



# RAFI COMMUNIQUE

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## The Gene Giants *Masters of the Universe?*

**Issue:** The 1990s saw a swift and bold concentration of power in the life industry. This trend accelerated in 1998 and shows no signs of abating in 1999, with the recent announcement that DuPont will pay \$7.7 billion to acquire the rest of Pioneer Hi-Bred, the world's largest seed company. A steadily shrinking number of corporate Gene Giants control expanding market share over agribusiness, food and pharmacy. These are the transnational enterprises that aim to manipulate, control, patent and profit from life. Market dominance combined with monopoly patents gives the Gene Giants unprecedented control over the products and processes of life – the biological basis for commercial food, farming and health.

**Impact:** Unchecked corporate power coupled with the vanishing role of public sector research will affect all areas of global health, agriculture and nutrition. Neglect of the public good is inevitable when the research agenda is determined by the private sector in pursuit of corporate profits. There is a widening knowledge gap between rich and poor, both within and between the industrialized North and the impoverished South. Access to food, health and nutrition – once considered a fundamental human right – is now subject to the whims of the free market system.

**Policy Fora:** Is anybody there? The concentration of economic power in the hands of the Gene Giants, and the privatization of science and technology is not being systematically addressed by intergovernmental bodies. These issues should be at the top of the list when UNESCO convenes its World Conference on Science in July 1999 in Bucharest. The Consultative Group on International Agricultural Research (CGIAR) – the world's largest international agricultural research network – runs the risk of irrevocably distorting its mandate to serve the world's poor farmers if it pursues the path of high-tech proprietary science in partnership with transnational Gene Giants. It must instead strengthen its research synergy with national programs and small farmers. The Food and Agriculture Organization, who 20 years ago held a major conference on agrarian reform and rural development, urgently needs to revisit and strengthen its commitment to farmers and food security. FAO must examine the implications of consolidation and the power of the Gene Giants for world food security.

*"In the 20<sup>th</sup> century, chemical companies made most of their products with non-living systems. In the next century, we will make many of them with living systems."*<sup>1</sup> – Jack Krol, DuPont's board chairman

### The Global Picture

This is RAFI's third annual report on the "life industry" – the giant, transnational enterprises that dominate commercial products for agribusiness, food and pharmacy. Loosely defined, the Gene Giants include the transnational enterprises that dominate commercial sale of pesticides, seeds, pharmaceuticals, food and animal veterinary products.

Corporate concentration is nothing new, but the pace of consolidation is accelerating. The value of global mergers and acquisitions in 1998 passed the *two trillion* mark – a

total of \$2.4 trillion – a staggering 50% increase over 1997. After the record setting \$80 billion merger of Exxon and Mobil announced in December – financial analysts speculate that 1999 could see the first billion-dollar merger.

To conclude that transnational corporations rival the power of the nation state is a gross understatement. Indeed, the *Economist* reported that when corporate executives were negotiating the merger of Travelers and Citicorp last year, one of the negotiators mused: "Can anybody stop us?" The only response was "NATO."<sup>2</sup>

One measure of economic globalization is the worldwide level of foreign direct investment (FDI).<sup>3</sup>

According to the United Nations conference on Trade and Development's (UNCTAD) 1998 *World Investment Report*, foreign direct investment by transnational corporations (TNCs) reached a record US \$430-440 billion in 1998.<sup>4</sup> Today, TNCs account for at least two-thirds of world trade.<sup>5</sup> Global cross-border mergers and acquisitions accounted for 58% of all FDI in 1997.<sup>5</sup>

Not surprisingly, UNCTAD reports that the world's largest TNCs are becoming increasingly transnational, with less dependence on their home country in terms of assets, sales and location of their employees. The premiere example is US-based Coca-Cola, a company that derives 80% of its operating profits outside the US. The value of global sales by foreign affiliates of TNCs rose from \$8.9 trillion in 1996 to \$9.5 trillion in 1997.

### Life Industry Sector

*"The common denominator of our business is biology. The research and technology is applied to discover, develop and sell products that have an effect on biological systems, be they human beings, plants or animals."*

- Daniel Vasella, CEO of Novartis<sup>7</sup>

Traditional boundaries between pharmaceutical, biotechnology, agribusiness, food, chemicals, cosmetics and energy sectors are blurring and eroding. Under the "life sciences" banner, transnational firms are using complementary technologies to become dominant actors in all of these industrial sectors. Major enterprises are restructuring to take advantage of the molecular revolution and the complementary use of technologies such as high-throughput screening, combinatorial chemistry, transgenics, bioinformatics and genomics.

*"The agricultural and medical marketplaces are very different but at the research level there is growing commonality. Technologies such as gene sequencing, combinatorial chemistry and high-throughput screening are as relevant to the agricultural as to the human health section."*

- Sir David Barnes, chairman of Zeneca<sup>8</sup>

A radical transformation of the global economy is well underway. Many of the world's largest chemical corporations are shifting out of commodity petrochemicals into biology – away from hydrocarbons to carbohydrates. As corporations embrace the biotechnological future, many are shedding old-fashioned industrial chemicals and concentrating on agribusiness, pharmaceuticals, and food. Consider, for example:

- As recently as 1996, Monsanto was the 4<sup>th</sup> largest chemical company in the United States. In a dramatic shift to biotechnology, Monsanto spun off its \$3 billion chemicals business as a separate company in 1997 (not including the company's profitable herbicide Round-

Up). Since 1996, Monsanto has spent over \$8 billion acquiring seed and agricultural biotechnology companies.

