# Unpacking the Pharma Biotech Engines

## How the leading pharmaceutical corporations are driving the biotech agenda

A Polaris Institute report
Prepared by Brenda Inouye

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Polaris Institute
312 rue Cooper Street, Ottawa ON K2P 0G7 Tel: (613) 237-1717 Fax: (613) 237-3359
e-mail/courriel: polarisinstitute@on.aibn.com www.polarisinstitute.org

## About this paper

This paper is a background paper to *Galloping Gene Giants; How big corporations are re-organizing their push for a biotech future and what can be done to challenge this agenda* (prepared by Tony Clarke with Brenda Inouye, February 2002). This paper is meant to be a tool for anti-biotech activists. It will hopefully be an informative introduction to the leading pharmaceutical corporations and how they are using biotech to advance their overall agenda. These leading corporations are what we refer to as the pharma biotech engines. The main sections of this paper are:

- A brief overview of why the leading pharmaceutical corporations have become key players in the biotech industry and the reasons people have begun to resist
- An introduction to the top pharmaceutical corporations and why they are so economically wealthy and politically influential
- The ways the top pharmaceutical corporations have incorporated biotech into their overall agendas, mainly in terms of key partners and technologies

The information in these sections is presented critically, and is intended to provide a strong rationale for why people should challenge and resist the pharma biotech engines.

This paper is one of a series of three background papers to *Galloping Gene Giants*. The other two papers focus on the biotech activities of: 1) the leading seed and agrochemical corporations and; 2) the leading food processing corporations. These papers will be supplemented with other tools such as fact sheets and corporate profiles to help anti-biotech activists develop campaigns that directly target the biotech engines. All of these resources will be available on our website www.polarisinstitute.org.

This paper, as well as the other resources mentioned above are part of the Polaris Institute's program 'Gearing up for the Biotech Century,' through which we will be working with various social justice networks concerned about issues related to genetic engineering, particularly the controlling corporate forces. We hope that our work will contribute to the larger Biojustice movement – one that will build upon various struggles.

## Acknowledgements

I would like to acknowledge the work and help of Colleen Fuller who contributed assistance in information, analysis and guidance to this work in its later stages. I would also like to stress the importance of ongoing struggles of indigenous rights groups, the disability rights movement, work of researchers and activists involved with patient rights campaigns and voices for academic freedom, which have all been essential contributions to this paper.

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# Introduction

The top pharmaceutical corporations in the world experience the highest profit margins amongst all industries. Profits have been largely driven by their patented $1 billion plus blockbuster drugs, which are meant to treat conditions more common in the industrialized North, like high cholesterol and ulcers. At the same time, the discovery of new blockbuster has slowed down and the patents on many of today's blockbusters are soon to expire. The top pharmaceutical corporations, or Big Pharma, are frantically looking for new ways to continue generating the kind of profits they've gotten used to. Shifting a greater focus to biotech is one of the solutions. While this is not a sudden decision, as genetically engineered (GE) drugs have been on the market since the early 1980s and leading pharmaceutical corporations such as Johnson & Johnson, Roche, Novartis and Bristol-Myers Squibb have invested billions into biotech research and development since the 1970s, biotech is quickly making head way within the pharmaceuticals industry. The top pharmaceutical corporations turned biotech engines are what we refer to as the pharma biotech engines – those entities with the economic wealth and political influence to drive biotech drugs forward. Pharma biotech itself refers to the use of biotech within pharmaceuticals.

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Already the pharma biotech engines and smaller biotech companies have released over 130 GE drugs on to the market and have many more in the pipeline. A few of these drugs have gained blockbuster status, including Eli Lilly and Novo Nordisk's recombinant/GE insulin. The pharma biotech engines have been aggressively pushing ahead with biotech. In terms of actual technologies, the engines have begun with developing GE proteins, such as GE insulin, marketing them as 'natural' versions of human proteins, and are moving towards such technologies as gene therapy and xenotransplantation, foreseeing markets worth tens of billions.

The pharma biotech engines are being strategic about how they promote biotech. Much of this strategizing is based on how the popular resistance against GE foods has shed a negative light on the agribusiness and food sectors. According to the SmithKline Beecham Science and Technology Officer in a 1999 article from *Financial Times* in 1999,

> *The negative image projected by the biotechnology industry in handling the genetically modified food debate will become a classic future business school study of ineptitude in public communication.*[1]

The biggest flaw in the early promotion of GE crops and foods, according to industry, was that there was not enough emphasis on 'consumer' benefits. Instead, leading seed and agrochemical corporations (e.g. Monsanto and DuPont) were promoting products like GE herbicide resistant seeds to farmers. Anti-biotech activists criticized the agribusiness industry for releasing products that would only further their agrochemical sales. Now most of the agro biotech industry's advertising, which appears in mainstream media, is focused on the messages that GE will 'feed the hungry' and 'improve nutritional value.' Meanwhile, to boost overall public confidence in biotech, public relations campaigns developed by the biotech industry are focused on compelling messages about the 'life saving' potential of biotech in medicine.

Pharmaceutical corporations are saying that GE drugs and therapies have 'cancer fighting' and 'disease preventing' potential. But, what are the realities behind these messages? Should they by challenged? Have people already begun to challenge them? If so, why?

## Reasons for Resistance

There are struggles that already exist in reaction to the pharma biotech industry, many of them have emerged from the exploitive history of the pharmaceuticals industry. The commercial applications of biotech have, in many ways, exacerbated the violations of the pharmaceuticals industry. The following are some of the main reasons for resistance against pharma biotech:

- **Biopiracy**
- **Ableism**
- **Unsafe drugs**
- **Expensive research and development**
- **University-Industrial complex**
- **Genetic pollution**

**Biopiracy:** The pharma biotech industry is on the hunt for 'rare' genes for genetic drugs and therapies. The most commercially attractive gene pools are in isolated population groups, such as certain indigenous communities. Many indigenous peoples have already been targeted by the pharma biotech industry. In the early 1990s Atencio Lopez began an international campaign against the stealing of genes from indigenous peoples. Atencio is an indigenous leader from the Kuna, or Dule, people of Kuna Yala or Dulenega Region, also known as Panama. Part of the campaign involved fighting the patenting of the cells by the U.S. government, of a Ngobe-Bugle, or Guaymi, woman. The Ngobe-Bugle people carry a virus (HLV2) similar to HIV, yet they do not develop the illnesses associated with the virus because they carry antibodies to protect them. The patented cells were part of the cell line infected with this virus. The cells are therefore of great interest to drug corporations for the development of AIDS drugs. While the patent for the cells was canceled by the U.S. government because of international pressure, cells from the Ngobe-Bugle woman, as well as cells from indigenous people from Papua New Guinea (for which the patents were also withdrawn due to pressure) and the Solomon Islands were still being kept in a U.S. laboratory as of 1997.[2]

The pharmaceuticals industry is on the hunt for 'rare' genes for genetic drugs and therapies. The most commercially attractive gene pools are in isolated population groups, such as certain indigenous communities.

**Ableism**: The biotech industry says that genetic technologies will help screen out and treat genetic 'defects.' Of course this message is based on a larger societal failure to accept and integrate people with disabilities. Discrimination against people with disabilities is not new. This is apparent through the development of certain technologies and the acceptance of them. For example, a test for detecting Down's syndrome during a woman's pregnancy has been around for about 40 years. Meanwhile, people with Down's syndrome did not ask that this test be developed.[3] Many people involved in the disability rights movement have been outspoken against genetic technologies that only increase discrimination against

people with disabilities. According to Dr. Gregor Wolbring, research scientist at the Department of Biochemistry and Molecular Biology, Faculty of Medicine, University of Calgary and founder of The International Center for Bioethics, Culture and Disability (http://www.bioethicsanddisability.org),

> *Disability is a social justice concept, the same as sexism (or) racism…Normal is a lack of variation. There is no such thing as normal. Normal is set up by a certain amount of people who have the power to decide, to define norms. It's the opposite of diversity because you have to adhere to that norm.*[4]

Disability rights activists demand that people living with disabilities be valued, and their lives improved through social access and acceptance rather than screened and 'fixed' out of existence.

