SB

85

SENATE COMMITTEE REPORT
FIRST COMMITTEE OF REFERRAL

DATE: 4/2/91 FURTHER: Finance

Date of 5-Day Notice: ____________
(in accordance with Uniform Rule 23)

DATE TURNED
INTO OFFICE: ____________

Resources Committee considered SSSB 85

Prohibiting certain sales of milk; authorizing embargo and detention remedies in case of violation of prohibition; making the commissioner of environmental conservation reponsible for enforcing the prohibition.

and recommended:

[ ] replace with ______ CS ____________________ [ ] same title
[ ] new title

[ ] attached amendment(s)

[ ] ____________________ letter of intent adopted

[ ] do pass

[ ] do not pass

[ ] no recommendation

[ ] individual recommendations

[ ] further referral to ____________________

ATTACHES NEW FISCAL NOTE(S):

Department(s)/Date:

[ ] fiscal note(s) ____________

Department(s)/Date:

[ ] zero fiscal note(s) ____________

[ ] appropriation-no fiscal note

[ ] Governor's bill w/fiscal note

SIGNING DO PASS:

OTHER RECOMMENDATIONS:

Chair: Signature and Recommendation

AMERICAN LEGISLATIVE EXCHANGE COUNCIL
The State Factor

Volume 17, Number 3 February 1991

THE BIOTECHNOLOGY EVOLUTION: A LEGISLATOR'S GUIDE

See pg. 14

Introduction

As biotechnology enters the 1990s, a wide range of issues and trends will impact the development of this emerging industry. While some will present new challenges brought on by the introduction of a new technology, others are ones every high-technology industry must address. These factors will in part be determined by state legislators.

Clearly, biotechnology's potential is enormous -- and the stakes are high. Whether pharmaceuticals for the treatment of disease, or healthier, safer foods for consumers, biotechnology's end products promise to offer a wealth of economic and social benefits which many believe will rival the computer boom which played such a large role in the economic growth of the 1980s.

State governments are continually searching for ways to promote economic growth, improve and expand their infrastructures, increase their educational standards, and create additional employment. As state governments conduct their search, they would be well-advised to turn increasingly to biotechnology companies and programs as important components in charting the path to optimum growth. Biotechnology, as with other high-technology industries, offers tremendous economic development possibilities whose limits have yet to be tested.

Biotechnology is a rapidly expanding industry and, as such, offers the promise of new jobs and increased revenue. As a high-technology industry, biotechnology relies heavily on a strong academic environment due to the constant exchange of ideas between industry and universities. State governments find this exchange of knowledge particularly inviting because it raises educational levels in their states. States can rely on biotechnology to bring in revenue and to attract a highly-skilled, highly-educated work force. This is positive for the overall economic development of any state.

Moreover, as biotechnology companies expand into manufacturing, they create a need for a diverse work force. These production jobs do not require advanced degrees and would be available to those with high school diplomas or the equivalent. Thus, biotechnology has the potential to create many jobs at various educational levels.

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Many states are recognizing biotechnology as one of the increasingly rare fields where the U.S. retains a decisive leadership role in international markets. Accordingly, it is incumbent upon all the key players -- including federal and state government leaders -- to ensure that we retain our competitive edge both nationally and internationally.

There are several methods by which a state can promote development of biotechnology in their state. States may provide funds or programs for biotechnology training at state universities or colleges, financial assistance or tax incentives that would be less burdensome to biotechnology companies, research parks supported by states primarily for biotechnology purposes, and centers where biotechnology companies and members of the academic community may meet to foster technology exchange. States can provide predictable and stable climates within which the industry can grow and mature, while ensuring public confidence in the process.

Yet a great deal of uncertainty, confusion, and fear continues to exist in the halls of state government with regards to America's emerging biotechnology industry. This edition of *State Factor* provides an overview of the science of biotechnology and serves as a legislative primer for elected officials interested in pursuing what promises to be one of the great technological booms of the 21st Century.

What is Biotechnology?

Biotechnology is the use of living organisms and biological agents to produce goods. This includes common products such as foods, beverages, and pharmaceuticals. While the use of microorganisms to produce medicines, such as antibiotics, goes back only several decades, the cultivation of plants and the use of yeast in food production goes back to antiquity.

One new biotechnology, recombinant DNA technology (also referred to as genetic engineering), became possible when scientists learned how to utilize certain enzymes that could be used like scissors and paste to isolate and rearrange genes with precision. Using these enzymes, researchers have been able to identify the genes that produce specific proteins. These enzymes also allow scientists to insert genes into plasmids, rings of genes that can move into and out of bacteria.

Once a certain gene is inserted into a plasmid, the plasmid can carry the new genetic material into bacteria. Inside the bacteria, the gene begins to produce its specific protein. In effect, the bacteria become miniature protein factories.

Scientists are using biotechnology to develop bacteria that can make proteins that can be used in vaccines and drugs. When grown in fermentation vessels, these bacteria produce large quantities of proteins for use as human or animal health products.

Recent developments in plant biology have allowed scientists to move genes in and out of plants. Thus, plants can be modified by genetic engineering to improve agronomic properties such as disease and insect resistance and food quality.

In addition, genetically engineered bacteria, plants, and animals are being developed for use in agriculture. Biotechnology has the potential to make farming more reliable, reduce the farmer's input costs, produce higher quality foods, and protect the environment.

Safety Record

Although the techniques used in biotechnology are relatively new, scientists already understand a great deal about their possible effects on health and the environment. In fact, no previous technology has been so thoroughly studied at such an early stage in its development as has biotechnology.

Biologists turned their attention to the issue of biotechnology safety shortly after the first genetic engineering experiments were conducted. Scientists took the unprecedented step of self-imposing a moratorium on recombinant DNA research. In 1975, at a special conference held in Asilomar, California, scientists developed a set of guidelines for ensuring the safety of genetic experiments.

Several years later, similar guidelines were formally adopted by the National Institutes of Health to govern university research. Biotechnology companies have voluntarily complied with these guidelines or their own higher standards. The NIH guidelines have been relaxed over the years as thousands of trouble-free experiments have provided sufficient evidence that biotechnology research is safe.

Paralleling the 1970s debate over the safety of laboratory experiments is a more recent debate over the safety of field testing of genetically engineered organisms. Environmental legislation passed by Congress in the 1970's, together with other federal laws, has provided the necessary framework for protection of the public health and the environment.

Biotechnology in Medicine

The human body is an exquisite example of nature's art. In health, its inner systems are finely tuned, in balance with one another. In sickness, the balance is disturbed and the body's natural ability to protect itself from disease is disrupted.

Aided by recent advances in biotechnology, medical researchers are beginning to understand how the body maintains its delicate balance. With this knowledge, researchers are discovering how human proteins and other natural substances can be used to treat, or even prevent, diseases that have stymied the medical community for generations.

Some diabetics, for example, can not produce insulin, a protein that helps control the amount of sugar in the blood. The absence of insulin results in dangerously high blood sugar levels. Injecting insulin in appropriate amounts restores the body's normal blood sugar balance.

In addition to supplying a missing or deficient protein, doctors can use appropriate proteins to stimulate and assist natural disease-fighting processes. One protein can dissolve the blood clots accompanying heart attacks before they cause death or permanent injury. Other proteins stimulate the body's immune system to kill cancer cells. Some proteins stimulate production of red and white blood cells.

