corporate arms to encourage and sponsor technology transfer through the creation of on-site business ventures. This new paradigm, which originated in the mid-1980s, is ubiquitous in Canadian universities and has grown to be an integral part of medical research commercialization.[46] These "business development offices" or "technology transfer agencies" act as a rule as industrial liaisons (i.e., creating a bridge allowing human capital and intellectual property to flow from university labs to the marketplace) and provide such services as patent-protection filing assistance or guidance, business start-up planning, marketing and distribution agreements, venture-financing options, and so forth. In Atlantic Canada, biopharmaceutical companies have particularly benefited from the assistance of the Seabright Corporation Ltd.

45. For further readings on this subject, see Zucker and Darby (1996).

46. This trend is not limited, however, to the commercialization of medical research. In general, it also applies to various knowledge-based and high-tech fields such as electronics, bioengineering, precision instruments, telecommunications, etc.

(Memorial University, Newfoundland), AVC Inc. (University of Prince Edward Island), NU-TECH (Dalhousie University, Daltech, Nova Scotia Agricultural College, and the University College of Cape Breton), and the Business Development Office of Dalhousie University's Faculty of Medicine. Overall, about a dozen biopharmaceutical firms fall into this category, and eight of them are actually joint ventures between the university and researchers. Their activities, although varied (nutraceuticals and other therapeutics, veterinary diagnostics, and biological products), take place mostly upstream in the industrial process and revolve around R & D projects. And because most of them emerged after 1990, several remain at the start-up phase. The firms in this category tend to be much smaller than those in the previous group: the average has six employees, while the largest has no more than twelve.

In addition to university spinoffs, biopharmaceutical companies in Atlantic Canada have also adopted other types of industrial strategies. In general, these companies operate mostly downstream in the value chain. For example, a handful of firms specialize in the sale and distribution of pharmaceutical products, both prescription and OTC drugs, throughout the four Atlantic provinces (wholesalers). These companies provide work for approximately 160 people in the region, and their sales volume is considerable. As service providers, however, their operations focus almost exclusively on the intraregional distribution of pharmaceutical products stemming from large multinational firms established chiefly in Central Canada. Only a few local biopharmaceutical firms maintain commercial relations with these companies, as the majority concentrate their efforts on national and international trade-service brokers in order to take advantage of a more extensive distribution network (the next section provides an in-depth look at the commercial relations of regional biopharmaceutical firms).

Finally, there are several firms (approximately seven) turning out innovative products with less-formalized in-house R & D capabilities; in some cases they are completely lacking in R & D capacity (only about three firms). These companies are much smaller in size (with, on average, less than nine employees), and apart from their own qualities, they strongly focus on market-related know-how from customers and suppliers, relying mainly on informal transfer channels and indirect exchanges of knowledge. In contrast to most university spinoffs — where scientific discoveries and technological innovations give rise to a "technology push" — these companies react more to a

current "demand pull" arising from changes in consumer needs. For example, traditional medicinal products derived from plants, herbs, and other natural sources are increasingly sought after as alternatives to modern medicines and pharmaceuticals. The same can also be said of nutraceuticals. Indeed, the diffusion of know-how and new clinical research supporting the role of essential fatty acids (EFA) in the prevention and mitigation of major diseases such as arthritis and cancer has led to the creation of various companies manufacturing EFA products from plant and marine sources: e.g., tree needle extracts (L & D Pharmaceuticals), fish and marine oils (Wesleyville Hatchery), and seaweed and kelp (Newfoundland Aqua Products Inc.). The majority of firms that fall into this category are health and nutraceutical companies. Markets for these products are just beginning to emerge, and regional entrepreneurs are reacting quite spontaneously to these new opportunities. As one entrepreneur notes: "My interest in marine nutraceuticals first started off as a hobby, but when I realized the tremendous potential for such niche products, I decided to take it up a notch and launch into the business."[47] The bulk of these firms have only been established within the last ten years (with many still at the start-up phase), and the degree of industrial organization, although uneven from firm to firm, remains relatively basic and very flexible. In most cases, collaborations or partnerships with public research institutions are negligible.

### *Commercial strategies: open to the world*

Sales of pharmaceutical products in the four Atlantic provinces reached an estimated $692 million in 1999 (see table 4), accounting for approximately 8.0 percent of the Canadian market (almost identically matching the region's population share, which was about 7.8 percent of the country's total population). Reflecting a similar trend in population patterns, market growth in Atlantic Canada has been slower than in other parts of the country. Over the last decade, for example, the average annual growth rate of regional pharmaceutical sales has lingered around 5 percent, while national sales have been growing at the quicker pace of 7 percent. This is not, however, hindering sales of regional biopharmaceutical firms.

47. Interview with industry executive (Newfoundland), January 2000.

**Table 4**

**Pharmaceutical Sales in Canada, by Region, 1999**

| Regions | Millions of Dollars | Market Share (%) |
|---|---|---|
| Atlantic provinces | 691.5 | 8.0 |
| Quebec | 2,212.2 | 25.5 |
| Ontario | 3,461.0 | 39.9 |
| Prairies | 1,275.8 | 14.7 |
| British Columbia | 1,037.6 | 12.0 |

*Source:* IMS Health, *Canadian Drugstore and Hospital Purchases*, 2000.

As the tide of globalization sweeps across all markets, knowledge-based industries are at the forefront of the wave. The biopharmaceutical industry, in particular, is characterized by a high degree of international integration. We have already indicated that industry consolidation through mergers and acquisitions extends well beyond national borders. Upstream, companies are increasingly looking to new sources of R & D for product diversification via strategic alliances and partnerships. Downstream, commercial strategies revolve around elaborate distribution networks that span the world. With only a few exceptions, Atlantic Canadian firms are very much outward looking.

Indeed, only a minority of biopharmaceutical companies focus their commercial activities on the market in Atlantic Canada. For instance, about 10 percent of all firms consist of subsidiaries of Canadian and foreign-owned companies strictly involved in the local distribution of pharmaceutical supplies.[48] Essentially, these companies act as intermediaries, and their commercial linkages amount to one-way trade corridors: big pharmaceuticals, headquartered in Ontario, Quebec, or beyond our national boundaries, sell their merchandise across the four Atlantic provinces. The end result is the same as in the case of large multinational pharmaceutical manufacturers: the majority of sales are repatriated to head offices outside the region. Another group of firms, approximately 14 percent of the total, are still at the start-up phase, seeking either business and/or scientific partnerships to further develop their products before launching them into the marketplace. Hence, the real value of analyzing market strategies can be found in the remaining 76 percent of firms located in Atlantic Canada.

48. This group of companies does not include regional sales representatives of large multinational pharmaceutical manufacturers, since they sell their products directly to hospitals, pharmacies, governments, and wholesalers.

As we have seen previously, the emergence of new segments of the pharmaceutical industry, combined with a multitude of technological advancements, has brought substantial changes to the industry's value chain. Ultimately, most Atlantic Canadian biopharmaceutical firms design their commercial strategies to profit from the new possibilities created by such structural changes. Indeed, their approach is to offer highly specialized products targeting, in most cases, very selective niche markets that are poorly served by broad-lined big pharmaceuticals (such a strategy is called *focused differentiation*).[49] Entry into such markets is relatively easy, and small companies avoid head-to-head competition with large multinationals. Again, a quick look at the different companies that make up the industry in Atlantic Canada reveals the concentration of activities in specific niches. From nutraceuticals to other leading-edge biological products, vaccines to diagnostics, small firms are moving in and capitalizing on new opportunities in several specialized fields.

The downside of such an approach is that it can lead to a very fragmented industry, which, to some extent, is the case here in the Atlantic provinces. Cooperation among firms is minimal at best as each strives to develop its own channels and networks. A study carried out by the Nordicity Group Ltd. et al. on knowledge-based industrial clusters in Atlantic Canada notes that while specialization allows companies "a certain competitive differentiation, it also means reduced competition and growth opportunities."[50] From an intra-regional perspective, one would think this might be particularly worrisome when competing in a small market environment, because domestic rivalry puts pressure on companies to constantly innovate and upgrade/improve. This is not the case, however, since firms are not only relying on regional markets for sales, but they are also looking at international markets as an outlet.

In fact, one of the positive side effects of industry segmentation has been the creation of windows of opportunity for global-focus strategies. For instance, despite the prevailing concentration of small, independent biopharmaceutical firms in Atlantic Canada, more than 70 percent of them are turning to export-based strategies for the

49. For more on this subject, see Michael E. Porter, *The Competitive Advantage of Nations* (New York: The Free Press, 1990), 39.

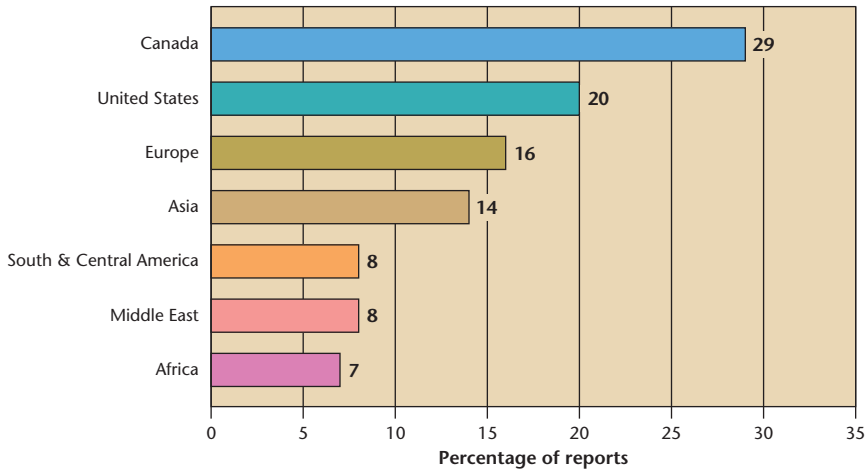
50. Nordicity Group Ltd. et al., *Prospects for Growing Knowledge-Based Industrial Clusters in Atlantic Canada*, Part 1 — *Concepts, Analysis and Recommandations* (31 July 1997), 20.

sale and distribution of their products.[51] Naturally, regional entrepreneurs first look to the national market for a commercial outlet (see figure 13). In all, 29 percent of trade links are established with other Canadian provinces, and commercial relations with Ontario and Quebec respectively are the most important within Canada.

But with the emergence of larger economic entities in various regions of the world, the reduction or complete elimination of tariff and nontariff barriers, and the standardization of regulatory requirements, new export opportunities abound. For example, under the North American Free Trade Agreement (NAFTA), the duties on finished products (i.e., under dosage form) were completely phased out as of 1 January 1998. Furthermore, having met a number of safety and effectiveness criteria set by various U.S. regulatory agencies (the FDA, USDA, etc.),[52] the flow of biological products such as insulin, serums, plasma, and vaccines is currently exempt from customs.

**Figure 13**

**Distribution of External Commercial Relations of Atlantic Canadian Biopharmaceutical Companies, by Region, 1997–98**




*Sources:* *Pharma, Biopharma & Nutraceuticals Canada Directory* (1999), *Canadian Biothechnology Directory* (1999), *Diagnostics Canada Directory* (1999), and Strategis – *Canadian Companies Capabilities* (1999), Pharmaceutical Manufacturers Association of Canada (1999), Canadian Pharmacists Association (1999); compilation by Sébastien Breau.

51. Although most firms did not divulge their export volumes, we suspect that they represent a large portion of their sales figures. One industry executive reported that more than 90 percent of his company's sales revenues stemmed from exports.

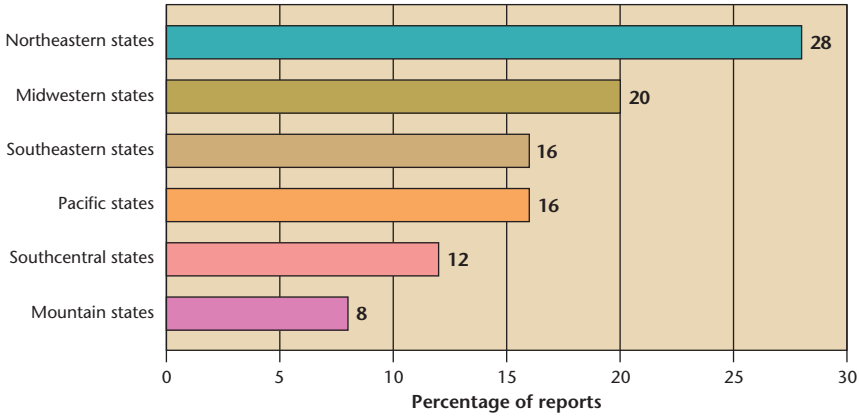
52. Biopharmaceutical products entering the U.S. must undergo a seven-step testing, review, and follow-up process.

As one company executive said, "Although the regulatory process is still somewhat cumbersome, NAFTA has allowed us to gain quicker and more cost-effective access to the U.S. market which is very lucrative."[53] Today, Atlantic Canadian biopharmaceutical products are distributed in practically every American state (in fact forty-nine of the fifty states). Commercial ties to the northeastern states are particularly strong (see figure 14) and cover the entire range of products. For Atlantic Canadian biopharmaceutical entrepreneurs, the New England market in particular is seen as crucial, both for regional sales and as a prospective port of entry to the American market. Therefore, it is important that governments and industry continue their efforts to strengthen business links with the New England states. To do so, Atlantic Canadian biopharmaceutical entrepreneurs must have access to promotional events (i.e., trade shows) held in the U.S. in order to boost their profiles (and the region's profile as well) and make contacts which could lead to possible alliances with larger companies, distributors, and wholesalers.

Governments should also explore new avenues that would accelerate regulatory processing and approval times of biopharmaceutical applications. One such possibility would be to improve preapproval

**Figure 14**

**Distribution of Commercial Relations of Atlantic Canadian Biopharmaceutical Companies with the United States, by Region, 1997–98**




*Source:* Ibid.

53. Interview with industry executive (Prince Edward Island), March 2000.

inspection results.[54] As it stands, the U.S. regulatory process for biopharmaceuticals is typically much more onerous than that of most European countries. In vitro diagnostic products, for example, can take up to three times as long as in European countries, requiring validated proof of the accuracy and efficiency of tests. For this reason, producers in Atlantic Canada often turn to European countries first for new-product validation and hands-on market substantiation before launching these products in the U.S. market.

Other U.S. regions with strong trade relations with Atlantic Canada include the midwestern states (20 percent), the southeastern states (16 percent), and the Pacific states (16 percent). It is worth mentioning that several Atlantic Canadian biopharmaceutical firms have a strong presence in California's diagnostics market. Areas identified as important for diagnostic substances and kits are the following: DNA-based diagnostics, non-invasive sensors, in vitro diagnostics, new markers for diseases (such as prostate cancer, hepatitis, and osteoporosis), and tests based on body fluids other than blood (i.e., urine- or saliva-based).[55] Interestingly, only one Atlantic Canadian biopharmaceutical firm has evolved beyond its regional boundaries and established subsidiary companies abroad: Diagnostic Chemicals Limited of Prince Edward Island has distribution centres in Connecticut and Mexico, which together employ approximately forty people.