**Unsafe drugs:** There have already been serious questions raised about the safety of GE drugs. In 2002, the Society for Diabetic Rights made a public demand that Health Canada make insulin from pork and beef more widely available. This demand was made because GE insulin has caused fatal and serious adverse reactions in diabetics. Since its release onto the market in 1982 in the U.S and 1983 in Canada, governments and drug corporations have made it difficult to obtain animal insulin, which had been proven safe and effective over 70 years of use. As of January 2001, Health Canada had received 465 reports of adverse reactions, which included 8 deaths, linked to GE insulin. In the U.S., there have been 92 reported deaths and 4,000 reports of adverse reactions linked to the drug. In comparison, only 9 diabetics reported adverse reactions to pork insulin, and none to beef.[5] Patient rights groups, like the Society for Diabetic Rights, are demanding for access to safe drugs, and in turn for a rigorous regulatory system and independent testing of products.

**Expensive research and development**: Sharon Batt, co-founder of Breast Cancer Action Montreal, has raised concerns about the costs of GE drugs. Investments in the development of GE drugs, not to mention the bulky marketing costs, are limiting access to drugs. Roche's Herceptin, a GE drug for metastatic breast cancer, costs Canadian patients $(CAD) 16,000 for a 6-month period. Roche has made no effort to make the drug more accessible to women with advanced breast cancer in Canada. Instead, the corporation has suggested that it is the responsibility of provincial governments to subsidize costs for treatments. (While the Ontario and British Columbia governments cover Herceptin under medicare, other provinces have not because of the adverse effects, such as cardiac dysfunction, it causes in patients). Furthermore, some patients' rights groups are asking if these new drugs are even necessary, and point out that the focus of the drug industry should be on making existing essential drugs (proven safe through use over many years) accessible. Some also argue that the billions of research and development dollars spent on GE technologies, should be spent on prevention. Batt argues,

> *feminist discourse about breast cancer and genetics has concentrated on the ... reductionist emphasis on genetics to the exclusion of environmental triggers – as the basis of cancer*.[6]

**University-Industrial complex:** Mainly through public-private partnerships, universities have been key players in the biotech industry's development. Some university professors and researchers have risked their jobs by speaking out on the conflicts of interest that are inherent in partnerships between the private sector and universities. More have remained silent. Academic freedom and independent research are becoming increasingly obsolete as labs receive more and more funding from companies. As a result, universities' roles move further and further away from providing services to the community.

**Genetic pollution:** Already, concerns have been raised about increased levels of drug compounds being released into the environment. According to Health Canada, traces of antibiotics, estrogen (from contraceptive pills) and compounds from antidepressant drugs have been found in Canada's water system. What will the long-term environmental health impacts be of the consumption of GE drugs? And, as more and more microorganisms and animals are genetically engineered and cloned, what will the impacts of their eventual release (as byproduct waste) be? Which communities will be most affected?

The struggles that already exist, and those that are likely to emerge, are the bases upon which we can develop a larger movement against the pharma biotech industry. We can support these struggles in a number of different ways. One way is to begin to understand how the pharma biotech engines operate. What are the economic and political strengths of the leading pharmaceutical corporations? How have they have integrated biotech within their overall agenda? What are the implications of the pharma biotech engines on peoples' health and well-being? The following sections will explore these questions in a way that will hopefully provide insight into why the pharma biotech engines must be challenged.

# Part I: Why is Big Pharma so Big?

There are clear reasons why the leading pharmaceutical corporations are considered "Big Pharma." Economically, Big Pharma has **economic strongholds**, such as extremely attractive profit margins, which are largely a result of their patented blockbuster drugs. Looking beyond these aspects of Big Pharma, are the reasons why these corporations experience the economic wealth they do. The leading pharmaceutical corporations have a long history of **exploiting people**, including indigenous peoples, impoverished people and people living with disease. At the same time, heavy **influence over key players,** such as governments, doctors, patient groups and the media, has enabled Big Pharma to establish and maintain a leading position in the global economy. And even as Big Pharma is experiencing some economic downturns, there are **emerging trends,** such as mega-mergers, restructuring of operations and the applications of biotech, within the sector that continue to provide opportunities for economic growth.

## Economic Strongholds

This section will discuss two of the most notable economic strongholds of the leading pharmaceutical corporations:

- **High profit margins**
- **Blockbuster drugs**

**High profit margins:** The pharmaceuticals industry is a lucrative one. When it comes to profit margins, the world's leading pharmaceutical corporations are the envy of the business world. While the top Global Fortune 500 industry sectors' average profit margin sits at 2.4 percent, the pharmaceuticals industry brought in a whopping 16 percent profit margin in 2001. In that same year, the world's top 11 pharmaceutical corporations each had drug sales of more than $(USD) 10 billion. These 11 corporations include Glaxo SmithKline, Pfizer (recently announced that it would acquire Pharmacia), Merck,

**Top 11 Pharmaceutical Corporations, 2001** (All sales figures in USD)

| Corporation | Drug Sales (billions) | Total Sales (billions) |
|---|---|---|
| Pfizer* | $25.5 | $32.3 |
| Glaxo SmithKline | $25.0 | $29.7 |
| Merck | $20.4 | $47.7 |
| AstraZeneca | $15.9 | $16.5 |
| Aventis | $15.7 | $15.7 |
| Bristol-Myers Squibb | $15.3 | $19.4 |
| Johnson & Johnson | $14.8 | $33.0 |
| Pharmacia | $13.8 | $13.8 |
| Novartis | $12.1 | $19.2 |
| Roche | $11.2 | $17.4 |
| Eli Lilly | $10.1 | $11.5 |
| Total | $179.80 | $256.20 |

* In July, 2002 Pfizer announced that it would acquire Pharmacia. The merged corporation will have $48 billion combined sales in 2002, which will include $39

AstraZeneca, Aventis, Bristol-Myers Squibb, Novartis, Pharmacia, Roche, Johnson & Johnson and Eli Lilly. (See "Top 11 Pharmaceutical Corporations, 2001" table). Combined, their drug sales were more than $(USD) 179 billion, making up over half of total sales of the leading 50 pharmaceutical companies worldwide. Comparatively, $179 billion is 18 times the amount that is needed to treat people living with HIV and AIDS in Africa, and 12 times the amount needed to treat people living with HIV and AIDS globally[7,8].

**Blockbuster drugs:** Having at least one or two major blockbuster drugs on the market, as well as a few in the pipeline, is crucial if leading pharmaceutical corporations want to stay on top. In 2000, for example, AstraZeneca – the fourth largest pharmaceutical corporation in the world – brought in sales of $(USD) 6.3 billion with its blockbuster drug Losec™ (generic name Prisolec), a treatment for gastrointestinal conditions. Losec is the biggest selling drug globally and made up almost half of AstraZeneca' total drug sales in 2000. Merck's cholesterol drug Zocor is the second highest selling drug and was worth $(USD) 5.28 billion in sales in 2000, that's almost one third of the company's total drug sales.

### Two Thumbs Up: What makes those blockbusters a hit?

- Pharmaceutical corporations don't need to price blockbusters at low competitive costs because they are protected through long-term patent regimes. This means that corporations can keep drugs at high prices regardless of the needs of people and ability of generic companies to develop cheaper versions of patented drugs. In North America patents generally last for 20 years, and begin during research and development (R&D) stages, which is another factor in corporations' rush to drugs from R&D to market stage. Once on the market, a drug might have patent protection for 10 years. Drug corporations can also extend patent protection of blockbusters up to five years by developing 'new' formulations (changing the molecular structures), while marketing them to the same patient group.

- The difference between research and development costs versus revenues for blockbusters is significant. The average cost of researching and developing a drug is approximately $(USD) 400 million over 8 to 12 years, with revenues of at least $(USD) 1 billion per year, for as many as 15 years.