- In 1998, Hoechst (Germany) spun off Celanese, its big American chemical subsidiary, in order to meet its goal of getting out of the chemical industry by the end of 2000.<sup>9</sup> In December 1998 the company announced it would merge with Rhone-Poulenc (France), creating, at least temporarily, the world's biggest life sciences company.
- Life industry giant, Bayer (Germany) is rapidly expanding its life sciences operations. In September 1998, for example, Bayer spun off its Agfa subsidiary, and spent \$1.2 billion to acquire the diagnostic division of Chiron, one of the world's largest biotech companies. In September, Bayer invested \$465 million in Millennium Pharmaceuticals, the largest to date in field of genomics drug research.
- DuPont, until recently the world's largest chemical producer, took dramatic steps to bolster its life sciences' business in 1998 and early 1999. In May, DuPont announced that it would divest its petroleum subsidiary, Conoco, the world's 9<sup>th</sup> ranking oil company. The largest-ever initial public offering for a US company raised a record \$4.4 billion. According to DuPont's chief executive, Charles Holliday, the sale gave DuPont the cash it needed to "rapidly accelerate" investment in the life sciences.<sup>10</sup> DuPont wasted no time, spending \$2.6 billion to acquire Merck & Co.'s 50% share in their joint venture, DuPont Merck Pharmaceutical, for \$ 2.6 billion. On March 15, 1999 DuPont announced that it would pay \$7.7 billion to acquire the remaining 80% stake in Pioneer Hi-Bred International Inc., the world's largest seed company.

In today's knowledge-based economy, intellectual property assets have surpassed physical assets such as land, machinery or labor as the basis of corporate value.<sup>11</sup> Life industry companies are securing and protecting information and technology via monopoly patents, and that quest is, in many cases, driving a restructuring of the industry.

*"The impact of globalization on our business cannot be overstated...Today, the new corporate wealth creation of our time comes from those companies who command ideas -- not from those who manufacture things."*

- John H. Bryan, CEO of Sara Lee Corp.

As if to demonstrate the value of intellectual property assets, the cover of Novartis' 1997 annual report announces that the company holds more than 40,000 patents.

### 1998 in Review

1998 saw the break-up of two announced mega-mergers. The union of Glaxo Wellcome and SmithKline Beecham failed to materialize, and the proposed alliance of

American Home Products and Monsanto also collapsed. At the end of 1998, however, a wave of mergers swept across Europe.

- In early December, Germany's Hoechst and France's Rhone-Poulenc merged to form Aventis - "the world's biggest life science company." With combined sales of \$20 billion per annum, Aventis becomes a global powerhouse and leapfrogs to the world's top ranking firm in sales of pharmaceuticals, agrochemicals and veterinary medicines. The combined research and development budget for Aventis will reach a staggering \$3 billion - that's equivalent to the budget for the 15-year Human Genome Project, or, it's roughly 40% of all funding for agricultural research in the private sector.
- Days later, UK-based Zeneca Group PLC and Astra A.B. of Sweden announced the largest-ever European merger. If completed, the merger would transform two second-tier drug firms into a leading pharmaceutical firm with \$14.3 billion in sales. With combined assets in excess of \$70 billion, the new company will be larger than the 1997 gross national product of 93 of the world's developing nations.<sup>12</sup>
- Also in December, Sanofi S.A. and Synethelabo, both of France, agreed to combine in a \$10.4 billion stock swap.
- In the US, the world's biggest grain exporter, Cargill, announced in November 1998 that it would buy the grain assets of one of its few surviving competitors, Continental Grain Co. According to the National Farmers Union (USA) the proposed merger would allow Cargill to control 45% of the global grain trade; including more than 40% of US maize exports and a third of US soybean exports.<sup>13</sup> The proposed merger is now under review by the US Justice Department.

By all accounts, the urge to merge is not over. As one industry analyst put it, the question isn't which company

is going to be next, "It's better to ask, who's not going to be next? Now, everybody wants to play."<sup>14</sup>

### Food and Beverage Industry - The Mega Gene Giants

The food and beverage giants are the true titans of the life industry. They are likely to become more visible and dominant players in the next 5-10 years. The total retail value of global food sales is estimated at \$2,000 billion - or six and one-half times larger than that for pharmaceuticals. Put another way, the 1997 revenues of the world's largest food and beverage corporation (Nestle - \$45.3 billion) easily surpassed the entire commercial seed industry (\$23 billion), the entire agrochemical industry (\$31 billion) and the animal health industry (\$17 billion). Nestle's 1997 revenues were more than 3 times the revenues of the leading pharmaceutical corporation (Aventis - \$13.7 billion).

In the near future, with growing emphasis on "output traits," crops and animals will be modified for end-users - the giant food processing industry. Among the genetically engineered "value-added" maize and soybean varieties scheduled to debut in 2000 are maize varieties with better amino acid balance; soybean varieties that produce oils with better shelf life; improved amino acid mix in soybeans, etc.<sup>15</sup> These varieties will not be grown as traditional or "generic" commodities. The introduction of proprietary, value-added crops will involve contractual links between the seed company, the farmer, the grain elevator and the processing company. In an era of bioserfdom, farmers are systematically eliminated from farm-level management and decision-making; they become renters of proprietary germplasm from the Gene Giants of their subsidiaries.

