

Recombinant Bovine Somatotropin (rbST): A Safety Assessment

Initially presented at the Joint Annual Meeting of the
American Dairy Science Association®,
Canadian Society of Animal Science, and
American Society of Animal Science

Montreal, Canada
July 14, 2009

Updated on March 22, 2010

Richard Raymond, M.D.

Connie W. Bales, Ph.D., R.D.

Dale E. Bauman, Ph.D.

David Clemmons, M.D.

Ronald Kleinman, M.D.

Dante Lanna, Ph.D.

Stephen Nickerson, Ph.D.

Kristen Sejrsen, Ph.D.

Recombinant Bovine Somatotropin (rbST): A Safety Assessment

Executive Summary

According to estimates from the Food and Agricultural Organization (FAO) of the United Nations (UN), in 50 years, the world's food needs will increase by 100 percent, and 70 percent of that increase will have to come from increased agricultural efficiencies and advances. There is just not sufficient and sustainable water, land and other natural resources to meet these food needs without the help of innovations in farming and agriculture.

Recombinant bovine somatotropin (rbST) is one example of the kinds of efficient food production practices that will help feed the world in the future. rbST is a supplement that increases milk production in healthy lactating cows, allowing farmers to produce safe, nutritious milk that is not only more affordable because of efficient farming practices, but is also produced in a more environmentally responsible way. Milk from rbST-supplemented cows, like all milk – organic, conventional, or rbST free – is a good and wholesome source of vital nutrients.

Supplementing cows with rbST increases milk production by an average of approximately 15 percent in the U.S. dairy cow population and reduces the cost of production of a glass of milk, therefore potentially making milk more affordable for the consumer. By increasing milk production per cow, the number of cows needed to maintain the current milk supply is decreased, thereby saving natural resources. The use of rbST to increase milk production in just 15 percent of the U.S. dairy cow population would reduce the carbon footprint of milk production equal to taking approximately 390,000 cars off the road or planting approximately 290 million trees annually. Contrary to some claims, there is no measurable impact on animal health when rbST is used to supplement dairy cattle. Moreover, three decades of research regarding rbST and human health have found no scientific evidence of any link between drinking milk

from cows supplemented with rbST and any human health risks, including the decline in age of puberty and the risk of breast cancer.

The safety of milk and meat from cows supplemented with rbST has been comprehensively and consistently documented. To date, there have been more than 90,000 scientific publications relating to somatotropin. Cow-related scientific investigations have also been extensive involving academic, government and industry scientists worldwide. A limited literature search for “bovine somatotropin” and “recombinant bovine somatotropin” yielded more than 1,300 and 500 scientific publications, respectively.

Based on the foundation of strong evidence of safety, rbST was approved for commercial use in the United States by the Food and Drug Administration (FDA) in 1993. Specific to human safety, regulatory authorities, together with their scientific assessment bodies, in more than 50 countries, including Australia, Canada, the Commission of the European Communities (Committee for Veterinary Medicinal Products), South Korea and the United States, have determined that milk and meat products from cows supplemented with rbST are safe for consumption by people of all ages. In addition, scientific bodies such as the World Health Organization (WHO) and the Food and Agriculture Organization (FAO), via their Joint Expert Committee on Food Additives (JECFA), have reached the same conclusions. Furthermore, all major dairy markets have no restrictions on the import of dairy products from rbST-supplemented cows.

Consumers can be reassured of the safety of milk from cows supplemented with rbST from the recent U.S. experience. Milk from rbST-supplemented cows has been a part of the U.S. food supply since receiving FDA approval more than 16 years ago and its use has not been associated with any scientifically documented detrimental effects on human health.

Introduction

In 1993, the U.S. Food and Drug Administration (FDA) approved the use of recombinant bovine somatotropin (rbST) for increasing milk production in lactating dairy cows, and its commercial use began in 1994. As of

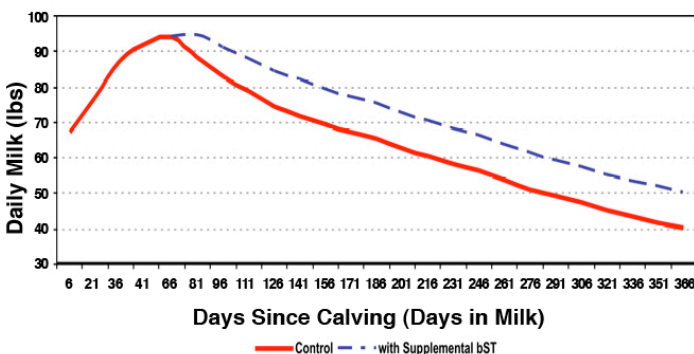
2009, more than 30 million cows in the United States have been supplemented with rbST, bringing nutritious and wholesome milk to the public along with economic and environmental benefits to society.

Specific to human safety, regulatory authorities, together with their scientific assessment bodies, in more than 50 countries, including Australia, Canada, the Commission of the European Communities (Committee for Veterinary Medicinal Products), South Korea and the United States, have determined that milk and meat from cows supplemented with rbST are safe for consumption by people of all ages.^{1,2,3,4} In addition, scientific bodies such as the World Health Organization (WHO) and the Food and Agricultural Organization (FAO) of the United Nations, via their Joint Expert Committee on Food Additives (JECFA), and the National Institutes of Health (NIH), via their Technology Assessment Conference, have reached the same conclusion. In fact, all milk – organic, rbST free and conventional – is well recognized to be natural, pure and safe.

According to estimates from the FAO, in 50 years, the world's food needs will increase by 100 percent, and 70 percent of that increase will have to come from technological advances as there is not enough land, water and other natural resources to meet that need without the help of innovations in farming and agriculture.^{5,6,7} Innovative and efficient food production practices, like the use of rbST, will help to feed the world by allowing farmers to make the most of land and natural resources.

Supplementing cows with rbST increases milk production by an average of approximately 15 percent (4.5 kilograms [10 pounds] per cow per day) in the U.S. dairy cow population and reduces the costs of production of a glass of milk, helping keep this vital source of worldwide nutrition more affordable. [Refer to Figure 1.] By increasing milk production per cow, the number of cows needed to maintain the current milk supply is decreased, thereby saving natural resources. In fact, use of rbST to increase milk production in just 15 percent of the U.S. dairy cow population reduces the carbon footprint of milk production equal to taking approximately 390,000 cars off the road each year.⁸

Figure 1. Typical Example of Lactation Production Curve



Contrary to some claims, there is no measurable impact on animal health and no scientific link between drinking milk from cows supplemented with rbST and any human health issues, including the decline in age of puberty and the risk of breast cancer.

In spite of overwhelming scientific evidence and support, questions have been raised about the safety for humans of the milk produced from cows supplemented with rbST and concerns have been expressed about animal welfare.

To address these questions and concerns in a constructive manner based on scientific research, Elanco, the company that manufactures and markets rbST, initiated an assessment with a group of independent scientific experts to develop an expert paper focusing on the science behind the product. These physicians, nutritionists and animal scientists came together twice as a group, in March and April of 2009, for meetings chaired by Richard Raymond, M.D., former Under Secretary for Food Safety at the United States Department of Agriculture (USDA), and sponsored by Elanco, during which the following paper was independently developed by these experts. The experts updated the paper in early 2010 with the most recent scientific information available.

This paper will explore in more depth what rbST is and how it works; the impact of rbST use on production efficiency; the many scientific reports detailing its safety in humans and animals; the nutritional content and quality of milk produced by rbST-supplemented cows; the economic impact of rbST use on the consumer; and the environmental advantages from its use.

General/Biology

Q1. What is rbST and how does it work?

Somatotropin (ST), also known as growth hormone, is a natural protein hormone that is produced by the pituitary gland. In lactating dairy cows, bovine somatotropin (bST) is a major regulator of milk production; it does this by coordinating the metabolism of body tissues so that more nutrients can be used for milk synthesis.^{9,10} Indeed, a characteristic of healthy, high producing cows is a greater pituitary secretion of somatotropin. Modern recombinant DNA technology allows the production of somatotropin in commercial quantities. Known as recombinant bovine somatotropin (rbST), it is biologically equivalent to the natural pituitary-derived somatotropin, and rbST supplementation markedly improves the productivity of lactating dairy cows. rbST use is initiated on or about

day 60 of a cow's lactation cycle when milk production normally begins to decrease. rbST supplementation prolongs an increased level of milk production and is, therefore, a management tool for dairy producers that helps supplemented cows produce milk at a level more like the farmer's most productive cow.

Human Health Aspects of rbST

Q2. Is there any difference among the various types of milk – organic milk, rbST-free milk and conventional milk? If so, is it meaningful or relevant from a human health standpoint?

Milk is a nutritious food and its composition does not differ whether it is labeled as conventional, rbST free or organic.¹¹ Milk and dairy products labeled as rbST-free or organic are niche products marketed by producers following a particular management system. There is no FDA-approved test that can differentiate between milk from rbST-supplemented and non-supplemented cows. If properly handled, all milk, regardless of the production system, is natural, pure and safe.

Q3. What evidence do we have that shows milk from cows supplemented with rbST is safe for humans? How much of this is recent (i.e., post-rbST approval)?

The safety of milk from cows supplemented with rbST has been comprehensively and consistently documented. To date, there have been more than 90,000 scientific publications relating to somatotropin, thereby providing a strong knowledge base for understanding the biology of somatotropin. Cow-related research has also been extensive; a limited literature search for "bovine somatotropin" identified more than 1,300 scientific publications and more than 500 publications relating to "recombinant bovine somatotropin." Many of these studies were conducted in the late 1980s and in the 1990s because the safety of milk from rbST-supplemented cows had to be established before it could be approved for use in the human food supply.

Based on the foundation of this strong evidence of safety, rbST has been approved for commercial use in more than 20 countries, in addition to the United States. Additionally, since rbST was first approved for commercial use in the global market in March 1990, and later approved for commercial use in the United States in November 1993, milk and meat from cows supplemented with rbST has been determined as safe by regulatory authorities, together with their scientific assessment bodies, in more than 50 countries, including

Australia, Canada, the Commission of the European Communities (Committee for Veterinary Medicinal Products) and South Korea. Also, its human safety is recognized by at least 20 respected and leading institutions and organizations, both in the United States and internationally. This support comes from health organizations such as the American Medical Association, the World Health Organization (WHO) and the Food and Agricultural Organization (FAO), via their Joint Expert Committee on Food Additives (JECFA), and the Royal College of Physicians and Surgeons of Canada; as well as governmental regulatory and oversight agencies, such as the U.S. Food and Drug Administration (FDA) and the Inspector General of the U.S. Department of Health and Human Services. (A comprehensive listing of these entities and key findings from them regarding the human safety aspects of rbST is attached to this paper as Appendix A.)

Consumers can be reassured of the safety of milk from cows supplemented with rbST based upon the U.S. experience. Milk from rbST-supplemented cows (more than 265 billion liters [70 billion gallons] from more than 30 million cows as of 2009) has been a part of the U.S. food supply since rbST approval in 1993 and its use has not been associated with any scientifically documented detrimental effects on human health.

Q4. Why is rbST not approved for use in certain countries such as Canada as well as in Europe?

While the human safety of dairy and meat products from dairy cows that have received rbST has been recognized in more than 50 countries by their regulatory authorities, together with their scientific assessment bodies, there are more than 20 countries in which rbST has been approved for commercial use, in addition to the United States. It is important to note that all countries, including Canada and the Commission for the European Communities, that have affirmed the safety of milk from rbST-supplemented cows, allow imported milk or dairy or meat products from these cows. Indeed, none of the major dairy markets that allows the import and sale of U.S. dairy products have restrictions on milk or dairy products from cows supplemented with rbST. Furthermore, none of them requires special labeling of such products.

The reasons for some countries not having yet approved rbST for commercial use are varied, ranging from concerns about animal welfare and safety within their indigenous production systems, production quota-based marketing, concern for the commercial viability of small producers, social customs, and

general opposition to technological advances used to promote more efficient food production, whether they are related to animal or crop production.

Q5. What effect does bovine growth hormone have when given orally to children with severe growth deficiencies?

