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BIOTECHNOLOGY COMPANY WILL SELL BIO-ENGINEERED HUMAN PROTEINS TO INFANT FORMULA MANUFACTURERS

ISSUE: GenPharm International announces plans to sell bio-engineered human proteins, produced in the milk of transgenic cows, as ingredients for the infant formula industry.

IMPACT: Bio-engineered human proteins such as lactoferrin have the potential to make infant formula more "nutritionally complete." The danger is that it will give infant formula manufacturers a powerful new marketing tool and revive unethical marketing practices that have led to death and illness for millions of children, especially in the Third World.

Will the infant formula product be labeled so that consumers are aware that it contains bio-engineered human proteins? Will the Third World be used as a testing ground before it is approved in industrialized countries?

Transgenic farming, using patented processes for creating bio-engineered livestock, will also promote genetic uniformity in livestock and accelerate the growth of contract farming.

WHEN: GenPharm plans to begin selling bio-engineered human proteins to infant formula companies in 1996. The company has a formal agreement with Bristol-Myers Squibb, and negotiations are reportedly underway with other pharmaceutical corporations that sell infant formula products.

FINANCIAL STAKES: Infant formula is a (US) $4 billion market worldwide.

GenPharm International Will Sell Genetically Engineered Human Milk Proteins to Infant Formula Companies

Earlier this year, GenPharm International, a biotechnology company based in the Netherlands and the United States, announced its plans to sell bio-engineered ingredients to the makers of infant formula, a worldwide market of (US) $4 billion. The company will produce these ingredients, including proteins contained in human breast milk, in the milk of transgenic dairy cattle.

Instead of using costly fermentation or cell culture facilities to produce genetically engineered proteins in the laboratory, GenPharm is one of several biotech companies that seeks to use transgenic farm animals as a cheap and continuous production system to produce large quantities of pharmaceuticals or foreign proteins in their milk.

GenPharm is the owner of the world's first transgenic dairy cow (Herman, a bull) born in December, 1990. Herman was bio-engineered by company scientists in the pre-embryo stage to carry the foreign gene for producing human lactoferrin. A genetically-engineered segment of DNA, called a transgene, was microinjected into a fertilized bovine egg that grows to become an embryo *in vitro*. The embryo was later implanted non-surgically into Herman's mother. The transgene engineered by GenPharm, which the company calls a "proprietary expression cassette," gives the

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cow the necessary genetic information to produce, upon lactation, foreign proteins at high levels in its mammary gland. The company's goal is to use Herman's female offspring to produce both high-volume nutritional proteins and high-value therapeutic proteins. GenPharm has applied for U.S. and world patents on the process used to create transgenic animals like Herman.

With artificial insemination, a bull like Herman can produce 10,000 calves a year. The company is confident that the genes passed on to Herman's offspring will be expressed in commercially relevant levels. According to GenPharm, a single cow can produce more than 300 kg of bovine milk protein per year at production costs as low as one cent per gallon.

Ingredients for Infant Formula

Herman, the transgenic dairy bull, is already producing female offspring that will carry human proteins in their milk. The foreign genes will enable the cows to express two essential human proteins in their milk--human lactoferrin and human lysozyme--that are not present in infant formula. These proteins, which have specific antibacterial and iron-transport properties, are too expensive to produce in adequate quantities by conventional cell culture methods.

Bristol-Myers Squibb, one of the world's largest pharmaceutical corporations, has a collaborative agreement with GenPharm to use the human protein-carrying bovine milk in its infant formula products.[1] (Mead-Johnson Nutritional Group, a subsidiary of Bristol-Myers Squibb, markets infant formula internationally.) The company would not comment on their plans to market infant formula containing bio-engineered proteins, saying that it is premature to speculate because the product is not yet available. (NOTE: RAFI does not know for sure if the formula product will be sold at a premium price and targeted to affluent consumers, or whether it will be marketed worldwide).