As genetic engineering and related technologies become more widely used to alter the function and performance of plants, animals and common ingredients, the food and beverage industry is likely to enter into strategic

alliances, mergers and acquisitions with seed, biotech and agro-chemical and pharmaceutical firms. Just as chemical and pharmaceutical enterprises have spent billions acquiring seed and biotech firms, acquisition of these same enterprises may prove irresistible to food and beverage transnationals. On the other hand, the pharmaceutical giants generally have higher profit margins, they are science and technology-based and have more cash to plow into major investments. Given current trends, we will likely see huge buy-outs and alliances between drug and food giants. How long before a Nestlé or Unilever devours a Glaxo or Novartis (or maybe vice versa?), or a ConAgra consumes a Dow?

### **World's Top 10 Food & Beverage Companies**

Company	1997 Food & Drink Sales (US Millions)	Food & Drink as % of Total Revenues
Nestle SA (Switzerland)	45,380	95%
Philip Morris Co. Inc. (US)	31,890	44%
Unilever Plc/NV (UK & NL)	24,170	50%
ConAgra, Inc. (US)	24,000	100%
Cargill, Inc. (US)	21,000	38%
PepsiCo, Inc. (US)	20,910	100%
Coca-Cola Co. (US)	18,860	100%
Diageo (UK) Guinness + Grand Metropolitan (UK)	18,770	93%
Mars Inc. (US)	14,000	100%
Danone (France)	13,970	94%

Source: RAFI, based on information from Seymour Cooke Food Research International

**Medicinal Foods:** With the development of so-called "functional foods" and "nutraceuticals" the lines between food and medicine are blurring, further enticing food processors, agbiotech firms and drug companies to merge complementary interests in food, biotechnology and pharmaceuticals.

Companies such as DuPont, Kellogg, ConAgra, Mars, Astra/Zeneca and others are rushing to engineer foods that claim to enhance health and wellbeing. According to industry analysts, the sale of foods touting healthy properties is expected to soon reach \$29 billion a year, from virtually zero in 1990.<sup>16</sup> (Note that \$29 billion is higher than the global commercial seed market - \$23 billion.)

The growing market for functional foods is already driving some of the world's largest food companies to seek alliances with pharmaceutical and biotech companies, and it will likely be a further catalyst for giant mergers and acquisitions in the future.

The following examples illustrate the functional food phenomenon:

- Food and beverage giant PepsiCo secured exclusive use of Procter & Gamble's fake fat, Olestra, the key ingredient in PepsiCo's new line of fat-free snack foods.
- Agribusiness giant Archer Daniels Midland is developing a non-dairy frozen dessert using soy protein that it says is low fat, cholesterol and lactose free and a source of vitamin E.
- Unilever will soon introduce a margarine that has cholesterol-lowering ingredients derived from wood pulp. The product will sell for 3-4 times the price of normal margarine. According to one analyst: "[The product] should not be compared with ordinary margarine but with what people pay for healthcare products."<sup>17</sup>
- DuPont has 40 clinical trials underway with soy protein. The company's goal is to develop soy-based foods that lower cholesterol, and combat osteoporosis or cancer.<sup>18</sup>

**Seed and Agrochemical Industry**

The commercial market for genetically engineered seeds expanded dramatically in scale and geographic scope in 1998. It was matched by unprecedented public opposition to genetically engineered crops and widespread concern about genetically engineered foods - especially in Europe.

- From 1986 - 1997, approximately 25,000 transgenic crop field trials were conducted by 45 countries on more than 60 crops and 10 traits. Of this total 15,000 field trials were conducted during the first ten-year period, and 10,000 in the last two years.<sup>19</sup>

**World's Top 10 Agrochemical Corporations**  
The top 10 agrochemical corporations account for \$26.2 billion or 85% of the \$30.9 billion agrochemical market worldwide.

Company	1997 Revenue (US Millions)
Aventis Group (France) pending	\$4,554
Novartis (Switzerland)	\$4,199
Monsanto (USA)	\$3,126
Zeneca/Astra (UK) - pending	\$2,674
DuPont (USA)	\$2,518
Bayer (Germany)	\$2,254
Dow AgroSciences (USA)	\$2,200
American Home Products (USA)	\$2,119
BASF (Germany)	\$1,855
Sumitomo (Japan)	\$717

Source: RAFI, with information provided by AGROW: World Crop Protection News

- Almost 28 million hectares of genetically engineered crops were grown worldwide in 1998. Soybean, maize, cotton, canola/rapeseed and potato were the five principal transgenic crops grown in 1998. Transgenic soybean and maize accounted for 52% and 30% of global transgenic area respectively. Herbicide tolerance was the dominant trait, accounting for 77% or 12.9 million hectares of all transgenic crops; insect resistance accounted for 22%, or 3.7 million hectares of the global transgenic area.<sup>20</sup>
- According to the International Seed Trade Federation, the world market for genetically engineered seeds is expected to reach \$2 billion by the year 2000 and will triple to \$6 billion by 2005. The Federation predicts that the market for bioengineered seeds will reach \$20 billion in the year 2010.<sup>21</sup>

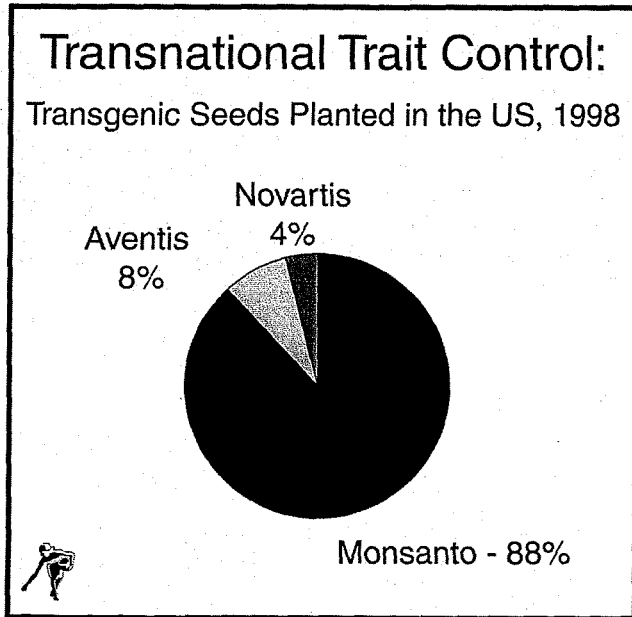
**Area of Transgenic Crops Planted (million hectares)<sup>22</sup>**