SOME DISEASES THAT MAY BE TREATED OR PREVENTED WITH BIOTECHNOLOGY

Condition	Number of People Affected in the United States	Drug or Vaccine
Heart Attack	1.5 million per year	TPA
Cancer	One million new cases per year	Interferon-alpha Interleukin-2 Tumor necrosis factor Colony stimulating factors Monoclonal antibodies armed with cancer-killing drugs
AIDS	More than 1.5 million infected with the HIV	CD4 Interferon-alpha Interleukin-2 Colony stimulating factors Genetically engineered vaccines
Diabetes	600,000 to 1.1 million need insulin	Human insulin
Dwarfism	1,700 children received growth hormone	Human growth hormone
Hemophilia	20,000	Factor VIII purified with monoclonal antibodies Genetically engineered Factor VIII
Anemia	500,000 people, including 90,000 on kidney dialysis and more than 100,000 with AIDS	Erythropoietin
Acute tissue rejection episode in kidneys	4,500 kidney transplant patients may experience tissue rejection per year	Orthoclone OKT3
Hepatitis B	---------	Hepatitis B vaccine

Gene Therapy

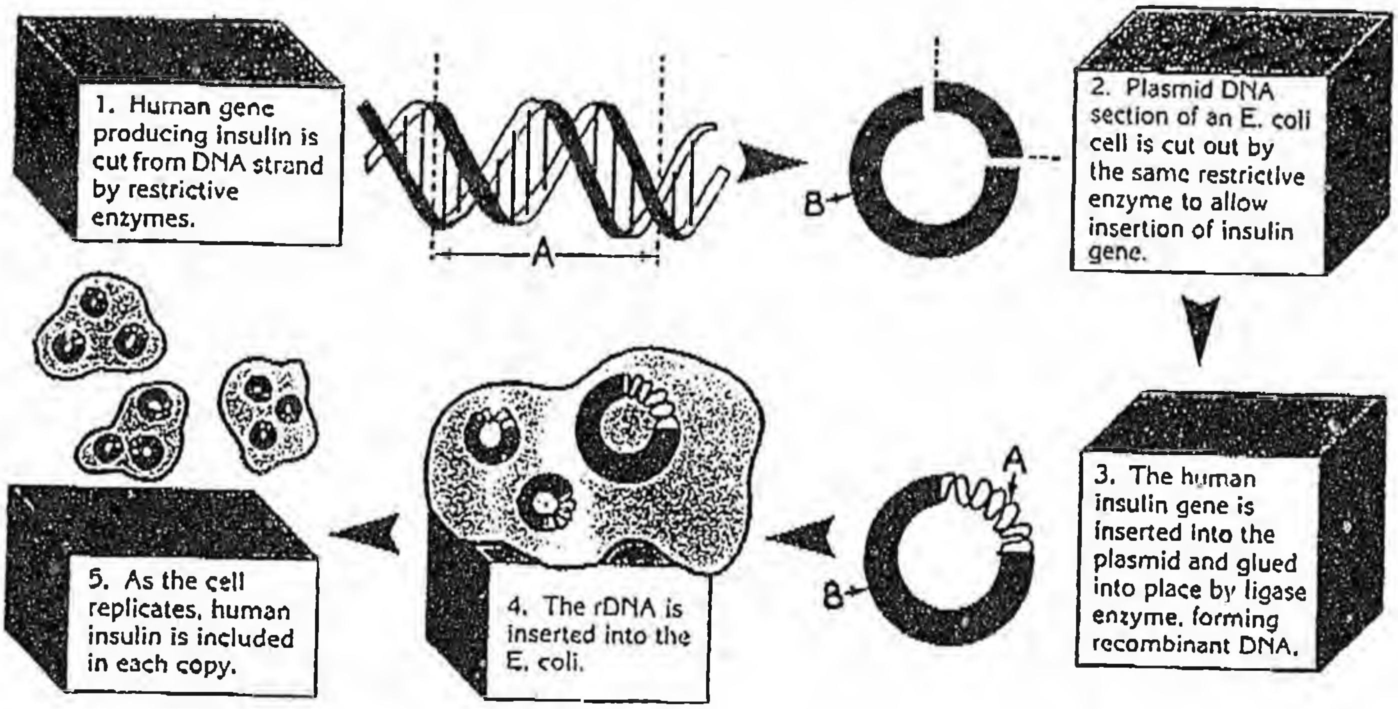
Human genetics is in the midst of a revolution. In the mid-1970s, about all that could be done was study inherited diseases and track their frequency. Now it is possible to locate and identify those genes that cause hereditary diseases. As scientists learn more about defective genes, the role they play in disease, and their locations relative to each other, they are able to create a type of map. This process, called genetic mapping, allows for the development of tests to diagnose diseases. Further study of the gene may provide new directions for human gene therapy.

Scientists have pinpointed the gene that causes cystic fibrosis, a disease that affects the digestive and respiratory systems so severely that, if not diagnosed early, premature death is often the result.

While their is no known cure for cystic fibrosis, early diagnosis can lead to therapy that can improve both the quality of life and the life expectancy of the patient.

Defective genes have been linked to other diseases as well, including Duchenne muscular dystrophy, adult polycystic kidney disease, a familial form of Alzheimer's disease and a familial form of colon cancer.

MAKING HUMAN INSULIN



Fighting Heart Disease

Heart attacks occur in people whose arteries have been narrowed by the accumulation of cholesterol. If a blood clot enters one of the coronary arteries, which supply blood to the heart muscle, it may become lodged in a narrowed section of the artery, thereby cutting off blood flow to a portion of the heart muscle. Without quick and effective treatment, the heart may be damaged permanently.

Each year, 1.5 million people suffer heart attacks. More than 540,000 of those attacks are fatal. Many of these patients can be saved from death or permanent disability by using a genetically engineered drug called tissue plasminogen activator, or TPA.

TPA is naturally-occurring protein that is able to dissolve blood clots. TPA is present in the blood, but in amounts too minute to prevent a heart attack.

When a heart attack strikes, doctors can inject genetically engineered TPA into the patient's blood. The protein travels to the clot, breaks it up within minutes, and restores blood flow to the heart muscle. By quickly restoring blood flow, TPA helps prevent life-threatening damage to the heart muscle.

In 1987, the U.S. Food and Drug Administration approved the use of TP. and it is now available in most hospitals. Eventually, the drug may be us by ambulance crews -- or heart patients themselves -- to stop heart attac. even before the patient reaches the hospital.