Ironically, Bristol-Myers Squibb is one of three manufacturers of infant formula in the U.S. that has stated it does not plan to use milk derived from dairy cows treated with the controversial, genetically engineered bovine growth hormone (see update on BGH that follows). According to John Stauber of the U.S.-based Pure Food Campaign, the company has agreed in writing that it will not accept milk from BGH-treated cows, regardless of whether or not it is approved for sale by the U.S. Food and Drug Administration.

According to GenPharm's Chief Executive Officer, Jonathan J. MacQuitty, GenPharm will begin selling bio-engineered ingredients to infant formula companies in 1996. The company will need approximately 2,000 transgenic cows producing 10,000 liters of milk a year to launch the business.[2] MacQuitty told *Biotechnology Newswatch* that he expects parents to buy milk on the recommendation of their doctors, whom GenPharm is already wooing.

Will mothers be willing to buy infant formula containing bio-engineered ingredients extracted from the udders of transgenic cows? Not to worry, says the company: *"We're making these proteins exactly the way they're made in nature,"* MacQuitty told *Biotechnology Newswatch. "Human milk is the gold standard, and formula companies have added more and more [human-like elements] over the past 20 years,"* said MacQuitty.[3]

Early Warning for Third World Consumers

RAFI's concern is that bio-engineered infant formula will give infant formula manufacturers a new marketing strategy, with serious implications for infant health and development, especially in the Third World. Will bio-engineered formula be marketed as a "new and improved," nutritionally-complete product, containing all the beneficial proteins found in human breast milk? Will the product be labeled so that consumers know it contains bio-engineered proteins? As we have already seen with the case of bovine growth hormone, it is possible that this novel product of genetic engineering will be marketed in the Third World before it is approved for commercial sale in the North. In the United States, there are no existing policies to regulate products derived from transgenic animals. Regulatory programs will need to be developed before they can

be commercialized and approved for human consumption.

It is important to be clear. At this point, nobody knows for sure whether or not infant formula containing bio-engineered human proteins will present new risks for human health simply by virtue of containing bio-engineered ingredients. The immediate danger is that transnational companies will use the "nutritionally improved" formula ("just like mother's milk") to launch aggressive new marketing campaigns. MacQuitty told RAFI: "*These ingredients could be quite important for formulas in developing countries.*"[4]

The issue is not new. It is a tragic fact that millions of babies, the vast majority in the Third World, have died because of artificial feeding practices promoted by transnational food and pharmaceutical corporations. Bottle feeding is associated with malnutrition and greater likelihood of infectious disease, other illness, and death of young children. By interfering with breastfeeding, bottle feeding has been identified as a major world health problem.

The International Baby Food Action Network (IBFAN), a strong global citizens network with organizers from 67 countries, has been battling the unethical marketing practices of infant formula manufacturers since 1979.

IBFAN played a major role in the development of a United Nations' Code of Marketing of Breast-Milk Substitutes in 1980, and, even more importantly, has increased consumer awareness worldwide that there is no substitute for breastmilk. Even so, the Code of Marketing has been adopted as law in only a handful of countries. Most countries are still considering legislation, voluntary measures, or further studies.

As a new product of genetic engineering seeks to penetrate new markets or expand market share in old ones, the concern is that there will be a resurgence of unethical marketing practices by the infant formula industry. The danger is greatest in the Third World.

RAFI has shared this analysis with IBFAN which continues to monitor industry practices and observance of the Code of Marketing, and works to promote breastfeeding worldwide.

"Identity-Preserved" Transgenic Farm Animals will Enhance Corporate Concentration in Animal Agriculture

According to a recent issue of the *Biotech Reporter*: "*Transgenic farm animals that produce pharmaceuticals in their milk represent a relatively "easy" technology and potentially substantial profits to companies producing them. They may even create a whole new industry of identity-preserved agriculture for livestock.*" (*Biotech Reporter,* May, 1993, p. 1-2).