- Top selling blockbusters are developed to treat chronic conditions mainly occurring in the North, such as ulcers and high cholesterol. In the U.S. one in ten people will develop an ulcer in her or his lifetime, while one in four American adults is diagnosed with high blood cholesterol. Most blockbusters are targeted at age-related conditions. In North America and Europe, the baby boom population is aging. In the U.S., people over 50 consume 74 percent of all prescription drugs. The fastest growing therapeutic categories – arthritis, cholesterol, central nervous system disorders and cardiovascular disease – all target age-related illnesses. Meanwhile, the pharmaceutical industry is not interested in developing drugs to treat serious illnesses in the South because people there cannot afford to pay the high prices corporations charge for drugs.

- Over the years, there has been a direct correlation between the increase in spending on direct-to-consumer (DTC) marketing – that is advertising specific drugs directly to people –and blockbuster revenues. In the U.S., DTC advertising for drugs can be found just about anywhere, from television, print ads in magazines and subway stations, radio to the internet, just like soap and cars. In 1999, Pfizer spent $(USD) 45 million on DTC advertising for its blockbuster cholesterol drug Lipitor; sales for the drug increased by a whopping 56 percent to $(USD) 2.7 billion.

## Exploitation

The pharmaceuticals industry has become profitable by exploiting people -- mainly indigenous peoples, impoverished people and people living with disease -- across the world.

In a 1993 report by the Working Group on Indigenous Populations (under the United Nations Commission on Human Rights) indigenous observers expressed concern about the exploitation of indigenous peoples by corporations. The following is an excerpt from the report,

> *although indigenous medicine was often portrayed as primitive or even dangerous, 7,000 natural compounds used in modern medicine had been utilized by indigenous healers for centuries. The annual market value of pharmaceutical products derived from medical plants discovered by indigenous peoples exceeded US$ 43 billion...Pharmaceutical companies continued to patent products and reap huge profits from the commercial exploitation of traditional knowledge.*[9]

The application of gene based technologies into pharmaceuticals makes **indigenous communities** even more targeted, as their genetic makeup has become commercially attractive to industry.

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**People living in poverty** have been targeted by the pharmaceuticals industry. Pharma giants have been using people in parts of Africa, Eastern Europe, Latin America and Russia for cheaper clinical trials, for example. Ethics review boards are often inexperienced and less money is provided per subject in these regions. In the U.S., for example, it costs an average of $(USD)10,000 per patient per clinical trial, while in Russia the figure drops to $(USD) 3,000. The number of clinical trials in the South has increased over the years. In 1994, Eli Lilly tested 590 patients in Africa, the Middle East and Central and Eastern Europe. In 2001, the company was expected to run tests on 7,309 people in those regions.[10] Meanwhile, drugs are targeted for the affluent. This is apparent from the geographic breakdown of global sales of drugs. Fifty percent of the world's pharmaceutical sales come from North America, 24 percent from Europe and 13 percent from Japan. The remaining 13 percent are from Africa, Latin America, Australia and the rest of Asia.

Access to essential drugs for **people living with illness and disease** is limited by the leading pharmaceuticals corporations through patent regimes, and, in turn, high pricing. For example, in South Africa, where more than one in five adults is estimated to be infected with HIV or AIDS, Pfizer's Diflucan™ (generic name fluconazole) – a widely used antiviral drug for the treatment of HIV and AIDS — was been priced at $(USD) 8.92 per pill, while the average monthly wage for employed South Africans in 1999 was $(USD) 7.00. Pfizer has made back more than ten times the research and development cost of Diflucan, which was, by law, only available through Pfizer in South Africa.

People living with illness and disease are also subject to adverse reactions from drugs. Rezulin, a diabetes drug sold by Warner-Lambert (now Pfizer) caused 63 confirmed deaths during its time on the

market, from 1997 to 2000. It is suspected, however, that the actual death toll is 10 times higher. Regulators tried to stop Rezulin from getting approved, as well as tried to get it off the market after approval, but faced opposition from Warner-Lambert and senior government officials. In the fall of 1996, Dr. John L. Gueriguian, a United States Food and Drug Administration (FDA) medical officer reviewing the drug, claimed that Rezulin should not be approved due to its potential harm to the liver and heart in diabetics. Warner-Lambert, however, pressured the FDA to approve the drug. Some FDA drug reviewers even received threats from their superiors if they were to speak publicly about their negative findings on Rezulin.[12] During the 29 months it was on the market, Warner-Lambert made $2.1 billion in sales on Rezulin. Meanwhile, other effective diabetes drugs were already on the market.

The trend of releasing new patented drugs on the market to replace older effective generic versions is shockingly common in the pharmaceuticals sector. Most new drugs on the market are replacements for cheaper generic versions. When it comes to biotech, the replacement of animal insulin products with GE insulin is a good example. According to a 1993 study by the U.S. Office of Technology Assessment, of the 348 drugs brought to market by the 25 leading U.S. pharmaceutical corporations between 1981 and 1988, 97 percent were copies of existing medications. Of the 3 percent offering new therapeutic results, more than half were eventually withdrawn from the market because of unanticipated side effects.[11]

## Influence Over Key Players

The pharmaceuticals corporations have applied significant pressure over the key players in order to acquire the economic wealth and political influence they have. These key players are:

- **Governments**
- **Doctors**
- **Patient groups**
- **Media**

**Governments**: Governments are increasingly influenced by the pharmaceuticals industry through aggressive lobbying. The drug industry is one of the biggest spenders when it comes to lobbying government. In the 1999-2000 election cycle in the U.S., pharmaceutical corporations spent over $(USD) 177 million on lobbying – that beats the expenditures of the oil and gas, tobacco, automobile and food processing corporations combined. This scale of spending has been favourable for industry.

Going back to 1992, the U.S. Congress allowed the Food and Drug Administration (FDA) – the main government body in the U.S. that regulates drugs – to accept drug company subsidies, in the form of 'user fees.' This move meant the hiring of some 600 additional people to review marketing applications and therefore the approval of more drugs, more quickly – exactly the goal of industry. Because of user fees, the time to review new drug applications has decreased from three years to one. According to Jeff Trewitt from industry group PhRMA (the Pharmaceutical Researchers and Manufacturers Association), "*there's a more constructive sense of collaboration between FDA and the companies*,"[12] with user fees in place. Between 1996 and 2000, the FDA approved a record 184 new drugs – that's approximately double than in the previous 4 years. Furthermore, in 1997, Congress allowed for "fast track" drug approvals, which decreases FDA's review time of companies' clinical drug trial results from one year to 6 months.

Regulations on patents have also been a major lobbying focus for pharmaceutical corporations. In Canada, Pharmaceutical Manufacturers Association of Canada (PMAC) was the main influence in the passing of Bill C-91, which allows multinational drug corporations to have a 20-year patent on new drugs, and is based on U.S. drug patent legislation. The purpose of the bill was to eliminate Bill C-22, which allowed companies to create and sell generic versions of patented drugs through what is called a compulsory license. Compulsory licensing encourages a number of companies to produce and sell generic versions of drugs and therefore establish competitive, i.e. lower, prices. (At the time that PMAC was pushing the government to pass Bill C-91, its president was the former Minister of Consumer and Corporate Affairs, Judy Erola). On the international level, there was the establishment of the World Trade Organization's (WTO) Trade-Related Aspects of Intellectual Property Rights (TRIPs) rules that give leading pharma giants the clout across borders to destroy generic drug businesses, particularly those in the South, that develop essential drugs at low costs to make them more accessible. PhRMA – the biggest pharmaceutical industry group in the U.S. – was one of the main groups that drafted the TRIPs agreement.

It is estimated that in Canada, pharmaceutical companies spend over $ (CAD) 20,000 per year per doctor (physicians and specialists) promoting their products[14]. In the U.S., the drug industry spent a total of $(USD) 16.4 billion in 2001 promoting its products to doctors, mainly through providing free samples, hiring sales representatives to make 'information' visits to doctors and by running print ads in medical journals.