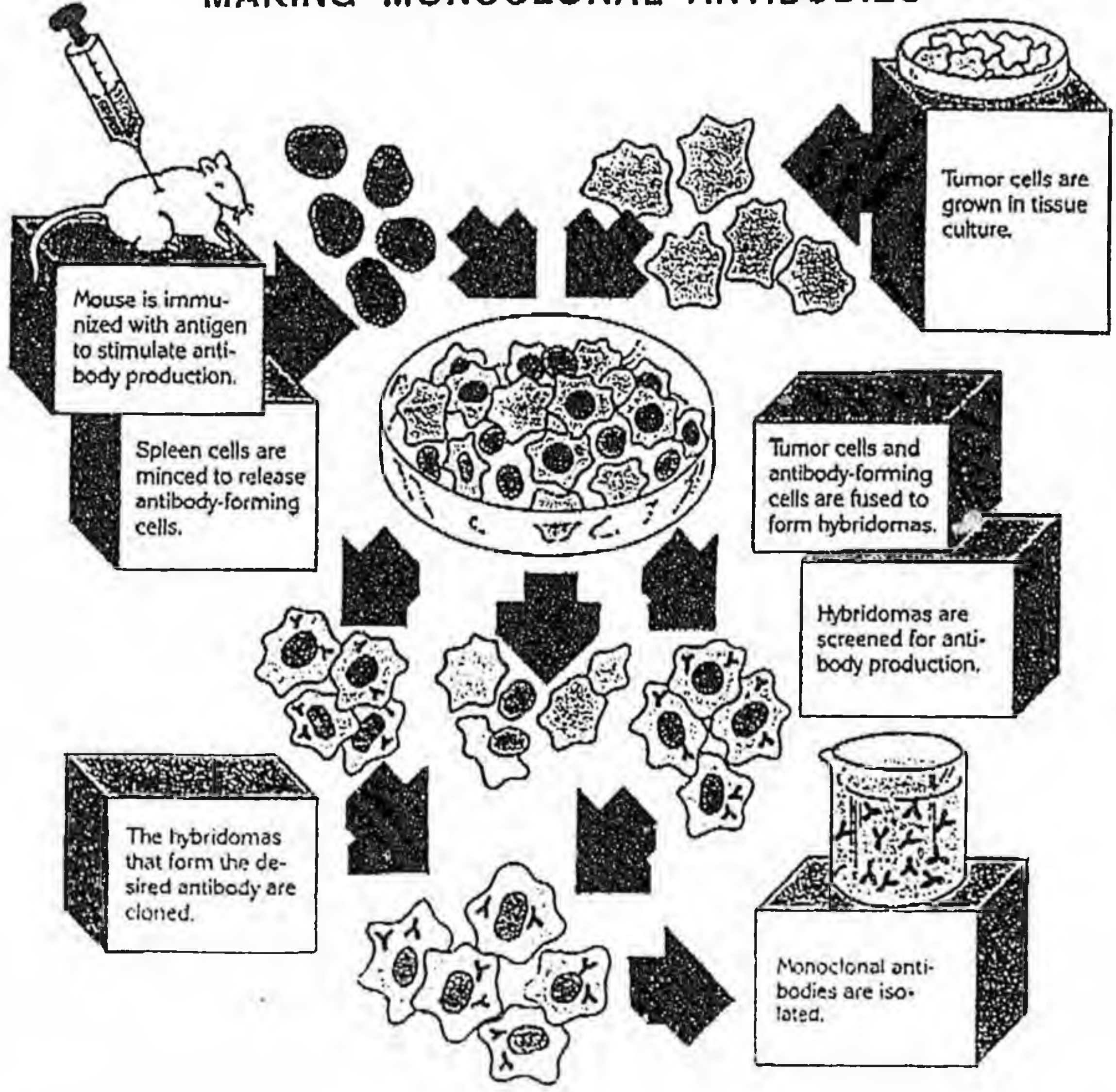
New Weapons for the War on Cancer

Cancer is an error in cell development. Normal cells grow and reproduce rapidly when they are young, and then slow down or stop reproducing when they mature. Somehow, cancer cells get tricked into staying immature, therefore reproducing wildly.

Despite the nation's War on Cancer, declared in the early 1970's, cancer is still second only to heart disease as a killer. Each year, nearly one million Americans develop cancer, and 480,000 die.

Biotechnology is used to treat cancer in three ways. Some genetically engineered proteins, called lymphokines, appear to attack cancer cells directly, or they may trigger the body's immune system to attack the cancer. Other genetically engineered proteins, called growth factors, appear to push cancer cells to maturity, slowing down the cell's rampant reproduction. And monoclonal antibodies, also derived through biotechnology, are armed with radioactive material, cancer drugs, or other poisons to search out and destroy cancer cells.

MAKING MONOCLONAL ANTIBODIES



One genetically engineered lymphokine, alpha-interferon, is used to treat people with hairy cell leukemia, a cancer that several hundred Americans develop each year.

Before alpha-interferon, a diagnosis of hairy cell leukemia was a virtual death sentence. People with the disease required frequent blood transfusions and became highly susceptible to infections. There were no effective long-term treatments.

Today, alpha-interferon can restore people with hairy cell leukemia to normal health. The protein appears to bind to the surface of the cancer cell, halting its growth.

In addition to alpha-interferon, doctors are experimenting with other genetically engineered lymphokines to treat cancer patients. Interleukin-2 activates special white blood cells, called killer cells, which can destroy cancer cells. These activated killer cells may prove to be an effective treatment for people with advanced skin or kidney cancer.

Another group of proteins, called colony stimulating factors, trigger production and activity of cells of the immune system. Colony stimulating factors may prove useful in marshalling the body's defenses against cancer and AIDS. Colony stimulating factors may also help restore normal blood production in patients with severe anemia or those undergoing bone marrow transplantation.

Fighting Anemia in Dialysis Patients

Anemia is caused by low levels of red blood cells usually the result of erythropoietin deficiency. Erythropoietin is a glycoprotein that is normally produced by the kidneys and circulated through the bloodstream into the bone marrow. Once in the bone marrow, erythropoietin stimulates the development of immature stem cells into mature red blood cells. When kidneys fail, proteins like erythropoietin are no longer produced. Since dialysis is not able to replace the lost proteins, most patients with chronic renal failure develop anemia.

However, scientists have developed a recombinant erythropoietin, known as EPO, that is able to replace the erythropoietin that failed kidneys are no longer able to produce. EPO provides dialysis patients with the levels of erythropoietin necessary to produce normal levels of red blood cells. Through the use of EPO doctors have helped many of the 100,000 patients with renal disease lead a more normal life.

EPO is safer than blood transfusions, the traditional method of treating anemia. Blood transfusions increase the number of red blood cells and offer the patient temporary relief, but there are risks involved. Through transfusions it is possible to contract undetected blood-borne infections such as AIDS, non-A or non-B hepatitis. Also, patients that receive frequent transfusions may develop large amounts of iron in vital organs, a condition known as iron overload. Finally, patients may form antibodies that may not allow them to receive a successful kidney transplant, the only known cure for kidney failure.

<u>Counterattacking the AIDS Epidemic</u>

Even though it kills fewer people than heart disease or cancer, acquired immune deficiency syndrome (AIDS) is feared more than other disease. Striking suddenly in the 1970's, it has already killed tens of thousands of people. More than 1.5 million people have been infected with the human immunodeficiency virus (HIV), which causes AIDS, and most of them will die of the disease unless a cure is found soon.

HIV infection destroys a portion of the immune system known as the T-4 lymphocytes. Without these T4 lymphocytes, the patient is defenseless against a wide range of diseases that a healthy body normally keeps in check without difficulty.

With the aid of biotechnology, biomedical researchers have been able to identify the virus quickly, understand it, and mount a counter-attack against it. To help prevent the spread of the HIV, researchers have employed monoclonal antibody technology to develop a laboratory test that shows whether or not blood is contaminated with the virus. Using the test, blood banks can now screen donated blood to ensure that it is not contaminated with the HIV.

Several genetically engineered proteins, including some of those originally developed as cancer therapies, are being examined as possible treatments for AIDS or for the infectious diseases that accompany AIDS.

A protein called CD4, found on the surface of T-4 cells, acts as a gate allowing the virus to enter cells. Doctors hope to be able to flood the patients' bloodstream with genetically engineered CD4, thereby providing million of decoys that the virus could attack instead of entering into T-4 cells.

Lymphokines such as alpha-interferon and interleukin-2, which stimulate the body's immune response, are being used experimentally in conjunction with AZT, a conventional drug that slows reproduction of the virus. Another experimental AIDS drug, dideoxycytidine (DDC), was discovered using biotechnology methods which help researchers identify promising new pharmaceuticals. The FDA recently approved a new use for a biotech derived drug, erythropoietin (EPO). EPO had previously been approved for treatment of dialysis patients with chronic renal failure. The new use will significantly reduce the need of blood transfusions for some people with AIDS who suffer debilitating anemia due to AZT therapy and low levels of naturally occurring erythropoietin. As the search for AIDS treatments continues, other scientists hope to halt the epidemic by developing vaccines.

Traditionally, vaccines have been made from killed or weakened viruses. Although unable to produce disease, a killed or weakened virus stimulates the body's natural defenses against the virus. If an immunized person is later infected with the natural virus, the stimulated immune system quickly destroys the invader.

Currently, scientists cannot use the entire HIV in searching for a vaccine, even weakened or killed, because it may become reactivated in the body and cause AIDS rather than conferring immunity. Instead, scientists hope to develop a vaccine using only a portion of the HIV, such as a piece of the protein coat that surrounds the virus.

Several biotechnology companies are using genetic engineering techniques to remove genes from the virus that carry the code for the HIV's protein coat. Inserted in bacteria or other cells, these genes can produce quantities of the protein-coat fragments for experimental use as AIDS vaccines.