Overseas, companies have also established commercial ties with European countries (16 percent), Asia (14 percent), South and Central America (8 percent), the Middle East (8 percent), and Africa (7 percent). In particular, firms in the four Atlantic provinces are taking advantage of the rapidly expanding nutraceuticals market in both European and Asian countries. Pacific Rim countries have also been the target of highly specialized diagnostics products for the aquaculture industry, with several firms instituting business relations with Japan, Hong Kong, and Thailand.

Moreover, because of their smaller size and in an effort to overcome limited resources in gaining access to foreign markets, marketing alliances, the use of distributor/trading companies, and other types of distribution arrangements play an important role in the expansion of commercial interests, both nationwide and abroad.

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54. Canada, Department of Foreigh Affairs and International Trade, *The Biotechnology Market in New England* (Team Canada Market Research Centre and Canadian Trade Commissioner Service, July 1999).

55. Canada, Department of Foreign Affairs and International Trade, *The Human Diagnostic Market in California* (Team Canada Market Research Centre and Canadian Trade Commissioner Service, July 1998).

Approximately 40 percent of Atlantic Canadian firms rely on such partnerships as tools for developing trade strategies. Several company executives also mentioned the use of various industry associations as well as trade shows to establish marketing relationships with overseas companies; they also pointed to the use of customs brokerage firms to ensure that customs clearance is not an impediment to their overall supply-chain management. This means an increased focus on customs regulations, internal customs compliance programs, adherence to preferential tariff rules, and improved information management.[56] Additionally, the Canadian government, which recognizes the importance of international partnerships and the benefits of encouraging and fostering international business development, has introduced a number of programs and initiatives (see box 2) to help small firms in the biopharmaceutical and other industries sharpen their competitive advantage.

It is important to underline the fact that besides forging alliances in order to expand the coverage of their sales force, biopharmaceutical companies are also developing other types of partnerships with each other. For example, Atlantic Canadian firms with technical alliances sharing resources and access to different products or processes averaged between four and six alliances each. In contrast to a 1997

**Box 2**

**Examples of Government Programs and Initiatives to Develop Export-Based Strategies**

- The Program for Export Market Development is aimed at increasing export sales by sharing the costs of activities that companies normally could not or would not undertake alone, thereby reducing risks involved in entering a foreign market.
- Both the Canadian Commercial Corporation and the Export Development Corporation offer financing, insurance, and better payment terms to small businesses.
- The Department of Foreign Affairs and International Trade, via its Corporate Partnering Group, has developed a strong network of business agents.

56. Livingston International (world leader in trade services).

nationwide industry survey conducted by Ernst & Young,[57] this is much lower than for the average Canadian biopharmaceutical company, which has 8.2 alliances. It does, however, tie in with the profile of lower-end medium, small and very small enterprises, which, according to the same survey, average between five and eleven alliances each. This is further proof that a biopharmaceutical cluster is crystallizing in the region. As we shall see in the next section, more and more firms are teaming up with universities, in particular with those that have medical schools and are affiliated to teaching hospitals. Service companies are setting up in the region and offering a wide variety of supporting business activities. Together with the industrial biopharmaceutical firms we have just described, they form the basis of a new emerging cluster.

## The Big Picture: The Cluster Perspective

So far, our analysis has focused primarily on private sector firms directly involved in the production/value chain that serves as the backbone of biopharmaceutical industrial activity in Atlantic Canada. Concluding our analysis at this point, however, would provide only limited insight into the workings of the industrial system. To get a more comprehensive and practical picture of the economic dynamics at work, we need to study the regional infrastructure that supports biopharmaceutical firms. In other words, we should examine the industry from a *cluster* point of view. In short, clusters can be defined as "networks of production of strongly interdependent firms linked to each other in a value-adding production chain."[58] As well, clusters cover partnerships and alliances with universities, technical colleges, various public research institutions, knowledge-intensive business services, consultants, financial institutions, incubators, research parks, and other supporting organizations. This section sets out the major elements that make up this supporting infrastructure and looks at some of the strengths and weaknesses of the biopharmaceutical cluster in Atlantic Canada.

### *Private-public sector interaction*

It is widely known that universities and public sector research institutions are crucial to the success of private R & D. In the pharmaceutical industry, the traditional view is that the public sector usually funds

57. Ernst & Young, *Coming of Age: Fourth Report on the Canadian Biotechnology Association*, Canadian Biotech '97 (Ernst & Young, 1997).

58. T. Roelandt and P. Hertog, "Cluster Analysis and Cluster-Based Policy Making in OECD Countries: An Introduction to the Theme," in *Boosting Innovation: The Cluster Approach* (OECD Proceedings, 1999), 9–23.

basic research, which is then transferred to the private sector to conduct applied research and transform it into new products. However, more recent studies of the interaction between public and private sector research suggest otherwise. One landmark study on such linkages in the pharmaceutical industry was carried out by Cockburn and Henderson.[59] They examined both quantitative and qualitative information in scientific papers published throughout the 1980s and early 1990s and concluded that the relationship between the public and private sectors is much more complex than a simple basic-applied dichotomy. In fact, they found that the "information exchange between the two sectors appears to be very much bi-directional, with extensive co-authoring between researchers in pharmaceutical firms and researchers in the public sector."[60] At the outermost limit, one could argue that the boundaries between the public and private sectors, particularly in the biopharmaceutical industry, have become increasingly blurred. A case in point is the fact that roughly 40 percent of new biopharmaceutical-university spinoffs in Atlantic Canada are for-profit companies — companies created by university researchers seeking to commercialize their breakthroughs and supported by university-based technology transfer agencies (via joint ventures).

We should remember that the role of universities and other public sector research institutes is not only to generate and publish new knowledge from research work (important as that is) but also to stimulate industrial innovative success by increasing overall human capital (in Atlantic Canada, more than 2,050 university degrees were granted in health- and biomedical-related fields in 1996 alone)[61] and by directly supporting private companies in solving problems. Whether it is through R & D cooperation projects, consultancies, contract research undertakings, personnel mobility, or teaching expertise, scientific knowledge flows back and forth between the public and private sectors.

From a cluster perspective, the geographic distribution of new science or knowledge-based industries (e.g., the biopharmaceuticals sector) is largely determined by the geographic distribution of uni-

59. I. Cockburn and R. Henderson, *Public-Private Interaction in Pharmaceutical Research* (Irvine, CA: Science, Technology and the Economy colloquium, National Academy of Sciences, 20–22 October 1995).

60. Ibid.

61. *Education in Canada*, Statistics Canada – cat. no. 81–229, 1998.

versities and the human capital they embody.[62] According to our research, approximately 61 percent of biopharmaceutical firms in Atlantic Canada have collaborative technical alliances with universities that cover a broad range of research activity. Clearly, the regional academic infrastructure is one of the strengths of the biopharmaceutical cluster, and it is worth highlighting some of its assets.

Nova Scotia is unquestionably the university hub of Atlantic Canada, and at the heart of it is Dalhousie University.[63] The university's Medical School houses strong research capabilities in areas such as cancer cell biology, neurosciences, infectious diseases, cardiovascular diseases, transplantation immunology, epidemiology, molecular genetics, population health, and clinical trials (the next chapter will explore in greater detail some of the R & D investments in these areas). The Medical School also encourages interdisciplinary research, which helps create synergies among different departments and organizations — the Vision 2000 program was implemented to promote such a team approach. Parallel to the Medical School, the College of Pharmacy combines with the Faculty of Science's biochemistry and molecular biology departments to add another dimension to pharmaceutical and medical research.

Beyond the university campus itself, Dalhousie maintains an extensive network of affiliated teaching hospitals. In Halifax alone, there are three such hospitals: the Queen Elizabeth II Health Sciences Centre (the Maritimes' biggest health care institution with the single largest volume of clinical trial activity), the Nova Scotia Hospital (the province's principal psychiatric centre), and the IWK Grace Health Centre (specializing in pediatrics, obstetrics, and maternity). It should also be noted that both Acadia University (Wolfville) and Saint Mary's University (Halifax) benefit from specialties in aquaculture, bioorganic chemistry, and other health-related biotechnologies.

In Newfoundland, Memorial University is home to Atlantic Canada's other medical and pharmacy schools, which are both located within the Health Sciences Centre in St. John's. Basic research activities centre mainly on immunology, neurosciences, cardiovascular and renal physiology, and molecular biology. Through the Newfoundland Centre for Health Education, researchers at Memorial University are also active in clinical trials (i.e., the Clinical Epidemiology Unit, the Health Research

62. For more details, see Zucker and Darby (1996) and Saxenian (1994).

63. With a total of eleven universities, Nova Scotia has the highest number of universities per capita in Canada.

Unit, and the Patient Research Centre). Affiliated institutions include the General Hospital (the main teaching hospital), the Charles A. Janeway Child Health Centre, the Grace General Hospital, the St. Claire Mercy Hospital in New Waterford, and the Newfoundland Cancer Treatment and Research Foundation. Moreover, departments within the Faculty of Science, such as the biochemistry, biology, and chemistry departments, are also actively involved in medical and biotechnological research.

Although New Brunswick and Prince Edward Island do not have medical schools, universities in the two provinces play an important role in biopharmaceutical research. For instance, the Atlantic Veterinary College at the University of Prince Edward Island conducts both basic and clinical trials research in the areas of veterinary and fish health/aquaculture (diagnostic services). The university's Clinical Research Centre also promotes and supports human health clinical research in the province. In New Brunswick, the Université de Moncton's Food Research Centre has established a solid reputation in the field of functional foods and nutraceuticals. In addition, the Saint John Regional Hospital, which is affiliated with Dalhousie's Medical School, is a leader in cancer cell biology, neurosciences, diagnostic imaging, and clinical trials (via the Clinical Trials Division, a joint venture funded by the provincial government, ACOA and industry players such as Astra Pharma Inc., Eli Lilly Canada Inc., Glaxo Wellcome Inc., Hoffmann-La Roche Ltd., Merck Frosst Canada Co., and Pfizer Canada Inc.).

The knowledge infrastructure also includes local partnership links with other public sector research institutes. In discussing clustering as a new form of growth strategy for regional economies, Lagendijk and Charles write: "The essential role of the state is being redefined as that of an *animateur*, a facilitator of networking and institution building. Following this logic, the state should not try to take ownership of cluster initiatives, but should primarily work as a catalyst, a broker that brings actors together and supplies initial funding for research and the initiation of the networking process. Knowledge is an essential component of this role as catalyst."[64] Throughout the four Atlantic provinces, nearly 30 percent of private sector biopharmaceutical companies are involved in strategic alliances with at least one government organization.

64. A. Lagendijk and D. Charles, "Clustering as a New Growth Strategy for Regional Economies? A Discussion of New Forms of Regional Industrial Policy in the United Kingdom," in *Boosting Innovation: The Cluster Approach* (OECD Proceedings, 1999), 127–153.

The sharing of knowledge and networking with the aim of generating new economic activity is the primary goal of one such catalyst, the National Research Council of Canada. In particular, several biopharmaceutical firms have benefited from collaborative R & D programs with the Institute for Marine Biosciences (IMB) in Halifax, one of five NRC biotechnology laboratories in Canada. Through its aquaculture program, IMB scientists collaborated with Jellett Biotek Ltd. of Dartmouth, Nova Scotia, to develop an in vitro cell bioassay called MIST (Maritime In-Vitro Shellfish Test) kits. Among other things, the institute assisted in validation studies and provided toxin standards, which are included in every kit. More recently, the same partnership resulted in the development of a rapid method for detecting paralytic shellfish poison toxins in shellfish samples, and there is ongoing work on other diagnostic kits for marine biotoxins.

The IMB is also at the cutting edge of genomics research in Canada. In conjunction with the Dalhousie Faculty of Medicine, IMB maintains and operates a joint DNA-sequencing facility within the institute's molecular biology laboratory. As researchers continue their quest for a better understanding of the relationship between genes and diseases, the IMB assists its partners by means of targeted DNA sequencing, protein characterization, and other sophisticated analyses using bioinformatics tools (via the Canadian Bioinformatics Resource). It also gives local researchers access to national and international networks of collaborators, which include the following organizations: Argonne National Laboratory (U.S.), Base 4 Bioinformatics Inc. (Ontario), Glaxo Wellcome (Ontario/UK), Institut Pasteur (France), Kinetek (B.C.), Max-Planck Institute for Biochemistry (Germany), Microtek International Ltd. (B.C.), MDS-SCIEX (Ontario), and Xenon Bioresearch Inc. (B.C.). Genomics research at the IMB is poised to increase rapidly, given that the February 2000 federal budget provided $160 million to fund the activities of five genome science centres across the country; Halifax is expected to be the site of one of them.

Other NRC initiatives include the Industrial Research Assistance Program (IRAP), which supports innovative SMEs with projects at the precommercialization stage. IRAP is a financial assistance program supporting the development, application, and diffusion of "enabling technologies" such as biopharmaceuticals.

At the provincial level, the government of Nova Scotia has been particularly aggressive in promoting public-private partnerships and the development of the biopharmaceutical industry. In 1994 it established In*NOVA*corp to expand the province's knowledge-based

industries (three sectors are targeted: life sciences, information technology, and advanced materials and engineering), and in collaboration with the Atlantic Canada Opportunities Agency (ACOA) and Nova Scotia's Department of Economic Development, it created the Life Sciences Industry Partnership (LSIP) with the specific goal of doubling the size of the province's life sciences industry between June 1998 and June 2001. LSIP provides scientists, researchers, and entrepreneurs with access to venture capital, business advisory services (strategic marketing, business planning, etc.), and business incubation facilities. In*NOVA*corp's latest foray includes the BioScience Enterprise Centre in downtown Halifax, also home to Ocean Nutrition Canada Ltd. The provision of physical infrastructure and administrative support are key elements in encouraging the growth of biopharmaceutical start-ups. According to Steve Armstrong, the director of Life Sciences at In*NOVA*corp, biopharmaceutical firms cultivated within incubation centres are approximately six times more likely to succeed than "non-incubated" start-up companies. This type of private-public partnership has definitely sparked life in the biopharmaceutical industry, helping to attract young entrepreneurs, diversify the industrial base, and increase awareness of the life sciences sector, thus making Nova Scotia a centre for health-related business developments.[65] Several other incubators as well as research/business parks in Atlantic Canada facilitate the creation of local conditions supportive of the biopharmaceutical (and the general) innovation process (see box 3 for a quick listing of these incubators/business parks).