**Doctors:** It is estimated that in Canada, pharmaceutical companies spend over $ (CAD) 20,000 per year per doctor (physicians and specialists) promoting their products[13]. In the U.S., the drug industry spent a total of $(USD) 16.4 billion in 2001 promoting its products to doctors, mainly through providing free samples, hiring sales representatives to make 'information' visits to doctors and by running print ads in medical journals. It is estimated that in the U.S., drug corporations hire 4,000 to 5,000 sales representatives to launch one blockbuster drug. How effective is all of this? Much of the spending – 64 percent of it – was on samples given to doctors. In a survey conducted by IMS Health, it was found that 70 percent of 2,300 physicians surveyed were more likely to prescribe a brand-name drug based on a patient request if a sample is available and can be provided during an office visit. Meanwhile, many patient requests in for drugs in the U.S. often originate from corporate television, newspaper and radio advertisements, also referred to as direct-to-consumer (DTC) marketing. While DTC is not yet legal in Canada, many patients are exposed to drug ads through American sources. And, as we shall see, Canadian pharmaceutical and advertising lobby groups are advocating for the legalization of DTC in Canada.

**Patient groups:** While doctors are being wooed by pharmaceutical corporations, so are patient groups. For example, leading pharma giants Bristol-Myers Squibb, Glaxo SmithKline, Pfizer and Pharmacia are amongst the $(USD) 100,000 + contributors to the American Cancer Society (ACS). While pharmaceutical corporations appear to be doing good for patient groups by providing donations and free samples of their products, the reality is that these gifts come with many strings attached. Pharmaceutical corporations have put pressure on patient groups to conceal the connections between environmental pollution and disease, as well as to promote their products over non-patentable, non-drug forms of treatment and prevention. For instance, AstraZeneca (then Zeneca) started Breast Cancer Awareness Month in 1985. At the time it has happened to be a leader in the chemicals and agrochemicals sectors. Its

motivation was not only to paint a positive picture of itself as a leading chemical producer, but also to promote its drug tamoxifen. Tamoxifen, sold as Novaldex, is marketed as a treatment that reduces the risk of breast cancer, yet actually has carcinogenic properties itself and can even be fatal in some patients. Over 10 million patients have used it and it is the world's largest selling drug for breast cancer. In 2001, sales for Tamoxifen were $(USD) 630 million.

**Media**: Patient groups are also being used by corporations in public relations schemes. According to pharmaceutical marketing experts, by getting patient groups to speak on behalf of the company, advertising becomes more effective. In Canada, for example, the Cancer Advocacy Coalition, is an industry front group that lobbies for government policies that favour leading pharmaceutical corporations. While it poses as a 'grassroots' organization, its main sponsors are actually pharma giants Aventis, Bristol-Myers Squibb, Glaxo SmithKline, Roche and Pharmacia. Within the same year of its establishment, in 2000, the Coalition developed a media strategy that advocated for a faster drug review process and greater financial backing by government for expensive cancer treatments. The strategy generated a great deal of media attention, which is not surprising since drug companies in Canada are supported by the Alliance for Access to Medical Information (AAMI), which includes the Canadian Newspaper Association, the Canadian Association of Broadcasters, The Institute of Communications and Advertising and Magazines Canada. AAMI, along with Canada's Research-Based Pharmaceutical Companies, whose president Murray Elston was formerly health minister of Ontario, are lobbying the Canadian government to make direct-to-consumer marketing legal. AAMI has met with more than 70 members of parliament to argue its case. If direct-to-consumer marketing is allowed, this would mean an extra $ (CAD) 400 million in revenues per year for AAMI members.[14]

## Emerging Trends

Like many sectors, the pharmaceuticals industry is always looking for opportunities for growth, particularly since patents on many of their blockbuster drugs are soon to expire. Some of the emerging trends have included:

- **Mega-mergers between leading pharma players**
- **Restructuring of operations**
- **Advancement of biotech**

**Mega-mergers:** Many patents on today's top blockbusters are soon to expire. Furthermore, leading pharmaceutical corporations are concerned that there are too few potential blockbusters in the pipeline. This is one of the reasons we have seen several mega-mergers between leading pharma players over the past couple of years. In 2000, Glaxo Wellcome bought up SmithKline Beecham for $(USD) 76 billion, and became Glaxo SmithKline – then the largest pharmaceutical corporation worldwide. That same year, Pfizer bought Warner-Lambert for $(USD) 116 billion. As well, Pharmacia & Upjohn bought agribusiness and pharmaceutical company Monsanto for $31 billion. Then, in July 2002, Pfizer announced that it would buy Pharmacia for $(USD) 60 billion. This will make the Pfizer the biggest pharma corporation, with annual sales for 2002 projected at $(USD) 48 billion. (As part of the merger, agribusiness unit Monsanto will be spun-off). By merging, corporations have been able to pool research and development (R&D) resources and cut costs through employee layoffs. Merging has also enabled pharma giants to increase their product lines by gaining a broader range of products across multiple therapeutic areas (e.g. cardiovascular, central nervous system, alimentary/metabolism, respiratory, anti-

infectives, etc.).

**Restructuring:** Another way the pharma giants are trying to stay on top of hefty profit margins and blockbuster success is through restructuring into units that focus on particular therapeutic areas. Pfizer, Glaxo SmithKline and Novartis have recently announced that they are splitting their R&D efforts into units specifying in such areas as central nervous system, cancer and cardiovascular – catering to chronic and widespread conditions that mainly affect populations in the developed North. According to industry analysts, these semi-autonomous units make corporations' research and development more commercially focused. In many ways, it also allows these corporations to maintain adequate management over shockingly huge budgets and operations.

**Biotech**: Pharma giants are also looking to keep up with their profits and sales growth through what they call the 'revolutionary breakthroughs' of biotech. An article in *Fortune* magazine provides some insight into the financial potential of biotech for the pharma industry,

> *The cure for Big Pharma's blockbuster blues lies almost certainly in drugs tied to the deciphering of the human genome. The genomics opportunity is enormous, verging on overwhelming. In the history of the pharmaceuticals industry, only about 500 basic "targets" have been identified – disease-causing functions in cells or viruses that can potentially be fixed with the right new chemical compound. But with growing understanding of how DNA makes or mismakes proteins, the basic functional molecules of the body, it is expected that the number of potential new targets could soar to 10,000.*[15]

So with the pharma industry's so-called 'blues' over expiring patents on blockbusters, it becomes clear that interest in biotech is financial. With biotech, the industry is continuing its trek for high profit margins. As we shall see, the pharma giants have an increasingly hefty stake in biotech and are aggressively pushing forward to get the profits they want, using similar exploitive measures on vulnerable communities, and influencing tactics with key players.

# Part II: Enter Biotech

Through biotech, pharmaceutical corporations are in a rush to develop new products that will bring in sales comparable to current blockbusters. The following are some facts that indicate the advancement of biotech drugs:

- Since the early 1980s, over 130 GE drugs have been released to market in the U.S.
- By 1993, global sales from GE drugs were $(USD) 8 billion. In 2000 sales were up to $(USD) 22.3 billion.
- Two of the top blockbusters – Procrit/Eprex and Epogen – now on the U.S. market are genetically engineered.
- While sales in biotech drugs only make up 10 percent of the $ (USD) 254 billion global pharmaceuticals market, the pace of GE drugs being released to market has significantly increased over the past several years. More than half of the 133 biotech drugs currently on the market in the U.S. were approved between 1996 and 2001.
- Currently, 30 percent of drugs undergoing clinical trials are being developed by the biotech industry.
- The U.S. is the biggest consumer of GE drugs, representing 43 percent of the market, while Europe represents 27 percent, Japan 24 percent and the rest of the world 6 percent.

How have GE drugs come to occupy such a significant presence within the pharmaceuticals industry? Who have the leading pharmaceutical corporations worked with to get their products to market? What types of technologies are being developed? What are the implications of the ways in which these technologies have been developed, and of the technologies themselves? The following sections will explore these questions, providing some detail to the facts above, which signify the growing presence of pharma biotech.