In the 1950s, there was interest in giving bovine growth hormone injections to children who were deficient in human growth hormone to help them achieve normal growth. Unfortunately, in these children, it was shown definitively that bovine growth hormone had no effect on growth in humans.^{12,13,14} This means that even if milk had high concentrations of bovine growth hormone, the hormone would not stimulate human cells to grow. Furthermore, when bovine growth hormone is given orally, it is broken down by digestive enzymes. Therefore, for these two major reasons, it is logical to conclude that bovine growth hormone in milk cannot stimulate human tissues to grow.

Q6. What safety studies supported the approval of rbST?

Long before safety studies were required, and as early as the mid-1930s, Russian scientists injected more than 500 cows with pituitary extract (containing bST) and found an increase in milk yield without deleterious side effects.¹⁵ Subsequently in the 1940s, English scientists, in attempts to increase milk production to alleviate food shortages during WWII, discovered that bST was the biologically active ingredient in pituitary extracts, and that milk production could be safely increased when given to cows without affecting milk quality.¹⁶ Later, clinical studies in the 1950s attempting to treat human dwarfism with bST found neither a growth response nor any adverse health effects, basically because the chemical structure of bST differs substantially from that of human somatotropin (hST).^{9,13,14,17} Based on these initial studies, the FDA concluded that bST was not active in humans.

After the enactment of the Federal Food, Drug, and Cosmetic Act (1938), the FDA required that for approval of any new animal drug, the food from treated animals must be safe for human consumption. Twenty-five years ago (1984), which was nine years prior to the U.S. FDA's approval of rbST for commercial use by the dairy industry (1993), the FDA concluded that milk from rbST-supplemented cows was safe for human consumption as well as wholesome in composition based on their review of published research data of the time, and allowed milk from rbST-supplemented cows studied under research conditions to be sold for commercial use.^{18,19,20}

Subsequently, from 1984 to 1993, more than 1,500 scientific studies, reviews, professional papers, and surveys further examined the role of rbST and determined that milk and milk products were safe for human consumption.²¹ Based on these amassed data, as well as results of post-approval trials, the human safety of dairy products originating from cows receiving rbST has been confirmed in more than 50 countries and recognized by numerous medical associations and scientific societies, including the FDA, the National Institutes of Health (NIH), WHO and FAO via their Joint Expert Committee on Food Additives (JECFA), all of which concluded that 1) all cows' milk contains bST, 2) there is no compositional change in milk from cows receiving supplemental rbST, and 3) milk from cows supplemented with rbST poses no human health or safety concerns for consumers of dairy products.

Q7. What post-marketing studies have been conducted on rbST with respect to human health?

The functions and effects of bST have been extensively investigated in animals and humans for more than 70 years.^{9,12,13,14,15,16,22} While most of the scientific studies related to the safety of rbST and human health were done as part of the FDA's pre-approval process, there have also been extensive follow-up studies and observations confirming the safety of rbST with respect to human and animal health. Within the past 25 years, we have learned to purify this hormone, determined its structure and synthesized it using recombinant DNA technology. The recombinant form of bST has the same biological functions as the native form. Naturally-occurring bST causes cows to produce milk, and they will increase their voluntary feed intake to support the increase in milk production. rbST does exactly the same thing. The milk obtained from cows supplemented with rbST is identical in every way to milk from non-supplemented cows. bST, both native and recombinant, is not recognized by the human body and has no function in humans.^{9,10,17,20} Moreover, native and recombinant bST are digested in the gastrointestinal tract and do not enter the blood stream.^{12,20}

Q8. Are hormones increased in milk from cows supplemented with rbST?

Hormones are naturally present in all the foods we eat, regardless of whether they are sourced from animals or plants. Dairy products are natural, nutritious foods and science has shown that milk from rbST-supplemented cows is indistinguishable from organic or rbST-free milk. In fact, milk label claims are not related to any meaningful differences in the milk compositional variables

measured.¹¹ Conventional, rbST-free and organic milk are compositionally similar; they have the same nutrient composition and the same trace levels of hormones regardless of the milk production system used.

Because of the lack of a difference in the milk, no scientifically proven, FDA-approved test exists that can identify the procedures and management systems used in producing the milk.

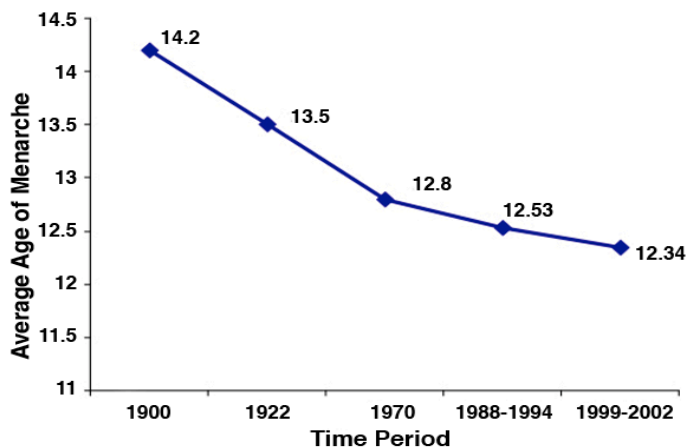
Q9. There has been a gradual decrease in the age at onset of puberty in females. What evidence exists that rbST has not affected this change?

Scientific evidence shows there is no change in the composition of milk from cows supplemented with rbST, and therefore no changes are present in the milk and dairy products from rbST-supplemented cows that could affect the age at puberty.

The decrease in age at onset of puberty has, for the most part, used menarche (onset of a girl's first menstrual flow) as the measurement most consistently reported.

The first reported studies appeared around 1940, with several large studies reported periodically thereafter.²³ These major studies reveal that the average age of menarche of all girls in the United States has shown a constant rate of decline from 1940 to the present.²⁴ [Refer to Figure 2.]

Figure 2. Average Age of Menarche of U.S. Girls Who Had Reached Menarche (1970, 1988-1994 and 1999-2002)²⁴



The most often-referenced surveys of the age of menarche are the National Health and Nutrition Examination Surveys (NHANES) conducted by the U.S. Centers for Disease Control and Prevention (CDC). Comparing the NHANES study of U.S. girls conducted

from 1988-1994 to an earlier study reported in 1973, the decline in age at menarche was four months over approximately two decades, or two months per decade. A comparison of the NHANES study of girls in the United States from 1988-1994 to the study of girls in the United States for NHANES 1999-2002 again shows a decline in age at menarche, of two months over approximately one decade.^{24,25} [Refer to Figure 2.] This last comparison coincides with the time period since the FDA approval of rbST for commercial use, and the results do not show any change from the rate of decrease in age of menarche when compared to the 50 years of studies that preceded this most recent analysis.^{25,26}

Q10. What environmental factors are known to play a role in the onset of puberty in boys and girls?

Many environmental factors influence the age of puberty in boys and girls.^{27,28} Body weight and rate of weight gain are strong influences. The increasing weight and height of boys and girls over the past century have been associated with earlier onset of puberty. Malnutrition and under-nutrition delay the onset of puberty. Other influences that delay the onset of puberty include: high altitude, chronic infections, and chronic illnesses, such as inflammatory bowel disease and cystic fibrosis. In all of these chronic conditions, nutritional status and weight gain are important determinants of the onset of puberty. Specific foods or non-nutrient substances in foods, such as hormones, have not been associated with changes in the age of puberty on a population-wide basis.

Q11. What are the breast cancer incidence trends in the United States over the last 30 years or so?

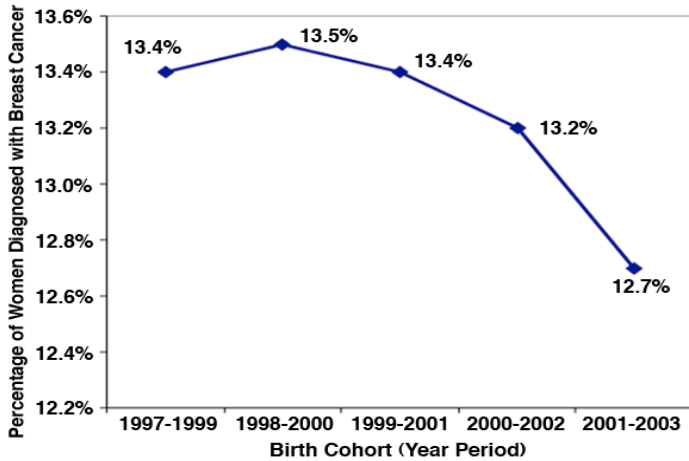
Age-adjusted incidence rates for breast cancer cases in the United States are lower today than they were in 1994 when rbST commercial use began.²⁹

The changes in incidence rates of breast cancer cases from 1975 to 2008 present very encouraging news because the recent trends show decreasing incidence rates. From 1980 to 1987, breast cancer incidence rates increased by 3.7 percent. From 1987 to 2001, the rates increased by only 0.5 percent, and from 2001 to 2005, breast cancer rates decreased by 3.1 percent.

Another way of looking at these positive trends is to look at the probability that a female born in the United States will be diagnosed with breast cancer in her lifetime. In the birth period of 1998-2000, that

probability was 13.5 percent (or one out of every 7.4 infant females) while the probability for the birth period of 2001-2003 was 12.7 percent (or one out of every 7.9 infant females).³⁰ [Refer to Figure 3.]

Figure 3. Lifetime Probability of Developing Breast Cancer (Girls Born 1997-2005)³⁰



Q12. What factors are known to contribute to the development of breast cancer?

The etiology of breast cancer is still largely undetermined. Living in a Westernized society and increasing age are the only consistently identified risk factors for breast cancer for most women living in the United States.^{24,29,31} Most factors that are agreed upon by the scientific community as risk factors actually increase the risk by very small percentages. Factors most solidly linked to an increased risk of breast cancer are having a first-degree relative with breast cancer and/or having the high-penetrant genes, BRCA1 and BRCA2, which account for the majority of inherited breast cancers.

Other factors known to increase the risk of breast cancer include obesity in post-menopausal women, early age of onset of menarche (first menstrual period), delayed pregnancy, no or little breast feeding of infants and nulliparity (no pregnancy history). There is a very small increase in risk with long-term use of oral contraceptives and hormone replacement therapy. There is no clear evidence that dietary exposure, with the exception of alcohol, is associated with an increased risk of breast cancer.

Milk contains ruminant, vaccenic, butyric and branched chain fatty acids, whey protein, calcium and vitamin D, all of which have the potential to protect against breast cancer.³²

Q13. Does drinking milk from cows supplemented with rbST increase breast cancer risk?

Drinking milk does not increase breast cancer risk, regardless of whether the milk is organic, rbST free or conventional.

There are many peer-reviewed studies that show no association between consumption of milk and incidence of breast cancer. A recent report that reviewed more than 40 case-control and 12 cohort studies concluded that evidence "...does not support an association between dairy product consumption and the risk of breast cancer."³²

As stated before, there has actually been a decline in the rate of breast cancer during the time period that rbST has been approved for commercial use.

Q14. Can people who have cancer safely drink milk from rbST-supplemented cows?

bST and rbST are biologically identical and neither have been associated with the development of cancer. The major reasons why this is so include:

1. When bST is consumed orally, it has no biological effect. This has been confirmed in a number of scientific studies.^{12,20}
2. bST is not biologically active in humans, even if it were to be injected right into the bloodstream.^{12,13,14,17,18}
3. If all dairy cows in the United States were supplemented with rbST, the amount of IGF-I contained in the daily recommended amount of milk in the United States (three 8-ounce glasses) would be approximately 0.04 percent of that produced daily by the human body.^{33,34} (See responses to Q15, "What is IGF-I?" and Q19, "Are the levels of IGF-I in the milk of rbST-supplemented cows elevated?")

These important facts help explain the consensus among regulatory agencies and medical and scientific communities that milk from rbST-supplemented cows is safe for consumption by all population groups. In fact, it is important to encourage milk consumption as part of a healthy diet to aid in health maintenance and decrease the likelihood of chronic diseases, including cancer.^{35,36,37} Milk is one of the most nutrient-dense foods in our diet. This means that in a calorie-for-calorie comparison with other foods, it provides very high amounts of a variety of essential nutrients. As

a rich source of protein, vitamins and minerals, milk supports a healthy and robust natural defense system in the body, enhancing the ability of the body to fight off challenges, including cancer. In addition to enhancing body host immune responses overall, milk contains a number of bioactive ingredients specifically known to help prevent certain cancers. These include whey protein, vitamin D, calcium, branched chain fatty acids, and two fatty acid isomers with potential anticancer effects – ruminic acid and vaccenic acid.³²

Q15. What is IGF-I?