Industry and professional associations, of which there are around ten in Atlantic Canada, are another vital component of the supporting services infrastructure. One of the leading organizations is the Nova Scotia Biotechnology and Life Sciences Industry Association (BioNova), which brings together more than seventy companies and institutions. BioNova's initiatives are designed to develop relationships (through alliances with various government departments), information, networking, and education (via training seminars and workshops). It is estimated that 55 percent of its member companies are closely linked to the regional biopharmaceutical industry.

There are also other models of partnership organizations. As counterparts to industry associations and university-based technology transfer offices, a few private sector enterprises are involved in the

65. The employment growth rate in the life sciences sector in Nova Scotia from December 1998 to December 1999 was in the region of 40 percent, at least double the national growth rate (see the Nova Scotia Life Sciences Industry Report 2000).

promotion and development of biopharmaceutical firms. In New Brunswick, while backing the general regional biotechnology industry, BioAtlantech Inc. is at the source of new biopharmaceutical business opportunities. For example, in a joint venture with a consortium

**Box 3**

**Business Parks/Incubators in Atlantic Canada**

| Type | Ownership | Location |
|---|---|---|
| **Incubators** | | |
| BioScience Enterprise Centre | In*NOVA*corp | Halifax (NS) |
| AgriTECH Park | In*NOVA*corp, Nova Scotia Agricultural College | Truro (NS) |
| Technology Innovation Centre | In*NOVA*corp | Dartmouth (NS) |
| The Genesis Centre | Seabright Corporation (Memorial University) | St. John's (Nfld.) |
| **Research Parks** | | |
| Parc scientifique – Université de Moncton (potential) | Université de Moncton | Moncton (NB) |
| **Business Parks** | | |
| West Royalty Industrial Park | PEI Business Development Inc. | Charlottetown (PEI) |
| Burnside Business Park | Halifax Regional Municipality | Dartmouth (NS) |
| Woodside Industrial Park | Halifax Regional Municipality | Dartmouth (NS) |
| Ragged Lake Business Park | Halifax Regional Municipality | Halifax (NS) |
| Nova Scotia Science Park (proposed) | Halifax Regional Municipality | Halifax (NS) |
| Greater Fredericton Knowledge Park (potential) | Greater Fredericton Economic Development Corporation | Fredericton (NB) |

of blueberry growers, it established Vaccinium Technologies Inc. to explore some of the functional food and nutraceutical applications of small fruits (i.e., natural antioxidants). Of the five biopharmaceutical firms in New Brunswick, four have ties with BioAtlantech Inc.

A different type of business organization is also lending a hand in marketing and attracting new investment to the Halifax region. Incorporated in 1996, the Greater Halifax Partnership (GHP) is a private enterprise bringing together the business community and the public sector. It recently embarked on a cooperative venture with the Dalhousie Medical School (and its Business Development Office)[66] to investigate the commercial viability of current research projects at the university. Of the more than three hundred active research projects, several are expected to have the potential to become successful commercial ventures.[67] For the scientists concerned, the agreement between the GHP and Dalhousie Medical School will provide easier access to investors and capital and allow them to sharpen their business skills through training and education programs. In addition to regrouping local resources, the GHP is also looking beyond the region with a series of national and international marketing campaigns. One of its five international marketing programs is specifically tailored to develop relations with Sweden, the province's largest international investor and an important player in the biopharmaceutical industry at the research level (there are several ongoing research projects between Nova Scotia universities and the Swedish pharmaceutical giant Astra Pharma Inc.).

### *Business services*

The biopharmaceutical cluster also consists of other supporting activities, including specialist suppliers and business service providers. The relationship between these service companies and those involved in industrial/primary activities has for the most part been reciprocal. On the one hand, the creation and expansion of an industrial foundation has opened the way for the development of service providers. On the other hand, the growing network of service providers has facilitated the start-up process and the progress of manufacturing firms, reinforcing overall industrial localization.

In the four Atlantic provinces, a group of approximately sixty firms provide such supportive activities. These firms tend to be of recent

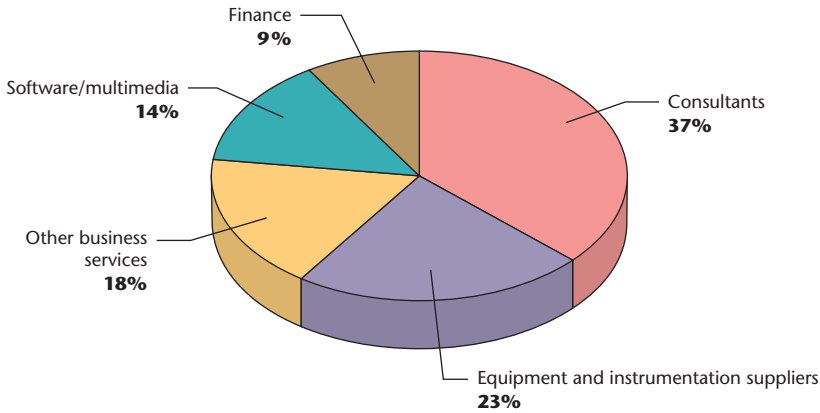
66. The BDO itself is an innovative model of private-public sector partnership. It is run by BioMed Management, a private company providing hands-on management expertise for biopharmaceutical start-ups.

67. Dr. Noni MacDonald, dean of the Dalhousie Medical School.

origin (in all, 61 percent of these firms were founded after 1990) and small- or medium-sized. Geographically, the vast majority (i.e., 81 percent) are located in Nova Scotia, bolstering the province's already impressive infrastructure.[68] In addition, the areas of expertise or activity of these firms are wide ranging (see figure 15).

**Figure 15**

**Breakdown of Private Sector Service Providers in Atlantic Canada according to Activity, 1997–98**




*Source:* Ibid.

One of the leading group of companies include suppliers of various equipment and instrumentation devices. There are also firms offering exclusive products, such as Precision Glassblowing Ltd. (which fabricates custom scientific glassware for R & D and industrial uses), and those providing multiple products and services, such as Can-Med Surgical IMP Supplies Ltd. (the largest independently owned supplier of health care products in Atlantic Canada). But despite the apparently significant volume of business they do, local suppliers remain rather scarce, and biopharmaceutical firms are inclined to rely on outside suppliers, again mainly from Ontario and Quebec.

There has also been a definite boom in firms specializing in consulting services, that is to say firms providing advice to improve corporate strategies and operations. Taken together, about 37 percent of service providers fall into this category. Beyond mainstream management and market consultants, a growing number of firms are focusing on selected services. For instance, BDH Science Communications

68. The dispersion of service companies in the other Atlantic provinces is as follows: New Brunswick accounts for about 15 percent of total firms, while Newfoundland and Labrador and Prince Edward Island share the other 4 percent.

(Bedford) and CanTox Inc. (Halifax) concentrate on scientific writing, that is, the preparation of scientific reports, technical submissions, news articles, and other similar kinds of communications. CanTox Inc. also provides assistance with risk-assessment reviews and regulatory affairs, thus helping clients launch new products into the marketplace. BioFocus Inc. also draws on past experience in the area of rapid diagnostic in vitro testing to support companies in the commercialization of products. Aside from being consultants, the common thread that runs through these firms is that they allow industrial companies to become more productive by removing the burden of having to perform every organizational function. Indeed, by contracting out specific functions (regulatory affairs, marketing, etc.) to such specialized service providers, biopharmaceutical firms can focus on internal operations and product development.

Small innovative software and multimedia developers have also mushroomed in response to the growing needs of the biopharmaceutical and health research community. On the software front, several companies design and manufacture products. FEOM Holdings, for example, has put together a protocol called MediTrac for tracking medical histories, a practical package for researchers conducting clinical trials. Britech Information Systems Ltd. develops various software products for laboratories, diagnostic imaging, and medical records. Digital Image FX Inc., also a software development company, is using the latest advances in virtual reality technology to create a medical simulation software package (in partnership with Dalhousie University) which, via a telemedicine system, could act as a *distance diagnostic unit*.

Telemedicine, by itself, is an entirely new field in the medical and pharmaceutical world. By means of telecommunications and information technologies, physicians and pharmacists can get in touch with more remote locations for timely consultations, remote diagnoses, and even patient treatment without being in physical contact with the patient. The provinces of Newfoundland and Labrador, New Brunswick, and Nova Scotia are all leaders in this field, and there is considerable potential for growth in the specific areas of integrated networks, home telecare and associated services, telelearning aspects of health, and corporate wellness.[69] Newfoundland, through its Telemedicine and Educational Technology Resources Agency (TETRA), has developed strong telecommunications expertise in health care delivery and has completed a variety of projects in Africa, Jamaica, and

69. For further readings on this subject, see Canada, Industry Canada, *Telehealth in Canada: Clinical Networking, Eliminating Distances* (Industry Canada, 1997).

the Philippines. Tecknowledge Health Care Systems of Dartmouth is another regional company making significant inroads into telemedicine. Within Nova Scotia, it set up the IWK Grace Children's Telehealth Network and took part in the implementation of the Nova Scotia Telehealth Network (i.e., a vast telecommunications system linking all forty-one health facilities across the province). In New Brunswick, with the help of other high-tech Internet/Intranet applications, Total Pricing Systems Inc. provides various information services to pharmaceutical manufacturers and their internal sales and marketing representatives. Certainly, the influence of multimedia technologies will continue to grow and present new opportunities for regional entrepreneurs.

In Atlantic Canada, one of the weakest links in business services is the availability of financial resources and venture capital, more specifically of seed capital. In a firm's growth cycle, the seed stage occurs after the first commercialization steps of R & D (to this point, the financing is usually by personal investments and research grants) and prior to full-fledged sales and marketing (when venture capital comes into play). Tapping into seed funds (such as the Eastern Technology Seed Investment Fund) in Atlantic Canada is possible, but very few regional biopharmaceutical firms have achieved this. As for venture capital, we will see in the following chapter that the situation is slowly improving, but the fact remains that there is only one regional venture-capital fund company making equity and quasi-equity investments in local businesses. Various other sources of financing are available, however (e.g., Canadian Medical Discoveries Fund, Working Ventures Canadian Fund, Business Development Bank of Canada, banking institutions, etc.), but again, very few Atlantic Canadian biopharmaceutical firms actually benefit from them.

### *Sowing the seeds of growth: the cluster's strengths and weaknesses*

The biopharmaceutical cluster in Atlantic Canada received its biggest boost from changes in the pharmaceutical industry itself. Until now, we have seen that because the bulk of firms provide products and services aimed at specific niche markets and new smaller yet emerging industry segments, they can compete internationally on a level playing field without necessarily butting heads with large multinational enterprises focusing on the most profitable segments. Their small size also makes them more flexible than big corporate structures and allows them to adapt quickly to shifting customer demands. And in spite of a comparatively small and fragmented regional market, the lack of domestic rivalry is, to some degree, compensated for by openness to global strategies, an integral part of the cluster's resilience.

The growth of biopharmaceuticals is also closely connected to the rapidly expanding biotechnology sector in the four Atlantic provinces. Health information technologies show exciting potential and new opportunities, while provincial governments and industry associations continue to be proactive in promoting the life sciences sector in their respective provinces. At the same time, the regional academic infrastructure provides an important source of highly trained personnel and is a solid basis for research and development activity.

These are some of the advantages of the biopharmaceutical cluster that allow us to investigate the origins of the region's *competitive advantage*. But what about some of the cluster's weaknesses? For example, we have already mentioned that access to adequate financing can be a problem affecting the development of biopharmaceutical firms, particularly at the early stages of development. Although improving, the process of technology transfer is sometimes sluggish because of a lack of experience in the commercialization and licensing of new products. Likewise, the fact that in many cases small biopharmaceutical firms are essentially built around one individual (i.e., the company founder) makes them vulnerable after his or her retirement.

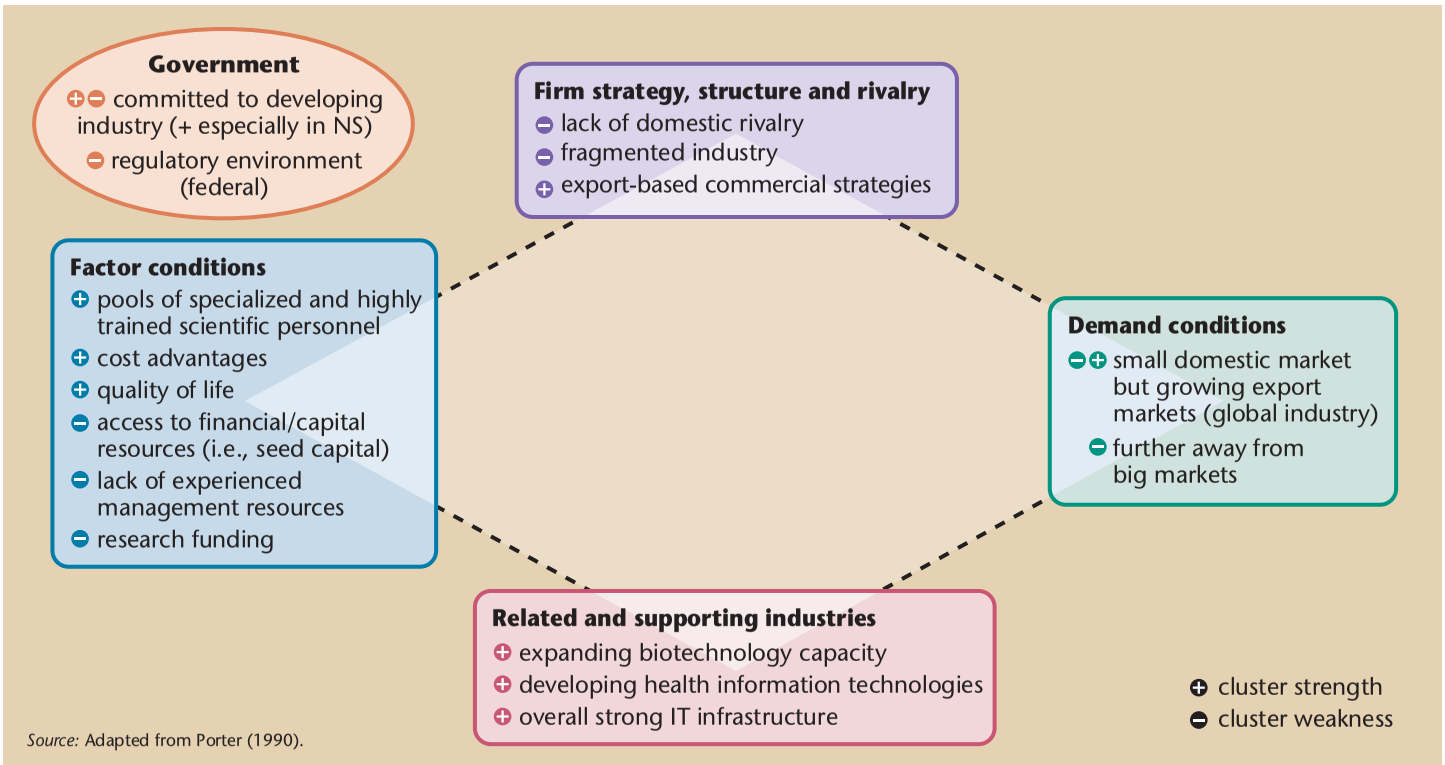
This leads us to ask questions about other forces at work in cluster dynamics. For instance, how does the regulatory environment affect industrial expansion? Are biopharmaceutical firms reinvesting in research and development, and even more generally speaking, what has been the evolution of R & D spending in Atlantic Canada? Does the actual tax climate attract outside investments in R & D? What about other cost advantages? Regarding the issue of human resources, it seems that one of the main challenges facing the industry is the lack of an experienced management workforce.