## Pharma Biotech Partners

The leading pharmaceutical corporations have been able to maneuver their way into biotech largely as a result of their partnerships with a number of players, including public and private bodies. Certainly, the influence that pharmaceutical corporations have on governments has been essential to the pharma biotech industry's development. Meanwhile, private-private partnerships have also been essential for the pharma biotech engines. Multinationals, as opposed to smaller biotech companies, not only have the capital to support drug development, but also the regulatory and marketing expertise to get a product to market. Meanwhile, the actual technological developments are more possible with the expertise available in smaller biotech companies. In certain cases, the multinationals end up purchasing the smaller companies. The private-private partnerships can focus on a number of different areas, including genomics and drug development. The main partners we will explore are:

- **Governments**
- **Universities**
- **Genomics companies**

**Governments**: Both the Canadian and U.S. governments have been key proponents of biotech by implementing policies favourable to the industry as well as helping out with the large research and development costs required to support it. In Canada, the Canadian Biotechnology Strategy, initially established in 1983 as the National Biotechnology Strategy, calls for growth in the biotech sector and boasts of job creation and a boosted economy from the manufacturing and sale of new drugs. On the financial front, the Canadian government has also been active. Between 2000 and 2001, the Canadian government handed over $(CAD) 300 million to Genome Canada. Genome Canada is a federally funded 'non-profit' corporation and "*the primary funding and information resource relating to genomics and proteomics in Canada*."[16] Since 2000, Genome Canada has invested over $(CAD) 290 million in biotech companies across Canada, which has been matched by other funding, making the total $(CAD) 580 million for 56 genomics projects. In the U.S., since 1988, more than $(USD) 3.3 billion of public money has gone to the Department of Energy and the National Institutes of Health for the Human Genome Project.

At sub-national levels, provincial and state governments are also providing support to the industry. Providing tax credits to biotech companies and sponsoring industry conferences, for instance, are some ways support is given. In turn, local and municipal governments are encouraged to sustain the biotech industry as part of their local economic development strategies, which often involve the participation of universities and business groups. Cities across North America are encouraging biotech investments in their local economies. Together, all levels of governments have been influenced by the biotech industry's agenda.

One of the key defining factors of biotech research and development (R&D) is that it is expensive. This is why public money is necessary for the pharma biotech industry to succeed. Put simply, the costs of biotech R&D are more than the industry can handle on its own.

We already have a good idea of how influential the pharmaceuticals industry has been on governments, and what some of the implications have been on the regulatory review of drugs. What about the implications with biotech in the picture? One of the key defining factors of biotech research and development (R&D) is that it is expensive. This is why public money is necessary for the pharma biotech industry to succeed. Put simply, the costs of biotech R&D are more than the industry can handle on its own. In fact, only a small portion of biotech companies in North America are even profitable because research and development costs are so high, making returns on investments difficult to recapture.[17] It is worth asking how these investments are affecting the public health care system in Canada, and how they might be contributing to the growing private health care industry in North America in general.

**Universities**: In an article in *Red Herring,* biotech editor Stephan Herrera writes, "*Academic research is the lifeblood not only of most U.S. biotech startups, but also of 'big pharma*.'"[18] Similarly, Lita Nelson, director of technology licensing at MIT, argues

> *I don't think the biotechnology industry would exist without university-industry collaborations. Almost every new biotech company traces its origins directly back to an agreement with a university.*[19]

Most biotech companies into which big pharma invests, have been founded by researchers coming directly from university labs, lured by the prospects of prestige and larger salaries in the private sector.

These companies, known as spin-offs, are generally smaller than the multinational pharmaceuticals in terms of staff and annual sales, and are focused on fewer product developments. In the U.S., the University of California (UC) and the Massachusetts Institute of Technology (MIT) have been very important universities for the pharma biotech industry. Six of the ten top selling biotech drugs currently on the market came from UC research, and one in six biotech companies in California were founded by UC scientists. Meanwhile, 42 biotech companies have been founded by MIT faculty and alumni, including top companies such as the top three biotech drug companies: Genentech; Biogen; and Amgen. Combined, these companies employ 10,000 people and bring in revenues of more than (USD) $3 billion – almost one quarter of the total revenues of U.S. biotech companies.

In Canada, in 1999 alone, 454 companies were created as 'spin-offs' from universities, the majority of which were in biotech. The University of Guelph and the University of Waterloo are two key universities that have collaborated with the biotech industry in Canada from the early 1980s onward. Other Canadian universities that are heavily involved in industry-led biotech research and development include the University of Saskatchewan, Queen's University, Dalhousie University and the University of Toronto. Spin-off companies, along with patented technologies, are often made possible through technology transfer offices. Most universities have their own "technology transfer office," that act as both a promoter and facilitator of commercial developments on campus.

The conflicts of interest that arise due to corporate-university deals are inevitable. A study by Dr. Thomas Bodenheimer, a professor at the University of California San Francisco, indicates that close ties between corporate sponsors and academic medical researchers create a number of trends, including publication biases, where corporate sponsors publish only favourable results and 'ghostwriting,' where academic researchers get paid to add their names to journal articles written by corporate marketing departments.[20] Inherent within conflicts of interest is the threat to academic freedom and the silencing of researchers' true findings. The following cases are two contrasting examples of what can result from corporate influence over university research. The first case involves Dr. Nancy Olivieri from the University of Toronto, who was pressured by the sponsoring drug company Apotex to withhold critical information on the side effects of one of its drugs. The second case involves Dr. James Wilson of the University of Pennsylvania who tried to keep research results from the public because of his own financial ties to Genovo, the sponsoring company to a gene therapy clinical trial.

University of Toronto: In 1993, drug company Apotex (Toronto, Canada) and the University of Toronto (U of T) signed an agreement for Dr. Nancy Olivieri's work in genetic blood disease research at the university's Hospital for Sick Children. As part of the agreement, Dr. Olivieri was to conduct a clinical trial for Apotex's drug Ferriprox™ (generic name deferiprone) – meant to treat a rare blood disorder called thalassaemia. When Olivieri discovered that Ferriprox was causing harm to some of her patients, she informed Apotex. Apotex vice president Michael Spino then threatened her with legal action if she were to tell her patients about her findings on the drug, as she would be breaking a confidentiality clause in the contract she had signed with the company. Olivieri decided to inform her patients. Then, in 1997, Dr. Olivieri published her findings that Ferriprox is ineffective and causes severe liver toxicity. After Olivieri went public with her findings, she temporarily lost her position at the university. During this scandal, U of T was in the process of negotiating a donation from Apotex of $(CAD) 92 million for a new biomedical building.[21] While as a result of pressure from faculty and other medical experts, Olivieri was given her position back, the situation that she faced is not unique within the increasingly corporatized academic research world.

University of Pennsylvania: In September 1999, 18-year old Jesse Gelsinger died when a dose of genetic material was injected into his liver for the treatment of ornithine transcarbamylase deficiency (OTCD), a rare metabolic disorder that he had been treating with a low-protein diet and drugs. The study was conducted at the University of Pennsylvania's Institute for Human Gene Therapy, and sponsored by biotech company Genovo, to test the safety of a treatment for babies with a fatal form of his disorder. Most patients in gene therapy experiments are seriously or terminally ill. Though Jesse was not forced into this experiment, he was neither of these. Jesse's was the first reported death linked to gene therapy. Researchers working on the study did not follow regulations as they should have. Mainly they failed to report adverse effects to the FDA, such as the fact that several patients preceding Jesse suffered from serious side effects, while monkeys had died in similar experiments.[22] Dr. James Wilson, director of the Institute for Human Gene Therapy, also happened to be the founder of Genovo. Genovo was providing one-fifth, that's $(USD) 25 million, of the annual budget of the Institute. (In addition, a portion of the lab's funding for its gene therapy research comes from the U.S. government through the National Institutes of Health). Genovo also had exclusive rights to commercialize Dr. Wilson's discoveries. Both Wilson and the university owned stock in Genovo at the time of the gene therapy experiment on Jesse.[23]

**Genomics companies**: As a basis for any work on GE drug development, multinational pharmaceutical corporations, smaller biotech drug companies and universities have come to rely on work being carried out by genomics companies. Genomics is the study of an organism's genes and their functions. For industry, the purpose of genomics is to identify genes that express what are referred to as 'therapeutic proteins' (e.g. insulin), or genes that in someway can be linked to disease, like cancer. From a technical point of view, genomics is the basis for GE drug development. The most recent 'milestone' in genomics was in June 2000 when the Human Genome Project and biotech company Celera Genomics announced that they had completed mapping out, or sequencing, the human genome. What this means is that HGP and Celera researchers had mapped the location of genes in a chromosome and then identified each sequence of base pairs in each gene. (Once the order of base pairs in a DNA molecule is known, the next step is determining the structure of proteins encoded by that DNA). Subsequently, this 'milestone' sent biotech stocks soaring.