Transgenic livestock used as production systems for pharmaceuticals and other high-value ingredients are proprietary products. The biotechnology industry refers to them as "identity-preserved" animals because they will remain proprietary products--with little danger of being copied or stolen by others. In order to preserve their identity, however, they will not be made available for sale to traditional farmers who might wish to breed them. Once a company like GenPharm has produced transgenic animals in sufficient numbers, it will hire farmers under contract to tend the "identity-preserved" livestock. These farmers will thus become "renters of transgenic livestock" rather than independent dairy farmers who raise their own breeding stock. According to Dr. Tracy Wilkins of Virginia Tech Biotechnology Laboratory, "*The company would own the cows, which would be the only ones on the farm, and contract for the milk to be delivered to the company's plant.*"[5]

Large-Scale Commercialization of Transgenic Animals will Promote Greater Genetic Uniformity in Livestock

Artificial insemination and embryo transfer are the delivery mechanisms by which new genetic biotechnologies are delivered to animals for propagation. Artificial insemination is not new. It enables a single bull to sire thousands and thousands of progeny. Embryo transfer will play an increasingly important role in commercial animal biotechnology because it allows genetic improvement through both sire and dam (both parents). According to GenPharm, "*The removal of immature eggs*

from elite donor cattle using echoscopic visualization, combined with in vitro embryo development, allows the genetic makeup of bovine embryos to be completely controlled."[6]

To date, cloning of calf embryos *in vitro* allows genetic engineers to produce as many as 11 genetically identical offspring from a single embryo. Scientists speculate that, with technological advances in "nuclear transplantation," the number of clones derived from animal embryos could be unlimited at some point in the future.[7] In order to accelerate genetic improvement in proprietary animals, and to achieve rapid propagation of precious transgenic animals, commercial biotechnology companies are likely to maximize use of these technologies, and in the process, engineer thousands of animals characterized by extreme genetic uniformity.

The combination of new and existing technologies will accelerate and reinforce current trends of genetic uniformity in commercial livestock breeds, and could result in the loss of valuable livestock genetic diversity. The concern is that identity-preserved livestock "owned" and controlled by commercial biotechnology firms will reinforce genetic dilution or replacement of traditional livestock breeds.

Industrial breeding stocks are not an adequate genetic reservoir for the future. The genetic diversity found in animal breeds is the foundation for continued evolution and opportunity in agriculture. Animal genetic diversity allows farmers and breeders to select their stocks in response to changes in the environment, prevailing diseases, market conditions and societal needs, all of which are largely unpredictable.

The problem of genetic uniformity in livestock is not new, but the application of new biotechnologies to animal agriculture is likely to compound the problem.

Sources Consulted

1. Biotechnology Newswatch, "GenPharm's bull ready to breed herd of cows to put human milk in a bottle", 1 June 1992, p.12.

2. Biotechnology Newswatch, January 18 1993, p.3.

3. Chase, Marilyn, "GenPharm to Use Bull to Enter Market for Infant Formula", Wall Street Journal, January 15 1993.

4. Letter from Jonathan J. MacQuitty to RAFI, dated April 27, 1993.

5. Quoted in Biotech Reporter, May 1993: Wrage, Karol, "Transgenic Farm Animals Turn Big Profits: A New Industry of I-P Livestock?", pp.1-2.

6. GenPharm International, "The Power of Transgenic Technology", a booklet published by GenPharm, 1993.

7. First, Neal L., "Animal Biotechnologies: Potential Impact on Animal Products and their Production", in Animal Biotechnology: Opportunities and Challenges, NABC Report 4, 1992, p.4.

Company Profile

GenPharm International is a biotechnology company founded in 1988, with offices in Leiden, the Netherlands and Mountain View, California, USA. The company's goal is to develop and commercialize pharmaceutical and nutritional products based on transgenic animal technology.