All of these pros and cons can be summarized by borrowing Michael Porter's "diamond" framework, which also recapitulates the four determinants of competitiveness (i.e., demand conditions, related and supporting industries, factor conditions and firm strategy, and structure and rivalry — and because of the importance of its role, we also include government as an outside force). Figure 16 presents a glimpse of how the answers to the above questions influence the cluster.

Typically, the birth and development of an industry are triggered by an advantage in factor conditions, related and supporting industries, or market conditions. In the case of the biopharmaceutical industry in Atlantic Canada, however, all three determinants contribute to cluster formation. The following chapter examines in greater

Figure 16

The Diamond of the Nascent Biopharmaceutical Cluster in Atlantic Canada




*Source:* Adapted from Porter (1990).

length the rationale behind this analysis and sheds light on some of the topics affecting the industry. Keeping in mind that the diamond model provides the basis for medium- to long-term structural competitiveness, we conclude by looking at some of the public policy issues with respect to promoting the cluster's growth.

# III

# Factors Affecting the Development of Biopharmaceuticals in Atlantic Canada

In a study on innovation clusters in Germany, Spielkamp and Vopel write: "Although an entrepreneurial spirit and the willingness to take risks in the development of new technologies are business characteristics which cannot be substituted by any governmental action, governmental R & D and innovation policy has to contribute to a dynamic innovative system. Readiness to innovate could also be encouraged by legislation. Therefore, the provision of favorable basic conditions has to go hand in hand with the development of co-operative networks within the innovative system. The funding and promotion of research, the stimulation of the exchange of knowledge between science and industry, and the creation of an environment that fosters innovative activities are vital characteristics of a comprehensive innovation policy."[70] The theme here is essentially how to mould development strategies that nurture the creation of factor conditions favourable to innovative industries. To do so, we must recognize some of the major topics shaping Atlantic Canada's biopharmaceutical cluster, notably the legislative environment, support for R & D activity, human resources development, and access to financial backing.

## Legislative Issues

Because of their direct effects on human and animal health, pharmaceutical and biopharmaceutical products are subjected to rigorous regulatory controls. And since the industry is global in nature, the commercial success of domestic biopharmaceutical firms relies heavily on the efficiency of Canada's regulatory framework and its intellectual property protection laws.

70. A. Spielkamp and K. Vopel, "Mapping Innovative Clusters in National Innovation Systems" in *Boosting Innovation: The Cluster Approach* (OECD Proceedings, 1999), 91–123.

### *Regulations*

In Canada, pharmaceuticals and health-related biotechnologies are regulated by various government departments, both at the federal level (Health Canada — Food and Drugs Act, Environment Canada — environmental protection, Transport Canada — transportation of dangerous goods, Department of Foreign Affairs and International Trade — export/import regulations, and Human Resources Development Canada — occupational safety regulations) and the provincial level (especially with regard to environmental, transportation, and occupational health and safety statutes).[71] For pharmaceutical and biopharmaceutical products, the fundamental piece of legislation is Health Canada's Food and Drugs Act, which was proclaimed in 1953. In brief, it sets out the requirements with which vaccines and therapeutic and diagnostic products must comply. It is the Health Protection Branch, via its Therapeutic Products Program (TPP), that demands that new products undergo a thorough process of clinical trials (pre-clinical and phases I–IV) to determine if they are safe and effective before reaching the marketplace.

In terms of scientific rigour and safety regulations, Canadian standards and quality assurance measures are world renowned. According to a report by the National Biotechnology Advisory Committee, Canada's comprehensive regulatory procedures could actually turn out to be a competitive advantage for the commercialization of biotechnologies, and the "label *Approved in Canada* could become internationally synonymous for safety."[72]

The hiccup, though, is that all of these requirements impose numerous constraints on the production and sales of biopharmaceuticals, often retarding the launch of new products. This, in turn, affects general public health care benefits and can have a significant impact on industrial development.[73] For example, because biopharmaceutical products cannot be produced for sale to other countries before first being approved for sale in the Canadian market, an expeditious approval system can prove helpful in attracting outside buyers to domestic manufacturers.

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71. Through the Patented Medicines Prices Review Board of Canada, drug prices are also regulated at the federal level.
72. National Biotechnology Advisory Committee. *Sixth Report 1998: Leading in the Next Millennium*. Ottawa: Industry Canada, 1998, 58.
73. See, for example, Krista Foss, "Loosening the Cap on Drug Approvals," *Globe and Mail*, 30 May 2000, R5.

Moreover, swift approval times translate into faster commercialization of products and longer periods of market exclusivity, allowing manufacturers to recoup initial R & D investments. From the point of view of international competitiveness, this is crucial for luring new clinical research investments from big transnational pharmaceutical companies. As pointed out in the Pharmaceutical Manufacturers Association of Canada's (PMAC) *Annual Review, 1998–99,* "Canadian clinical trial approval times must be competitive with those of the U.S. and European agencies if the placement of studies in Canada is to be encouraged and supported by pharmaceutical company head offices. Timeliness is key for Canada to attract more clinical trials, be more competitive, and have our researchers, clinicians, and patients benefit from this important research."[74]

However, even if delays were shortened significantly in the mid-1990s (following the 1992 release of the Gagnon report on the drug review process), Canada's average review and approval times continue to lag behind other competing countries. In comparison to the U.S., for instance, the average drug approval time in Canada is much longer. Over the 1996–98 period, the TPP's average approval time for new drugs was 608 days, whereas the Food and Drugs Administration, its U.S. counterpart, had an average of 496 days, a difference of 112 days. Since 1996, the gap between the two countries has actually widened. In several European countries, the approval process is even more rapid than in the U.S. (see table 5). Diagnostic products, for example, can be approved within an 80-to-120-day period if manufacturers already hold their European Union facility inspection (such as the ISO 9000 series of quality standards), making it one of the preferred point-of-market entries.

With the ever-increasing use of biotechnologies,[75] the strain on Canada's regulatory system is not about to abate unless more resources are dedicated to it. In this regard, the just recently released report of the Committee on the Drug Review Process (of the Science Advisory Board to Health Canada) tabled several recommendations addressing the issue of timeliness. Among them, priority is given to allocating sufficient resources to enhance the professional scientific capacity of Health Canada, tackling pending applications, and

74. Pharmaceutical Manufacturers Association of Canada, "The Value of Innovation for All Canadians," *Annual Review, 1998–99*.

75. Several biotherapeutic product setbacks have been linked to inadequately designed clinical studies: Phases II and III of clinical trials have been especially problematic, and the sixty-day review period for each of those stages is considered too lengthy.

**Table 5**

**Average Approval Times for New Drugs in Five Different Countries (in Days), 1996–98**

| Country | 1996 | 1997 | 1998 | 1996–98 |
|---|---|---|---|---|
| Canada | 584 | 660 | 560 | 608 |
| Australia | 514 | 533 | 562 | 536 |
| United States | 578 | 528 | 344 | 496 |
| Sweden | 383 | 340 | 352 | 360 |
| United Kingdom | 348 | 285 | 422 | 344 |

*Source: The Canadian Medical Association Journal* (22 February 2000).

guaranteeing acceptable timeliness of all applications.[76] The hope is that these recommendations will be implemented.

Although provinces are not responsible for the regulatory approval of new drug products sold in Canada, they play a key role in the authorization of drugs dispensed by pharmacists. Since the 1970s, in an effort to improve and maintain the well-being of their residents, provincial governments have established drug reimbursement programs for selected target groups (e.g., seniors, social assistance beneficiaries, etc.). All drugs and related products that are deemed to be "entitled services" and eligible for funding are listed on provincial drug formularies. Although not all drug products are covered (exceptions include items such as cough syrups, antihistamines, etc.), admissibility to provincial formularies is vital to the commercial success of new medications.

The rising cost of drugs is at odds with the cost-containment measures of governments, which have just recently begun to restore much-needed money to the health care system. Indeed, while most provincial governments struggle to control their purse strings, drug costs remain one of the fastest-growing components of health care spending. As a percentage of total health expenditures in Canada, the price of drugs has doubled since the beginning of the 1980s, while physicians' fees over the past ten years have been dropping.[77] This has led to a backlash as more provinces now require added justifications in defence of the advantages and/or supplementary costs associated with each new drug (i.e., reflecting the growing trend in pharma-

76. Canada, Health Canada, *Report of the Committee on the Drug Review Process of the Science Advisory Board to Health Canada* (February 2000).

77. Canadian Institute for Health Information, *National Health Expenditure Trends, 1975–2000*, 2000.

coeconomic assessments) prior to including it in their formulary (remember that provincial formularies are listings of all the medications that physicians can prescribe and that are covered by publicly funded drug plans). Hence, the review process is more time-consuming, which is creating bottlenecks in provincial formularies.

What is more, though provincial plans are fundamentally comparable, they are becoming increasingly distorted by the fact that each of them has a unique set of policies to assess the reimbursement eligibility of drugs. In some instances, expensive drugs considered breakthroughs that have no existing medication to compare them with have had only limited access to provincial drug programs. A study by the Department of Health Care and Epidemiology at the University of British Columbia revealed wide-ranging disparities in the approval rate of new drugs. Saskatchewan, for example, had the highest approval rate with 81 percent of drugs included in the provincial plan, whereas in Prince Edward Island, only 17 percent were approved.[78] Ultimately, timeliness and admissibility to provincial formularies constitute additional regulatory hurdles in the Canadian system as well as extra criteria for potential R & D initiatives of big pharmaceuticals in certain provinces.

In Prince Edward Island, for example, more than two hundred new drugs, already approved by the TPP, are currently awaiting review by the province's pharmacy advisory board for inclusion in its formulary. The result is that drugs "take about two years to be evaluated in Prince Edward Island, compared with six to 18 months in most other provinces."[79] As it happens, with the exception of Nova Scotia, the Atlantic provinces rank last in regard to the length of time required to review new drug products. Again, from an inter-Canadian perspective, timely access to provincial drug benefit programs is becoming an increasingly important factor in persuading innovative firms to undertake research projects in specific provinces. The result when they do is more investment dollars for researchers and the regional research infrastructure. Although large multinational companies have boosted their R & D investments in Atlantic Canada over the last few years, a more flexible review process could bolster the attractiveness of the region's clinical research network. None the less, the increase in R & D activity has also been part of a nationwide trend, buttressed by more robust patent protection (Bills C-22 and C-91).

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78. A. Anis et al., *A Dog's Breakfast: Prescription Drug Coverage Varies Widely Across Canada* (Vancouver: UBC, 1998).

79. Carol McLeod, "Backlogs Affect PEI Pharmacists," *Pharmacy Post* (December 1999).

### *Patent protection*

When innovation is at the heart of the matter, as in the case of biopharmaceutical entrepreneurs, the ability to patent new products and/or industrial processes is another critical factor in commercial success. In the life cycle of a new product, patents are usually issued at the early stages of development, when R & D is still proceeding and before submission to the regulatory review and approval process. Once endorsed, products then typically benefit from approximately seven to ten years of market exclusivity. The length of protection provided by a patent is thus very valuable in determining a firm's profitability.

In Canada, patents relating to pharmaceutical products date back to the 1920s, when compulsory licensing for foods and medicines was first introduced. It was only in 1969, however, that the law was amended to allow imports of active ingredients, triggering the development of the generics industry. The Patent Act was again amended in 1987, when Bill C-22 extended the length of patent protection from the previous seventeen-year period to twenty years (that is, from the date of filing a patent application) and provided patent holders a minimum of seven years of market exclusivity. As for manufacturers of generic products, they could still obtain compulsory licenses during the term of patents. This would change, however, when in 1993 Parliament passed Bill C-91, which put an end to compulsory licensing, meaning that generic producers had to wait until patents expired before launching copies of products. But perhaps the most significant impact of Bill C-91 was the commitment made by PMAC members to reach and maintain an average R & D-to-sales ratio of 10 percent by 1996. This invigorated research spending in Canada as multinational pharmaceutical giants increased their R & D investments: from 1988 to 1998, PMAC members R & D-to-sales ratio shot up from 6.5 percent to 12.7 percent.

After a review of the bill in 1997, the dispute over patents between brand name and generic producers has abated (although it is never far from the surface), and the focus has shifted from national concerns to the internationalization or harmonization of intellectual property (IP) laws and the new challenges resulting from patenting biotechnologies. The advances in genetic research, for instance, are raising concerns over traditional patentability principles all over the world. So far, the Canadian system has allowed patents for single-celled organisms (e.g., yeast cells, algae, bacteria, etc.), but not genes. In contrast, Canada's major trading partners — particularly the U.S. and European

countries — have already begun granting patents on higher life forms such as plants and transgenic animals. A classic example of some of the problems incurred by such divergences is the ongoing saga of the Harvard onco-mouse.[80]

Concerns over economic and international trade matters are also at the forefront of the growing intricacies of patent protection rights. In 1996 the Agreement on the Trade-Related Aspects of Intellectual Property Rights, between the World Trade Organization and the World Intellectual Property Organization, took effect, establishing minimum standards of IP protection among participating countries. This is a further step towards greater coordination of intellectual property practices within the international community. It also shows the significance of having robust patent protection in Canada so that it can sustain its competitiveness, especially vis-à-vis the U.S., major European countries, and Japan.