Country	1997	1998
USA	8.1	20.5
Argentina	1.4	4.3
Canada	1.3	2.8
Australia	0.1	0.1
Mexico	0.1	0.1
Spain	0.0	0.1
France	0.0	0.1
South Africa	0.0	0.1
<b>TOTAL</b>	<b>11.0</b>	<b>27.8</b>

Source: Clive James, 1998

Particularly striking is not just the number of hectares on which transgenic crops are grown, but the fact that a handful of Gene Giants completely dominate the market for bioengineered seeds. According to estimates compiled by the Sparks Companies, in the US (the world's largest transgenic seed market), Monsanto's transgenic seeds accounted for 88% of the total transgenic crop area in 1998.<sup>23</sup> AgrEvo (now Aventis) accounted for 8%, and Novartis' transgenic seeds were planted on just 4%.

While leading competitors such as DuPont and American Home Products are expected to commercialize new transgenic crops soon – the market will still be controlled by an elite group of Gene Giants.



### Terminator and Traitor Technology

The infamous Terminator technology identified by RAFI in March 1998 is a technique for genetically altering a plant so that the seeds it produces are sterile. It is a threat to agricultural biodiversity and the wellbeing of 1.4 billion rural people who depend on farm-saved seed and local plant breeding. In January 1999 RAFI revealed that virtually all the Gene Giants (Monsanto, Novartis, Astra/Zeneca, DuPont, BASF, Rhone Poulenc) are working on their own genetic seed sterility patent claims. Over two dozen new patents reveal that engineered seed sterility is not an isolated research agenda, it's the Holy Grail of the agricultural biotechnology industry.

**Traitor technology:** The new generation of Terminator patents goes beyond the genetic neutering of crops. The patents reveal that companies are developing suicide seeds whose genetic traits can be turned on and off by an external chemical "inducer" – mixed with the company's patented agrochemicals. In the not-so-distant future, we may see farmers planting seeds that will develop into productive (but sterile) crops only if sprayed with a carefully prescribed regimen that includes the company's proprietary pesticide, fertilizer or herbicide. The latest version of Monsanto's suicide seeds won't even germinate unless exposed to a special chemical, while Astra/Zeneca's technologies outline how to engineer crops to become stunted or otherwise impaired if not regularly exposed to the company's chemicals. A Novartis patent (US 5,789,214) describes a process for chemically regulating a number of developmental processes in plants – such as germination, sprouting, flowering, fruit ripening, etc. The patent specifically mentions that the chemical regulator can be applied to plants in combination with a fertilizer or herbicide. RAFI calls it "Traitor Technology." (For more information and in-depth analysis, see *RAFI Communique*, "Traitor Tech: The Terminator's Wider

Implications," January/February, 1999. Available on the internet: <http://www.rafi.org>)

If companies can genetically program suicide seeds to perform only with the application of proprietary pesticide or fertilizer, it means they will dramatically increase sales of their patented agrochemicals and other proprietary inputs. Chemically-dependent suicide seeds are a dazzling technological achievement and a brilliant marketing strategy, but it's grim news for farmers, the environment and global food security.

*"Seeds are software. And we have the seeds."*

- Alfonso Romo Garza, owner of Empresas La Moderna, a Mexico-based seed company that controls 25% of the global vegetable seed market.<sup>24</sup>

In mid-1998 RAFI produced a *Communique* on seed industry consolidation which gives a comprehensive picture of who owns whom in the global seed industry. (See *RAFI Communique, Seed Industry Consolidation*, July/August 1998.) Today, the top 10 seed companies control over 30% of the \$23 billion commercial seed market. But corporate market share is much higher in specific seed sectors and for certain crops. For example:

- 40% of US vegetable seeds come from a single source.<sup>25</sup> The top 5 vegetable seed companies control 75% of the global vegetable seed market.<sup>26</sup>
- Just 4 companies (DuPont, Monsanto, Novartis, Dow) control 69% of the North American seed corn market.<sup>27</sup>
- Just 4 companies (Monsanto, DuPont/Pioneer, Novartis, Dow) control at least 47% of the commercial soybean seed market. An estimated 10% of the market is in public varieties. An estimated 25% of North American soybean seed is farmer-saved, not newly purchased.<sup>28</sup>
- At the end of 1998, Monsanto controlled 87% of the US cotton seed market.<sup>29</sup> (Since then, Monsanto has divested some interests in cotton seeds as a preemptive move to gain regulatory approval of its takeover of Delta & Pine Land.)

Following DuPont's March 1999 announcement that it would acquire the rest of Pioneer Hi-Bred International for \$7.7 billion, the *Wall St. Journal* said the deal "effectively divides most of the US seed industry between DuPont and Monsanto."<sup>30</sup>

### Crop Genomics Research Accelerates

Scientists are using advanced genomics as a means of identifying, mapping and understanding the expression of crop genes, and their link to agronomically important traits. The goal is not only to construct genetic maps of plant species, but also to link the genetic structure of the plant with its protein activity.<sup>31</sup>

In July 1998 Novartis announced that it will spend \$600 million over 10 years to establish the "Novartis Agricultural Discovery Institute," a new in-house effort

dedicated to plant genomics research. The company says it will be the world's biggest crop gene mapping project. The California-based institute will employ about 180 scientists.