The search for a vaccine has been slow, however, because the virus is continuously changing. Several different strains of the virus have already been identified, and no single vaccine is likely to be effective against all of them. Doctors do not expect a vaccine to be widely available before 1995.

Other Diseases

In the seventeen years since the first gene was spliced, a number of proteins have become widely available to diagnose, treat, and prevent disease. Heart disease, cancer, AIDS, diabetes, and anemia are just five of many diseases biotechnology will help treat in the coming years. Here is a sample of some of the other conditions for which biotechnology products are available:

Dwarfism. Children lacking sufficient growth hormone cannot grow to normal height without regular injections of human growth hormone. Traditionally, these children were treated with limited supplies of growth hormone extracted from cadavers. However, in 1985 cadaver-derived hormone was removed from the market after several children died from a rare virus that contaminated the hormone. Unlike cadaver-derived hormone, genetically engineered growth hormone is a safe therapy for the 1,700 children being treated for dwarfism.

Hemophilia. Hemophiliacs are constantly at risk of internal bleeding because their bodies cannot produce sufficient amounts of a protein called Factor VIII, which controls blood clotting. Transfusions of Factor VIII from human blood can control the disorder, but these transfusions contain only one percent Factor VIII and also may transmit viral diseases. In the early 1980s, some hemophiliacs were infected with HIV from transfusions and they are still susceptible to hepatitis from contaminated transfusions of Factor VIII.

Today, scientists are utilizing monoclonal antibody technology to produce Factor VIII that is 99 percent pure. Studies also are under way to develop genetically engineered Factor VIII which is completely pure and incapable of transmitting disease.

Organ rejection. When a patient receives a kidney or other transplanted organ, the patient's immune system may recognize it as an invader and attack it. This rejection may cause a transplant to fail, and in some cases, it may be fatal. By using monoclonal antibodies, doctors can eliminate T cells, those elements of the immune system responsible for organ rejection.

Hepatitis B vaccine. Hepatitis B is one of at least three hepatitis viruses that cause a systemic infection that can disrupt liver function. The hepatitis B virus is an important cause of viral hepatitis with no specific treatment for this disease. However, through biotechnology, scientists have developed a safer hepatitis B vaccine. The Centers for Disease Control (CDC) estimates that there are approximately 0.5 to 1 million chronic carriers of hepatitis B virus in the United States and that pool of carriers is growing by 2% - 3% per year.

Biotechnology in Agriculture

Biotechnology utilizes a variety of techniques for developing new products and improving microbes, plants, and animals. In agriculture, biotechnology has the potential to make farming more reliable, reduce the farmer's input costs, produce higher quality foods, protect the environment through the substitution of biodegradable products for non-biodegradable products, and help developing nations feed their people.

Agriculture is a nation's most essential enterprise. The ability to produce food, fiber, and other agricultural products largely determines the standard of living that people in that nation will enjoy. Nations have prospered or perished through the success or failure of their agriculture.

However, farming is a risky business. Weeds compete with crops for moisture and nutrients. Insects and plant disease take their toll. A late frost in spring or an early frost in autumn can destroy an entire season's produce. Too much rain can be just as devastating as too little.

Some of the problems faced by farmers today require both political and economic solutions. Technological changes, however, can alter the forces that make farming an unpredictable and sometimes unprofitable occupation. Many of these changes will arise from the field of biotechnology.

Biopesticides

In the past, chemical pesticides have been the main line of defense against pests. Farmers annually spend $20 billion worldwide -- $5 billion in the United States alone -- on crop protection products, primarily synthetic chemicals. In the United States, farmers spend $1.6 billion on agricultural chemicals to control insect pests. For example, in 1988 it was estimated that 34-38 million acres of corn were treated with chemical pesticides to control damage caused by the insects corn rootworm and corn borer. These insect pests respectively cause $900 million and $500 million worth of damage annually to the U.S. corn crop.

Growing public concerns about water contamination, chemical pesticide resistance, dietary exposure to pesticide residues, and worker exposure to chemicals have led farmers to search for alternative methods of pest control. Many agricultural scientists believe that biotechnology offers a politically and economically acceptable alternative.

Many biopesticides do not remain in the environment -- a major environmental benefit. The active elements produced by bacterial pesticide products are fragile molecules which are quickly broken down when exposed to the sun or other natural elements. This characteristic of biopesticides should eliminate public concerns about residues on crops and in groundwater.

Biopesticide technology is based on potent, naturally occurring microorganisms, such as *Bacillus thuringiensis* (B.t.). Discovered at the turn of the century, B.t. has been used without risk in the United States for almost three decades by home gardeners, farmers, and forestry officials. Its active component, a protein crystal, specifically attacks the alkaline stomachs of target pests. Higher organisms, however, such as mammals, fish, birds and other non-target species remain unthreatened by this highly specific bioinsecticide. Inconsistent performance of these products has, however, resulted in a relatively small market. Today's biotechnology techniques permit the development of B.t. products which are as effective as chemical pesticides without their disadvantages.

In order for protein toxins to be effective as commercial insecticides, they must remain active for an adequate period of time under field conditions. As a result, various methods of extending the activity of bioinsecticides are now being developed. One method involves spraying the insecticidal proteins directly onto crops. As insects feed on the sprayed crops, the protein is activated in the insect's stomach whereupon the insects immediately stop eating. Another method involves inserting the B.t. gene directly into the genetic makeup of crops. This method gives the crops a built-in resistance to insects. Similarly, the B.t. gene can be inserted into a third party, such as a microorganism that lives within the plant's sap. These organisms -- known as endophytes -- multiply within the host plant and move throughout the plant's vascular system forming a microscopic defense against feeding insects. This process resembles vaccines moving throughout a person's vascular system to defend against harmful disease. Another system has been developed which protects the B.t. toxin in a natural microcapsule within which it is produced, formulated, and sprayed on crops. The resulting product consists of a potent protein toxin with an inert microcapsule.

Companies engaged in agricultural biotechnology are aiming toward the same goal -- providing attractive alternatives to the farmer that will allow him to be competitive in the marketplace.

In addition to biopesticides, work is also underway to develop effective bioherbicides and fungicides. While biopesticides will not eliminate the need for chemical pesticides in many cases, the two types of products will be used in concert with each other toward the same goals. Advances in agricultural biotechnology, however, will eventually make it possible to develop pesticides of greater potency, certainty, and with broader applications than current products.

Through the development of more potent biopesticides and improved delivery systems, biotechnology will provide excellent control to the farmer. In cases where a product must be able to control a large spectrum of pests, biotechnology provides industry with the tools to deliver multiple biotoxins into delivery systems while still maintaining the safety to the surrounding ecosystems. In addition, using biotechnology techniques, organisms can be developed that can provide more toxic dosages to the target pests so that the pest's feeding is halted after only a couple of bites, therefore, causing only minimal damage to the plant.

Plant Biotechnology

Although plant science is a relative modern discipline, its fundamental techniques have been applied throughout human history. When early man went through the crucial transition from nomadic hunter to settled farmer, cultivated crops became vital for survival. These primitive farmers, although ignorant of the natural principles at work, found that they could increase the yield and improve the taste of crops by selecting seeds from particularly desirable plants.

Farmers long ago noted that they could improve each succeeding year's harvest by using seed from only the best plants of the current crop. Plants that, for example, gave the highest yield, stayed the healthiest during periods of drought or disease, or were easiest to harvest tended to produce future generations with these same characteristics. Through several years of careful seed selection, farmers maintained and strengthened such desirable traits.

The possibilities for improving plants expanded as a result of Gregor Mendel's investigations in the mid-1860s of hereditary traits in peas. Once the genetic basis of heredity was understood, the benefits of cross-breeding, or hybridization, became apparent: plants with different desirable traits could be used to cultivate a later generation that combined these characteristics.