For smaller biopharmaceutical firms, strong patent protection is no less important as it confers not only protection of their innovations but also credibility in the eyes of potential investors — credibility that is crucial in the beginning stages to winning early investments. Apart from subsidiaries of larger national or international firms, about a dozen biopharmaceutical firms in Atlantic Canada currently have patents.[81] An examination of patents in the context of the granting organization reveals a number of trends. For example, only a quarter of all patents were registered with the Canadian Intellectual Property Office, while the lion's share were issued by other international organizations. More and more, innovators are turning to the World Intellectual Property Organization (WIPO) to file their patent applications under the Patent Cooperation Treaty (35 percent of patents held by biopharmaceutical entrepreneurs in the region were granted under the auspices of the WIPO). The chief advantage of the PCT is that it makes it possible for inventors to seek simultaneous patent protection in all the contracting countries by filing a single international patent application. The alternative would be to apply in each country, a process that can be very expensive.

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80. Although in 1998 the U.S. Patent Office granted a patent for this genetically engineered mouse (used in laboratories for cancer research), the Canadian Commissioner of Patents rejected Harvard's application for a Canadian patent in 1995. In 1997 an appeal was heard before the Federal Court of Canada; litigation is still pending.

81. This does not include pending patent applications nor unpublished patent applications (patent applications are only published after an eighteen-month period of secrecy).

Atlantic Canadian biopharmaceutical companies also initiate a large number of patent applications to the U.S. Patent and Trademark Office (roughly one-third of biopharmaceuticals have U.S. patents). In general, firms do this in order to get technologies recognized in one of the biggest and potentially most-lucrative markets. But they also file patents with the U.S. patent office because it is usually less expensive and much more rapid. Indeed, similarly to its regulatory approvals, the U.S. assigns superior resources and patent officers to process the fast-growing number of claims. In addition, since 1995, innovators can file a provisional application, which is a simplified filing with a lower initial investment; it allows the applicant twelve months to assess the invention's commercial potential before committing to the higher cost of filing and prosecuting a nonprovisional application. This is particularly attractive to small biopharmaceutical firms who want to avoid hastily filing broadly based patents only to be challenged later on, often because of overlapping claims and the unavoidable ambiguity of gene patents, by deep-pocketed rivals, who can afford expensive and exhaustive legal contests.

Furthermore, universities, aware of the value of patents, not only have entered the race but are actually setting the pace in the Atlantic provinces. Together, they share more than sixty-five patents relating to biopharmaceuticals. The Seabright Corporation, the commercialization office of Memorial University, has been particularly skilful in assisting *academic entrepreneurs* to file and obtain patents (it alone has more than thirty patents to its credit). In some instances, these same academic entrepreneurs went on to form companies such as Bio-ID and PA Pure Additions. In Nova Scotia, NU-TECH is also evolving as a resource centre for issues concerning intellectual property protection.

To sum up, the implications of both regulatory approvals and intellectual property laws are central to the development of the biopharmaceutical industry in Atlantic Canada. For start-ups and smaller producers, they convey confidence and provide a protected position in which to make developmental investment decisions. For larger manufacturers, they help in raising R & D funds and influence their choice of where to locate these investments, a crucial element for R & D activity in Atlantic Canada.

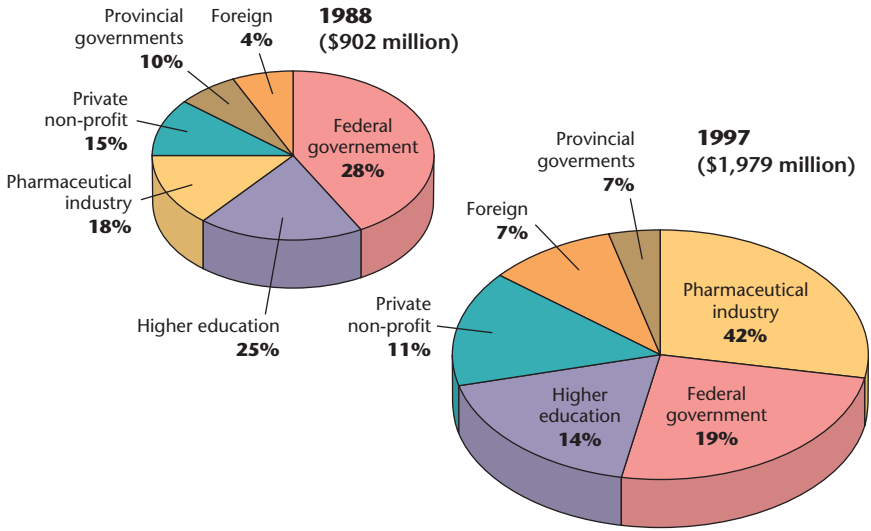
## Research and Development Then and Now

Innovation through research and development is a key driver in the growth of the biopharmaceutical industry. It is largely through new product development arising from basic research that companies are able to continue making inroads into the expanding international marketplace.

In Canada, more specifically in Ontario and Quebec, one of the principal reasons for the development of the research infrastructure in the health field has been an increase in R & D spending by large multinational pharmaceutical companies, a result of improved patent protection provided by Bills C-22 and C-91. In fact, it is estimated that gross R & D expenditures in the health sector have more than doubled over the period 1988–97, from $902 million to almost $2 billion (see figure 17). The share of funding stemming from business enterprises has grown considerably since 1988, with total

**Figure 17**

**Gross R & D Expenditures in Canada's Health Field by Funding Source, 1988 and 1997**




*Sources:* Statistics Canada, 1998, and *1997 PMAC Anual Statistical Survey* (as reported in *PMAC's 1999 Annual Review*).

investments by PMAC members representing some $825 million in 1997.[82] For the same period, the PMPRB (Canada's watchdog on patented medicine prices) reported that the PMAC's ratio of R & D expenditures to sales revenues increased from 6.5 percent to 12.7 percent, surpassing the 10 percent target committed to by PMAC members back in 1993 following the passage of Bill C-91.

Unfortunately, Statistics Canada does not publish a similar breakdown by province of gross domestic R & D expenditures in the health field (health sciences are lumped in with natural sciences and engineering). None the less, it is still possible to examine some of the major components of health research investment to see if indeed Atlantic Canada is getting its fair share of R & D funding.

In keeping with the nationwide profile, the largest portion of biopharmaceutical R & D activity in the four Atlantic provinces is funded by multinational pharmaceutical companies. Over the period 1989–98, R & D spending in the region by these pharmaceuticals rose from $3.1 million to $19 million, a more than sixfold increase that was almost twice the national rate and four times the U.S. growth rate. This reflects in large part the commitment of brand name manufacturers (i.e., under Bill C-91) to redistribute clinical research investments on a regional basis.

A breakdown of increased R & D spending in Atlantic Canada (see figure 18) reveals that the largest part, 41 percent of the total in 1998, goes to hospital-based researchers to carry out applied research directed towards clinical trials. In fact, in Atlantic Canada, as in the rest of the country, clinical research is the most substantial kind of research being done. For example, in 1998, 79.3 percent of applied research outlays were dedicated to clinical trials.[83] Most of the clinical studies that take place in Atlantic Canada involve phases III and IV trials. Once preliminary evidence suggesting the effectiveness of a new drug has been obtained from earlier trials (phases I and II),[84] phase III trials are carried out to gather additional information about effectiveness and product safety on a larger scale using a controlled and uncontrolled patient base that usually involves five hundred

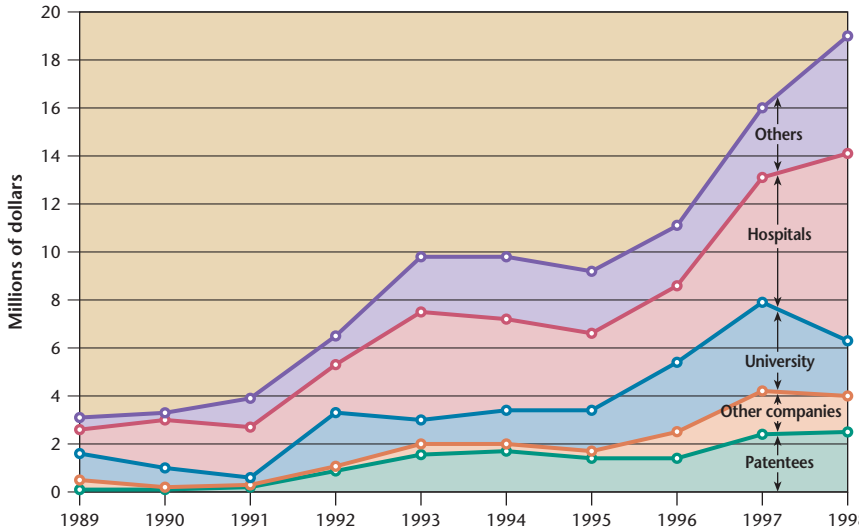
82. This figure includes PMAC members that do not report to the PMPRB because either they do not yet have a product on the market, or their products may not be patented. In comparison, the PMPRB reported that innovative manufacturers invested $725 million in R & D in 1997.

83. PMPRB, *Eleventh Annual Report* (31 December, 1998).

84. Phase I trials concern the introduction of a new drug into humans (a small control group of healthy individuals) to determine its metabolic and pharmacological effects, whereas phase II trials focus on using the drug on patients affected by the disease it is designed to treat.

**Figure 18**

**Growth of R & D Expenditures by R & D Category, Atlantic Canada, 1989–98**




*Source:* PMRPB.

to three thousand patients. They also allow for comparison with other existing drugs or treatments. Phase IV trials, also called post-marketing surveillance trials, measure the performance of new drug products in real-life situations.

Much of the increase in R & D spending in Atlantic Canada can be attributed to the establishment of the Clinical Trials Atlantic Corporation (CTAC). Funded by the MRC/PMAC Health program and ACOA, CTAC was formed in 1994 as a nonprofit, independent company with a five-year mandate to attract more clinical research investment to the region. To do so, it acted as an umbrella organization that simultaneously promoted and developed research networks between several academic institutions and teaching hospitals throughout Atlantic Canada by providing training, patient recruitment, and administrative support. During its brief existence, total R & D spending in the region more than doubled. Having excelled in marketing the region's research expertise and infrastructure, CTAC fell victim to its own success. In 1999 its mandate came to an end, and it passed on its role to individual localized groups, who are now recognized as the points of entry for clinical studies in the pharmaceutical industry.

The dispersion of R & D investment by province again reflects the predominance of Nova Scotia's well-established medical research infrastructure, which attracted 65 percent of pharmaceutical R & D spending in 1998. The organization of clinical research activity in the province is structured around the Centre for Clinical Research, part of the Queen Elizabeth II Health Science Centre. With more than twenty years of clinical research experience to its credit, it brings together some 250 researchers and investigators. Some of its more recent research initiatives include a $6 million five-year population-based study to measure and improve the quality of care for victims of cardiovascular disease (*Improving Cardiovascular Outcomes in Nova Scotia*), a $1.3 million clinical trial on Alzheimer's disease (which will involve other Maritime sites as well), and a $750,000 study on how to reduce the risk factors associated with cardiovascular disease in employees (a partnership between Hoechst Marion Roussel Canada Inc., Atlantic Blue Cross Care, and the Atlantic Health and Wellness Institute in Halifax).

R & D spending in Newfoundland accounts for roughly 20 percent of regional industry outlays. Since 1994, the Patient Research Centre (part of the Newfoundland Centre for Health Evaluation) has been responsible for promoting and coordinating clinical research activities in the province, making good use of the broad-based disciplines of investigators. More recently, in September of 1999, the Newfoundland Center for Applied Health Research was established with a mandate to increase the province's capacity to perform high-level research on applied health issues (i.e., health and welfare public policy issues and clinical decision making). Currently, pharmaceutical companies are engaged in a three-phase study on the optimal use of antibiotics, and Novartis Pharmaceuticals Canada is sponsoring the creation of a Human Genetics academic chair at Memorial University's Faculty of Medicine. Several other on-going public-private partnership programs (such as the Mind Your Health program) were designed to increase the public awareness of health issues and to continue to reinforce Newfoundland's research infrastructure.

Although there is no medical school in New Brunswick, pharmaceutical R & D spending in the province has increased significantly over the last few years. It accounted for approximately 14 percent of Atlantic Canada's research expenditures in 1998, compared to only 5 percent in 1990. An important development was the foundation of the Clinical Trials Division (CTD) in 1997, the result of a joint partnership between the provincial government, ACOA, and six multinational pharmaceu-

ticals. Part of the Atlantic Health Sciences Corporation in Saint John in Southwestern New Brunswick, the CTD was designed to help organize clinical trials research throughout the province. In the short time since its formation, R & D spending in the province has increased more than twofold, and the prospects for further investments are favorable as efforts to build integrated networks of researchers continue to be made.

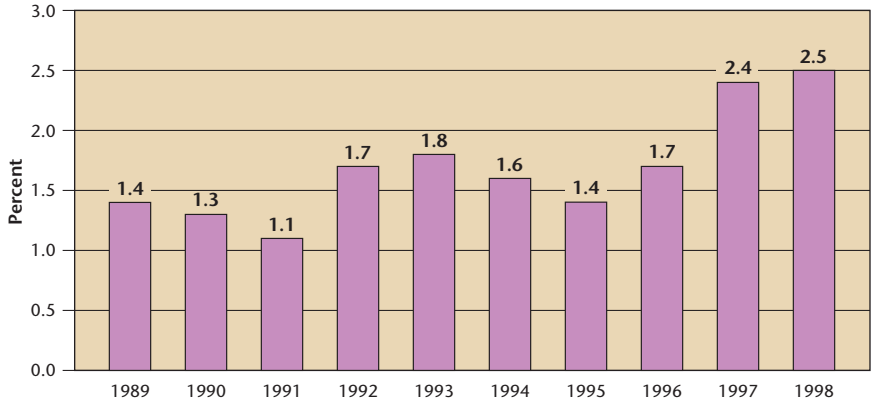
Investment in R & D in Prince Edward Island amounts to a meagre 1 percent of regional outlays. Clinical trials are carried out mainly in family practice units in association with research centres based in either New Brunswick or Nova Scotia. At present, some of the clinical trials underway in the province include treatments for asthma, stroke, diabetes, depression, and new pediatric vaccines.

In spite of Atlantic Canada's recent success in attracting more R & D investment in clinical trials from international pharmaceutical companies, in 1998 the regional share of total R & D investment by the pharmaceutical industry in Canada was rather low at 2.5 percent (see figure 19). This is exacerbated by the fact that government spending on health-care-related research, with the Medical Research Council of Canada (MRC) as the primary source of funding for basic research, steadily dwindled throughout the 1990s.

For example, R & D expenditures by the MRC in Atlantic Canada totaled $6.9 million in 1997–98 (78 percent of which went to Nova Scotia and 20 percent to Newfoundland), a decline of approximately 12 percent from 1993–94 and slightly above the 9.2 percent drop

**Figure 19**

**Share of R & D Investment in Atlantic Canada, 1989–98**




*Source:* PMPRB.

at the national level for the same period. On a per capita basis, this translates into roughly $2.90 invested per Atlantic Canadian in 1997–98, whereas the national average was significantly higher at $7.60 per person. These figures pale in comparison to government funding for basic biomedical, clinical, and health research in other G7 countries. Per capita spending in the U.S., for instance, was more than $60 in 1997–98.[85] Not only are R & D expenditures much higher in the U.S., but they have been continually rising over the course of the decade (in 1990, federal R & D expenditures in the U.S. equaled $40 per citizen).