IGF-I (insulin-like growth factor-I) is a protein that stimulates growth and maintenance of skeletal tissue in normal people. Humans have IGF-I in their blood and it is produced in most body tissues. Without adequate IGF-I, humans do not grow normally. They are very short, have weak bones that break easily, have small brains and mental retardation.

Q16. What is the effect on human health of IGF-I in milk from cows supplemented with rbST?

In cows supplemented with rbST, there is a slight increase in the amount of IGF-I in the milk. The IGF-I that is in the milk from cows supplemented with rbST is the same IGF-I that is in non-supplemented cows' milk. The amount of IGF-I that is present in milk from rbST-supplemented cows does not exceed the range that occurs in herds and dairy cows not supplemented with rbST.^{20,34,38} Therefore, there is no evidence that this amount of IGF-I would pose a health hazard.

The American Cancer Society's (ACS) paper on rbST, last revised on Feb. 17, 2009, finds that "...there is no evidence that drinking milk, produced with or without rBGH treatment, increases circulating IGF levels into the range of concern."³⁹ The ACS paper also found that, "One study estimated that the additional amount of IGF-1 that might be absorbed by humans, assuming no degradation and complete absorption, represents 0.8% of normal gastrointestinal secretion and 0.09% of the daily production of IGF-1 in adults."³⁹ This study by the Joint Expert Committee on Food Additives (JECFA) indicated that the daily intake of 1.5 liters of milk per day will provide an amount of IGF-I that is equal to less than one one-thousandth (or 0.09 percent) of that produced by the human body on a daily basis.^{33, 34}

Consequently, the amount of IGF-I absorbed by the intestine from milk is negligible. Because the body produces so much IGF-I, the amount absorbed, if any, does not cause a detectable increase and body tissues are exposed to no more IGF-I than if no milk

was consumed.⁴⁰ Additionally, IGF-I has never been shown to transform a healthy cell into a cancer cell. The digestive secretions, such as saliva, contain an amount of IGF-I that has never been shown to cause intestinal cell transformation.^{39,41,42,43,44,45,46} (An IGF-I Fact Sheet outlining the impact of IGF-I on human health safety is attached to this paper as Appendix B.)

Q17. How is IGF-I broken down by the digestive process, and is any of it absorbed intact?

The majority of IGF-I is broken down by the digestive process like any other protein. Because the body produces so much IGF-I every day, the amount of IGF-I absorbed by the intestine is minuscule when compared to the amount produced by the body.^{34,41,47,48} Therefore, the amount of IGF-I in milk – either from cows with or without rbST supplementation – does not cause any measurable change in the amount of IGF-I that is present in a normal healthy human being.

A paper by Hoppe et al, and another by Anderle et al, discuss the effect of milk protein on children's growth.^{49,50} The papers show that ingestion of the bovine milk protein casein results in increased levels of IGF-I in the circulation. However, the studies deal with the beneficial effect of animal protein in general and casein in particular on growth. The increased longitudinal growth in the children being studied was considered a benefit. Thus, the improved intake of the milk protein/casein leads to increased physiologic/endogenous production of IGF-I. There is no mention of increased uptake of milk IGF-I as the "cause" of the increased levels of IGF-I seen in these growing children.

Q18. Is IGF-I broken down by pasteurization of the domestic milk supply and other heat methods used in infant formula processing?

IGF-I is not broken down by pasteurization of cows' milk. Sterilization of liquid formula completely denatures IGF-I and other similar proteins. Processing of the dry milk powder does not denature IGF-I. Some activity remains in the processed powder, although when the powder is mixed with the other components of the formula, standard assays do not detect it, likely because of interference by the other components of the formula. The amount of biologically-active IGF-I remaining in the powder is inconsequential compared to the amount of IGF-I the infant itself produces in secretions (such as saliva, bile and pancreatic secretions). It should also be noted that IGF-I is a constituent of human breast milk and concentrations are enhanced in human colostrum. Colostrum is the first milk secreted at the end of pregnancy, or

after birth; it is rich in antibodies that confer passive immunity to the newborn. Finally, it is recommended that infants under a year of age not be fed standard cow's milk because the concentration of nutrients is not optimal to support growth and development.

Q19. Are the levels of IGF-I in the milk of rbST-supplemented cows elevated?

In cows supplemented with rbST, there is a slight increase in the amount of IGF-I in the milk. However, if several lots of milk are examined from several different farms, generally the range of concentrations of IGF-I is so broad that even following supplementation of rbST it is impossible to detect a difference among milk from individual cows or farms of rbST-supplemented cows compared between those not using rbST.^{20,34,38} However, taking into account that there is some small increase in IGF-I in milk from rbST-supplemented cows this degree of increase is very minor compared to the total amount of IGF-I produced daily by intestinal secretions. Therefore, it does not contribute to any measurable change in total body IGF-I levels in blood or in intestinal secretions. For instance, the daily amount of IGF-I produced in human saliva and other digestive secretions is equivalent to the amount of IGF-I that would be consumed by drinking more than 270 glasses of milk (8 ounces or 237 milliliters) in a single day.³⁴

Furthermore, the American Cancer Society's 2009 paper on rbST finds that "...IGF-1 concentrations are slightly higher (to variable degrees, depending upon the study) in milk from cows treated with rBGH than in untreated milk. This variability is presumed to be much less than the normal variation of IGF-1 in cow's milk attributable to parity and stage of lactation."³⁹

Q20. Are the levels of antibiotics in the milk of rbST-supplemented cows elevated?

The FDA established a Post-Approval Drug Monitoring Program to further address milk safety from rbST use. The program included tracking violations for antibiotic residues in milk; results demonstrated that use of rbST had no effect on violative drug residues and they reaffirmed that "...bST is indeed safe and has no adverse effect on the milk supply."⁵¹ It is noteworthy that, in the United States, while dairy cows are being treated with antibiotics for illnesses, including mastitis, milk from these treated cows does not go into the human food chain because of the possibility of human allergies to the antibiotic that might be present as a residue. In addition, for each antibiotic, there is a scientifically determined withdrawal period

for the elimination of the drug from the cow's system, during which none of the cow's milk enters the human food chain. Dairy producers are also very careful not to allow milk with antibiotics into their manufacturing facilities because the presence of antibiotic residues in milk may affect the production of milk products relying on the addition of microbial cultures.

Mastitis is a major reason for treating dairy cows with antibiotics; however, investigations into the effect of rbST on mammary health have demonstrated no effect on the severity or duration of clinical or subclinical mastitis. Indeed, post-approval data summaries and field trials in commercial herds demonstrated that rbST was not associated with significant changes in subclinical or clinical mastitis.^{52,53,54,55,56,57} Thus, use of antibiotics to control this disease would be no different between rbST-supplemented and non-rbST-supplemented cows. Additionally, the majority of mastitis that is treated with antibiotics is clinical mastitis, most of which occurs during the first 60 days of lactation, a period during which rbST is not being used.⁵³

Q21. Is there a test to detect the differences between milk from rbST-supplemented cows and milk from non-supplemented cows?

There is no scientifically proven, FDA-approved test for cows' milk to determine whether or not the cows have received rbST supplementation.

Extensive scientific testing shows that there is no biological or nutritional difference between milk from cows supplemented with rbST and milk from unsupplemented cows. This means that the milk content of important nutrients including protein, fat, vitamins and minerals is not altered in any way when cows receive supplementation with rbST.¹⁷

Q22. Does rbST have any influence on the residue of pesticides in the fat of milk?

Pesticide residues are an indication of misuse in the production of plant-based human foods or animal feeds. The use of rbST supplements requires no special feeds or diet formulations. Use of rbST does not increase exposure to the residue of pesticides. Milk is the most monitored product in the American food supply to ensure its safety and wholesomeness. Milk is tested for antibiotic residues and thoroughly inspected several times during the journey from farm to grocery store shelves. The USDA also analyzes milk and dairy products for pesticide residues and the most recent tests indicate no violation of residue standards established by the Environmental Protection Agency (EPA).⁵⁸

Q23. Why has Codex not adopted a standard or approved rbST for supplementation in dairy cattle?

The Codex Alimentarius Commission was created in 1963 by the WHO and FAO, agencies that are both under the umbrella of the United Nations. It consists of 180 countries to date, and its major purpose is to create policies and standards that universally promote food safety and fair trade practices. It is a democratic organization with each member country getting one vote, no matter how large or small. When policies are being promulgated, they must go through committees made up of member country representatives. The process is quite lengthy with appropriate avenues and opportunities for discussion. To become final policy, a proposal must go through eight steps, with a consensus decision or votes being taken at each step along the way. rbST entered into the Codex process in 1990, with the scientific human safety assessment reported in 1992. The proposed standard regarding rbST reached Step 8 (final step) of the Codex process in 1999 and has been held there since that time.^{34,59}

Opponents of rbST use have made statements that Codex considers the supplement to be “unsafe,” or that Codex has “banned” its use and has “repeatedly refused to recognize its safety.” These statements are not a true reflection of the Codex process. First of all, Codex does not have the authority to “ban” any product or additive. It can, however, develop maximum risk levels of drugs, residues, etc. Secondly, the rbST discussion has passed through the first seven steps of the Codex eight-step process. At each step along the way, it was determined that rbST posed no food safety or public health risk. The concerns expressed have been in regard to “other legitimate factors” and the elaboration of Codex standards.

The report of the seventh session of the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF) includes in its recommendations that Maximum Residue Limits (MRLs) and the Acceptable Daily Intake (ADI) be “not specified.” “Not specified” is a term applicable to a veterinary drug for which there is a large margin of safety for the consumption of its residues based on available data and that therefore there is no need to specify a numerical ADI or MRL. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) has also performed a thorough scientific evaluation of rbST and, as reported in the seventh report from CCRVDF cited earlier “...concluded that the margin of safety was so large taking into account the proposed use, potential intake of residues and available toxicity data that they represented no hazard

to human health and did not require a numerical ADI or MRL to be specified.”⁵⁹

The policy statement regarding rbST has reached Step 8 (final step) of the Codex process but has not yet passed Step 8. It is at this level that all 180 countries vote, or decide, for or against the policy becoming a universal standard. Codex follows the approach that consensus is ideal for a policy to be adopted. Oftentimes a vote will not be asked for if there is no consensus and it will be delayed until opposition questions can be answered or concerns resolved. Failure to pass Step 8 does not necessarily indicate that the majority are opposed to passage. In fact, a policy would not likely get to Step 8 if a majority opposed it because of the multiple steps and committees it must have passed through to get to the final step.

If Codex adopted the recommendations of the CCRVDF for rbST policy that would make the ADI and MRL standard “not specified,” that decision could possibly allow countries where rbST is approved for commercial use to use the World Trade Organization’s influence against a country if at some time in the future that country chose not to allow importation of milk or dairy products from cows supplemented with rbST. The Codex standard is designed to ensure public health and facilitate the trade of safe food products.

Animal Health Aspects of rbST

Q24. Is rbST harmful for cows?

Somatotropin is a natural protein present in the bloodstream of lactating mammals, with the greater concentrations observed immediately after parturition (giving birth). The approved supplementation of lactating cows with rbST occurs during the second part of their lactation, after which they have passed the most stressful part of the lactation. The health effects were extensively studied before rbST was approved by the FDA. Subsequent data summaries and post-approval studies on commercial dairy farms, some evaluating the response of more than 200,000 lactation cycles for cows on several hundred farms, have indicated cows receiving rbST are of normal health.^{52,53,54,55,56,57,60,61,62}

Animal health variables that were evaluated included the cost of veterinary services, culling rates, reasons for culling, incidence of lameness, reproduction, somatic cell count and incidence of mastitis. The results demonstrated that these variables were unchanged on farms where rbST was used to supplement compared to farms where rbST was not

used. Consistent experimental data confirming rbST effects have been collected in different countries, by different research groups.²¹

The physiological behavior of rbST-supplemented cows has been consistently shown to be similar to the behavior of superior milk-producing cows, those with the genetic capacity to produce more milk. There is an increase in their milk production, a matching increase in voluntary feed intake, and later in lactation these cows replenish their body reserves through dietary intake as support for the next lactation.⁹

Cows receiving rbST replenish their body reserves during the latter part of lactation in the same manner as unsupplemented cows. Consistent with this biological response, in their next lactation, neither milk production nor their health status was adversely affected in rbST-supplemented cows, as demonstrated by data collected in the field with thousands of cows before and after rbST was approved. Supplementing cows with rbST increases milk production by maintaining milk production to resemble a farmer's best cows.^{9,52,57,63}

If cows are stressed or have health problems, their milk production is decreased because they require more nutrients for maintenance and have fewer nutrients available for milk production. Genetically superior cows and those supplemented with rbST have the opposite response – they have increased milk production with a higher percentage of their nutrient intake being used for lactation. Health problems common to all milk-producing cows, such as acidosis, lameness and mastitis (udder infections) are observed in rbST-supplemented cows at the same low frequency as that which occurs in unsupplemented cows producing the same amount of milk.