In November 1998 Novartis and the University of California at Berkeley (Department of Plant and Microbial Biology) signed an unprecedented \$25 million, 5-year agreement. Although the agreement specifies that Novartis cannot dictate what research will be performed with its money, the company will have first rights to negotiate an exclusive license on a fraction of all the research developments in the laboratories – whether or not the projects were supported by Novartis funds.<sup>32</sup> Critics charge that the alliance gives a private company unprecedented ability to influence the research agenda at a state-owned university, and it will allow public goods to be appropriated for private profit.

Since 1996, virtually every major seed/agrochemical company has invested in plant genomics research. Driven by the increased efficiency of genomics technology and fierce competition among major agbiotechnology firms, investments in crop genomics accelerated dramatically in 1998 (see table).<sup>33</sup> Particularly noteworthy is the very minor participation of public sector researchers in agricultural genomics. After the Gene Giants and their genomics partners stake patent claims to molecular bits and pieces of commercially important plant genomes – what will be left for the public sector? With patents in hand, the Gene Giants have the legal right to determine who will get access to plant genomic material and at what price.

### The World's Top 10 Seed Corporations

The top 10 seed companies control approximately 32% of the \$23 billion seed trade worldwide.

Company	1997 Revenue (US Millions)	Comment
DuPont/Pioneer Hi-Bred (US)	\$1,800+	DuPont will buy the the remaining share of Pioneer for \$7.7 billion.
Monsanto (USA)	\$1,800 (est.)	Estimate of the total sales volume of all Monsanto seed acquisitions made by October, 1998. <sup>34</sup>
Novartis (Switzerland)	\$928	Formerly Ciba Geigy and Sandoz.
Groupe Limagrain (France)	\$686	French cooperative.
Advanta (UK and NL)	\$437	Owned by AstraZeneca and Royal VanderHave.
AgriBiotech, Inc. (USA)	\$425	The company has completed over 30 acquisitions (forage and turfgrass) since 1995.
Grupo Pulsar/Seminis/ELM (Mexico)	\$375	Pulsar is giant agro-industrial corporation that owns Empresas La Moderna, majority shareholder of Seminis, Inc. A merger is proposed with Seguros Comercial America. The new company will be called Savia.
Sakata (Japan)	\$349	Vegetable/flower/turfgrass.
KWS AG (Germany)	\$329	Major sugar-beet seed company.
Takii (Japan)	\$300 (est.)	Privately-held.

Source: RAFI

### Recent Agricultural Genomics Deals

Company/Institute	Partner	Date	Action
AgrEvo (Germany)	Gene Logic	1998	3-yr., \$45 million genomics alliance.
Dow (US)	Biosource Technologies	1998	3-yr. genomics research alliance.
DuPont & Pioneer (US)	CuraGen	1998	\$5 million per annum expansion of plant genomics research alliance
DuPont (US)	Lynx Therapeutics	1998	5-yr., up to \$60 million. Focus on maize, soybeans, wheat & rice.
Genoplante - French Genome Initiative (FR)	See right.	1998	Focus on genomics in European crops. Public/private alliance involving Rhone-Poulenc, Biogemma, Sigma/Serasem, Florimond Desprez, INRA, CIRAD, ORSTOM and French universities
Monsanto (US)	Incyte Pharma.	1998	Broad access to Incyte's gene expression technology.
Monsanto (US)	GeneTrace	1998	\$17.2 million, plant & animal ag. genomics technology

Novartis	Novartis Ag. Discovery Institute	1998	10-yr., \$600 million plant genomics institute.
NSF Plant Genome Project (US govt.)	University of Missouri (US)	1998	\$11 million for maize genomics research
Zeneca (UK)	John Innes Center & Sainsbury Laboratory (UK)	1998	10-yr., \$80 million for advanced genomics and wheat.
Zeneca Agro (UK)	Alanex	1998	3-yr. agreement for screening of Alanex's compound library.

## Truth and Consequences

### RAFI's REALITY CHECK

#### FOOD

**The Facts:** The top 10 food and beverage corporations account for sales of over \$233 billion. According to industry analysts, the top 10 companies account for an estimated 16% of global retail food sales.<sup>35</sup>

**Reality Check:** New estimates from the Food and Agriculture Organization of the United Nations indicate that there are 828 million chronically undernourished people in the world, an increase since the 1997 World Food Summit.<sup>36</sup>

#### PHARMACEUTICALS

**The Facts:** The top 10 pharmaceutical firms control 35% of the \$297 billion pharmaceutical market. The average profit margin of the ten largest firms in 1996 was 30 per cent.<sup>37</sup> Analysts predict that the global pharmaceutical market will grow 7.8% annually to \$406 billion in 2002. North America, Europe, Japan and Latin America are projected to account for 85% of the worldwide pharmaceutical market.

**Reality check:** One-fifth of humanity has no access to public health services and one half lacks regular access to essential drugs.<sup>38</sup> Inequalities are widening both within and between the industrialized countries and the South. Average life expectancy is 22 years longer in industrialized countries than in LDCs.