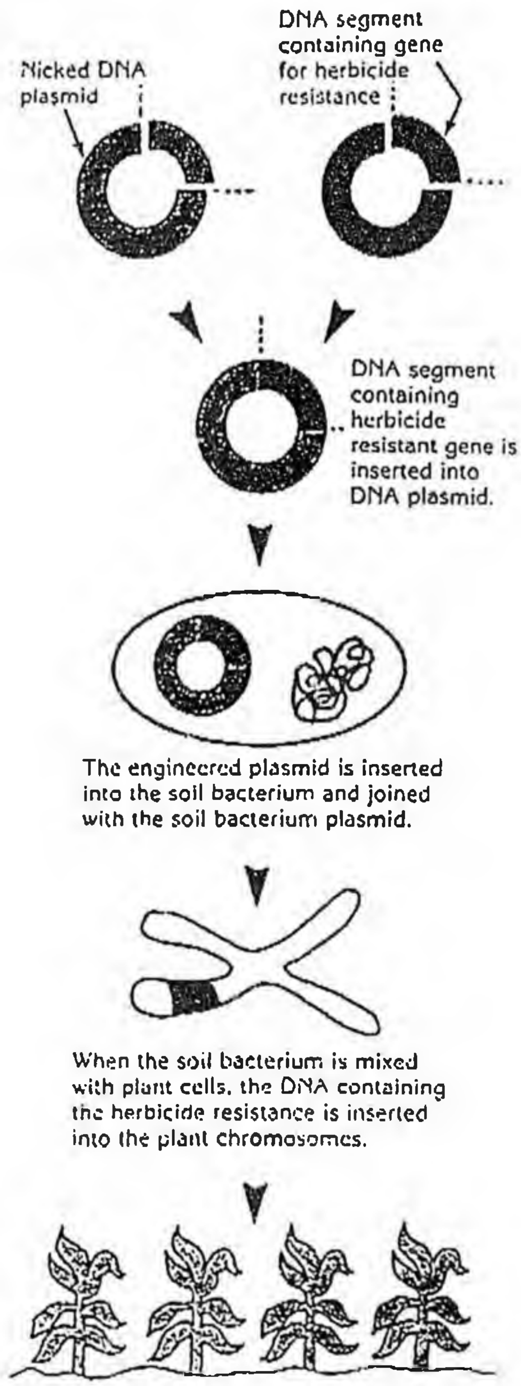
Understanding of the scientific principles behind crop improvement practices has come only in the last hundred years. But the early, crude techniques, even without the benefit of sophisticated laboratories and automated equipment, were a true practice of biotechnology -- guided natural processes to improve man's physical and economic well-being.

Today, applied plant science has three overall goals: increased crop yield, improved crop quality, and reduced production costs. Biotechnology is proving its value in meeting these goals. Progress has, however, been slower than medical and other areas of research. Because plants are genetically and physiologically more complex than single-cell organisms such as bacteria and yeasts, the necessary technologies are still in development.

In one active area of plant research, scientists are exploring ways to use genetic modification to confer desirable characteristics on food crops. Similarly, agronomists are looking for ways to harden plants against adverse environmental conditions such as soil salinity, drought, alkaline earth metals, and anaerobic (lacking oxygen) soil conditions.

One new development in the area of plant biotechnology is herbicide-tolerant crop plants. These plants are genetically modified to resist applications of herbicides that will kill the targeted weeds. This is important to agriculture as weeds compete with crop plants for moisture and nutrients, thus decreasing the farmers yield. New crop plants selected for herbicide tolerance will increase the farmer's options in selecting his use of herbicides. These plants will enable him to choose environmentally softer new herbicides with appropriate weed spectrum and low application rate. Herbicide-tolerant plants not only reduce the use of agricultural chemicals, but they also reduce the economic burden to the farmer by eliminating the costs associated with excess labor and materials.

PLANT BIOTECHNOLOGY



Genetic engineering to improve characteristics -- such as taste, texture, size, color, acidity or wetness, and ripening processes -- of food crops, such as fruits and vegetables, are being explored as a much better strategy than the traditional method of cross-breeding.

Research in this area of agricultural biotechnology is complicated by the fact that many of a crop's traits are encoded not by one gene but by many genes working together. Therefore, scientists must first identify all of the genes that function as a set to express a particular property. This knowledge can then be applied to altering the germlines of commercially important food crops. For example, it may eventually be possible to transfer the genes regulating nutrient content from one variety of tomatoes into a variety that naturally grows to a larger size. Similarly, by modifying the genes that control ripening, agronomists hope to provide supplies of seasonal fruits and vegetables for extended periods of time.

Biotechnological methods for improving field crops, such as wheat, corn, and soybeans, are also being sought, since seeds serve both as a source of nutrient for people and animals and as the material for producing the next plant generation. By increasing the quality and quantity of protein or varying the types of these crops, scientists can improve their nutritional value. For example, a major protein of corn has very little of two amino acids, lysine and tryptophan, which are essential for human growth. Increased amounts of these amino acids could make corn products a source of improved protein.

BST: Improving Milk Production Efficiency

More than half a century ago, researchers discovered that a cow's milk production is regulated in part by the release of a protein secreted from the pituitary gland called bovine somatotropin (BST). Studies showed that when the cow's natural BST is supplemented, milk production can increase dramatically -- and the ratio of feed intake to milk output is lowered at the same time, making the cow a more efficient producer.

For a long time, this knowledge was of no practical use, since BST had to be extracted from the pituitaries of slaughtered cattle. But the advent of recombinant DNA technology now permits commercial production of mass quantities of BST which has the same biological effect as that produced by cows themselves.

If the Food and Drug Administration (FDA) approves BST for general use, dairy farmers will have a new management tool with the power to significantly increase their herds' efficiency. Recent on-farm studies demonstrate that supplemental BST can boost an individual cow's milk production 10 percent to 25 percent with only 5 percent to 15 percent more feed. Because milk production increases within a few days after supplementation begins, farmers will be able to quickly adjust production to meet demand, thereby helping to assure consumers of a steady, reasonably priced milk supply.

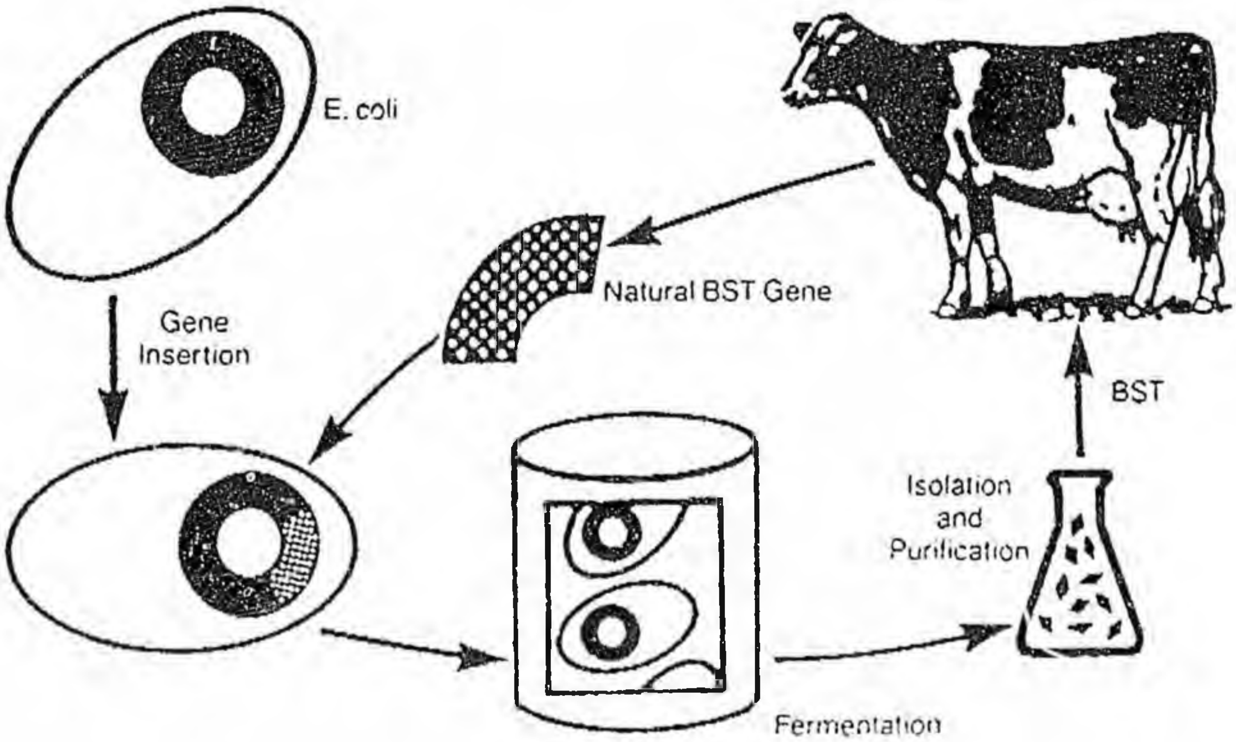
And, because supplemental BST will not require capital investment up front (unlike many other new farm technologies), its benefits will be equally accessible to operators of small and large dairy farms.