Q25. Is rbST used to mask poor animal health and/or poor animal care?

Using rbST costs money and its use provides no benefit on farms where the performance of the herd is limited by inadequate nutrition or poor quality of management. Quite to the contrary, to get an economic return the recommended use of this technology is only on farms where cows are fed and managed properly.

When farm management is inadequate, including when health and nutritional care is poor, the farmer will simply not obtain any milk production advantage in using this technology. The farmer would lose the money invested in rbST. Thus, the statement that rbST could be used to mask poor animal health is contrary to our knowledge of the biology behind the rbST response. It is also not justifiable economically.

Several studies in different countries have shown that when cows do not have enough feed or are subject to poor management, there will be no response to rbST supplementation.^{64,65,66}

Q26. Have follow-up studies been conducted since the approval of rbST regarding herd and animal health related to rbST?

Subsequent to the 1993 approval, the use of rbST has continued to be examined under a wide range of conditions and management systems and results are remarkably consistent worldwide. These results have also been verified through the commercial use of rbST. Studies conducted on commercial herds have observed an increased milk yield in rbST-supplemented cows as compared to unsupplemented cows, but there were no differences in overall cow health, cow longevity or the quality of the milk being produced.^{52,55,56,57,60,61,62}

The FDA Center for Veterinary Medicine also maintains a national reporting system for adverse drug experiences (ADE). In 1999, the FDA stated that "...the number and nature of the adverse events reports raised no new animal concerns."⁶⁷ In 16 years, more than 30 million cows in the United States have been supplemented with rbST. Also, subsequent to the initial approval of rbST by the FDA, recent scientific studies have been submitted via normal regulatory process, and the initially approved product label has been updated to reflect these most recent scientific findings.

Q27. How is rbST metabolized in the dairy cow's body?

A consistent and sustainable high level of milk production has been demonstrated after supplementation of lactating cows with rbST. The experimental results that were used to request approval of the technology, as well as the evaluation of tens of thousands of cows in post-approval research, confirm a sustained response to rbST throughout the first lactation and a similar response is observed with supplementation in subsequent lactations.

The biology of this response has been well investigated and is well understood by animal physiologists.^{9,10} Naturally occurring hormones, including somatotropin, reach different cow tissues, binding to cell receptors and coordinating the use of nutrients to support lactation. Exactly the same process of hormone binding to its natural target tissues occurs when cows are supplemented with rbST. Cows respond by similar coordinated changes in the metabolic activities

of liver, mammary gland and other tissues to support an increase in milk production of approximately 15 percent. The biology described above has been extensively studied in animals.

In other words, the cow maintains the same metabolic priorities for milk production normally effective in early lactation. Researchers have demonstrated that superior cows used by farmers today have the ability to better maintain milk production levels throughout the lactation cycle.^{19,63} This is called “persistence” and is generally associated with healthier cows that are capable of maintaining good milk production through the entire lactation period. Cows supplemented with rbST also can maintain greater milk production up to the time of ceasing lactation, demonstrating there is no burnout, and that they remain healthy. [Refer to Figure 1.]

Genetically superior cows and cows supplemented with rbST can increase milk production only when they are well managed and can consume good quality feed.

Q28. What effect does rbST have on the quality of milk and the somatic cell count?

The quality or composition of milk, including the proportion of butterfat, protein and lactose, is not altered by supplementing cows with rbST. Likewise, there is no effect of rbST on the mineral (e.g., calcium) or vitamin content of milk. Moreover, the manufacturing qualities of milk are not influenced by rbST, including cheese-making properties such as yield, composition, and sensory characteristics of resulting cheeses. Factors such as genetics, diet, breed of cow, age, stage of lactation, environment and season, and milking practices such as milking interval, milking rate, frequency of milking and milking routine cause the variability observed in milk quality and composition; however, these factors would have equal effects in rbST-supplemented and non-supplemented cows.^{9,19}

The somatic cell count (SCC) is another assessment of milk quality, specifically a reflection of mammary health such as inflammation caused by bacterial infection or mastitis. Research trials prior to registration of rbST for commercial use did indicate there may be a slight increase in SCC with its use. This risk, however, is substantially smaller than risk from other factors that exist on all farms, such as season of the year, age, breed, stage of lactation, farm sanitary conditions and parity.⁶⁸

Q29. Does the change in use of rbST over the years affect mastitis cases in dairy cows?

Prior to approval of rbST, the Veterinary Medicine Advisory Committee (VMAC) of the FDA Center for Veterinary Medicine (CVM), held a public hearing to evaluate rbST and the relationship to mastitis and antibiotic use. They concluded that “...in view of the much larger variations in the number of mastitis cases normally observed due to herd, season, parity, and stage of lactation, the use of sometribove (rbST) would not be an important factor in considering the overall incidence of mastitis per unit of milk produced. Therefore, CVM has concluded that the use of sometribove (rbST) in dairy cows will not result in an increased risk to human health due to the use of antibiotics to treat mastitis.”⁶⁸

There have also been post-approval publication of studies involving hundreds of commercial dairy herds and publication of large experimental data summaries. Variables have included mastitis incidence, cultures for mastitis organisms, somatic cell counts, culling rates and veterinary costs. These studies found no evidence that commercial use of rbST represented a significant concern for mastitis or antibiotic use.^{52,53,54,55,56,57,59}

The majority of mastitis cases occur in early lactation (within the first two months), a period during which rbST is not being used to supplement cows. Investigations into the effect of rbST on mammary health have demonstrated no significant effects on the severity and duration of clinical or subclinical mastitis in dairy cows.^{52,53,54,56,57}

The prevalence of mastitis in any dairy herd is dependent on the husbandry practices employed to prevent and manage this disease, such as milking hygiene, animal housing and cow comfort, and environmental sanitation. In order to maximize economic returns from their cows, dairymen are continuously upgrading their mastitis management practices to minimize this disease. Factors associated with mastitis of which producers have less management control are season of the year, parity, stage of lactation and cow age.⁶⁹

Q30. Does the change in use of rbST over the years correlate to changes in antibiotic-resistant bacteria in cows?

The primary use of therapeutic antibiotics in dairy cows is to treat clinical cases of mastitis. Even in herds not using rbST, there is no evidence supporting the view that use of therapeutic antibiotics leads to resistant strains of mastitis-causing bacteria in dairy cows. A study of antibiotic usage over the past four decades,

initiated by the National Mastitis Council, found no scientific evidence to suggest that antibiotic resistance is an emerging human health problem in milk and dairy products.⁷⁰

Q31. Does rbST shorten a dairy cow's lifespan in the herd?

The effects of rbST use on cow performance and health were an important part of the FDA's evaluation that led to the approval of rbST for commercial use in the United States. In the 16 years since commercial use of rbST began, studies have continued to examine effects on cow health and well-being including effects on culling, veterinary costs, lameness, reproduction and mastitis. These follow-up studies showed an increase in milk production when rbST supplements were used but there were no differences in cow health, culling or longevity.^{52,55,56,57,60,61,62}

In fact, an examination of USDA dairy slaughter rates demonstrated no difference in slaughter (culling) rates between the seven years (1986-1993) prior to rbST approval and the 14 years (1994-2008) after approval. Likewise, there was no difference in seasonality of culling rates pre- and post-approval.⁷¹ Typically, slaughter rates are higher in the winter and fall and lowest in spring and summer, and for 11 out of 12 months of the year, slaughter rates for post-approval years were numerically equal to, or lower than those, for pre-approval years of rbST. Even for the years 2001-2003, the period representing the highest years of rbST use, slaughter rates for post-approval years were numerically lower than pre-approval years for seven out of 12 months of the year.

Finally, the dairy herd represents the livelihood of the dairy farmer. Farmers are very cognizant of the health and performance of their herd and would not use any technology or practice that had adverse effects. Likewise, the herd veterinarian and nutrition/management consultants would recognize if cows were adversely affected and these professionals would not recommend practices that negatively affect the health and performance of the dairy herd. Since its first use in 1994, rbST has proven to be a valuable management tool that allows dairy producers to improve their herds' productivity, and to date more than 30 million dairy cows have received rbST supplements.

Q32. Is there evidence of rbST being associated with injection site problems?

A mild transient swelling of 3-5 cm in diameter may occur at the injection site beginning approximately three

days after injection, persisting up to six weeks. Some cows may experience swellings of up to 10 cm that remain permanent but are not associated with animal health problems. The typical injection site swelling is of cosmetic concern only.²

Environmental Aspects of rbST

Q33. What is the environmental impact of using rbST?

The use of rbST allows each cow to produce approximately 4.5 kilograms (10 pounds), or approximately 4.5 liters (1.2 gallons), of extra milk per day. This translates to an increase in milk production by an average of approximately 15 percent with rbST use. This means that six cows supplemented with rbST can produce the same amount of milk as seven unsupplemented cows, which represents one less cow producing manure, consuming feed and water, using electricity for milking and requiring human effort for husbandry. In fact, the use of rbST in just 15 percent of the U.S. dairy cow population reduces the carbon footprint of the current milk supply production equal to taking approximately 390,000 cars off the road each year or planting approximately 290 million trees annually.⁸

If just 15 percent of the U.S. dairy herd was supplemented with rbST, the environmental gains of this reduction in the environmental impact would be equal to freeing up 540,000 acres of farmland currently used to produce dairy feedstuffs, a reduction in enough fossil fuel to heat more than 15,000 homes and a reduction in water sufficient to supply about 10,000 homes.⁸

On an individual basis, by consuming milk from rbST-supplemented cows, a family of four drinking the U.S. recommended allowance (RDA) of three 8-oz glasses (237 ml) of conventional milk per day would reduce their annual carbon footprint of the current milk supply by 345 pounds of carbon dioxide, which is equivalent to planting 25 trees annually.

The use of rbST is a management tool that improves agricultural sustainability and reduces the carbon footprint per unit of milk. All food production has an environmental impact. However, FAO estimates that in the next 50 years, the world food production must be increased by 100 percent to provide adequate nutrition for the increasing global population.⁷ Thus, innovative food production practices like rbST supplementation that increase the efficiency of food production

while mitigating the environmental impact will be of even greater importance in the future for the global production of food.

Q34. Are there rbST residues being left in the environment through the use of rbST?

The composition of all milk – organic, rbST free and conventional – is indistinguishable.¹¹ Moreover, rbST is made up of the same amino acids as other proteins, and proteins are digested and degraded. Therefore, there is no difference in the environmental effect by supplementing cows with rbST as compared to unsupplemented cows since there is no residue in either case.

Economic Aspects of rbST

Q35. What is the economic impact of drinking milk from cows supplemented with rbST?

The economic benefits of rbST are partitioned between the technology supplier, dairy producers, processors, retailers, consumers and the different levels of government.⁷² What segment of the dairy chain benefits, and by how much, is very difficult to predict and/or estimate. Milk and dairy products are commodities, and like all other commodities their costs of production and sale prices are subject to the laws of supply and demand. And like all commodities, there are many variables that can enter into the supply and demand equation.

By using nine cents per gallon as an estimated average savings that is passed on to the consumer purchasing milk and dairy products from cows supplemented with rbST, the maximum savings would be \$2 billion dollars. If only 20 percent of dairy cattle were supplemented with rbST, the annual savings to consumers in the United States would be approximately \$400 million.

Supplement lactating dairy cows every 14 days beginning at 57-70 days in milk until the end of lactation. When calculating net carbon footprint, manufacturing processes and total environmental costs must be considered. The label contains complete use information, including cautions and warnings. Always read, understand, and follow the label and use directions.