In the US, prescription drug costs have risen an average 17% per annum in recent years; and national spending on prescription drugs has more than doubled in the last decade.<sup>39</sup> A 1998 report estimates that adverse reactions to prescription drugs are killing about 106,000 Americans each year – more than automobile accidents.<sup>40</sup>

#### AGROCHEMICALS

**The Facts:** The top 10 agrochemical corporations control 85% of the global pesticide market, valued at \$31 billion.

**Reality check:** Up to 25 million agricultural workers in the South – 11 million in Africa – may be poisoned each year by agrochemicals, and hundreds of thousands die.<sup>41</sup> Over 500 species of insects and mites are reported resistant to one or more insecticides<sup>42</sup>; 216 weed species are resistant to at least one class of chemical weed killers.

#### SEEDS

**The Facts:** The top 10 seed corporations control 32% of the commercial seed market valued at \$23 billion. In the US, the cost to farmers of seeds, fertilizers and agricultural chemicals shot up 86% between 1987-1997.<sup>43</sup>

**Reality check:** Seed oligopoly is a fact of life. The disappearance of public sector plant breeders, coupled with consolidation in the seed industry and the specter of Terminator seeds, puts farmers at the mercy of a handful of Gene Giants. Terminator threatens the livelihoods of 1.4 billion people who depend on farm-saved seeds. The top 4 companies control 69% of the North American maize seed market. The top 5 vegetable seed companies control 75% of the global vegetable seed market. The transgenic seed market is virtually controlled by five Gene Giants: DuPont, Monsanto; Novartis; Astra/Zeneca; Aventis.

#### ANIMAL PHARMACEUTICAL

**The Facts:** The top 10 veterinary medicine firms control 60% of the \$17 billion dollar animal health industry.

**Reality check:** The animal pharmaceutical industry is plagued by emerging crises related to animal and consumer health. The European beef cattle industry collapsed following the bovine spongiform encephalopathy (BSE) and related food safety crises; there is growing evidence of the link between low-level use of antibiotics in animal feed and the rise of antibiotic-resistant bacteria in human medicine. Though scarcely acknowledged by industry, there is a perilous loss of animal genetic resources worldwide. Domestic animal breeds are disappearing at an annual rate of 5%, or 6 breeds per month.<sup>44</sup> According to FAO, the status of almost one-third of all livestock breeds is endangered or critical.

**Animal Pharmaceutical Sector:  
The Gene Giants' Orphan Industry?**

With industry-wide revenues of \$17 billion, the animal pharmaceutical industry represents only about 5% of the giant human pharmaceutical market. Industry analysts refer to animal health as a "mature" market, with only modest growth (3%+) in recent years. Nevertheless, the growing synergy between animal veterinary medicine and the human pharmaceutical market is clear. For example, biotech companies are producing human proteins in cows' milk; they are hoping to grow spare-part human organs in pigs; and there is a rapidly growing market for antidepressants for dogs (really).

According to Fountain Agricounsel, the animal health division of most pharmaceutical and agrochemical corporations dilutes the profit margin of the parent company.<sup>45</sup> The animal health industry depends on the economic muscle and R&D budgets of the Gene Giants. Of the top 20 companies, only two are stand-alone businesses with a primary focus on animal health.

Consolidation in the animal pharmaceutical sector continues. Analysts predict that the survivors will include a top tier of four or five mega-size companies with revenues of at least \$2 billion (there is only one in that category today) driven by genomics research and technology.

Traditionally, the food animal sector accounts for 75% of the animal health industry revenue. During the 1990s, however, the "companion animal market" (that is, domestic pets) in the industrialized world revolutionized the animal health market and the focus of current R&D. Today, the companion animal market is second only to the cattle species sector in size. Fountain Agricounsel predicts that within five years the companion animal sector will account for over one-third of the industry's total revenue and over half of the total operating profits. Though the statistics may be difficult for some to comprehend, analysts conclude that, "Many pet owners are willing to spend for the health and well being of their pets at a level equal to or greater than what they spend for themselves and their family."<sup>46</sup>

The animal health industry is plagued by growing consumer concerns about food safety and animal welfare. In North America, the risk of pathogen-related food-borne illnesses has become a daily occurrence - ranging from massive re-calls of E. coli contaminated hamburger meat, to dangerous salmonella outbreaks in meat and egg products. The European beef industry suffered a virtual collapse following the bovine spongiform encephalopathy (BSE) crisis. In January 1999 Canada's national health agency declined to approve the use of Monsanto's genetically engineered bovine growth

**World's Top 10 Veterinary Medicine Companies**  
The top 10 animal health firms control approximately 60% of the \$17 billion dollar animal health industry.

Company	1997 Sales (US) Millions
<b>Aventis Group</b> Merial Animal Health/Hoechst Roussel Vet pending	\$2,258
<b>Roche Vitamins Inc.</b>	\$1,603
<b>Pfizer Animal Health</b>	\$1,329
<b>Bayer Animal Health</b>	\$947
<b>Rhone-Poulenc Animal Nutrition</b>	\$731
<b>American Home Products (Ft. Dodge Laboratories)</b>	\$700
<b>BASF</b>	\$682
<b>Schering-Plough Animal Health</b>	\$627
<b>Novartis Animal Health</b>	\$611
<b>Eli Lilly (Elanco Animal Health)</b>	\$590

Source: RAFI, based on material provided by Fountain Agricounsel, LLC

hormone, citing concerns over the drug's impact on animal health and welfare.<sup>47</sup>

**Human Genomics Companies**

RAFI has been monitoring the growth and evolution of the human genomics companies since 1994. These are the companies that aim to de-code, map, identify and patent the functional characteristics of "commercially relevant" human genes. These high-tech, entrepreneurial companies were founded on venture capital and the promise of patented products and processes. The majority of genomics companies has no commercial products or profits - only patents. For genomics companies, survival depends on strategic alliances and equity investments from the Gene Giants, or subscription fees to proprietary genome databases.