Some dairy farmers have been concerned that introduction of BST could lead to significant over-production of milk, causing milk prices for dairy farmers to fall. Several economic studies, however, have indicated that because of gradual adoption of BST by dairy farmers and its use on only *some* animals in a herd, additional milk production nationally from BST is likely to be modest and manageable. Thus, the USDA has forecast that BST use could increase the milk supply nationwide only 2 percent to 5 percent during the first few years of its use.

Field research to date indicates that cows receiving supplemental BST and managed properly exhibit no detrimental effects from either the BST or their increased milk output. This on-farm research is part of an extensive battery of studies required of companies developing BST by the FDA. These tests include work to demonstrate that BST poses no immediate or long term health hazards for BST-supplemented cows or their offspring. Other required studies relate to assuring that BST is effective, that a quality product can be manufactured, and that its use causes no environmental harm. To date, more than five years of research and millions of dollars have been invested by companies developing BST products to meet FDA's testing requirements for safety and effectiveness.

Milk produced with the help of supplemental BST is no different in composition from the milk of unsupplemented cows. All milk contains traces of the BST generated by the cow; the BST levels in milk from supplemented cows are in the same range as those levels that have always been found in milk.

HOW IS BST PRODUCED?



Furthermore, *all* BST -- whether produced by the cow herself or given supplementally -- is safe for human consumption. BST ingested with milk and other dairy foods is broken down in the digestive system, like all other proteins.

The human safety of BST was further demonstrated in the 1950s when researchers attempted to use BST derived from the pituitaries of cattle as treatment for human dwarfism. They found that even when BST was injected (thereby avoiding breakdown in the digestive system) there was still no effect on the human body.

The FDA certified the human safety of supplemental BST in 1985, and since then has allowed the marketing of milk and meat from cows involved in on-farm tests of BST's long-term effects on the animals. A recent NIH study confirms BST's safety.

In coming years, biotechnology will have a significant and beneficial impact on the production of food from farms animals. Milk produced with the help of supplemental BST may be among the first evidences on the grocer's shelf of this technological advancement.

Waste Management and the Environment

The raw materials and by-products of biotechnology are mostly intrinsically harmless. The advantages of biotechnological approaches to cleaning up the pollution caused by traditional industries are already evident, and in some cases more than one goal can be achieved in a single process. For example, methane fuel production by biotechnology not only generates a useful product, but simultaneously removes domestic and agricultural waste.

Even the smallest communities throughout the developed world have employed biotechnology in one key role -- that of sewage disposal. In these, microorganisms are used to purify waste water by breaking down a variety of solids contained in the effluent. Because of the variety of microbes involved, and the variable composition of sewage, precise details of how this works are not entirely clear. The fact that the methodology has changed little since it was first introduced is a testimony of its effectiveness.

Bacteria such a *pseudomonas* break down a range of products including hydrocarbons. Plasmids from several different strains have been added to a single cell with the aim of generating a bacterium effective for oil spills. This may be the effective answer in the long term, but for the moment mixtures of microbes are used successfully to remove oil and gasoline spills.

Mixtures of microbes and enzymes also have been designed to deal with paper mill waste. The paper-making industry generates a particularly noxious waste known as sulfite liquor. If discharged into rivers and lakes, it rapidly depletes the oxygen in the watercourse with disastrous consequences. In order to cope with this, a solution was devised in Finland which involves passing the effluent over *Paecilomyces* fungi, which both purifies the waste liquid and supports the growth of numerous microbes. These can be sold for animal feeds, so this is a further example of a waste disposal process with a useful by-product. Methanogenic bacteria can also be used to purify paper-making waste, producing a useful energy source -- methane -- in the process.

Finally, biotechnology has the potential for cutting in half the costs of acid rain mitigation imposed by the 1990 reauthorization of the federal Clean Air Act. "Acid rain" is thought to result when materials containing sulfur and/or nitrogen are oxidized and allowed to escape into the atmosphere. Small-scale test plants have shown the practicability of a biotechnological approach to remove these harmful wastes through the use of bacteria which rely on sulfur compound as its energy source.

Regulation of Biotechnology

Biotechnology companies are regulated by the U.S. Environmental Protection Agency, the U.S. Department of Agriculture, the U.S. Food and Drug Administration, and the Occupational Safety and Health Administration. In 1986, the White House's Office of Science and Technology Policy issued a framework for coordinating the activities of all federal agencies involved in regulating biotechnology.

Under federal regulations, organisms with new genes from unrelated species must be evaluated for safety before being tested outdoors. Federal regulatory agencies review data from laboratory and greenhouse experiments to determine whether test organisms are toxic to humans, animals,. or to determine if they are beneficial to plants and insects.

Government agencies have set up scientific advisory boards to advise them on the safety of proposed field tests of genetically engineered plants and microorganisms. These expert panels have recommended approval of the proposed tests. A number of these field tests have been completed, with no evidence of harm to the environment.

Scientific evidence indicates that biotechnology is safe. Genetically engineered organisms look and behave much like their traditional counterparts, which have been used safely in agriculture for many years.

Economic Considerations

Biotechnology is considered an important investment market for the 1990s. The market for biotechnology products will be expanding as the 1990s bring about tremendous increases in the number of biotechnology derived products introduced into the marketplace. As a whole, the biotechnology industry is not yet profitable, but the industry has reported increasingly higher revenues and sales during the last several years. Biotechnology companies predict that in the next five years there will be a ten-fold increase in sales and twenty-five-fold increase in sales in the next ten years. In order to achieve these goals, however, biotechnology companies must find new ways of raising capital.

In bringing biotechnology to the market place, companies must spend an enormous amount of money. In order to continue conducting research, biotechnology companies have had to develop unique ways of raising capital. To this point, most of the money raised by biotechnology companies has been through venture capital and private equity. These methods of raising capital will remain important to small companies, but larger companies will be searching for ways to expand their horizons. In the future, biotechnology companies will increasingly be looking towards strategic alliances, mergers, and public equity as a means of increasing funds.

Many biotechnology companies currently rely heavily on strategic alliances with large pharmaceutical companies. At the moment, strategic alliances are the most important means of raising capital for some biotechnology companies. Strategic alliances provide an important marketing strategy for companies that wish to sell products both in the U.S. and abroad. Through strategic alliances many biotechnology companies have been able to raise capital and increase both research capability and regulatory expertise.

Mergers appear to be on the rise and experts are predicting that the industry may be going through the first stage of consolidation. Most mergers involve biotechnology companies and large pharmaceutical companies. This arrangement usually benefits both parties as the pharmaceutical companies have a ready-made means of entering the biotechnology industry and the biotechnology companies are able to increase their resources (i.e., research and development, marketing, and manufacturing) as they prepare to bring their products to the marketplace.