The success of the MRC/PMAC research program has also been limited in Atlantic Canada. The goal of the partnership, which began in 1993, is to bolster the interaction between PMAC (now Rx & D) member companies and health researchers in universities, hospitals, and other research institutes across Canada by funding studentships, research chairs, operating and equipment grants, clinical trials, and other university-industry programs. Less than 2 percent of the $237 million invested in research activity during phase I of the program (i.e., from 1993 to 1999) was earmarked for Atlantic Canadian institutions.

The outlook for R & D investment in the region is expected to brighten over the next few years. As phase II of the program gets underway and the MRC is transformed into the Canadian Institutes of Health Research (CIHR), federal funding for health research should grow rapidly. In 1999 the Regional Partnership Program (RPP), initially launched in 1996 by the MRC to boost medical research funding in Saskatchewan, Manitoba, Nova Scotia, and Newfoundland, got a shot in the arm when the federal government expanded the program to include New Brunswick and Prince Edward Island. Over the next five years, an extra $8.6 million will be made available for health research grants in Atlantic Canada through the RPP.

Other opportunities to tap into more funding for medical research will multiply as more financial resources are dedicated to the CIHR's budget, the upshot of renewed investments by the federal government in innovation and research after several years of fighting the deficit. In fact, the CIHR's research funding is expected to double over the next three years, from $248 million in 1998–99 to $500 million by 2001–02. By 2004, some believe that the CIHR's budget could well surpass the $1 billion mark.[86]

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85. The Coalition for Biomedical and Health Research (see the Web site at www.cbhr.ca/trends/98-1-mrc.htm).

86. "No Tears at Wake for Research Council," *Globe and Mail*, 22 March 2000, A7.

The challenge, however, for the Atlantic provinces research institutions will be to put together multidisciplinary research projects addressing the organization's new raison d'être, which is based on the following four aims: basic biomedical research, applied clinical research, research on health care systems and services as well as social studies, and culture and the health of populations. As indicated by Dr. Howard Dickson, associate vice president for research and international relations at Dalhousie University, "The ability to develop large interdisciplinary research teams capable of studying complex medical problems from all its angles represents the future for health related R & D in the region."[87] It is the formation of these multifaceted research teams that will be crucial in securing larger group grants. So far, however, this remains a weak link in Atlantic Canada's research infrastructure because of the lack of resources needed to mobilize such groups.

That weakness could be alleviated by additional investments in local and provincial funding for medical research. With the exception of Nova Scotia, where the Dalhousie Medical Research Foundation offers $750,000 for local research activities and the newly created Nova Scotia Health Services Research Fund administers a total contribution of $200,000 per year, provincial medical research funding has had meagre pickings in Atlantic Canada, a situation that is viewed as a serious impediment to industrial development in the region.

Furthermore, as research networks are developed in each province, it will become increasingly important to create synergies at the Atlantic Canadian level in order to pool human expertise and attract larger research projects. One of the few occasions when universities, governments, and industry from all four Atlantic provinces joined forces was when they worked together to have a Genome Research Centre established in the region. The centre is to be one of five in the country that together will make up Genome Canada, a consortium of university researchers, pharmaceutical firms, agribusinesses, and several government agencies whose goal will be to overcome Canada's weaknesses in genomics R & D and make it internationally competitive in the field. Given the region's strength in microbial and comparative genomics and bioinformatics (concentrated at the NRC's Institute for Marine Biosciences), the centre will probably have a main facility in Halifax and possibly satellite facilities at UNB, UPEI, and Memorial University. With genomics now one of the main pistons

87. Interview with Dr. Dickson, 18 April 2000.

powering target discovery, validation, and compound development in the pharmaceutical and biopharmaceutical industries, the centre will enhance the region's overall research capabilities and should help attract more R & D investment.[88]

In addition to the stimulus of private pharmaceutical R & D investment and the opportunities and challenges that lie ahead for increased government funding, research tax advantages can also be a magnet for more R & D dollars. Quebec has been particularly successful in aggressively pursuing such avenues. It proposes a host of tax relief measures for R & D conducted in the province, including a fully refundable tax credit of 20 percent of wages paid in Quebec for carrying out research activity. For this reason, it is not surprising that Quebec ranks first in the Conference Board of Canada's latest provincial ratings of R & D tax incentives.[89] As for the Atlantic provinces, Newfoundland ranks second, thanks in large part to a 15 percent fully refundable Scientific Research and Experimental Development tax credit that was implemented in 1996 (the program in fact applied to R & D expenditures in the province starting in 1995). Nova Scotia, which has a similar R & D tax credit, ranks fourth in the Conference Board ratings. New Brunswick, on the other hand, which only offers a 10 percent non-refundable R & D tax credit, placed seventh, while Prince Edward Island, with no specific provisions for R & D, finished ninth.

These are all issues with an important effect on how R & D is conducted in Atlantic Canada. And yet even if universities, teaching hospitals, and other public institutions were to come increasingly involved in research projects with international pharmaceutical companies, the spillover from these projects would not fully trickle down to regional biopharmaceutical firms. For one thing, approximately 40 percent of firms are still not linked to public research institutions. And for another, only 43 percent of firms are associated or have technical partnerships with big pharmaceutical companies.

Besides developing alliances with these multinational corporations, the issue for small biopharmaceutical firms is how to secure

88. Preliminary reports estimate that the centre represents a $50 million to $100 million opportunity for the Atlantic region (see the Web site at www.atlanticgenomecentre.ca).

89. Jacek Warda, *Measuring the Attractiveness of R & D Tax Incentives: Canada and Major Industrial Countries* (December 1999). In this report, the minimum benefit-cost ratio (aka the B-index) is used to compare the relative support for private sector investment in R & D delivered through a tax system. From an international perspective, Canada offers the most attractive treatment for R & D of all G7 countries.

private capital resources to support the lengthy R & D process. Over 80 percent of all biopharmaceutical firms in the region maintain in-house laboratory facilities. Actual R & D budgets, however, vary widely across the industry and are generally considered small when benchmarked with other regions. Newer enterprises, for example, tend to reinvest a larger proportion of their sales in R & D in order to solidify their industrial position, whereas firms with an established product line dedicate more resources to marketing and distribution. Regional biopharmaceutical companies, on average, allocate only 7 percent of their sales to R & D. This is a low ratio considering that larger pharmaceuticals in Canada normally allocate 11 to 12 percent of their sales to R & D.[90] As we will see in the next section, one of the most pressing concerns facing the development of the region's biopharmaceutical industry is the lack of access to private capital.

## Venture Capital and Other Financial Resources

Investing in R & D is at the heart of new biopharmaceutical discoveries. The products they give rise to are then commercialized and companies are formed based on them, all of which involves attracting and accessing the appropriate financial resources. Historically, venture capital investment in emerging companies across Canada has lagged behind other countries such as the U.S. and the U.K.[91] This is changing, however, as total venture capital investments have increased almost sixfold since 1994, reaching $2.72 billion in 1999: approximately $500 million of that was invested in biotechnology and in the medical devices and health-related fields.[92]

As one might expect, Ontario, Quebec, and British Columbia are the focal points of these investments. In fact in 1999, 82 percent of venture capital investment was concentrated in those three provinces. Quebec has been particularly adept at fostering an entrepreneurial climate in the health and biotechnology sectors by means of specialized funding firms such as BioCapital (created by the Fonds de solidarité des travailleurs du Québec), Sofinov (a subsidiary of the Caisse de dépôt et placement du Québec), and GeneChem. The availability

90. In the U.S. and U.K., the average R & D expenditure as a percentage of sales is even higher, reaching a 15 to 20 percent ratio (Centre of Medicines Research, U.K.).

91. For further readings on this subject, see Coopers and Lybrand Consulting, *Assessment of Competitiveness of Canadian Pharmaceutical R & D* (Ottawa, 24 May 1996) (prepared for Industry Canada).

92. Statistics prepared for the Canadian Venture Capital Association by Macdonald & Associates Limited, 1999 (see the Web site at www.canadavc.com).

of venture capital in Atlantic Canada has also risen sharply. Over the 1997–99 period alone, investments have nearly tripled, rising from $22 million to $61 million. This is due in large part to the influx of new capital resulting from the creation of ACF Equity Atlantic Inc. in 1996, the region's first home-grown venture capital fund, and its $30 million endowment.

Still, despite the growing pool of venture capital, only a few firms have been successful in securing such financing. For example, while labour-sponsored funds have been a driving force behind the commercialization of academic science in other parts of the country, only a handful of Atlantic Canadian biopharmaceutical firms have been able to take advantage of the financial assistance of such funds. The first was Chitogenics of Halifax, which in early 1998 landed a $1.5 million investment from Working Ventures Canadian Fund, the largest labour-sponsored fund in the country. With the exception of this single investment, it is only in the last few months that the financial resources of other leading funds, such as the University Medical Discoveries Inc. (UMDI intervenes at the earliest stages of technology transfer), have begun to trickle down to Atlantic Canadian firms. The same can be said of the newly created venture capital funds set up by private banks to target the life sciences and health care businesses.

There are several reasons why companies are having trouble accessing these new sources of funding. In their 1997 study of selected industrial clusters in Atlantic Canada, the Nordicity Group Ltd. et al. list the following problems:[93]

- Reluctance of entrepreneurs to give up equity to obtain funding
- Entrepreneurs' lack of experience in dealing with venture capitalists
- Lack of role models and success stories
- Lack of mentors

These are all valid points and stem from the fact that the sector, which is only beginning to emerge, has yet to develop a significant and critical mass. The real problem, however, may be more elementary. Remember that in high-growth sectors, venture capitalists are

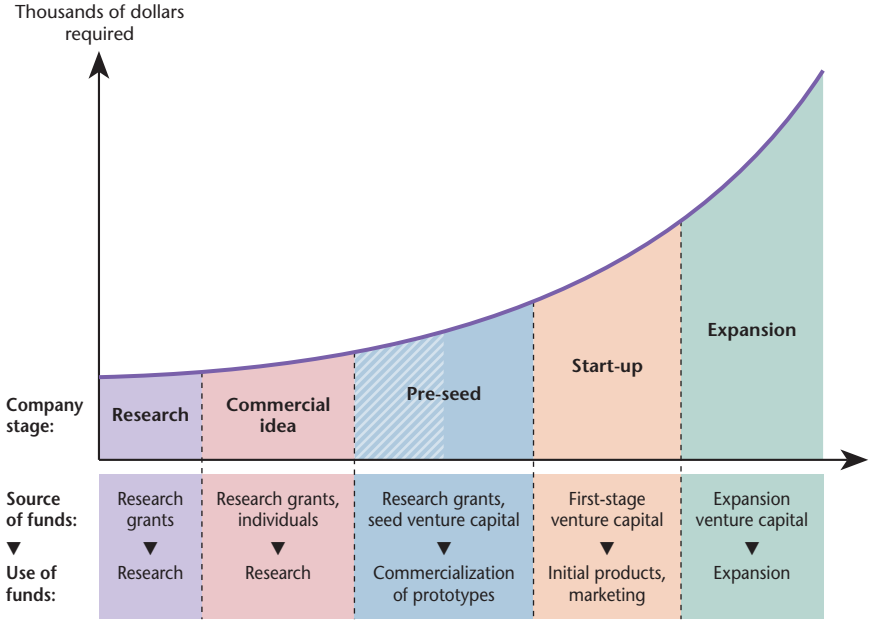
93. Nordicity Group Ltd., Syntel Consulting Inc., and Horizon Consulting Ltd., "Prospects for Growing Knowledge-based Industrial Clusters in Atlantic Canada," part 1 of *Concepts, Analysis and Recommendations* (July 1997) (prepared for the Atlantic Canada Opportunities Agency).

essentially guided by two criteria: (1) how to make money quickly and (2) how to build up a business. In more practical terms, this means tenfold returns on their investments and erecting barriers to potential competitors. In the biopharmaceutical industry, these barriers are supplied by patent protection. This, it seems, is the area where the opportunities presented by local entrepreneurs fail to satisfy the criteria of venture capitalists.

Indeed, in order to obtain patent protection with a view to attracting venture capital, a product must already be well developed and the company has to be at the somewhat advanced stage of commercialization where it is gearing up for sales and marketing efforts. As we have seen, however, from the point when a patent demand is filed to when it is issued, the endorsement process can be lengthy and expensive. In a company's growth cycle, this period coincides with the seed stage of financing (see figure 20). Before arranging start-up venture capital, biopharmaceutical entrepreneurs in Atlantic Canada require adequate funding to promote/advance a concept, further develop the initial product, and hire the necessary business personnel to help in other stages of the commercialization process.

**Figure 20**

**Stages in Company Growth and Corresponding Financing Needs**




*Source:* Adapted from Eastern Technology Seed Investment Fund's Web document.

Unfortunately, access to seed (and pre-seed) capital resources remains a problem for regional entrepreneurs and has put the brakes on the creation of new businesses.

To deal with the problem and to help realize the region's untapped scientific and commercial potential, the Medical School at Dalhousie University established its own in-house Business Development Office (BDO). Established in conjunction with the Canada Community Assistance Plan, Industry Canada, and the Greater Halifax Partnership, the BDO is a unique partnership led by a team of experienced business managers that has become particularly adept at matching new ideas and concepts with the suitable funds needed to carry out development. In just over a year, the BDO has taken four start-up companies under its wing, three of which have benefited from seed capital financing via the Eastern Technology Seed Investment Fund (ETSIF). One of the companies, NovaNeuron Inc., has also benefited from the financial support of ACF Equity, and just recently it was announced that Fusogenix will receive investment funding from UMDI.[94] To date, they are the only two regional biopharmaceutical companies to do so.

The participation of government in supporting biopharmaceutical start-ups, although difficult to measure because of the multiplicity of programs offered, has been generally positive, especially at the federal level. The Business Development Bank of Canada, for instance, has played an active role in setting up seed venture capital funds (it is one of the major financial backers of the aforementioned ETSIF).[95] The NRC, apart from its contribution to research initiatives, also helps SMEs create and adopt innovative technologies through its umbrella organizations such as the Industrial Research Assistance Program and the Canadian Technology Network (although these resources typically come into play at earlier stages of company growth).