Today, the process of sequencing DNA is much faster and cheaper than anyone imagined possible even five years ago. For example:

- In the mid-1970s it would take a laboratory two months to sequence 150 nucleotides (the molecular letters that spell out a gene).<sup>48</sup> Today, one commercial genome firm has the tools to sequence 11 million letters a day.
- The cost of DNA sequencing has dropped from about US \$100 per base pair in 1980 to less than \$1 today, and experts predict it will be less than a cent by 2002.<sup>49</sup>

The furious pace of discovery in the field of genomics is reflected in the growing number of patent claims related to partial gene sequences or ESTs (expressed sequence tag). In 1991, the US Patent and Trademark Office had applications pending on 4,000 EST sequences. In 1996,



there were a total of approximately 350,000 EST sequences to be examined, and as of September 1998, there were applications pending on over 500,000 EST sequences.<sup>50</sup>

In November 1998 California-based Incyte announced that it had received the first US patent on 44 ESTs.<sup>51</sup> The company's self-described aim: "Our goal is now to have sequenced, mapped and filed for intellectual property on the novel and most commercially relevant genes by the second half of the year 2000."<sup>52</sup>

*Our goal is now to have sequenced, mapped and filed for intellectual property on the novel and most commercially relevant genes by the second half of the year 2000."*

-- Incyte

The patenting of partial gene sequences is controversial; even the US government's National Institutes of Health objects to the patenting of ESTs. How, they ask, can standard patent criteria (novelty, non-obviousness and utility) be met in a case where the function of a partial gene sequence (the protein it encodes) is not even known? Claims on partial gene sequences may also preclude future patenting of a full-length gene containing an already patented sequence. After Incyte Pharmaceuticals announced that it received the first patent on partial gene sequences in late 1998, Leroy Hood, head of the University of Washington's department of molecular biology, announced that he would terminate research on a possible colon cancer screening test because his work involved a gene that is the subject of an EST patent application filed by Incyte.<sup>53</sup> This example illustrates how gene patents, instead of promoting innovation, are stifling research and hindering competition.

**Human Genome Project Privatized?** The Human Genome Project, a 15-year, \$3 billion project supported primarily by the US government and British partners, was launched in 1990 to map the entire human genome, the 80,000-100,000 genes that exist within our DNA. The Human Genome Project was conceived as an international, public sector initiative, a project too massive in scope and too expensive for any single country or company to undertake. With the advent of faster, cheaper sequencing technologies, the race to map the human genome now faces stiff competition from the private sector.<sup>54</sup> In May

1998 a new commercial venture announced that it would start and essentially complete the sequencing of the human genome in 2001, 4 years ahead of the US government's target date of 2005. The company, a joint venture between Perkin-Elmer and the US-based Institute for Genomics Research (TIGR) claims that the sequencing capacity of the company's state-of-the-art equipment far exceeds the total sequencing capacity of all existing genomics laboratories in the world.<sup>55</sup> The new company's goal is to become the "definitive source of genomics and associated medical information."<sup>56</sup> In August 1998 Incyte Pharmaceuticals trumped its commercial rivals, announcing that it would map most of the human genome within one year.<sup>57</sup>

After receiving additional financial support from the Wellcome Trust of London, the world's largest medical philanthropy, the Human Genome Project announced in September, 1998 that it would move up by two years, to 2003, its target date for completing the sequencing of the human genome.<sup>58</sup>

**Icelandic DNA Monopolized?** The human genetic gold rush continues worldwide. In early 1998 the prospect of nationwide collection and commercialization of human DNA made headlines when Hoffman-La Roche (Switzerland) and DeCode Genetics Inc. (Iceland) signed a \$200 million research collaboration to identify disease genes based on studies of Iceland's relatively isolated and strikingly homogeneous population.<sup>59</sup> The Icelandic situation has become an international test case for many of the ethical and intellectual property issues surrounding collection and commercialization of human DNA.<sup>60</sup> Despite opposition by growing numbers of Iceland's scientific and medical community, a bill was passed by the Icelandic parliament on 17 December 1998 that gives DeCode Genetics the right to collect current and retrospective medical information from Iceland's 270,000

## World's Top 10 Pharmaceutical Companies

The top 10 pharmaceutical corporations control 35% of the \$297 million dollar pharmaceutical market.

Company	1997 Pharma. Sales (US Millions)	Pharma. Sales % of Total Revenues
Aventis (Rhone-Poulenc + Hoechst) pending (France)	\$13,750	30%
Merck (US)	\$13,636	58%
Glaxo Wellcome (UK)	\$13,082	100%
Novartis (Switzerland)	\$10,943	51%
Astra/Zeneca - pending (UK)	\$10,000	69%
Bristol-Myers Squibb (US)	\$9,932	59%
Pfizer (US)	\$9,725	78%
American Home Products (US)	\$8,669	61%
Johnson & Johnson (US)	\$7,696	34%
SmithKline Beecham (US)	\$7,495	59%

Source: RAFI, based on information provided by Scrip's 1998 Pharmaceutical League Tables

inhabitants into a centralized, comprehensive database.<sup>61</sup> The new law gives DeCode Genetics exclusive rights to the commercial exploitation of genetic information for 12 years.