Leading genomics companies include Celera Genomics, Incyte Genomics, CuraGen, Gene Logic, Millennium Pharmaceuticals, Human Genome Sciences and Myriad Genetics. All of the leading pharmaceutical corporations, as well as the biotech drug companies (e.g. Amgen, Genentech and Biogen) have deals worth millions with these and other genome sequencing and bioinformatics companies to access genomic data in hopes that it will lead to greater and faster drug discovery targets. In some cases, genomics companies are also involved directly with drug development. To access Celera's genome databases, companies are required to pay, on an annual basis, in USD, between $5 million and $ 15 million, whereas academic labs are charged between $2,000 and $15,000.

Bioinformatics is the use of computer databases and software systems to collect, store, search and interpret molecular components of living things. Bioinformatics companies are referred to as 'toolkit companies' within the biotech industry. Meanwhile, genome sequencing companies are considered 'content companies.' Genome sequencing companies also include pharmacogenomics and proteomics. Pharmacogenomics is the study of how genetic variations, or single nucleotide polymorphisms (SNPs), amongst individuals and populations affect the ways people respond to drugs. Proteomics is the study of the full set of proteins encoded by a genome.

The pharma biotech industry is promoting pharmacogenomics as a way to predict adverse drug reactions in specific populations. In reality, the industry is hoping that pharmacogenomics will lead to the revival of failed drug candidates that have previously been abandoned because of lack of efficacy or adverse reactions. As well, there are hopes that pharmacogenomics will lead to cheaper drug development by targeting specific populations, with similar genetic profiles, thereby making clinical trials less complicated and time consuming. Meanwhile, health maintenance organizations (HMOs) are interested in the development of pharmacogenomics because they say it will help them reduce their costs by prescribing drugs that would cut down on the number of patient visits to hospitals or shorten patients' length of hospital stay. This means they are expecting to have access to information pertaining to peoples' genetic profiles. In 1998, 10 pharma companies – AstraZeneca, Bayer, Bristol-Myers Squibb, Roche (then Hoffman-La Roche), Glaxo SmithKline (then Glaxo Wellcome and Smith Kline Beecham), HMR (Herd Mundy Richardson Limited), Novartis, Pfizer and Pharmacia (then Searle), formed a two-year $(USD) 45 million alliance, known as the SNP consortium.

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Most disturbing, is that commercial SNP discoveries increase the exploitation of indigenous peoples, ethnically-distinct groups and people with disease and disability. As discussed briefly in the "Reasons for Resistance" section, the genes from these people are being hunted, stolen and patented for the benefit of the pharma biotech engines. The pharma biotech industry is continuing to take advantage of its powerful position within the global economy, which itself is based on colonialist rule over indigenous communities, as well as oppressive rule over people of colour and people living with disease and disability.

## Following the Money: Key Products and Technologies

This section will outline the major technologies in pharma biotech, both in terms of market value and track record, i.e. safety and feasibility. It will hopefully provide a general insight of what types of technologies are being developed from investments into biotech research and development and what the implications of the resulting technologies are. There are two major categories of pharma biotech technologies: The "First Wave" and the "Second Wave." The **First Wave technologies involve developing recombinant proteins derived from genetically engineered cells**, which are then taken as drugs. **Second Wave technologies involve genetically altering cells, tissues and organs**, and inserting them directly into humans. There are currently only First Wave products on the market.

### The First Wave - 'Natural Proteins'

**Technology:** Most biotech drugs that are currently on the market (see "Top 10 GE Drugs" table) are GE proteins, mainly hormones, interferons, antibodies –also referred to as monoclonal antibodies – and enzymes (see Appendix). Monoclonal antibodies have become a big focus for the pharma biotech engines,

mainly because they can target very specific substances in the body, and can therefore be used for many purposes. The pharma biotech industry is currently trying to develop plants that are genetically engineered to develop monoclonal antibodies, hoping that this will be a cheap method of production. Monoclonal antibodies can be used to treat very specific infections, for the diagnosis, monitoring and treatment of disease, or in autopsies, drug purification processes and screening for donor organs.

These GE proteins are developed by cloning genes and inserting them into cells, or 'bioreactors,' ranging from hamster ovarian cells to *Escherichia coli* (*E coli*) bacteria. In the case of the drugs Epogen and Procrit/Eprex the bioreactors are hamster ovarian cells. The human gene responsible for producing erythropoietin – a hormone that stimulates the production of red blood cells – is isolated, cloned and implanted into a hamster's ovarian cell. This cell then produces a recombinant or GE version of erythropoietin. Neupogen and Humulin, on the other hand, are produced using the *Escherichia coli* (*E coli*) bacteria instead of hamster cells. [Monsanto's recombinant bovine growth hormone (rBGH) used in the U.S. dairy industry is also produced using *E coli*]. This procedure of using organisms' cells has become a hot ticket for the pharmaceuticals industry as it provides a way to mass produce proteins that are considered valuable and are otherwise not available in quantities required for commercial purposes. At the same time, industry is marketing these products as 'human' and 'natural.'

**Products and Market value:** Two of the top ten blockbuster drugs currently on the market are GE drugs. These are Johnson & Johnson's Procrit/Eprex, which raked in $(USD) 3.4 billion and Amgen's Epogen, which brought in sales of $(USD) 2.1 billion in 2001. Sales of Procrit/Eprex made up 10.4 percent of Johnson & Johnson's annual sales for 2001, while Epogen brought in more than half of Amgen's entire annual revenues. These two products – meant to treat anemia caused by kidney failure, chemotherapy, HIV and major surgery – are actually the same drug developed by Amgen, but marketed by both companies. (Johnson & Johnson is able to sell the drug through a licensing agreement with Amgen). Johnson & Johnson has put a big push on Procrit, partially to alleviate competition with Amgen. Between 1998 and 2001 the company doubled the drug's sales crew to 600 representatives, as well as spent $(USD) 33.4 million on consumer ads within the first eight months of 2001 alone.

A third biotech blockbuster includes Amgen's Neupogen – a treatment for low white blood cell counts as a result of chemotherapy – brought in $(USD) 1.2 billion in sales in 2000. There are also Eli Lilly and Novo Nordisk's GE insulin for diabetes. Each company made approximately $(USD) 1.5 billion in sales on GE insulin in 2000.

The initial R&D stages of most GE drugs have been carried out by biotech companies such as Amgen, Biogen and Genentech, but financed by the larger pharmaceutical multinationals. The following are some examples of links between big pharma and biotech drug companies.

- In 1982 Eli Lilly began marketing Humulin (GE insulin) – the first ever GE drug approved for commercial use – through a licensing agreement with Genentech.

- Johnson & Johnson, through its biotech subsidiary Ortho Biotech, has an agreement with leading biotech drug developer Amgen for Procrit/Eprex. Through this agreement Ortho has rights to market Procrit.

- In 1998, Roche signed a licensing agreement worth $(USD) 40 million with Genentech for the marketing of Herception – a drug that Genentech had developed for the treatment of breast cancer. The agreement gave Roche exclusive marketing rights to Herceptin outside of the U.S.