Public equity will become increasingly important to biotechnology companies, especially larger companies, as more and more companies bring their products onto the market place. With increased numbers of products on the market, biotechnology companies should find a warm reception on the public equity market.

The United States is currently the world leader in biotechnology; however, as U.S. biotechnology companies face shrinking options within the U.S. for financing their businesses, some biotechnology companies may be forced to turn to foreign investors for capital. Many foreign investors have large amounts of money and supportive governments.

In the future, it appears that the U.S. will be facing its toughest competition from Japan. Japanese biotechnology is supported by large corporations which are well funded and have substantial resources. Japanese biotechnology is also aided by a business structure that appears to be more conducive to commercialization of biotechnology than does the U.S. system.

Intellectual Property Protection

In 1984, the Office of Technology Assessment identified intellectual property law as one of the 10 key factors influencing U.S. competitiveness in biotechnology. It remains so today.

The substantial investment required to bring a biotechnology product to the marketplace and the significant risk that many products will fall by the wayside make patent protection essential. Because biotechnology is a process by which innovative new products are produced, protection from unfair competition by foreign companies using U.S.-developed processes -- a policy that other countries have adopted to protect their own companies -- will help insure a strong and growing industry.

Also important is expeditious and thorough review of patent applications by the U.S. Patent Office. Until a company's patent application is approved, it may have difficulty raising the capital needed to further develop, produce, and market a product. The current backlog of biotechnology patent applications at the Patent Office currently stands at 15,000. Also, it takes the Patent Office approximately 26.3 months to review and act on a typical biotechnology patent.

Patent protection and expeditious review of patent applications are important to the biotechnology industry because the economic livelihood of many companies hinges on the issuance of patents in a timely manner. The backlog in the patent process has tied up the product development and marketing capabilities of many biotechnology companies. The excessive review period is proving to be costly to many biotechnology companies trying to bring their products to the marketplace.

Conclusion

States are increasingly eager to obtain the many economic benefits of biotechnology. Many states are promoting the development of biotechnology by funding research and training programs, tax and other financial incentives, and research parks and centers.

In order to effectively introduce biotechnology into their state and reap the greatest benefits from biotechnology, state legislators should carefully examine the existing federal regulatory framework and strive to avoid duplication in state laws affecting biotechnology. The achievement of a harmonious and stable market will be ensured through open and ongoing communications.

CREDENTIALS

This edition of *State Factor* was prepared by Mr. Jerry Taylor, director of ALEC's National Task Force on Agriculture, and Mr. Michael Tanner, director of ALEC's National Task force on Health Care. *State Factor* is intended for informational purposes only.

JAMA SUMMARY

Here's What Your Doctor Reads About Bovine Somatotropin.

An article in *The Journal of the American Medical Association (JAMA)* answered the important questions about bovine somatotropin for your doctor. The doctor learned that this product, sometimes called BST, is being developed for use by dairy farmers to help their cows produce milk more efficiently. It is currently under review by the Food and Drug Administration.

JAMA is a trusted source of information for physicians. All material published in it is reviewed and approved for scientific validity by a panel of physicians. Here is what it said about BST in the issue of August 22/29, 1990:

JAMA *Comments*

Is the milk safe?

The Food and Drug Administration (FDA) has investigated BST and concluded that when it is given to cows, the resulting milk is safe for human consumption.

"The FDA has answered all questions and concerns about the safety of milk from bST-supplemented cows for human consumption...."

Why is the milk safe?

1) BST is digested when consumed, and
2) it is not active in humans.

"It has no biological effect on humans for two reasons: When ingested, bST...[is] *broken down by digestive enzymes into amino acids and small peptides, as is any other protein in the diet; and even if bST did enter the body in substantial amounts, it is not biologically active."*

Does BST change the milk?

BST does not change the composition of milk; it does not change the flavor of dairy foods; it does not change the nutritional qualities of milk; it does not increase the normal trace level of BST in cow's milk.

"Bovine milk composition has been studied for many years, but never as rigorously as in relation to the use of bST.... Bovine somatotropin causes no changes in milk composition."

"...there will be no changes in the flavor or nutritional characteristics of dairy foods if dairy farmers use bST as a production management tool."

"Bovine somatotropin is normally present in trace amounts in milk from unsupplemented cows...studies using the recommended dose levels of bST have found that supplementary bST does not raise significantly the bST levels in milk obtained from supplemented cows."

Does BST do anything else?

BST does not work directly on the mammary gland. Instead, it stimulates the cow's liver to produce another protein hormone, called insulinlike growth factor I (IGF-I). This hormone, produced by all cows, regulates milk production and is found in all milk. The amount of IGF-I in milk increases modestly after BST supplementation but does not exceed normal levels, which vary during lactation. IGF-I is destroyed during the processing of infant formula and does not cause allergies in infants.

"These modest increases are less than the natural variation in milk IGF-I levels...that can occur across a lactation or between multiparous [mature] *and primiparous* [young] *cows...the modest rise in milk IGF-I concentration in milk produced by bST-supplemented cows is well within the endogenous levels in bovine and human milk and would have no impact on milk safety."*

"The high level of heat processing normally used to prepare infant formula from dairy ingredients has been shown to inactivate all IGF-I...."

About the Authors

The *JAMA* article on bovine somatotropin was written by two distinguished scientists. They both have recognized expertise in their fields and personal experience in research directly related to bovine somatotropin.

The primary author, William H. Daughaday, M.D., has been honored many times during his distinguished career as a pediatric endocrinologist. He has served on the faculty of the Washington University School of Medicine, served on many study groups commissioned by the federal government, practiced as a physician, served on numerous editorial boards for medical journals, and is a member of several professional and honorary societies such as the National Academy of Sciences and the American Academy of Arts and Sciences. In addition to these accomplishments, Dr. Daughaday has conducted research into purification of bovine insulinlike growth factor I from blood, under contract with Monsanto Agricultural Company.

The coauthor, David M. Barbano, Ph.D., is an associate professor of food science at Cornell University. He is considered an expert in cheese production and the chemical composition of milk and is a member of several professional organizations devoted to the dairy industry. He has conducted research into the chemical composition and processing characteristics of milk from cows receiving supplemental bovine somatotropin under an agreement between Cornell University and Monsanto Agricultural Company.

JAMA Editorial Criticizes Opponents of BST

In the August 22/29, 1990, issue of *The Journal of the American Medical Association*, an editorial criticizes those who oppose the use of bovine somatotropin. Written by Charles J. Grossman, Ph.D., the editorial accuses opponents of BST of using safety and health issues as a red herring for their real concerns, which he says are economic. Dr. Grossman says, "This tactic has resulted in both confusing and frightening the nonscientific public....

"Because milk produced from cows treated with bovine somatotropin is no different from the milk of untreated cows, it is both inappropriate and wrong for special-interest groups to play on the health and safety fears of the public to further their own ends."

Dr. Grossman explains that the economic concerns are based on a fear that smaller dairy farmers may not survive if BST is used. He points to "an intrinsic trend toward larger, more efficient dairy farms, a trend destined to continue regardless of whether this hormone is used.

"Studies have indicated that milk composition is no different in cows treated with bovine somatotropin and that the cows themselves are not adversely affected," Dr. Grossman says.

Safety for People: The FDA Reports on Bovine Somatotropin

Here is what the Food and Drug Administration (FDA) said in an article published in *Science*, August 1990. The article, written by FDA scientists Judith C. Juskevich and C. Greg Guyer, was reviewed for scientific accuracy by an independent panel of scientists prior to publication. It discusses bovine somatotropin, which is currently under review by the FDA.

FDA Comments

BST has been found to be safe for people.

The Food and Drug Administration has determined that milk and meat from cows receiving bovine somatotropin is safe for human consumption.

(Bovine somatotropin is abbreviated "BST", or "BGH" for bovine growth hormone, or "rbGH" or "rMet-bGH" for recombinant bovine growth hormone.)