Appendix A

United States and International Organizations Acknowledging Human Health Safety of Milk and Meat from Cows Supplemented with Recombinant Bovine Somatotropin (rbST)

Multiple respected and leading organizations, both international and domestic, as evidenced below, have stated publicly that there is no difference in the composition or nutritional value of milk based on production practices, and therefore there is no difference in the safety to humans when consuming milk regardless of the production practices employed on the dairy farm. It is the conclusion of the expert panel that milk is milk, whether the dairy farmer chooses to produce milk under organic conditions, with rbST supplementation, or without rbST supplementation, and that no FDA approved test exists today to differentiate between milk produced by these different production practices simply because there is no measurable difference in the milk itself.

The following 20 organizations have made statements, or published data in publications, using one or more of the following acronyms: bGH, rbGH, rBGH, bST, BST, and rBST. All of these acronyms are being used to represent the recombinant form of bST, recombinant bovine somatotropin (rbST). The following organizations have acknowledged the safety of dairy products from cows supplemented with rbST:

1. United States Food and Drug Administration (FDA): August 1990, March 1993, January 1999, April 2000, January 2007, April 2009

In the August 1990 issue of *Science*, Vol. 249:852-853, Ann Gibbons contributed an article called "FDA Publishes Bovine Growth Hormone Data." The commentary highlighted an "unprecedented move" by the FDA, who published an article authored by Juskevich and Guyer detailing the safety information related to rbST before it had been approved. The report by Juskevich and Guyer concluded:

- "...that the use of rbGH in dairy cattle presents no increased health risk to consumers."

Juskevich JC and Guyer CG. Bovine growth hormone: human food safety evaluation. *Science*. 1990 Aug 24;249(4971):852-84.

On March 31, 1993, the FDA Veterinary Medicine Advisory Committee issued Meeting Discussion notes, which conclude that:

- "...the use of sometribove in dairy cows will not result in an increased risk to human health due to the use of antibiotics to treat mastitis."

Food and Drug Administration, Veterinary Medicine Advisory Committee. The effect of sometribove on mastitis. FDA report from the public hearing. Gaithersburg, MD. March 31, 1993.

On April 21, 2000, the FDA Center for Veterinary Medicine (CVM) issued an update entitled, "FDA Responds to Citizen Petition on rbST," in response to a Citizen Petition from Mr. Robert Cohen. Highlights from the update include:

- "FDA has previously maintained and continues to maintain that levels of IGF-I in milk, whether or not from rbGH supplemented cows, are not significant when evaluated against levels of IGF-I endogenously produced and present in humans."
- "While some studies indicate that levels of IGF-I may statistically increase in the milk of rbGH supplemented cows relative to unsupplemented cows, reported increases are still within the normal variation of IGF-I levels in milk."
- The Agency pointed out that "...even if all of the IGF-I in milk is absorbed, and there is insufficient evidence that it would be, the levels of IGF-I in human plasma would not rise by 1%."
- "Like most dietary proteins, rbGH is degraded by digestive enzymes in the gastrointestinal tract and not absorbed intact."

Food and Drug Administration, Center for Veterinary Medicine. CVM Update: FDA Responds to Citizen Petition on BST. April 21, 2000. Last accessed March 5, 2010: <http://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm130325.htm>.

An article from the January 2007 issue of the FDA Veterinarian entitled, "Developments in New Animal Technologies Show Rapid Advancement: CVM Keeping Pace," revealed that while technology in the field was moving quickly, the FDA Center for Veterinary Medicine's review and approval process was still focused on safety:

- "This approach to producing drugs required new approaches by the FDA to review the manufacturing capabilities of the drug sponsor. However the drugs themselves are reviewed for safety and effectiveness similar to other new animal drugs developed using more conventional methods. A recombinant bovine somatotropin (rbST) product approved by FDA in 1993 to increase milk production in dairy cows is produced with this technology."

Food and Drug Administration, Center for Veterinary Medicine. Developments in New Animal Technologies Show Rapid Advancement: CVM Keeping Pace. FDA Veterinarian. 2007;XXII(1). Last accessed March 5, 2010: <http://www.fda.gov/downloads/AnimalVeterinary/NewsEvents/FDAVeterinarianNewsletter/UCM055713.pdf>.

On April 23, 2009, the FDA issued an update on rbST as a result of an audit claiming that certain health concerns were not addressed in the original application and review. In the update, entitled “Report on the Food and Drug Administration’s Review of the Safety of Recombinant Bovine Somatotropin,” the FDA reconfirmed that:

- “...there are no new scientific concerns regarding the safety of milk from cows treated with rbGH. The determination that long term studies were not necessary for assessing the safety of rbGH was based on studies which show that: bGH is biologically inactive in human even if injected, rbGH is orally inactive, and bGH and rbGH are biologically indistinguishable.”

Food and Drug Administration, Center for Veterinary Medicine. Report on the Food and Drug Administration’s Review of the Safety of Recombinant Bovine Somatotropin. April 23, 2009. Last accessed March 5, 2010: <http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm130321.htm>.

2. American Medical Association (AMA): March, June, August and December 1990, March 1991, October 1992, November and March 1993, April 2008

On March 21, 1990, C.J. Grossman published an editorial in the *Journal of the American Medical Association* entitled, “Genetic Engineering and the Use of Bovine Somatotropin.” The concluding paragraph stated:

- “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.”

Grossman C.J. Genetic Engineering and the Use of Bovine Somatotropin. *JAMA*. 1990;264:1028.

On August 21, 1990, the AMA issued a press release entitled, “Bovine Somatotropin: Is the Milk Safe?” The release cited a report and editorial in the August 1990 issue of the *Journal of the American Medical Association*, in which authors, William H. Daughaday, M.D., and David M. Barbano, Ph.D., declared that:

- “Bovine somatotropin causes no changes in milk composition of any practical importance to consumers. [...] The minor differences in milk composition shown between unsupplemented and bST-supplemented cows are well within normal biological variation in milk composition.”

Daughaday WH and Barbano DM. Bovine somatotropin supplementation of dairy cows. Is the milk safe? *JAMA*. 1990 Aug 22-29;264(8):1003-5.

At the request of the AMA’s Board of Trustees, after the organization’s 139th Annual Meeting, June 24-28, 1990, the AMA’s Council on Scientific Affairs researched the development, safety and FDA oversight activities related to rbST prior to its approval as a commercial product for use in the United States. As a result, the Council on Scientific Affairs produced a written report introduced at the 44th Interim Meeting of the AMA’s House of Delegates, December 2-5, 1990. There, the report was assigned to a Reference Committee, which recommended that the House of Delegates adopt the report. The House of Delegates adopted the Council’s report, which includes the following statement:

- “The Food and Drug Administration has sufficiently addressed the health safety issue and the many in-depth studies identified in this report have adequately addressed the economic and policy issues.”

American Medical Association Council on Scientific Affairs. I. Economic and Public Policy Issues Involving Bovine Somatotropin (Resolution 232, A-90). In: Proceedings of the House of Delegates, 44th Interim Meeting, Orlando, FL, 1990.

On March 20, 1991, the *Journal of the American Medical Association* published a report by AMA’s Council on Scientific Affairs entitled, “Biotechnology and the American Agricultural Industry.” The article references the reasoning behind FDA approval of rbST as follows:

- “1. BST is a protein, not a steroid hormone, and is therefore easily broken down in the digestive tract.”
- “2. Because BST differs structurally from the human counterpart, the bovine hormone has no effect on human growth hormone receptors.”
- “3. Native somatotropin exists in bovine milk and therefore human consumption of bovine somatotropin is not new.”

American Medical Association Council on Scientific Affairs. Biotechnology and the American Agricultural Industry. *JAMA*. 1991;265:1429-36.

In March, 1993, AMA provided expert testimony on the “Human Health Implications of Recombinant Bovine Somatotropin” to the Food and Drug Veterinary Medicine Advisory Committee. The AMA concluded:

- “...all currently available scientific evidence suggests that the use of recombinant bovine somatotropin by the dairy industry poses no threat to human health.”

On November 5, 1993, the AMA issued a media statement entitled, "AMA Supports FDA Approval of Bovine Somatotropin (BST)." The statement contains the following language:

- "The American Medical Association supports the FDA's approval of Bovine Somatotropin (BST), to safely enhance the milk production of dairy cattle. Agricultural biotechnology of this kind is the future of food production in the United States and should not be feared or impeded."
- "After prolonged analysis of BST, the American Medical Association's Council on Scientific Affairs found BST-supplemented milk to be completely safe and nutritionally comparable to cow's milk currently on grocery store shelves."
- "BST is a protein hormone that is produced naturally by cows to help them make milk. Supplementing cows with small amounts of BST has shown to increase their milk production by 10-40 percent per cow without harming the animal or altering the nutritional value of their milk."
- "On a global level the positive impact of BST is significant. Beyond the financial benefits of increasing milk yield, BST can help to reduce waste, control pollution, enhance the nutritional value of foods and ensure that an adequate food supply exists."

Schwarz MR. Press Release: AMA Supports FDA Approval of Bovine Somatotropin (BST). November 5, 1993.

In contrast to the positive statements above, in the April 2008 issue of the AMA newsletter, the AMA President advised the hospital community to source milk from rbST-free suppliers. It is believed that the statement represents an individual's opinion and that the AMA, as an organization, has not changed its official position on rbST.

3. National Institutes of Health (NIH): December 1990

At the request of the U.S. Congress, NIH convened the Technology Assessment Conference on Bovine Somatotropin on December 5-7, 1990. A panel was charged with reviewing scientific data and weighing the evidence on the safety of rbST. The study was published by NIH and also in the Journal of the American Medical Association, Vol. 265:1423-1425. Conclusions from the conference report include:

- "The composition and nutritional quality of milk and meat from rbST-treated cows is equal to that from untreated cows."
- "The composition and nutritional value of milk from rbST-treated cows is essentially the same as that of milk from untreated cows."
- "As currently used in the United States, meat and milk from rbST-treated cows are as safe as that from untreated cows."

National Institute of Health (NIH). NIH Technology Assessment Conference Statement on Bovine Somatotropin. JAMA. 1991;265:1423-25.

4. American Cancer Society (ACS): March 1994 and February 2009

In March 1994, the ACS issued a press statement from the Vice President for Epidemiology and Statistics, C.W. Heath, Jr., M.D., entitled, "Bovine Growth Hormone." The statement reads:

- "The U.S. Food and Drug Administration recently approved the use of biosynthetic bovine growth hormone (recombinant somatotropin or rbST) for use by dairy farmers to boost cow milk production by increased hormonal stimulation of lactation. Extensive testing and research has shown that rbST is indistinguishable from natural bovine growth hormone and thus entails no health risks for consumers. There are no valid scientific findings to indicate a risk of human carcinogenesis."

Heath CW Jr. Press Statement: Bovine Growth Hormone. American Cancer Society. March 1994.

In February 2009, ACS provided an update about recombinant bovine growth hormone on its web site. While ACS states that it has no formal position regarding rBGH, the update confirms the essence of the press statement from 1994:

- "Still, there is no evidence that drinking milk, produced with or without rBGH treatment, increases circulating IGF levels into the range of concern."

American Cancer Society. Recombinant Bovine Growth Hormone: Background. February 2009. Last accessed March 5, 2010: http://www.cancer.org/docroot/PED/content/PED_1_3x_Recombinant_Bovine_Growth_Hormone.asp.

5. International Dairy Federation (IDF): February 1994

In December 1987, the International Dairy Federation commissioned Group A-22 to prepare a Technical Report on Bovine Somatotropin. A preliminary report

was presented in the Annual Sessions in September 1992, and then following review and comments the IDF Permanent Commission approved publication of a Final Report. The Report concluded that:

- "...the milk from BST-treated animals has been deemed safe for human consumption by medical and health agencies in numerous countries."

Bauman DE et al. Somatotropin (BST): International Dairy Federation technical report. 1994. Bulletin of the IDF 293/1994, pp. 2-7.

6. Joint Food and Agriculture Organization (FAO) and World Health Organization (WHO) of the United Nations: February 1998

In February 1998, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) 50th Meeting took place in Rome. During the meeting, the following conclusions were made:

- "It was concluded that the use of rbST will not result in a higher risk to human health due to the use of antibiotics to treat mastitis and that the increased potential for drug residues in milk could be managed by practices currently in use by the dairy industry and by following label directions for use."
- "...the potential for IGF-1 to promote tumour growth will not increase when milk from rbST-treated cows is consumed, resulting in no appreciable risk for consumers."
- "... The Committee concluded that rbST can be used without any appreciable risk to the health of consumers."