The many R&D partnerships between the pharma biotech engines and smaller biotech comapanies and universities means high R&D costs, which are in turn reflected in the prices charged for GE drugs. For example, GE human growth hormones, such as Pharmacia's Genotropin, Genentech's Nutropin and Eli Lilly's Humatrope cost patients close to $(USD) 16,000 per year. Enbrel, a treatment for rheumatoid arthritis in adults and children, developed and marketed by Immunex, costs $(USD) 220 per week, and

**Top 10 GE Drugs, 2001**

| Drug | Year first approved by FDA | Year first approved by Health Canada | Developer | Marketer | Marketed treatment areas | 2001 Sales (USD, billions) |
|---|---|---|---|---|---|---|
| Procrit/Eprex | 1990 | 1990 | Amgen - Kirin joint venture | Jonhson & Johnson (Ortho Biotech subsidiary) | Anemia (low red blood cells) | 3.4 |
| Epogen | 1989 | N/A | Amgen - Kirin joint venture | Amgen | Anemia | 2.1 |
| Neupogen | 1991 | 1992 | Amgen | Amgen | Neutropenia (low white blood cells) | 1.3 |
| Humulin | 1982 | 1983 | Genentech | Eli Lilly | Diabetes | 1.1 |
| Avonex | 1996 | 1998 | Biogen | Biogen | Multiple sclerosis | .972 |
| Rituxan | 1997 | 2000 | IDEC | IDEC-Genentech (U.S) Roche (Canada ) | Non-Hodgkin's lymphoma | .819 |
| Enbrel | 1998 | 2000 | Immunex (acquired by Amgen) | Amgen - Wyeth Ayerst | Rheumatoid arthritis | .762 |
| Humalog | 1996 | 1996 | n/a | Eli Lilly | Diabetes | .628 |
| Betaseron | 1993 | 1995 | Chiron - Berlex (subsidiary of Schering) | Chiron - Berlex | Multiple sclerosis | .610 |
| Ceredase/ Cerezyme | 1991 | 1997 | Genzyme | Genzyme | Type 1 Gaucher's disease | .570 |

potentially needs to be taken for life. Roche's Roferon-A [recombinant interferon] is a drug for chronic hepatitis C, chronic myelogenous leukemia, hairy cell leukemia, and AIDS-related Kaposi's sarcoma, and costs patients over $(USD) 56,000 per year.

**Track record:** Drug safety and efficacy is a major issue facing patients taking GE drugs. GE insulin for diabetics was the first ever GE drug on the market has generated serious concerns amongst diabetics. According to a study by the British Diabetes Association – a group sponsored by Eli Lilly – between 15 and 20 percent of diabetics using the product complained of such side effects as reduced hypoglycaemic awareness, arthritis, muscle pain and weight gain.

Meanwhile, industry refuses to acknowledge these dangers. Eli Lilly spokesperson Doyla Chadwick, speaking in defense of the company against a class action lawsuit filed in the Federal Court in New Mexico in April 2000, stated

> *The safety of human insulin has been proven by regulatory authorities almost 20 years ago. Human insulin is identical to the insulin produced naturally by the body... and is less allergenic than animal insulin.*[25]

Eli Lilly's GE insulin was rushed through the FDA approval process in only 5 months on the false argument that numerous people with diabetes were dying from allergic reactions to animal insulins. As mentioned earlier, only 9 diabetics have reported adverse reactions to pork insulin, and none to beef, while 100 deaths related to GE insulin have been reported in North America. The claimants in the suit argue that Eli Lilly,

> *paid for, arranged for and caused rapid approval of Humulin(r) or Humalog(r) from the Federal Drug Administration despite having knowledge of the potential life-threatening side effects from those drugs and despite that the long-term effects of these drugs have not been determined.*[26]

The release of GE insulin is a good example of the drug industry's tactic of releasing a new, more expensive and patented drug to replace an older generic one.

## The Second Wave – 'New and Improved' Genes and Organs

### • Gene therapy

**Technology:** The process of gene therapy is described as replacing missing or 'flawed' genes in cells with 'healthy copies.' The cells into which the genes are inserted can either be cells originally taken from the patient's body or foreign cells from another organism. When genes are inserted into cells, the cells are then inserted into the body, whereby a particular organ is targeted for delivery. The transgenic cells are usually administered with a needle. The cells into which genes are inserted could also be either somatic (body cells) or germline (reproductive). Altering somatic cells would only affect the individual receiving the therapy, whereas changes in germline cells would affect following generations.

**Products and Market value:** It is estimated by the U.S. Federal Trade Commission, that the market for gene therapy will be worth $(USD) 45 billion by 2010. The first approved gene therapy treatment is expected to be on the market by 2004. There are currently 600 gene therapy clinical trials occurring

worldwide. Currently, more than 60 percent of clinical trials for gene therapy are for common cancers, such as lung and breast cancers. Aventis, Roche and Pfizer are leading pharma biotech engines that have invested in gene therapy for cancer treatments, and hope to have products out in the next several years. Aventis and Roche (through their partner companies and institutions) are working on gene therapy drugs that focus on the *p53* tumour suppressor gene. Researchers say that the *p53* tumour suppressor gene controls DNA repair and natural cell death and is mutated in more than half of all common cancers. They also point out that *p53* mutations in head and neck cancer are caused by tobacco smoke.[26] Meanwhile, experts point out that trying to insert genes into cancer cells, particularly when they exist in more than one site in the body, is a major limitation of gene therapy for cancer.

**Track record:** Over 3,000 people have taken part in clinical trials testing gene therapy – an area of medical research that has been around for just over 10 years and has not yet led to any approvals for commercial use. Jesse's Gelsinger's death (see "Pharma Biotech Partners" section, pg. 17) has created major uncertainties about the advancement of gene therapy. Following Jesse's death, the FDA temporarily suspended the University of Pennsylvania's gene therapy program. The FDA also discovered that gene therapy researchers at other universities and research institutions did not report over 600 adverse reactions and deaths amongst gene therapy volunteers to the agency, as they are required to do. As a result, the FDA has enforced stricter guidelines on monitoring gene therapy studies, such as requiring universities and other research institutions to submit monitoring plans and ensuring that gene therapy researchers are following these plans. The FDA also now conducts on-site inspections of clinical trials. It remains to be seen how effective these new measures will be since most gene therapy trials continue to be influenced by corporate interests.

## • Xenotransplantation

**Technology:** Xenotransplantation is the process of exchanging organs, tissues and cells between different species. Xenotransplantation between animals and humans has failed in the past mainly because animal cells and organs have not been able to survive in the human patient's immune system. Now the industry is attempting to genetically engineer donor animals – mainly pigs –with human genes so they will produce organs more acceptable to the human body.

**Market value:** With 180,000 people worldwide on waiting lists for organ transplants, the pharma biotech industry is keen to cash in on the market potential for xenotransplantation. It is estimated by analysts that the xenotransplantation market could be worth as much as $(USD) 6 billion by 2010, which would include sales from anti-rejection drugs in patients' post-operative stage. One estimate from 1995 suggests that for a xenotransplantation operation alone, it would cost upwards of $(USD) 250,000. Expenses associated with xenotransplantation would include costs of breeding, housing, feeding, medicating, testing, transporting and disposing of the remains of herds of GE animals. This figure does not include post-operative patient costs. Looking at costs for human-to-human organ transplantation is helpful in understanding how expensive xenotransplantation would be for the patient. Post-operative costs, which include anti-rejection drugs and other medications, are approximately $(USD) 11,000 in the first year, and as much as $(USD) 18,500 annually in following years. Immunosuppressive drugs are required for the rest of the patient's life. Some patients must undergo several transplants during their lifetime to replace organs that fail to be effective.[27]

Amongst the pharma biotech leaders, Novartis, which is also active in the anti-rejection/post-operative

drug market for human-to-human transplantations, is the most active when it comes to xenotransplantation. Since the early 1990s, biotech and pharmaceutical companies have shown a renewed interest in xenotransplantation, seeing profit potential both in terms of xenotransplantation itself as well as in the market for post operative immunosuppressant/anti-rejection drugs. In January 2002 researchers from the University of Missouri-Columbia and Immerge BioTherapeutics – a joint venture between Novartis and BioTransplant – announced that they had created the world's first miniature cloned pig with a specific gene that had been 'knocked out' of its DNA[28]. The knocked out gene is one apparently responsible for causing a virus that is harmful to human cells. Novartis also sponsors xenotransplantation research at several Canadian, U.S. and European medical centers, including the Ohio State University, University of Pennsylvania, University of Wisconsin, Stanford University and Massachusetts General Hospital in the U.S., and, in Canada, at the University of Western Ontario, University of Toronto, and University of Guelph.