Other agencies such as ACOA have had a considerable impact in providing public assistance for biopharmaceutical start-ups. It is estimated that since its beginnings, ACOA has financed approximately ninety private projects in the biopharmaceutical industry worth just over $17 million (73 percent of that was invested in Nova Scotia, 22 percent in Prince Edward Island, 4 percent in Newfoundland, and 1 percent in New Brunswick). In addition, the agency also supported

94. Although details are still sketchy at this time, UMDI is in the process of setting up a regional office (affiliated company) in Halifax in order to seek out new biopharmaceutical and medical investment opportunities in the region.

95. We were unable to obtain detailed information on the financial involvement of the BDC with local biopharmaceutical firms because of various issues of confidentiality.

the establishment of ACF Equity Atlantic and other pioneering ventures, including the Seabright Corporation in Newfoundland and In*NOVA*corp in Nova Scotia.

The problem with these programs, however, is that they are usually broad-based and not tailored to the specific needs of biopharmaceutical start-ups. Furthermore, the programs created by the federal government to encourage the development of knowledge-based industries have had little or no impact on the strengthening of some regional biopharmaceutical clusters. For example, support from the much-talked-about Technology Partnerships Canada (TPC) program has been insignificant in the four Atlantic provinces. TPC is a technology fund created in 1996 to support R & D and innovation in environmental, enabling, and aerospace and defense technologies, and it has so far contracted investments of $1.1 billion. Although the bulk of that money has been used to finance aerospace and defense initiatives, almost $340 million has been invested in enabling technologies. From September 1999 to April 2000, biopharmaceutical projects alone received $140 million from the fund. These projects, however, were earmarked for firms in Quebec and Ontario. TPC investments in Atlantic Canada have been limited to 1.5 percent of total funding and have supported the creation of about 330 jobs in the region (in contrast to the more than 23,230 jobs created or maintained by the program elsewhere in the country).

As for provincial government strategies (apart from general programs helping start-up firms get off the ground), Nova Scotia, through In*NOVA*corp and its Life Sciences Industry Partnership (LSIP), is spearheading proactive policy initiatives targeting the biopharmaceutical and other life sciences sectors. Designed as a public-private partnership to assist in the development of life sciences opportunities by offering a variety of business services (i.e., incubation, partnering facilitation, etc.), In*NOVA*corp also provides early-stage equity financing via the Nova Scotia First Fund. Thus far, 33 percent of In*NOVA*corp's investments (totaling about $2 million) have been in life sciences companies.[96] Though modest in comparison to other resources, In*NOVA*corp supplies the necessary investment that allows entrepreneurs to continue developing their products and services and to strengthen their companies by attracting more investment dollars from other sources, including other venture capitalists, chartered banks, etc.

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96. In*NOVA*corp, "The Power of Innovation," in *Annual Report, 1998–99*.

## Human Resources Development

The expansion of the biopharmaceutical industry in Atlantic Canada also depends on its capacity to attract, develop, and retain people with the necessary skills at all levels of the industry. This means access to both scientific/technical personnel as well as experienced management personnel to help, among other things, in the marketing, manufacturing, financing, patenting, and regulatory processes.

So far, it has been rather difficult to get a comprehensive picture of the dynamics at work in the employment structure of the regional biopharmaceutical industry. This is largely due to the lack of in-depth information and data on the development of the workforce in public research institutes, universities, teaching hospitals, and relevant provincial government departments. The picture has also been blurred by the growing linkages between public and private organizations and the sometimes overlapping duties of researchers backed by both types of institutions.

Therefore, our assessment of the expansion of the regional biopharmaceutical industry relates mostly to private sector business development and is based on a combination of three different data sources: company directories published by Contact Canada (i.e., *Diagnostics Canada Directory, Canadian Biotechnology Directory and Pharma, and Biopharma and Nutraceuticals Canada Directory*), Industry Canada's *Canadian Company Capabilities* database, and information from Canada's Research-Based Pharmaceutical Companies (which is based on an annual survey of member companies). And to refine the accuracy of the database, information from stand-alone corporate statistics was included when available.

In 1997–98, the biopharmaceutical industry in Atlantic Canada employed just over 1,250 people. Of that number, approximately 815 were directly employed by regional biopharmaceutical firms, while the remaining 438 worked for large pharmaceutical companies headquartered outside the region and predominantly engaged in marketing and sales functions. Although it is impossible to determine exactly how many people were employed in manufacturing and production or in sales, marketing, and distribution because of the varied tasks performed by each worker in many of the smaller integrated companies, we know that 361 people were involved in R & D activity.

More than half of the total biopharmaceutical workforce is in Nova Scotia: 698 employees in all (247 in R & D), most of them in and around the Halifax-Dartmouth area (see map 2). In New Brunswick, some 200 jobs (43 in R & D) are scattered around the cities of Fredericton, Moncton, and Saint John. Prince Edward Island accounts for 182 positions (32 in R & D), and all are in the vicinity of Charlottetown — by itself, DCL employs over 80 percent of the Island's biopharmaceutical workforce. In Newfoundland, there are 172 workers in the biopharmaceutical industry, and most are located in the St. John's area (see box 4 for an estimate of the industry's economic impact).

**Box 4**

**Estimating the Value of Economic Activity Generated by the Biopharmaceutical Industry in Atlantic Canada**

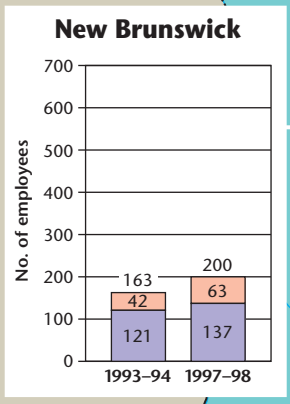
In economics, the concept of value-added is often used to measure economic activity in a specific industry. In short, it estimates net output by adding the market value of goods and services produced and subtracting the value of the purchased inputs (cost of materials, supplies, etc.) used in the production process.

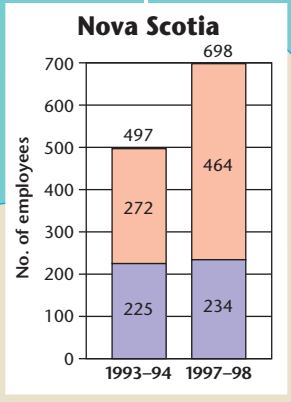
Using Statistics Canada's employment value-added contribution estimates, we are able to calculate the approximate output of the biopharmaceutical industry in the Atlantic provinces. The reader should remember, however, that this is only a gross estimate of the industry's economic impact. The data used to compute the value-added coefficients are based on the outdated 1980 Standard Industrial Classification of the pharmaceutical and medicine industry (SIC 3741, the closest proxy available), which, as we know, is too constraining for biopharmaceuticals. Furthermore, when a province or territory has only a few producers in an industry class (as is the case in Atlantic Canada), detailed statistics cannot be published for reasons of confidentiality; the real value of the industry is therefore unknown.

None the less, by combining provincial and national estimates of total value-added for biopharmaceuticals, the industry in 1997–98 injected approximately $160 million into the economy of the Atlantic provinces. Similarly, total wages and salaries paid out in the region totaled more than $51 million.

## Map 2

## Pockets of Employment Distribution and Provincial Employment Growth in the Biopharmaceutical Industry in Atlantic Canada, 1993–94 and 1997–98

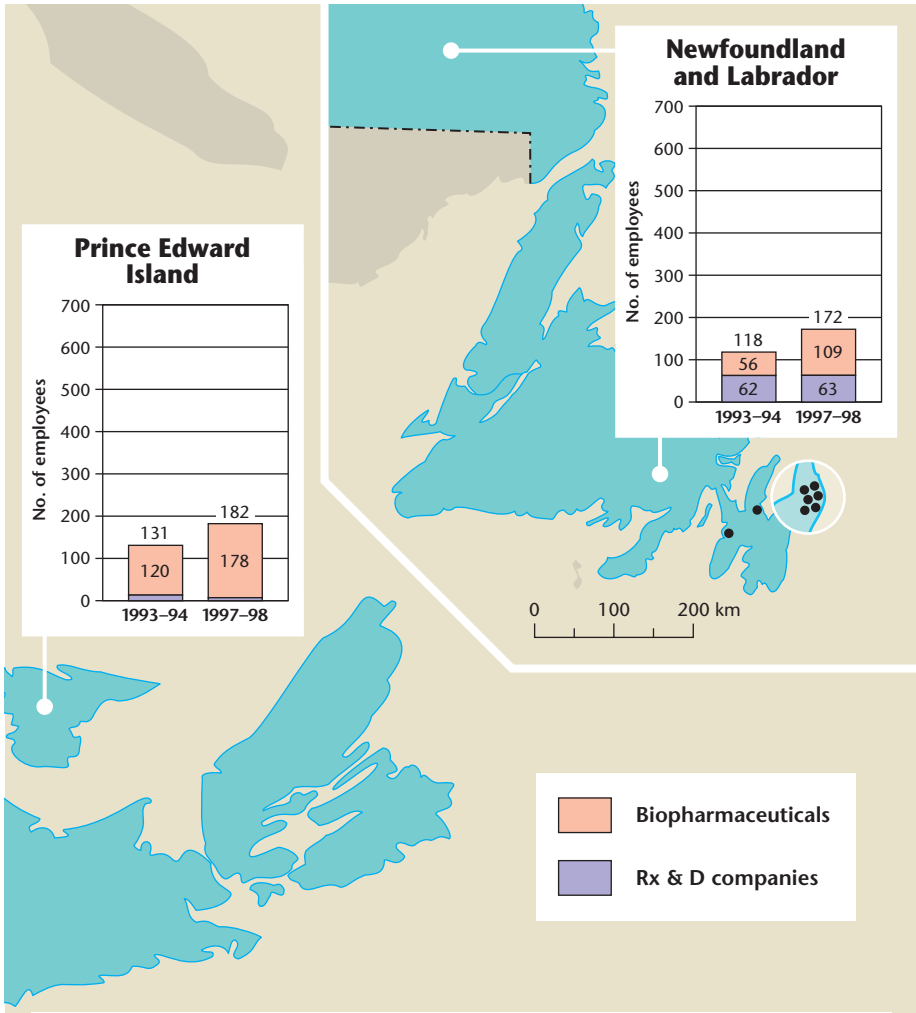



0 100 200 km

*Source*: Ibid.

Map by Mathieu Breau and Raymond Thériault, 2000.




## Average Annual Compound Growth Rates (from 1993–94 to 1997–98)

| | Total Employment (%) | Regional Bioph. Companies (%) | Rx & D Companies (%) | Overall R & D Positions (%) |
|---|---|---|---|---|
| Nova Scotia | 7.0 | 11.3 | 0.8 | 13.2 |
| New Brunswick | 4.2 | 8.5 | 2.5 | 12.4 |
| Prince Edward Island | 6.8 | 8.2 | -63.6 | 10.9 |
| Newfoundland | 7.8 | 14.2 | 0.3 | 11.1 |
| Atlantic Canada | 6.6 | 10.7 | 0.9 | 12.6 |

From 1993–94 to 1997–98, employment grew, on average, roughly 6.6 percent annually, resulting in the creation of almost 350 jobs in the biopharmaceutical sector in the four Atlantic provinces. This is quite considerable given that on the whole, the region's economy over the same period generated average annual employment growth of only 0.8 percent. What is even more impressive is that 95 percent of the jobs were created by regional biopharmaceutical firms. In fact, whereas the number of local positions generated by larger pharmaceutical companies with head offices outside the region has stagnated, regional companies have been churning out new jobs at the rapid pace of 11 percent, on average, per year (see corresponding table in map 2). The top performers in the region are Nova Scotia and Newfoundland, which are hotbeds of biopharmaceutical employment growth: the provinces' medical schools are the sources for vital R & D, and they supply a constant stream of highly trained scientific personnel.

Generally speaking, providing qualified scientific and technical personnel in the region has not been a problem thus far because of its strong academic infrastructure, which is able to train for and support basic and applied research activities. Recall that, in 1996, Atlantic Canada's twenty universities granted in excess of 2,050 degrees in fields pertinent to the biopharmaceutical industry, including biology, chemistry, medical studies and research, veterinary medicine, pharmacy, nursing, and other disciplines.[97] Roughly 11 percent of those were M.Sc. or Ph.D. degrees, which are preferred by companies with a strong emphasis on R & D.

Despite this seemingly large pool of skilled workers, however, there are two major concerns in the medium term concerning the demand for scientific personnel. The first deals with the scientific backgrounds required by the industry. As the knowledge surrounding biopharmaceuticals continues its rapid advance, companies are increasingly looking for graduates at the cutting edge of emerging fields who have already acquired experience in interdisciplinary research teams. Combinations between computer-based expertise such as bioinformatics or molecular modeling and up-and-coming disciplines such as genetics and gene therapy will become more and more valuable as firms deal with the integration of the more traditional sciences and the emerging information sciences.[98]

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97. Statistics Canada (1998), cat. no. 81–229.

98. Canada, Human Resources Development Canada, *Building Long-Term Capability Now: Canadian Human Resources Study in Biotechnology* (May 1996).

The second concern is attracting and then retaining a highly skilled workforce — those Ph.D.'s and postdoctoral fellows conducting world-class research who are most likely to initiate biopharmaceutical start-ups. The BDO at Dalhousie University's Medical School, for instance, reports that it takes an average of no less than nine to twelve months to recruit a postdoctoral researcher. And although it is difficult to track the interprovincial movements of scientific researchers, they along with other industry executives suggest that the distant lure of rich employment packages, lower income taxes, and better training and opportunities for career development is making it more difficult for Atlantic Canada to compete. Many of the bright, young scientific minds and potential entrepreneurs are leaving the region for better prospects in other parts of the country (i.e., Ontario, Alberta, and Quebec) or even in foreign markets such as the U.S. An analysis of Canada's genetic research community, for instance, revealed that the net out-migration of talent resulted in the loss of 30 percent of its star researchers (presumably most went to the U.S.). [99]

In some instances, entire companies pack up and relocate elsewhere; one example is Acta-Med Inc. This state-of-the-art CRO in ethical phytopharmaceuticals, which at present has a staff of approximately sixteen — a figure that is expected to triple by the end of the year — just recently shifted its operations from Fredericton to Montreal. Among the several reasons that prompted the move, two stand out: the availability of an experienced workforce at the forefront of emerging fields and, as we saw previously, a provincial tax climate that more aggressively encourages R & D investment.

The issue of the brain drain has lately begun to attract attention again in Canadian media circles, and government policy makers are under increasing pressure to take action to stem the loss of key talent throughout the knowledge-based industries. Policies to improve the regulatory framework, enhance the educational system, boost the research infrastructure, and reform the tax structure were some of the recommendations submitted to the House of Commons Standing Committee on Industry in February 2000 by the Coalition for Biomedical and Health Research.[100] It is hoped that the government's

99. Lynne Zucker and Michael Darby, "Star Scientists and Institutional Transformation: Patterns of Invention and Innovation in the Formation of the Biotechnology Industry," in *Proceedings of the National Academy of Sciences* (November 1996), 12709–12716.