Joint FAO/WHO Expert Committee on Food Additives. Joint FAO/WHO Expert Committee on Food Additives fiftieth meeting Rome, 17-26 February 1998 summary and conclusions. World Health Organization. Rome. 1998.

7. The Executive Branch of the Federal Government (The White House): January 1994

As part of the Omnibus Budget Reconciliation Act of 1993 and at the request of several Congressmen including Senators Feingold (WI) and Leahy (VT) and Representatives Obey (WI) and Sanders (VT), the Executive Branch of the Federal Government informally agreed to undertake a study of the potential impact of rbST. In January 1994, the White House issued its report entitled, "Use of Bovine Somatotropin (bST) in the United States: Its Potential Effects." Statements in the report include:

- "There is no evidence that bST poses a health threat to humans or animals. It has been studied

more than any other animal drug, been found safe by FDA and many other scientific bodies in the U.S., Europe, and around the world."

The Executive Branch of the Federal Government. Use of Bovine Somatotropin (BST) in the United States: Its Potential Effects. January 1994.

8. American Dietetic Association (ADA): February and November 1993

In a February 1993 issue of the *Journal of the American Dietetic Association*, the ADA stated its position on BST supplementation as:

- "It is the position of the American Dietetic Association that the techniques of biotechnology are useful in enhancing the quality, nutritional value, and variety of food available for human consumption, and in increasing the efficiency of food production, processing, distribution, and waste management."

The American Dietetic Association. The American Dietetic Association: Biotechnology and the future of food. *J. Am. Diet. Assoc.* 1993 Feb;93(2):189-92.

On November 5, 1993, the ADA issued a news release entitled, "The American Dietetic Association Supports Food and Drug Administration's Approval of BST." Highlights of the release include:

- "The evidence is clear that BST does not change the composition of milk, and consumers should have complete confidence in the milk supply," said ADA President Sara C. Parks, RD.
- A fact sheet issued by the ADA in 1993 says that, "BST is inactive in humans. It is broken down during digestion just like any other protein."

Schifari M and Steen K. Press Release: The American Dietetic Association Supports Food and Drug Administration's Approval of BST. The American Dietetic Association. November 5, 1993.

National Center for Nutrition and Dietetics, American Dietetic Association. Nutrition Fact Sheet: BST (BOVINE SOMATOTROPIN).1993.

9. International Food Information Council (IFIC): 1993 and 2008

A 1993 BST Fact Sheet from IFIC stated that:

- "BST is a natural component of cow's milk."
- "BST is safe and has no effect on humans."
- "BST is a protein and is digested like other proteins."
- "Milk is not altered by using BST."

International Food Information Council. BST Facts. 1993.

In response to the question, “Is rbST safe?,” included in a December 1, 2008 Q&A from IFIC, the answer reads as follows:

- “Yes. The Food and Drug Administration (FDA) approved the use of rbST (sometimes referred to as rbGH) in November 1993. FDA approved the product because it had determined after a thorough review that rbST is safe and effective for dairy cows, that the milk from rbST-supplemented cows is safe for humans, and that production and use of the product does not have a negative impact on the environment. In 2000, FDA upheld its original conclusion that milk from cows supplemented with rbST is safe for human consumption. FDA’s determination has been supported by numerous scientific and regulatory bodies including the Joint Food and Agricultural Organization/World Health Organization Expert Committee on Food Additives (JECFA), an international panel of experts in the fields of toxicology and chemistry of animal drug residues; the Commission of the European Communities; and the National Institutes of Health.”

International Food Information Council. Questions and Answers About Labeling of Milk Products Containing Recombinant Bovine Somatotropin (rbST). December 1, 2008. Last accessed March 5, 2010: http://www.foodinsight.org/Resources/Detail.aspx?topic=Questions_and_Answers_About_Labeling_of_Milk_Products_Containing_Recombinant_Bovine_Somatotropin_rbST_.

- “...any risk to the health of consumers of meat or milk obtained from treated animals”

Committee for Veterinary Medicinal Products, Commission of the European Communities. Veterinary Medicinal Products Containing Bovine Somatotropin: Final Scientific Reports. January 29, 1993.

12. Inspector General, Department of Health & Human Services (HHS): February 1992

At the request of Representative J.D. Conyers (MI), Chairman of the House Committee on Government Affairs, HHS conducted an audit of the FDA review of bovine somatotropin. The Audit Report concluded the following:

- “We found that research has been conducted to demonstrate both that bST is not harmful to humans and that bST levels in milk are not higher in bST-treated cows than in non-treated cows.”
- “In reviewing the concerns about bST, we found no evidence that would lead us to question FDA’s review of the human safety aspects of bST.”

Kusserow RP. Audit of Issues Related to the Food and Drug Administration Review of Bovine Somatotropin. Office of Inspector General, Department of Health and Human Services. February 21, 1992.

10. Institute of Food Technologists (IFT): May 1993

In a “Comment by the Institute of Food Technologists” by Dr. M. Susan Brewer to the Joint Meeting of the Food and Veterinary Medicine Advisory Committees to the Food and Drug Administration” on May 6, 1993, it was concluded:

- “First, there is no known health or safety risk to humans.”
- “Second, there is no discernable difference between milk from cows treated with bST and milk from untreated cows.”

Brewer MS. Comment by the Institute of Food Technologists. Presented at the Joint Meeting of the Food and Veterinary Medicine Advisory Committees to the Food and Drug Administration. May 6, 1993.

11. Commission of the European Communities, Committee for Veterinary Medicinal Products: January 1993

In the Final Scientific Report of the European Committee for Veterinary Medicinal Products, it is stated that rbST does not present:

13. U.S. Congress’ Office for Technology Assessment (OTA) Report: May 1991

In May 1991, the U.S. Congress requested that a study be conducted by the Office for Technology Assessment (OTA). The OTA study concluded:

- “Claims have been made that bST is unsafe in consumer food products... This report concludes just the opposite.”
- There is “... no change in milk composition as a result of bST supplementation.”

Congress of the United States Office of Technology Assessment. U.S. Dairy Industry at a Crossroad: Biotechnology and Policy Changes. May 1991.

14. State Medical Society of Wisconsin: January 1990

In January 1990, the Board of Directors of the State Medical Society of Wisconsin adopted a statement:

- “...that milk from cows treated with bovine growth hormone (BGH) does not pose a health hazard to humans.”

- The statement also concluded that “...synthetic bovine somatotropin (BST), also known as bovine growth hormone, produces no known unsafe biological, hormonal or hazardous effects on humans, either directly or indirectly through alteration of milk or meat.”

Wilke DB. Press Release: State Medical Society Finds BGH Milk Safe for Humans. The State Medical Society of Wisconsin. January 1990.

Kava R. Marketing rBST-Free Milk is Misleading. American Council on Science and Health. August 29, 2007. Last accessed March 5, 2010: http://www.acsh.org/factsfears/newsid.1043/news_detail.asp.

In a March 2008 article on the American Council on Science and Health’s web site, HealthFactsAndFears.com, ACSH Director of Nutrition, Ruth Kava, Ph.D., R.D., makes the following statements:

- “The fact is that there has never been any substantiated scientific study showing that milk from cows treated with rBST is any different from milk from untreated cows. The hormones are so similar that you can’t tell them apart, nor can the FDA.”

Kava R. Milking Consumer Fears. American Council on Science and Health. March 24, 2008. Last accessed February 26, 2010: http://www.acsh.org/factsfears/newsID.1145/news_detail.asp.

15. American Council on Science and Health (ACSH): September 1990, January and August 2007 and March 2008

The ACSH is an independent consumer education group comprised of physicians, scientists and policy advisors. In its review on rbST safety published in a booklet and accompanying press release, the Council stated:

- “The arguments against BST safety have been considered and rejected by FDA and most scientists.”
- “Although the opponents of BST have attempted to cloud the issue with non-science based concerns, the fact remains that BST is a safe and effective means of increasing our nation’s milk supply.”

American Council on Science and Health. BST = A Safe, More Plentiful Milk Supply. September 1990.

Whelan EM. Press Release: BST Equals A Safe and Plentiful Milk Supply. The American Council on Science and Health. September 1990.

In a January 2007 article on the American Council on Science and Health’s web site, HealthFactsAndFears.com, ACSH President, Dr. Elizabeth Whelan, is quoted saying:

- “Milk from rBGH-treated cows is indistinguishable from milk from non-treated cows. Giving cows rBGH does not change the composition or wholesomeness of their milk in any way, and treatment does not affect the amount of rBGH found in the milk.”

Chickering J. No Need to Mooove to rBGH-Free Milk. American Council on Science and Health. January 17, 2007. Last accessed March 5, 2010: http://www.acsh.org/factsfears/newsID.910/news_detail.asp.

In an August 2007 article on the American Council on Science and Health’s web site, HealthFactsAndFears.com, ACSH Director of Nutrition, Ruth Kava, Ph.D., R.D., states:

- “There’s nothing unhealthful or dangerous (to humans or cows) from using rBST.”

16. School of Public Health, University of California, Berkeley: May 1994

The University of California, Berkeley Wellness Letter (The Newsletter of Nutrition, Fitness, and Stress Management), concluded in May 1994:

- “Years of study have shown that milk from treated cows is safe.”
- “...increased levels [of IGF-I] from treated cows are within the normal range; the milk from treated and untreated cows can’t be distinguished on this, or any, basis.”

University of California, School of Public Health. Udder confusion. University of California Berkeley Wellness Letter. 1994 May;10(8):1-2.

17. Baylor College of Medicine, Department of Pediatrics, USDA/ARS Children’s Nutrition Research Center: February 1994

In a February 25, 1994 letter to the FDA Commissioner, the Honorable David A. Kessler, M.D., Baylor College of Medicine Professor of Pediatrics and Director, Children’s Nutrition Research Center, Dennis M. Bier, M.D., argued the following points:

- “Bovine somatotropin has no action on human breast epithelial cells, since it does not interact with the human somatotropin receptor on breast or any other human cell membrane.”
- “BST cannot stimulate any IGF-I production in humans.”

Bier DM. Letter to FDA Commissioner. Department of Pediatrics, Children’s Nutrition Research Center, Baylor College of Medicine, February 25, 1994.

18. Report of the Royal College of Physicians and Surgeons of Canada Expert Panel on Human safety of rbST: January 1999

In a January 1999 report, which was prepared for Health Canada, the Royal College of Physicians and Surgeons of Canada's Expert Panel on Human Safety of rbST, the following conclusions were outlined:

- "Cow's milk contains bST whether or not the cow has been treated with rbST. No increase in total bST concentration is observed in milk from rbST-treated cows and therefore no human risk related to BST consumed by this route is likely to result."

Report of the Royal College of Physicians and Surgeons of Canada Expert Panel on human safety of rbST. Health Canada. January 1999. Last accessed on March 5, 2010: http://www.hc-sc.gc.ca/dhp-mps/vet/issues-enjeux/rbst-stbr/rep_rcpsc-rap_crmcc_e.html 3/29/2008.

19. American Society for Clinical Nutrition (ASCN)*, American Institute of Nutrition (AIN)*, American Dietetic Association (ADA), and the Institute of Food Technologists (IFT) and the Food and Nutrition Science Alliance (FANSA): February 1994

FANSA was organized to provide public outreach and represents a national alliance of four food science and nutritional science organizations - the American Society for Clinical Nutrition, the American Institute of Nutrition, the Institute of Food Technologists and the American Dietetic Association. In 1994, FANSA put out a press releases regarding milk labeling as "rBST-free" or "rBGH-free," which concluded:

- "The drawback to an 'rBST-free' or 'rBGH-free' label are first that it might be misleading by giving the impression that the labeled milk is substantially different, which it is not."
- "Second, it might suggest that unlabeled milk poses a possible health risk, which it does not."

Brewer MS, Press Release: No Scientific Evidence to support labeling of milk from cows given BST. Food and Nutrition Science Alliance. February 25, 1994.

*Note that the ASCN and the AIN have merged and are currently known as ASN, the American Society for Nutrition.