A vocal minority of Iceland's scientific and medical community, including the Icelandic Medical Association, the Association of Icelanders for Ethical Science and the Icelandic Mental Health Alliance oppose implementation of the law and are advising doctors and their patients to refuse participation in the collection of DNA samples.<sup>62</sup> Opponents believe that the bill violates principles of privacy and informed consent and they object to a single company gaining exclusive rights to a valuable scientific resource. For example, the law allows only for individuals to opt out of the database, but does not require any other form of consent. Although the database is supposed to be confidential and anonymous, critics charge that personal information can be deciphered and that computer security measures proposed by the company are not adequate to insure confidentiality.

**The Specter of Biological Warfare:** The use of genetic research for biological warfare is an ominous trend that RAFI has monitored since 1987. It is almost impossible to distinguish between peaceful, humanitarian uses of genetic research and the development of genetic weaponry. According to Dr. Pauline Lane of the University of East London, "The line between medical research and warfare is often difficult to distinguish and...[it] is a difficult area to monitor."<sup>63</sup> A report released in January 1999 by the British Medical

Association warns that biomedical research could be perverted to develop "weapons which may become a major threat to the existence of Homo sapiens, and a development of biotechnology which perverts the humanitarian nature of biomedical science".<sup>64</sup>

The 1972 Biological and Toxic Weapon Convention (BTWC), signed by 141 countries, bans the development and production of biological weapons. But the Convention is impossible to enforce because it lacks mechanisms for oversight and enforcement. In 1998 negotiators met in Geneva to strengthen the BTWC. But efforts to develop a legally-binding compliance protocol were stalled because pharmaceutical and biotech representatives voiced concern about industrial espionage and the theft of intellectual property.<sup>65</sup> A conference to review the 1972 Convention is due in 2001.

In November 1998 the *London Sunday Times* reported that scientists are attempting to engineer deadly biological organisms to produce "ethno-bombs" that are capable of targeting human victims by ethnic origin.<sup>66</sup>

In early January 1999 Craig Venter of Celera Genomics told the American Association for the Advancement of Science that his company was on the threshold of constructing the world's first simple artificial life form, based on 300+ genes borrowed from a simple microbe. But Venter's team announced that it would halt further work because artificial organisms could be misused and become a template for deadly biological weapons in the hands of bioterrorists.<sup>67</sup>

## "Gene Juniors" - Leading Human Genomics Companies

Genomics Company (and year founded)	Alliances with Pharmaceutical Giants	Patent Portfolio	Comments
Axys Pharmaceuticals (US) 1998	Bayer, Boehringer Ingelheim, Roche, Bristol-Myers Squibb, Parke-Davis, Pharmacia & Upjohn, Rhone-Poulenc, Amgen	At least 4 issued in US; obesity genes and retinal dystrophies.	Arris Pharmaceuticals and Sequana Therapeutics merged in 1998 to form Axys
DeCode Genetics (Iceland) 1997	Hoffmann-La Roche, 5-yr. \$200 million deal	Research will focus on discovery of genes related to 12 common hereditary diseases.	DeCode wins exclusive monopoly rights to Icelandic DNA in 1998.
Genome Therapeutics (US) 1994	Schering-Plough, AstaAB, Bayer, Bristol Myers, Hoechst		Focus on pathogen genomics (drug-resistant bacteria) and human genomics
Genset (France) 1989	Abbott, Genetics Institute, Johnson & Johnson, Pharmacia & Upjohn, Synthelabo, American Home Products	Patents filed on prostate cancer genes.	Self-described leading European genomics company. Focus on genes for schizophrenia, osteoporosis, cardiovascular disease, obesity.
Human Genome Sciences, Inc. (US) 1992	Hoffmann-La Roche, SmithKline Beecham, Takeda, Schering-Plough, Synthelabo, Merck, Affymetric, Pharmacia & Upjohn	66+ patents allowed by US PTO. Patents pending on over 476 full-length human genes.	HGS claims it has isolated 95% of all human genes.

Incyte (US) 1991	Incyte's partners include 22 of the world's largest pharmaceutical companies.	93 issued US patents; applications pending on 1,500 full-length human genes and over 1.2 million partial gene sequences (ESTs)	Unlike most genomics companies, Incyte posted profits in 1998. The company acquired British firm Hexagen for \$5 million cash.
Millennium Pharmaceuticals (US) 1993	Pfizer, Eli Lilly, Asta AB, Wyeth-Ayerst, Monsanto, Bayer.	500+ US and intl. patents pending; 21 issued	Over \$1 billion in total pharma. alliances. Company expects to report first profits in 1998. Bayer's \$465 million alliance is largest to date in human genomics.
Myriad Genetics (US) 1991	Bayer, Novartis, Schering-Plough, Eli Lilly, Monsanto	14 issued US patents; especially portfolio of breast cancer genes	

Source: RAFI

<sup>1</sup> Krol is quoted in a case study prepared by Professor Jonathan West, Harvard Business School, "E.I. duPont de Nemours and Company," November 19, 1998, no. N-9-699-037.

<sup>2</sup> The story is told in the *Economist*, January 9, 1999, p. 21.

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<sup>4</sup> UNCTAD Press Release, "New Records Being Set in Global Foreign Direct Investment," UNCTAD, 2 November 1998, TAD/INF/2775.

<sup>5</sup> Personal communication with Masataka Fujita, International Investment, Transnationals and Technology Flows Branch, UNCTAD, 15 January 1999.

<sup>6</sup> UNCTAD Press Release, "Cross-Border Mergers and Acquisitions Dominate Foreign Direct Investment Flows," 2 November 1998, TAD/INF/2776.

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