**Track record:** While biotech proponents say that they will be able to breed pigs for xenotransplantation that are 'germ-free', many scientists point out that it is impossible to breed animals free of parasites harmful to humans. Furthermore, there have been serious questions raised on the feasibility of GE and cloned animals in general. For example, of 49 GE pigs bred by Imutran (a xenotransplantation subsidiary of Novartis), as many as one quarter were stillborn, died or killed soon after birth. PPL Therapeutics (the Scotland based company that "produced" Dolly the sheep – the first mammal to be cloned from an adult cell) has reported a 50 percent postnatal loss of cloned animals. Most attempts to clone animals have ended in failure, where fetuses are deformed and die in the womb, have oversized organs or are born dead. Others have died after birth, some two times as large as they should have been. Earlier this year, Ian Wilmut, co-creator of Dolly the sheep, published findings indicating that all of the world's cloned animals are genetically and physically defective.[29]

Earlier this year, Ian Wilmut, co-creator of Dolly the sheep, published findings indicating that all of the world's cloned animals are genetically and physically defective.[29]

There's also the problem of contamination. While proponents say that measures to keep GE animals and their carcasses from contaminating food chains and ecosystems will be strict, there is always room for human error. In January 2002 it was reported that 11 of the University of Guelph's EnviroPigs – pigs genetically engineered to produce less phosphorus in their feces – were accidentally used for animal feed. The carcasses were supposed to be incinerated, but ended up being shipped off to an animal feed plant[30]. At the same time, there are concerns that soil and groundwater would become contaminated from the disposal of animal waste and the carcasses of GE animals and their offspring. Meanwhile, animal welfare activists have also launched campaigns that oppose the use and treatment of animals in xenotransplantation experiments.

The track records of First and Second Wave technologies clearly challenge the pharma biotech industry's message that biotech will 'save lives' and 'get rid of disease.' Mainly certain GE drugs and therapies have proven dangerous and even fatal to patients' health, while costs of developing and using GE drugs are high. And, when we combine these factors with the violations and political and economic strategies of the pharmaceuticals industry as a whole, there is more reason to be critical of, and challenge the industry.

# Conclusion

The pharmaceuticals industry has a long and controversial track record. It has increasingly worked against public interests, motivated solely by profit and the desire for new blockbuster drugs, exploiting indigenous peoples, the poor and those living with disease and disability. Furthermore, the industry's economic wealth and political influence has been facilitated by its pressuring of doctors, governments, patient groups and media. Now with biotech in the picture there is even more reason for concern and for action. Pharma biotech engines are aggressively pushing ahead to ensure that the billions they have spent developing biotech drugs pay off. However, with a strong and coordinated resistance against the pharma biotech engines that asks critical questions about the economic and political influence behind the technologies being developed, this agenda can be challenged.

Within campaigns of resistance, we must recognize the groups that have already been challenging the drug corporations, particularly around biopirating, drug safety and access to essential drugs. Some of these groups include indigenous rights groups, humanitarian aid groups, patient rights groups and health care advocacy groups. Organizing campaigns that make links to the existing struggles is integral for an effective Biojustice movement. Many of these struggles have been identified in this paper. The following is a summary list of the reasons for these struggles, as they relate to the pharma biotech engines:

- **Biocolonialism** -- the stealing and patenting of cells, and in turn genes, from indigenous peoples, as well as ethnically-distinct groups and people with disease and disability, for the development of expensive drugs and treatments for the affluent.

- **Ableist society** -- perpetuation of discrimination against people with disabilities through genetic screening technologies and other gene-based technologies that aim to 'eliminate' disability.

- **Dangerous drugs** -- the release of unsafe drugs due to industry' influence over governments, and in turn, regulatory processes.

- **Expensive R&D** -- governments are using public money to subsidize the biotech industry because of the high costs involved in developing GE technologies. High costs have resulted in expensive GE drugs for patients ( on top of questions around drug safety).

- **Lack of independent research** -- much of the research on GE drugs and therapies occurs at universities and other public research institutions, which are directly influenced by industry.

- **Genetic pollution** -- the release of waste and byproducts from the development and use of GE drugs and therapies has potentially destructive impacts on peoples' health and environments

It is also important that we look very carefully at how to proceed in resisting pharma biotech within the larger framework of a biojustice movement. Firstly, existing struggles be respected. The lead should be taken from groups who are experienced and knowledgeable about the reasons listed above. Secondly, we must look critically at those campaigns whose objectives are limited and don't make links to the more fundamental questions. Anti-abortion groups, for example, have begun to speak out against the use of human embryonic stem cell research. Human embryonic stem cells are taken from cloned human fetuses, and are being used to develop cloned GE stem cells that can be implanted in humans for treatments of

various conditions, including Parkinson's disease and spinal cord injuries whereby cells and tissues in certain parts of the body have degenerated. In response to the controversy around the use of human embryonic stem cells, in 2001, President Bush restricted federal funding for research using these cells. Yet, as we know, the U.S. government is the biggest supporter of the biotech industry in all sectors, especially when it comes to pharmaceuticals. Also, the use of adult stem cells (located in the bone marrow) is still permitted, mainly for drug screening purposes. Multinationals like Novartis and Aventis have invested in biotech companies working on drug screening using adult stem cells.

The campaigns launched by anti-abortion groups, as well as from the U.S. government, on human embryonic stem cells, are worth looking at critically as an exercise to better advance the Biojustice movement. We must be careful not to narrow the demands and challenges to the pharma biotech industry. Companies and governments are always quick to respond, in limited ways, to narrow demands that revolve around issues that generate widespread controversy. They do this without responding to the larger and more fundamental issues. Campaigns must ask critical questions. Using the stem cell issue, for instance, who will benefit from the technologies being developed? What will the implications be on patients? How costly are the developments? What are the alternatives?

Identifying targets locally can be part of an effective strategy in campaign building. How do the pharma biotech engines show up near us? As biopirates, in university labs, in corporate headquarters and regional offices, through partner biotech companies, through government regulatory bodies, public awareness campaigns, through physicians and patient groups? By responding to these questions and understanding many of the reasons why the pharma biotech engines need to be confronted and challenged, we can begin to effectively shake the ground upon which the pharma biotech engines and their partners are sitting.

# Appendix

**Hormone** – a protein produced by a gland or tissue that is released into the bloodstream, which controls body functions such as growth and sexual development.

**Interferon** — a protein produced by body cells that fights viral infections and certain cancers by interfering with the ability of viruses to reproduce. An interferon can also boost the immune system.

**Enzyme** – a protein that acts like a catalyst and helps speed up chemical reactions in the body.

**Antibody** — a protein made by white blood cells that reacts with a specific foreign protein as part of the immune response.

**Monoclonal antibodies**: Of the 360 or so GE based pharmaceutical products and therapies being developed, about one third are monoclonal antibodies (mAbs). More than have of these mAbs are in their later stages of clinical trials. There are currently ten mAbs that have made it to market in the U.S. Three of these products – Synagis, Herceptin and Rituxan – are top selling GE drugs, bringing in sales of over $200 million per year.

MAbs are referred to as 'magic bullets' because it is said that they can target specific infections, leaving the rest of the body untouched. One of the current challenges, however, is the start-up cost for the large-scale production of mAbs using industrial tanks, generally referred to as bioreactors. It is estimated that the cost of building a facility that would have the capacity to manufacture four different mAbs, as well as be up to FDA standards, would cost $5 billion over three to five years.

For this reason, companies have turned to bioreactors of another sort – plants and animals. These organisms are genetically engineered to carry genes that produce selected antibodies. A transgenic mammal that would secrete mAbs in their milk can produce one gram of antibody for approximately $100, that's one third of the cost of traditional production methods. Johnson & Johnson and biotech company Centocor, for example, have a deal to producing a mAb called Remicade using transgenic goats. Dow and biotech company Epicyte have a deal to produce mAb producing corn plants for herpes treatment. Epicyte is also producing mAbs in corn that would bind to sperm and act as contraceptives.

In some cases, these 'plantibody' crops are being promoted to farmers who are looking to farm crops that could give them greater dollar value. Most farmers today are facing extremely difficult situations, as commodity prices for crops have decreased due to decreased government subsidies and elimination of production controls. The genetic contamination of GE food crops is already a reality. With GE crops containing drugs, there is even greater concern for genetic contamination into ecosystems, including our food chain.

# Notes

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