"...FDA scientists have determined that milk and meat from rbGH-treated animals are safe for human consumption."

Human safety was determined as part of the initial FDA review of BST research.

The FDA first announced its finding of human safety in 1985 after a review of research information provided by organizations developing BST under an Investigational New Animal Drug Application (INAD).

"Under an INAD application, pharmaceutical companies may conduct human food safety studies required for approval of their product. The results of these studies may be submitted to CVM [The Center for Veterinary Medicine, an office of the FDA] *while the compound is still undergoing investigation."*

The FDA has continued to evaluate research on human safety.

Ongoing research since 1985 has been continuously monitored by the FDA and has not caused the FDA to change its original position with regard to human safety.

"Because the FDA requires the pharmaceutical companies to submit all studies they conducted on their products, the agency continues to receive human food safety information even after the requirements have been met."

The final conclusions about the safety of BST are made by the FDA, not by the companies developing this product.

"The pharmaceutical companies provide descriptions of the human food safety studies and summaries of results but ultimately it is the FDA that decides on the integrity of the data."

The FDA findings of human safety of BST are based on three main facts:

1. **BST is inactive in humans.** The FDA cites two kinds of tests that demonstrate this: 1) actual injection of BST into humans and 2) tests of BST on human tissues.
2. **BST is not active when taken orally by humans or other species.** During research on BST, the FDA required each company developing BST to administer at least 100 times the dose for dairy cattle (relative to body weight) to rats for at least 14 days. There was no effect from this oral administration, even when the studies were continued for 90 days.
3. **Recombinant BST is biologically indistinguishable from BST produced by a cow.** The FDA cites research that compared the effects of recombinant BST with the effects of a cow's own BST. No biological differences were found.

"...GH derived from bovine...pituitaries is ineffective in humans...bGH does not bind to GH receptors in human tissues."

"No toxicologically significant changes were noted in the clinical chemistry, hematology, or urinalysis parameters determined in rats administered rbGH orally."

"These results indicate that the body does not treat rMet-bGH as a protein distinct from a naturally occurring BST variant."

Giving a cow BST does not increase the normal trace amount of BST in the milk.

The FDA did not require studies of BST presence in milk since BST is inactive in humans. However, such studies were conducted and showed no increase in the level of BST in milk when cows were administered normal doses.

"...these very limited studies suggest that milk concentrations of bGH do not increase significantly as a result of the treatment of dairy cows with rbGH at the proposed doses... bGH residues do not present a human food safety concern."

Pasteurization destroys BST.

The FDA cited research showing that any trace of BST that may be present in milk is at least 90 percent destroyed by pasteurization.

"...it has been determined that at least 90% of bGH activity is destroyed upon pasteurization of milk."

BST does not change the composition of milk or its nutritional value.

The FDA found that the milk is not changed by administration of BST to the cow.

(Variations of milk components such as protein, fat and lactose occur during a cow's normal lactation due to changes in food intake and other normal factors. BST did not alter these normal variations.)

"Milk composition of treated cows is well within the normal variation observed during the course of a lactation."

A secondary product of BST, IGF-I, was studied and dismissed by the FDA as unlikely to present any human food safety concerns. Also known as insulinlike growth factor, IGF-I is generated by the cow in response to the presence of BST. The FDA reported that IGF-I has no oral activity, is not found at levels significant for concern, and is denatured by the process used to prepare infant formula.

Overall conclusion:

The FDA has determined that the use of BST in cows is safe for humans.

"On the basis of this information, the FDA scientists concluded that the use of rbGH in dairy cattle presents no increased health risk to consumers."

Courtesy of Elanco Animal Health

Independent Findings on Human Safety of Bovine Somatotropin (BST)

An independendent study of BST was done by the National Institutes of Health (NIH), which has no connection with proponents or opponents of this product. The NIH is a federal agency responsible to the United States Congress and to the President. This project was sponsored by the National Institute of Child Health and Human Development, the National Institute of Diabetes and Digestive and Kidney Diseases, and the NIH Office of Medical Applications Research.

Bovine somatotropin, also called BST or BGH (bovine growth hormone), is a natural protein hormone produced by cows that regulates milk production. Supplemental BST, also called rBST (recombinant bovine somatotropin), is currently under development for administration to dairy cows.

The NIH Technology Assessment Conference on BST was held December 5 through 7, 1990. A thirteen-member panel of independent experts examined available scientific data and heard presentations by experts and critics. The panel consisted of specialists in the medical profession and related scientific disciplines, clinical investigators, and public representatives. It also included a dairy farmer.

Conclusions of the NIH panel were unanimous. Their conclusions on human safety are presented and summarized below.

The National Institutes of Health is a public agency that is part of the U.S. Department of Health and Human Services.

NIH Panel Conclusions on the Human Safety of BST

"In the unanimous judgement of the panel:

"The composition and nutritional value of milk from rBST-treated cows is essentially the same as milk from untreated cows.

"As currently used in the United States, meat and milk from rBST-treated cows are as safe as those from untreated cows."

	Summary	NIH Panel Conclusions
MILK SAFETY	**The safety and wholesomeness of milk are carefully protected in the United States.**	"Because milk is such an important food in the American diet, ...it receives critical attention of regulatory agencies to ensure its safety and wholesomeness." "Milk is the most monitored food in the American food supply."
MILK QUALITY	**Research shows that milk from cows receiving BST is unchanged in nutritional value.**	"The evidence indicates that the nutritional quality of milk and meat from rBST-treated cows is equivalent to that of milk and meat from untreated cows. Protein, fat, and mineral content, including calcium, of the milk are all within the range found in untreated cows."
MEAT QUALITY	**Meat from cows receiving BST was found to be unchanged in nutritional value, except for a reduction in fat content.**	"Meat derived from treated cows is lower in fat content but otherwise is nutritionally equivalent to that from untreated animals."

	Summary	NIH Panel Conclusions
BST IN MILK	It was found that giving a cow BST does not change the trace level of BST normally found in milk.	"The concentration of BST in the milk of cows treated with usual doses of rBST is no higher than the concentration in untreated cows."
	The trace level of BST in milk was found to be mostly destroyed by pasteurization.	"Pasteurization inactivates or destroys most of the BST in milk...."
	Research indicates that BST is digested and, even if it were not digested, could have no effect in humans.	"There are no data to suggest that BST present in milk will survive digestion or produce unique peptide fragments that might have biological effects. Even if BST is absorbed intact, the growth hormone receptors in the human do not recognize BST and, therefore, BST cannot produce effects in humans."
IGF-I	IGF-I, a protein produced by the cow in response to BST, has not been found to have effects harmful to humans.	
	IGF-I is digested.	"This protein will also be digested into its amino acid, di- and tripeptide constituents by gut enzymes."
	Even if IGF-I were not digested, there is no evidence that it would be biologically active in humans.	"...nor is there evidence of systemic biological effects in man from any IGF-I absorbed intact, because the amounts of IGF-I that might potentially be ingested are orders of magnitude less than those required to produce such effects."
	It has been found that IGF-I is not destroyed by pasteurization but is destroyed by the heat treatment used to prepare infant formula.	"*[Pasteurization]* has little or no effect on the content of IGF-I *[in milk from cows receiving BST]*.... The more intense heat treatment used in the manufacture of infant formulas inactivates approximately 90 percent of the IGF-I."
	The IGF-I content of milk was found to be slightly increased when BST is administered, but the amounts were found to be within normal experience.	"Milk from rBST-treated cows contains higher concentrations of IGF-I.... The amount of IGF-I ingested in 1 liter of milk approximates the amount of IGF-I in saliva swallowed daily by adults. Young children and infants already ingest IGF-I in commercially available cow's milk or in mother's milk."
IGF-II	IGF-II, another protein hormone produced by the cow, has not been found in increased levels in milk from cows receiving BST.	"The concentration of IGF-II does not increase with rBST treatment."