Bristol-Myers Squibb, based in New York, NY, USA, is one of the world's leading pharmaceutical corporations, with significant interests in infant formula. (Its subsidiary, Mead-Johnson Nutritional Group, markets infant formula worldwide.) The parent company ranks # 40 on Fortune Magazine's list of the 500 largest U.S.-based corporations, with 1992 annual sales of (US) $11,805 million. (Source: Fortune Magazine, April 19, 1993.)

It is important to note that many biotechnology companies worldwide are in the business of transgenic farm animals for the production of therapeutics and nutritional supplements. Briefly, these include:

- DNX, of Princeton, New Jersey, USA -- focusing on the production of human hemoglobin in swine blood, and the development of donor transplant organs from swine.
- Genzyme, Boston, Mass., USA -- production of transgenic goats that produce a protein for treatment of cystic fibrosis.
- Protein Pharmaceuticals Ltd., Scotland -- production of transgenic sheep producing alpha 1 anti-trypsin protein for treatment of emphysema.
- TransPharm of Blacksburg, Virginia, USA -- production of transgenic swine to produce milk containing a clot-preventing agent.

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RAFI Communique Update:

Bovine Growth Hormone in Mexico

In the United States and Europe, controversy continues over governmental approval of bovine growth hormone(BGH), a product of genetic engineering designed to increase milk production in dairy cattle. In the United States, despite opposition from consumer, farm and environmental organizations, rumours abound that the U.S. Food and Drug Administration will approve the product for commercial sale in the near future.

Lessons from Mexico

A recent article in *Hoard's Dairyman* (25 April 1993) reports on the use of bovine growth hormone on large dairy farms in Mexico, where the product has been available for commercial sale since mid-1991 (see *RAFI Communique, "Third World Marketing and Promotion of Biosynthetic Milk Hormone,"* October, 1990).

The magazine's staff visited seven large dairies, five of which were using BGH, in a region of northern Mexico known as "Mexico's Dairyland." The dairies in this region are large, resembling drylot dairies found in the southeastern United States. The two companies that are marketing BGH in Mexico, Dow Elanco and Monsanto, are competing aggressively for new customers, and thus the price of BGH has fallen from an average of 62 cents per cow per day, to as little as 35 cents per cow per day. BGH suppliers are also offering to furnish a person to make the BGH injections.

The response? There's no question that BGH increases milk yields in some Mexican herds, but the additional milk comes at a cost. Cows eat additional dry matter to compensate for the higher milk production. Also, the ration must be more energy dense, and that means a more expensive feed. At the Zaragosa Dairy near Delicias, when the managers boosted the energy level of the ration to compensate for higher production, they had a severe problem with acidiosis in the cows (acidiosis is a metabolic imbalance that affects the cows overall health as well as milk production).

At La Rebancha Dairy, in the Torreon region, BGH was used on an experimental basis, but the managers decided against further use. One dairy manager told *Hoard's Dairyman: "Our cows are producing well and have enough stress* [without BST]." La Rebancha provides milk to Alpura, the second largest dairy co-op in Mexico, with annual milk receipts of about 1 billion pounds. The co-op has chosen not to accept milk from cows receiving BGH supplements, because of the negative public relations. *"However,"* notes *Hoard's Dairyman, "BST use and its impact have not received widespread media attention in Mexico."*

Potential for Product Abuse Demonstrated

The article also reports on one aspect of the BGH experience in Mexico that indicates the potential for widespread misuse of the product:

> *"The dramatic response in milk production with BST coupled with the competition-induced lower prices have led people to use both the 14-day and 28-day interval products more often than recommended.*
>
> *"Impact of using BST in the large groups of cows in Mexico was so noticeable that herd managers saw that the response began to diminish before time for the next injection. As a result, on some dairies the 14-day interval products are being injected every 11 days, and the 28-day interval product is being used every 21 days. This adds to the cost per cow per day of using BST but results in a greater overall response."*