20. Regulatory Agencies Worldwide

rbST has been approved for commercial use in more than 20 countries, in addition to the United States, including: Brazil, Chile, Columbia, Costa Rica, Ecuador, Egypt, Guatemala, Honduras, Jamaica, Lebanon, Mexico, Panama, Pakistan, Paraguay, Peru, Salvador, South Africa, South Korea, Uruguay and Venezuela.

Insulin-like Growth Factor-I (IGF-I) Fact Sheet

I. Human Body IGF-I

A. Plasma concentration

Juskevich and Guyer. 1990. Science 249:875-883
Blum et al. 1993. J. Clin. Endocrinol. Metab. 76:1610-1616
FAO/WHO. 1998

- Adult = 120-460 ng/ml
- Adolescent = 180-780 ng/ml
- Infant = 17-250 ng/ml

B. Production rate (adult)

Guler et al. 1989. Acta Endocrinol. 121:753-758

- Total IGF-I 10,000,000 ng/day

C. Gastrointestinal secretions (adult)

Chaurasia et al. 1994. Regulatory Peptides 50:113-119
Vander, Sheman & Luciano (ed). 1990. Human Physiology, published by McGraw-Hill Publishing Co.
FAO/WHO, 1998

- Total IGF-I ~ 380,000 ng/day
- Secretion

Secretion	Volume (ml/day)	Concentration (average; ng/ml)	Total IGF-I secreted (ng/d)
Jenjunal chyme	1500	184.5	276,750
Pancreatic juice	1500	27.0	40,500
Gastric juice	2000	26.2	52,400
Bile	500	6.8	3,400
Saliva	1500	6.8	10,200

II. Cow Milk IGF-I and Digestion

NIH Technology Assessment Conference. 1990. NIH Proc.
Phillips et al. 1995. Pediatric Res. 37:586-592
Houle et al. 1997. Pediatric Res. 42:78-86
Donovan et al. 1997. J Pediatric Gastroenterology & Nutr. 24:174-182
FAO/WHO. 1998

A. Concentration

- Average 4-6 ng/ml at mid lactation
- Range 15-35 in early lactation (first 30 days) and 1-20 ng/ml at mid lactation

B. Milk IGF-I digestion

- IGF-I comprises approximately one-tenth of one millionth of total milk proteins and digestion in the gastrointestinal tract is like other dietary proteins.
- Studies providing physiological to pharmacological amounts of dietary IGF-I have demonstrated negligible amounts are absorbed as intact proteins.

III. Human IGF-I Production and Milk Equivalent (each glass equals 8 ounces or 237 milliliters)

- Daily IGF-I from saliva and other digestive secretions is equal to amount of IGF-I in ~270 glasses of milk
- Daily IGF-I from whole body production is equal to amount of IGF-I in over 7000 glasses of milk.
- IGF-I intake in a glass of milk is equal to ~0.01% of the body's daily production.

Prepared by D.E. Bauman, Cornell University
Updated March, 2010

Summary of author biographies

Richard Raymond, M.D., served as Under Secretary for Food Safety at the U.S. Department of Agriculture (USDA) for more than three years, retiring in October 2008. His responsibilities included overseeing the policies and programs of the Food Safety and Inspection Service (FSIS), and chairing the U.S. Codex Policy Committee, which provides guidance to U.S. delegations on the Codex Alimentarius Commission. Previously, he was director of the Nebraska Department of Health and Human Services Regulation & Licensure division, and he also served as Nebraska's Chief Medical Officer. He has served as president of the Association of State and Territorial Health Officials (ASTHO). He currently is a faculty affiliate at Colorado State University in the Department of Animal Health Sciences and serves as a public health consultant with the Nebraska Medical Association.

Connie W. Bales, Ph.D., R.D., is a Professor in the Department of Medicine at Duke University Medical Center. She is a Registered Dietitian (RD) and a Certified Nutrition Specialist (CNS) and has published broadly on nutrition and aging-related topics for more than two decades. She is a past-president of the American College of Nutrition and edits the Handbook of Clinical Nutrition in Aging and the Journal of Nutrition for the Elderly.

Dale E. Bauman, Ph.D., is Liberty Hyde Bailey Professor in the Department of Animal Science and the Division of Nutritional Sciences at Cornell University. His research on the metabolic regulation of nutrient use has led to the definition of biological concepts and contributed to the development of new technologies such as recombinant bovine somatotropin (rbST). His research on the biology of somatotropin has ranged from basic investigations to establish mechanisms of action to studies evaluating potential application. He has published more than 700 scientific peer-reviewed articles, invited reviews, book chapters and abstracts. He has received several awards from scientific and professional societies, the USDA Distinguished Service Award and was elected to the National Academy of Sciences. He has served on several USDA Advisory and NAS/NRC Committees, and as Chairman of the NAS/NRC Board on Agriculture & Natural Resources and President of the American Society for Nutrition.

David Clemmons, M.D., is Sarah Graham Kenan Professor of Medicine and Biochemistry at the University of North Carolina at Chapel Hill. He has conducted research on IGF-I (insulin-like growth factor-I) for 33 years and published more than 400 scientific articles

on this subject. His research has focused on several aspects of IGF physiology including normal growth and development, achievement and maintenance of normal bone and muscle size and integrity, as well as the role of IGF-I in pathophysiologic states such as diabetes, atherosclerosis and cancer.

Ronald Kleinman, M.D., is Charles Wilder Professor of Pediatrics at the Harvard Medical School; chair of the Department of Pediatrics and chief of the Division of Pediatric Gastroenterology and Nutrition at the Massachusetts General Hospital in Boston. He is the former chair of the Committee on Nutrition of the American Academy of Pediatrics; editor of the Nutrition Handbook, American Academy of Pediatrics 2008; senior editor of the Walker's Textbook of Pediatric Gastroenterology and Nutrition, Decker, 2008; and a member of the Institute of Medicine (IOM) Committee on National Standards for School Lunches and Breakfasts.

Dante Lanna, Ph.D., is Professor of Biotechnology and Animal Metabolism at University of Sao Paulo in Brazil, where he serves as the head of the Animal Growth and Nutrition Laboratory. He is also the Technical and Scientific Director of the Brazilian Feedlot Association and a consultant to the Brazilian government organization that regulates and authorizes the use of transgenic organisms (CTNBIO). He has published 71 peer-reviewed articles mostly on nutrient metabolism; 193 abstracts in scientific conferences; and edited or contributed on nine books. He has received nine awards by several scientific and professional societies.

Stephen Nickerson, Ph.D., is Professor of Lactation Physiology at the University of Georgia. He has conducted research in the area of bovine mastitis and milk quality, and has published more than 400 scientific articles on this subject. He has served as President of the National Mastitis Council, as Editor-in-Chief of the Journal of Dairy Science, and on the board of directors of the American Dairy Science Association. He has traveled to more than 30 foreign countries as invited speaker to present seminars on milk quality and mastitis control, and is the recipient of several signal awards for his research in these areas.

Kristen Sejrsen, Ph.D., is Associate Professor at Aarhus University, College of Agricultural Sciences, in Denmark. He has conducted research on the effect of rbST on growth, mammary development and milk yield in dairy cattle, including studies on the mechanism of growth hormone action, and the involvement of the growth hormone-IGF axis in mediating the effects of nutrition.

He has edited two books on rbST and published many articles on the subject. He is President of the European Federation of Animal Science (EAAP) and a member of the management committee for the OECD Co-operative Research Programme (CRP) for Biological Resources in Agriculture. He was a former member of the Scientific Committee for Animal Nutrition (SCAN) under the European Commission. He has received the International Dairy Production award by the American Dairy Science Association and The LeRoy Fellowship from the European Federation of Animal Science.

Conflict of interest statement

Dr. Raymond consults for Elanco in areas regarding public health and food safety, but owns no Eli Lilly and Company stock. He reports receiving consulting fees from Elanco and Fraser Stryker PC LLO, lecture fees from the Public Health Association of Nebraska, the University of Nebraska Medical Center, the East Central District Health Department and the Four Corners Health Department; and he receives no grant support. The lectures were not related to Elanco or Elanco products and no other potential conflict of interest relevant to this article were reported. Dr. Raymond is involved in food borne illness litigation work with Bonner Kiernan and Marler Clark, attorneys at law. He is also a regular contributor to Feedstuffs.com and Meatingplace.com.

Dr. Bales received compensation for her involvement in this rbST expert paper, but owns no Eli Lilly and Company stock. She reports receiving royalties from Springer Press and Taylor and Francis Group, a consulting fee for contributing to a health newsletter, and grant support from the National Institutes of Health (NIH). No other potential conflict of interest relevant to this article was reported.

Dr. Bauman received compensation for his involvement in this rbST expert paper, but owns no Eli Lilly and Company stock. He reports having previously received consulting fees from Monsanto, lecture fees from Elanco and is receiving grant support for research unrelated to rbST from Dairy Management Inc., BASF, Monsanto and USDA-CREES. No other potential conflict of interest relevant to this article was reported.

Dr. Clemmons consults for Eli Lilly and Company in areas pertaining to human growth hormone, but owns no Eli Lilly and Company stock. He has also received compensation for his involvement in this rbST expert paper. He reports receiving consulting fees from Eli Lilly and Company, lecture fees from Pfizer and no grant support. No other potential conflict of interest relevant to this article was reported.

Dr. Kleinman received compensation for his involvement in this rbST expert paper, but owns no Eli Lilly and Company stock. He serves on scientific advisory boards for General Mills, the Grain Foods Foundation and Burger King. He is a member of the Board of Directors for Project Bread in Boston; a member of the Board of Directors Global Child Health Foundation; and a consultant for Mead Johnson Nutritionals. No other potential conflict of interest relevant to this article was reported.

Dr. Lanna received compensation for his involvement in this rbST expert paper, but owns no Eli Lilly and Company stock. He reports receiving grant support from Provimi, Elanco, Church and Dwight, Purina, Cargill, Louis Dreyfus, Phibro and Fort Dodge and lecture fees from Phibro, Tortuga, Provimi, Pfizer, Purina and Marca; none of these grants or fees are directly related to rbST research. No other potential conflict of interest relevant to this article was reported.

Dr. Nickerson received compensation for his involvement in this rbST expert paper, but owns no Eli Lilly and Company stock. He reports receiving consulting fees from A & L Laboratories and Pfizer and grant support from Immucell Corp, Epicare and Monsanto. No other potential conflict of interest relevant to this article was reported.

Dr. Sejrnsen received compensation for his involvement in this rbST expert paper, but owns no Eli Lilly and Company stock. He reports receiving grant support from Upjohn and American Cyanamid. No other potential conflict of interest relevant to this article was reported.