100. "Canada's Biotechnology Preparedness: Encouraging Risk and Rewarding Success" (Brief submitted to the House of Commons Standing Committee on Industry by the Coalition for Biomedical and Health Research, Ottawa, 22 February 2000).

commitment to rejuvenate the CIHR and strengthen federal funding for health research will help retain some of our best scientists, both in Atlantic Canada and in other parts of the country.

Not only does the industry require strong scientific and technical capacity, it also needs skilled business managers. In fact, according to several industry leaders, the Achilles heel of Atlantic Canada's human resources program is the lack of management expertise for such knowledge-based industries. This was first underscored in a 1997 study of the region's biotechnology sector. In its report, Bicon Consulting states, "(…) there is a shortage of entrepreneurial science managers with the ability to raise capital, put together a business plan and build a company."[101] Given that the regional biopharmaceutical industry is still very young, it is understandable that such resources are limited. What is troublesome, however, is the fact that as the industry continues to grow over the next few years, the shortage of highly qualified managers is also expected to grow, thereby exacerbating the problem.

This was also echoed at the national level when the National Biotechnology Advisory Committee (NBAC) reported that "Canada has a serious lack of programs to nurture the management skills, such as product development, strategic alliance management, international regulation and technology transfer."[102] To reverse that trend, it recommends that in the longer term, industry and government work together with universities and business schools to design programs allowing industry executives to develop such talents. In Atlantic Canada, this has been the impetus for the creation of such organizations as the Genesis Centre at Memorial University in St. John's. Using a novel approach to team up entrepreneurs with experienced knowledge-based industry mentors, the centre focuses on facilitating the learning of successful business skills. Since its inauguration in 1997, the centre has graduated mostly information technology firms, but it is currently coaching a health-related software developer and an innovative, research-based dental/medical device manufacturer.

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101. Bicon Consulting Associates, *Opportunities for Biotechnology-based Business in Atlantic Canada*. Report prepared for the Atlantic Agri-Products Competiveness Council and the Atlantic Canada Opportunities Agency (January 1997), 4.
102. NBAC. *Sixth Report 1998: Leading in the Next Millennium*. Ottawa: Industry Canada, 1998, 14.

# Conclusion

In this study we have sought to explore the organization and development of the pharmaceutical and biopharmaceutical industry from a regional point of view. As we have seen, although large multinational companies are at the forefront of the biopharmaceutical industry, its value chain is changing. For instance, outsourcing or subcontracting of specific operations is now more common and allows smaller businesses to seize new opportunities. Biotechnologies have revolutionized traditional processes in the health and pharmaceutical fields, and at the same time they have also opened up various potential niches for small firms using these innovative technologies.

We have also seen that Canada is particularly well suited to take advantage of such opportunities, and that the momentum of biopharmaceutical activity in the four Atlantic provinces is gaining. Indeed, there is no doubt that clusters of industrial biopharmaceutical activity are beginning to take shape in Atlantic Canada. Over the last ten years, new biopharmaceutical companies in the Atlantic region have been springing up at an average annual rate of 10 percent, an astonishing rate of growth. Today, the region has fifty or so biopharmaceutical firms, a little over 5 percent of all such companies in Canada. This is quite impressive considering that since 1990, the number of regional biopharmaceutical firms has almost tripled. Without a doubt, the principal catalyst behind the industry's growth has been the emergence of biotechnologies and their multiple applications — more than 60 percent of regional firms rely on biotechnology-based activities. These companies are involved in the production of a wide array of nutraceuticals and other therapeutic products, as well as diagnostics, vaccines, and other biological products. In addition to company start-ups, the industry's vitality is also reflected in an impressive rate of employment growth. From 1993–94 to 1997–98, the sector has generated jobs at an average annual rate of nearly 7 percent, for a total of 350 net-new jobs across the four Atlantic provinces. Even more remarkable has been the corresponding 13 percent growth of R & D positions in the region.

Still, the regional biopharmaceutical industry remains somewhat fragmented and small. Almost half of the firms reported sales of less than $1 million and employed fewer than ten people. Furthermore, with companies providing very specialized products targeting niche markets at the international level, interfirm cooperation is negligible as each strives to develop its own channels and networks. By the same token, domestic rivalry between firms (rivalry encourages innovation and competitiveness) is limited.

The industry is also unevenly dispersed throughout the Atlantic region. By far the largest cluster of biopharmaceutical activity is located in the Halifax-Dartmouth area of Nova Scotia. Here, the several universities and federal research institutes provide an important backdrop for a significant pool of intellectual resources, a vital component of the industry. Smaller pockets of biopharmaceutical companies are also emerging in the St. John's area of Newfoundland, Charlottetown in Prince Edward Island, and in Fredericton, Moncton, and Saint John in New Brunswick.

None the less, these geographic concentrations or zones of industrial clustering are the focal points for investments in biopharmaceuticals, both private and public, and as such are the centres of initiative for building and upgrading the conditions needed to successfully expand the regional industry. It is clear that they are the impulse behind the underlying momentum in Atlantic Canada's biopharmaceutical industry.

From a public policy perspective, we can draw on the "diamond" analysis introduced at the end of chapter two in order to outline potential government strategies. It is important to bear in mind that the role of government is to amplify the "forces" within the diamond. Innovative industries, such as the biopharmaceutical industry, also require sustained investment in terms of both capital and human resources. Hence, the policy mix to help foster the development of the biopharmaceutical industry in Atlantic Canada must be wide-ranging, and not solely focus on attracting foreign investments via short-term cost advantages. Although it is important to be competitive from a cost-efficiency perspective, it is essential to promote the growth of local clusters. And it is during the early stages of industrial development that government intervention to stimulate *factor creation* is most efficient.[103]

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103. Michael Porter, *The Competitive Advantage of Nations* (New York: The Free Press, 1990).

One of the first steps is for governments to recognize the important socio-economic potential of regional biopharmaceutical developments, identify the sector as a priority area, and establish strategic industrial policies to foster its growth. Such policies could be adopted as part of a wider framework encompassing other sectors of biotechnological applications or knowledge-based activities. The government of Quebec, which first targeted the biotechnology sector in the 1980s, offers a good example of how sound industrial and science-technology policy can encourage the development of innovative industries. So far, at the provincial level (apart from Nova Scotia, which as we have seen, has promoted a series of government initiatives to raise the profile of its life sciences industry), the Atlantic provinces have been rather slow in introducing policies geared towards developing the biopharmaceutical industry.

It is also important that the federal government take the lead in establishing policies to create conditions conducive to a dynamic regional biopharmaceutical industry. To that end, the Atlantic Investment Partnership initiative has recently been undertaken. Although complete details of the program are not yet known, it is expected to include a $300 million Atlantic Investment Fund (AIF) designed to develop the region's knowledge-based economy and to build up its innovative capacity. The development and guidance of this fund are to be overseen by the ACOA, thereby making it one of the potentially leading biopharmaceutical industry champions in the region. To achieve that status, however, it will need to strengthen its focus on the biopharmaceutical sector as an industrial axis throughout the Atlantic provinces.

For example, ACOA could address the difficulties encountered by regional biopharmaceutical entrepreneurs in securing venture capital funding, more specifically their inability to attract the seed (and pre-seed) capital required to promote and advance an initial concept. To a large degree, this reflects the inexperience of entrepreneurs in dealing with venture capitalists — that is, their lack of necessary business skills required to put together and sell a promising idea to potential investors. To counter this, ACOA should bolster its assistance to commercialization and technology transfer agencies already in place in most universities, making sure they receive adequate funding to offer the proper administrative support needed to structure and package biopharmaceutical deals.

More funds should also be allocated to these organizations to pursue such avenues as patent protection filing, which can be a very lengthy and expensive process but is also crucial to the success of biopharmaceutical firms. Indeed, just as it is essential for emerging companies to have ready access to adequate financial resources in order to fund their growth, so patent protection can be indispensible if new entrepreneurs are to secure the necessary investments to develop a product. Patents, it will be recalled, convey confidence in the eyes of investors.

Securing intellectual property through greater patent protection is one way to improve access to seed and venture capital. Another way would be to realign policies within the existing framework of funding and support programs offered by federal agencies towards more knowledge-based industries and to develop initiatives that would help fill the void at the seed-capital level. In Quebec, for example, $T^2C^2$ was recently set up by the Business Development Bank of Canada, Sofinov, and other partners as a technology development firm supporting the emergence and start-up of new health sciences companies. Although beyond the scope of this study, further investigation of such successful undertakings focusing on the biopharmaceutical industry could be beneficial in serving as a guide to developing similar regional efforts.

Reinforcing the regional scientific infrastructure is another key element in fostering the development of the biopharmaceutical sector, as well as other innovative industries, throughout Atlantic Canada. The NRC will no doubt be a catalyst in this regard. Already, the Atlantic Investment Partnership has earmarked roughly $110 million for the expansion of its facilities in the region.[104] And in an effort to promote the commercialization of new technologies, it also plans to set up an incubation facility in Halifax, which will house ten to twelve start-up companies. This is especially good news for the already thriving Halifax biopharmaceutical cluster, but efforts must also be channeled to other focal points in Atlantic Canada so that the region can develop an integrated web of clusters.

There is also a real need for greater regional coordination of biopharmaceutical activity (policies, networking, etc.). For instance, provincial industry associations have helped weave closer ties between local, national, and international organizations in their respective

104. "Prime Minister Announces New Atlantic Investment Partnership" (NRC press release, Ottawa, 29 June 2000).

jurisdictions, but efforts to do so at a regional level have been modest. This is one area where ACOA, which has a mandate to work together with all four Atlantic provinces, could play an important role in implementing greater regional cooperation by working in conjunction with the provincial biotechnology industry associations — particularly with regard to the identification and promotion of the region's education infrastructure, research capabilities, and common promotional activities so as to develop the biopharmaceutical industry.

There is also a need for increased cooperation between research organizations, medical and veterinary schools, and business development and technology transfer agencies, both at the provincial and regional levels. Too often, these groups fail to work closely enough with one another, and at times even appear to be competing on the same initiatives. Similarly, as research networks are developed in each province, emphasis should be placed on creating synergies at the Atlantic Canadian level to pool human resources expertise and attract larger research projects. This could be achieved, for example, by developing *virtual networks* using the region's advanced telecommunications capabilities to link various organizations across the region. The common purpose that brought together governments, universities, and key industry players to found a Genome Research Centre in Atlantic Canada is a good example of better regional collaboration. With each province building on its strengths and expertise and as genome research itself becomes one of the driving forces behind biopharmaceutical development, the centre will contribute significantly to the region's research infrastructure and should help attract more R & D investment to Atlantic Canada.

Furthermore, because universities are excellent breeding grounds for biopharmaceutical start-ups, it is also important to continue developing alliances and partnerships between private and public sector institutions. Recent trends in R & D expenditures in the health field point to the business sector as an increasingly significant source of funding. Accordingly, universities must have the flexibility to adjust to the specialized needs of the industry. For example, research projects such as the ICONS study on cardiovascular disease in Nova Scotia could serve as a model for other similar public-private partnerships.

Universities will also have to assemble multidisciplinary research teams if they are to attract more R & D investments from federal government funds, such as the newly created CIHR. Again, this could be achieved by developing stronger research ties between universities in the region, possibly even creating interuniversity research teams

that combine the strengths of each of the players and are capable of tackling all dimensions of the complex issues in health research (from basic and clinical research to the societal and cultural dimensions of health). Resources should therefore be allocated to ensure the mobilization of such teams. Increased support of provincial medical research funds as well as the establishment of biopharmaceutical research funds could also help to bolster the region's R & D framework and attract outside companies and researchers. Finally, encouragement of research activity within firms can also be achieved by creating an overall friendlier R & D climate with various tax incentives (as is being done in Quebec).

Governments also influence *demand conditions* by regulating both intellectual property rules and product standards. In the eyes of domestic biopharmaceutical producers and large multinational pharmaceuticals, it is important that patent protection in Canada provide the same support to commercialization as it does in other leading countries. Equally important to nurturing a competitive environment are the stringent standards and quality assurance measures governing new products. The key, however, is that regulatory approval times be both rapid and efficient. Again, because international benchmarking shows that Canada continues to lag behind its major trading partners in this area, it is important that sufficient resources be allocated to solve the problem.

The same is true at the provincial level, where each government has the power to regulate drug formularies. The timeliness with which a new product is added to a drug formulary is a decisive factor in attracting pharmaceutical R & D investments to individual provinces. With the rising cost and complexity of new biopharmaceutical drugs, the review process is becoming more expensive and burdensome for provincial governments. So why does the region maintain four different drug programs (one for each province) for a relatively small population? Atlantic Canadian provinces should consider consolidating some of their programs instead of allowing interprovincial disparities in approval times to continue to grow. The issue was recently addressed by all four Atlantic premiers at the inaugural meeting of the newly established Council of Atlantic Premiers. In an attempt to bolster cooperation among the provinces, the premiers agreed to explore the possibility of a common regional process for new drug approvals. While this signals the start of a new round of consultations between provincial health officials, it is important that decision makers review some earlier recommendations and work together to

come up with a detailed cost-benefit analysis of potential changes to provincial drug formularies, such as the:

- "establishment of reciprocal product review and approval criteria, permitting the provinces to share the burden of new product evaluations, leading to a single product application review within the region, as opposed to four separate reviews. Sharing of the product review workload would not obligate any province to accept a new product for its benefits list of formulary;
- establishment of a common formulary for all four Atlantic provinces would further consolidate the provincial drug benefit programs, yielding additional administrative cost benefits and further streamlining the approvals process for pharmaceutical manufacturers. The logical extension of this concept would be the establishment of a common drug benefit program for all four provinces in the region; and,
- provision of preferential access to provincial/regional benefits lists and formularies for new products for which threshold levels of investment have been made in the development and/or manufacturing of the product in Atlantic Canada."[105]

These are all elements that can energize the process of creating advanced and specialized factors. Eventually, the aim is to develop a critical mass of companies and related technical infrastructure across the region that will be self-supporting. Clusters with specialized expertise can be created by both regional industrial and science/technology policy, and they in turn will become magnets that will attract other companies and promote the development of new business. Although the process has started, it will take time and a concerted effort by all parties concerned before a competitive biopharmaceutical industry can be established in Atlantic Canada.

105. Price Waterhouse, *A Study of the Pharmaceutical Industry in Atlantic Canada* (November 1993) (prepared for the Atlantic Canada Opportunities Agency), 109.

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# List of Tables

# List of Figures

# List of Maps