References

- 1 Report of the Royal College of Physicians and Surgeons of Canada Expert Panel on human safety of rbST. Health Canada. January 1999. Last accessed on March 5, 2010: http://www.hc-sc.gc.ca/dhp-mps/vet/issues-enjeux/rbst-stbr/rep_rcpsc-rap_crmcc_e.html 3/29/2008.
- 2 Freedom of Information Office Center for Veterinary Medicine, U.S. Food and Drug Administration. Freedom of information summary: Posilac® (sterile sometribove zinc suspension). November 5, 1993.
- 3 Committee for Veterinary Medicinal Products. Commission of the European Communities. Final scientific report on the Committee for Veterinary Medicinal Products on the application for market authorization submitted by the Monsanto Company for Somatech, 500 mg sometribove (recombinant bovine somatotropin) for subcutaneous injection. January 27, 1993.
- 4 European Commission. Press release: Commission proposes ban on BST. IP/99/798. Brussels, Belgium. October 26, 1999.
- 5 Green RE et al. Farming and the fate of wild nature. *Science*. 2005 Jan 28;307(5709):550-5.
- 6 Tilman D et al. Agricultural sustainability and intensive production practices. *Nature*. 2002 Aug 8;418(6898):671-7.
- 7 United Nations Food and Agriculture Organization. World Agriculture: toward 2015/2030. Rome, Italy. 2002. Last accessed March 5, 2009: <http://www.fao.org/docrep/004/Y3557E/Y3557E00.htm>.
- 8 Capper JL et al. The environmental impact of recombinant bovine somatotropin (rbST) use in dairy production. *Proc. Natl. Acad. Sci.* 2008 Jul 15;105(28):9668-73.
- 9 National Research Council. Metabolic modifiers – effects on the nutrient requirements of food-producing animals. National Academy Press. Washington, D.C. 1994.
- 10 Etherton TD and DE Bauman. Biology of somatotropin in growth and lactation of domestic animals. *Physiol. Rev.* 1998 Jul;78(3):745-61.
- 11 Vicini J et al. Survey of retail milk composition as affected by label claims regarding farm management practice. *J. Am. Diet. Assoc.* 2008 Jul;108(7):1198-203.
- 12 Hammond BG et al. Food safety and pharmacokinetic studies which support a zero (0) meat and milk withdrawal time for use of sometribove in dairy cows. *Ann. Rech.Vet.* 1990;21 Suppl 1:107S-120S.
- 13 Bennett LL et al. Failure of hypophyseal growth hormone to produce nitrogen storage in a girl with hypophyseal dwarfism. *J. Clin. Endocrinol. Metab.* 1950 May;10(5):492-5.
- 14 Froesch ER et al. Hyperglycemic effect without anabolic effect of beef growth hormone in man. *Diabetes*. 1957 Nov-Dec;6(6):515-22.
- 15 Asimov GJ and Krouze NK. The lactogenic preparations from the anterior pituitary and the increase in milk yield from cows. *J. Dairy Sci.* 1937 Jun;20(6):289-306.
- 16 Young FG. Experimental stimulation (galactopoiesis) of lactation. *Br. Med. Bull.* 1947;5:155-160.
- 17 Wallis M. The molecular evolution of pituitary hormones. *Biol. Rev. Camb. Philos. Soc.* 1975 Feb;50(1):35-98.
- 18 Daughaday WH and Barbano DM. Bovine somatotropin supplementation of dairy cows. Is the milk safe? *JAMA*. 1990 Aug 22-29;264(8):1003-5.
- 19 Bauman DE. Bovine somatotropin: review of an emerging animal technology. *J. Dairy Sci.* 1992 Dec;75(12):3432-51.
- 20 Juskevich JC and Guyer CG. Bovine growth hormone: human food safety evaluation. *Science*. 1990 Aug 24;249(4971):875-84.
- 21 Bauman DE et al. Somatotropin (BST): International Dairy Federation technical report. 1994. Bulletin of the IDF 293/1994, pp. 2-7.
- 22 Folley SJ and Young FG. The effect of anterior pituitary extracts on established lactation in the cow. *Proc. R. Soc. Lond. B. Biol. Sci.* 1938;126(842):45-76.
- 23 Chumlea WC et al. Age at menarche and racial comparisons in US girls. *Pediatrics*. 2003 Jan;111(1):110-3.
- 24 Steingraber S. The falling age of puberty in US girls: what we know, what we need to know. Breast Cancer Fund. August 2007. Last accessed March 5, 2010: <http://www.breastcancerfund.org/atf/ct/%7BDE68F7B2-5F6A-4B57-9794-AFE5D27A3CFF%7D/the%20Falling%20Age%20of%20Puberty%20report.pdf>.
- 25 Anderson SE and Must A. Interpreting the continued decline in the average age at menarche: results from two nationally representative surveys of US girls studied 10 years apart. *J. Pediatr.* 2005 Dec;147(6):753-60.
- 26 Herman-Giddens ME et al. Secondary sexual characteristics and menses in young girls seen in office practice: a study from the Pediatric Research in Office Settings network. *Pediatrics*. 1997 Apr;99(4):505-12.
- 27 Frisch R. Body fat, menarche, fitness and fertility. *Hum. Reprod.* 1987 Aug;2(6):521-33.
- 28 Euling SY et al. Role of environmental factors in the timing of puberty. *Pediatrics*. 2008 Feb;121 Suppl 3:S167-71.
- 29 National Cancer Institute, U.S. National Institutes of Health. Cancer trends progress report – 2007 update. Last accessed March 5: <http://progressreport.cancer.gov>.
- 30 National Cancer Institute. A Snapshot of Breast Cancer. Last accessed March 5, 2009: <http://www.cancer.gov/aboutnci/servingpeople/snapshots/breast.pdf>.
- 31 Pickle LW and Johnson KA. Estimating the long-term probability of developing breast cancer. *J. Natl. Cancer Inst.* 1989 Dec 20;81(24):1854-5.
- 32 Parodi PW. Dairy product consumption and the risk of breast cancer. *J. Am. Coll. Nutr.* 2005 Dec;24(6 Suppl):556S-68S.
- 33 Guler HP et al. Insulin-like growth factors I and II in healthy man. Estimations of half-lives and production rates. *Acta. Endocrinol. (Copenh)*. 1989 Dec;121(6):753-8.
- 34 Joint FAO/WHO Expert Committee on Food Additives. The fiftieth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Toxicological evaluation of certain veterinary drug residues in food; and summary and conclusions. World Health Organization. Geneva. 1998.
- 35 Murphy SP and Lindsay HA. Nutritional importance of animal source foods. *J. Nutr.* 2003 Nov;133 (11 Suppl 2):3932S-3935S.
- 36 Alvarez-Leon EE et al. Dairy products and health: a review of the epidemiological evidence. *Brit. J. Nutr.* 2006 Aug;96 Suppl 1:S94-9.
- 37 Elwood PC et al. The survival advantage of milk and dairy consumption: an overview of evidence from cohort studies of vascular diseases, diabetes and cancer. *J. Am. Coll. Nutr.* 2008 Dec;27(6):723S-34S.
- 38 Collier RJ et al. Factors affecting insulin-like growth factor-1 concentration in bovine milk. *J. Dairy Sci.* 1991 Sep;74(9):2905-11.
- 39 American Cancer Society. Recombinant Bovine Growth Hormone: Background. February 2009. Last accessed March 5, 2010: http://www.cancer.org/docroot/PED/content/PED_1_3x_Recombinant_Bovine_Growth_Hormone.asp.
- 40 Booth C et al. Growth factor regulation of proliferation in primary cultures of small intestinal epithelium. *In Vitro Cell Dev. Biol. Anim.* 1995 Mar;31(3):234-43.
- 41 Blum JW and Baumrucker CR. Colostral and milk insulin-like growth factors and related substances: mammary gland and neonatal (intestinal and systemic) targets. *Domest. Anim. Endocrinol.* 2002 Jul;23(1-2):101-10.
- 42 Clark RG. Recombinant human insulin-like growth factor-I (IGF-I): risks and benefits of normalizing blood IGF-I concentrations. *Horm. Res.* 2004;62 suppl 1:93-100.
- 43 Ryan J et al. Salivary insulin-like growth factor-I originates from local synthesis. *J. Endocrinol.* 1992 Oct;135(1):85-90.
- 44 Werner H and Katz J. The emerging role of insulin-like growth factors in oral biology. *J. Dent. Res.* 2004 Nov;83(11):832-6.

- 45 Burrin DG. Is milk-borne insulin-like growth factor-I essential for neonatal development. *J. Nutr.* 1997 May;127(5 Suppl):975S-979S.
- 46 Liu X et al. Enteral nutrients potentiate the intestinotrophic action of glucagon-like peptide-2 in association with increased insulin-like growth factor-I responses in rats. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* 2008 Dec;295(6):R1794-802.
- 47 Donovan SM et al. Orally administered iodinated recombinant human insulin-like growth factor-I is poorly absorbed by the newborn piglet. *J. Pediatr. Gastroenterol.* 1997 Feb; 24(2):174-182.
- 48 Food and Drug Administration, Center for Veterinary Medicine, Update: FDA Responds to Citizen Petition on BST. April 21, 2000. Last accessed March 5, 2010: <http://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm130325.htm>.
- 49 Hoppe C et al. Differential effects of casein versus whey on fasting plasma levels of insulin, IGF-I, and IGF-I/IGFBP-3. *Eur. J. Clin. Nutr.* 2009;63:1076-1083.
- 50 Anderle P et al. In vitro assessment of intestinal IGF-I stability. *J. Pharm. Sci.* 2002 Jan;91:1.
- 51 Food and Drug Administration, Veterinary Medicine Advisory Committee. Post Approval Monitoring Program for Posilac. December 18, 1996.
- 52 Collier RJ et al. Effects of sustained release bovine somatotropin (somatotribove) on animal health in commercial dairy herds. *J. Dairy Sci.* 2001 May; 84(5):1098-108.
- 53 White TC et al. Clinical mastitis in cows treated with somatotribove (recombinant bovine somatotropin) and its relationship to milk yield. *J. Dairy Sci.* 1994 Aug;77:2249-60.
- 54 McClary DG et al. The effects of a sustained-release recombinant bovine somatotropin (somidobove) on udder health for a full lactation. *J. Dairy Sci.* 1994 Aug;77(8):2261-71.
- 55 Ruegg PL et al. Effect of the use of bovine somatotropin on culling practices in thirty two dairy herds in Indiana, Michigan, and Ohio. *J. Dairy Sci.* 1998 May;81(5):1262-6.
- 56 Judge LJ et al. Recombinant bovine somatotropin and clinical mastitis: incidence, discarded milk following therapy, and culling. *J. Dairy Sci.* 1997 Dec;80(12):3212-8.
- 57 Bauman DE et al. Production responses to bovine somatotropin in northeast dairy herds. *J. Dairy Sci.* 1999 Dec;82(12):2564-73.
- 58 USDA/Agricultural Marketing Service. Pesticide Data Program (PDP). Last accessed March 5, 2010: <http://www.ams.usda.gov/AMSV1.0/ams.fetchTemplateData.do?template=TemplateC&navID=PesticideDataProgram&rightNav1=PesticideDataProgram&topNav=&leftNav=ScienceandLaboratories&page=PesticideDataProgram&>.
- 59 Codex Committee on Residues of Veterinary Drugs in Foods (CCRVD). Report of the Seventh Session of the Codex Committee on Residues of Veterinary Drugs in Food. World Health Organization/ Food and Agriculture Organization of the United Nations. Washington, D.C. October 20-23 1992.
- 60 Tauer LW and Knoblauch WA. The empirical impact of bovine somatotropin on New York dairy farms. *J. Dairy Sci.* 1997 Jun;80(6):1092-7.
- 61 Wells SJ et al. Effect of long-term administration of a prolonged release formulation of bovine somatotropin (somatotribove) in clinical lameness in dairy cows. *Am. J. Vet. Res.* 1995 Aug;56(8):992-6.
- 62 Santos JEP et al. Effect of bST and reproductive management on reproductive performance of Holstein dairy cows. *J. Dairy Sci.* 2004 Apr;87:868-881.
- 63 Hartnell GF et al. Evaluation of somatotribove in a prolonged-release system in lactating cows – production responses. *J. Dairy Sci.* 1991 Aug;74(8):2645-63.
- 64 Chalupa W and Galligan DT. Nutritional implications of somatotropin for Lactating Cows. *J. Dairy Sci.* 1989 Oct;72(10):2510-24.
- 65 Hoogendoorn CJ et al. Production responses of New Zealand Friesian cows at pasture to exogenous recombinantly derived bovine somatotropin. *Anim. Prod.* 1990; 51:431-439.
- 66 McGuire MA et al. Nutritional modulation of the somatotropin/insulin-like growth factor system: response to feed deprivation in lactating cows. *J. Nutr.* 1995 Mar;125(3):493-502.
- 67 Food and Drug Administration, Center for Veterinary Medicine. BST Update and Summary of Adverse Reaction Reports on Posilac. January 14, 1999. Last accessed March 5, 2010: <http://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm127668.htm>.
- 68 Food and Drug Administration, Veterinary Medicine Advisory Committee. The effect of somatotribove on mastitis. FDA report from the public hearing. Gaithersburg, MD. March 31, 1993.
- 69 National Mastitis Council, Cow factors in mastitis; and management and environmental factors in mastitis. *Current concepts of bovine mastitis.* Chapters 5-6. Madison, WI. 1996.
- 70 Erskine R et al. Bovine mastitis pathogens and trends in resistance to antibacterial drugs, National Mastitis Council research committee report, NMC Annual Meeting Proceedings, pp. 400-414. Madison, WI. 2004.
- 71 USDA-National Agricultural Statistics Service NASS. Last accessed March 5, 2010: http://www.nass.usda.gov/Data_and_Statistics/Quick_Stats/index.asp#top.
- 72 U.S. Congress, Office of Technology. U.S. Dairy Industry at a Crossroad: Biotechnology and Policy Choices--Special Report. OTA-F-470. Washington, DC. May 1991.

Posilac® is a registered trademark of Elanco's brand of recombinant bovine somatotropin.

© 2010 Elanco