

# Recombinant Bovine Somatotropin (rbST): A Safety Assessment

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## 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 with rbST increases milk production by an average of approximately 15 percent in the U.S. dairy cow population and reduces the costs 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 production level 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 over 90,000 scientific publications relating to somatotropin. Cow-related scientific investigations have also been extensive involving academic, government and industry scientists worldwide, with a limited literature search for “bovine somatotropin” and “recombinant bovine somatotropin” yielding over 1,300 and 500 scientific publications, respectively.

Based on the foundation of a 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 56 countries, including Australia, Canada, European Union member states, 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), the FAO and the National Institutes of Health (NIH), 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 also draw reassurance on 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 over 15 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, approximately 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.

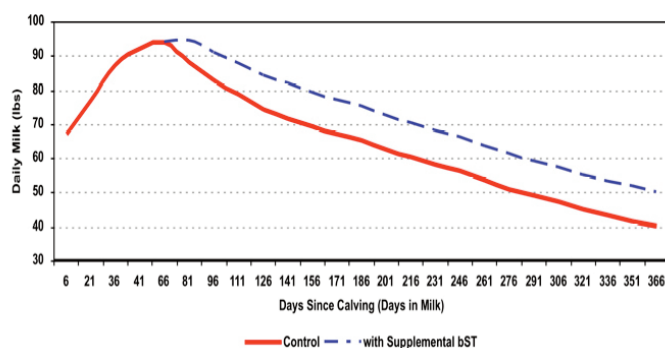
Specific to human safety, regulatory authorities, together with their scientific assessment bodies, in 56 countries, including Australia, Canada, European Union member states, South Korea and the United States, have determined that milk and meat from cows supplemented with rbST are safe for consumption by people of all ages.<sup>1,2,3,4</sup> In addition, scientific bodies such as the World Health Organization (WHO), the Food and Agricultural Organization of the United Nations (FAO) and the National Institutes of Health (NIH), 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 have increased 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.<sup>5,6,7</sup> 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 with rbST increases milk production by an average of approximately 15 percent (about 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,

Figure 1. Typical Example of Lactation Production Curve



This expert paper was developed by 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., and Kristen Sejrsen, Ph.D.

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the number of cows needed to maintain the current milk production level is decreased, thereby saving natural resources. In fact, the 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.<sup>8</sup> 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 this 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, animal scientists and environmental 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.

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.<sup>9,10</sup> 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 is usually 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 makes all cows produce milk more like the farmer's most productive cow does.

## **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.<sup>11</sup> Milks labeled as rbST-free or organic are niche products marketed by producers following a particular management system. There is no 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 over 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" indicates over 1,300 scientific publications and over 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 is now approved for commercial use in 20 different countries and it is recognized as safe by regulatory authorities, together with their scientific assessment bodies, in 56 countries, including Australia, Canada, European Union member states, South Korea and the United States. Its safety for human consumption is endorsed by more than 20 leading health organizations in the United States – including the National Institutes of Health, American Academy of Pediatrics, American Cancer Society, American Medical Association – and internationally – including the World Health Organization (WHO) and Food and Agricultural Organization (FAO).

Consumers can also draw reassurance on the safety of milk from cows supplemented with rbST from the recent U.S. experience. Milk from rbST-supplemented cows (over 70 billion gallons as of 2008) has been a part of the U.S. food supply since approval of rbST 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 confirmed in 56 countries by their regulatory authorities, together with their scientific assessment bodies, there are 20 countries where rbST is currently commercially used. It is important to note that all countries, including Canada and the European Union member states, 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 countries that allow the import and sale of U.S. dairy products have restrictions on milk or dairy products from cows supplemented with rbST and none of them require 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, 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 a lot of interest in trying to give 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.<sup>12,13,14</sup> 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 safe to say 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 2,000 cows with pituitary extract (containing bST) and found an increase in milk yield without deleterious side effects.<sup>15</sup> Subsequently in the 1940s, English scientists, in attempts to increase milk production and 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.<sup>16</sup> 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).<sup>9,13,14,17</sup> 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, 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 approval 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 at that time, and allowed milk from rbST-supplemented cows studied under research conditions to be sold for commercial use.<sup>18,19,20</sup>

Subsequently, from 1984 to 1993, more than 1,500 scientific studies, books, professional papers, and surveys further examined the role of rbST and determined that milk and milk products were safe for human consumption, and within five years after approval in 1993, two million cows in the United States – or 23 percent of the cows in the country – were being supplemented annually with rbST.<sup>21</sup> 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 56 countries and approved by numerous medical associations and scientific societies, including the FDA, WHO, FAO and NIH, 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.<sup>9,12,13,14,15,16,22</sup> 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.<sup>9,10,17,20</sup> Moreover, native and recombinant bST are digested in the gastrointestinal tract and do not enter the blood stream.<sup>9</sup>

## 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.<sup>11</sup> 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.

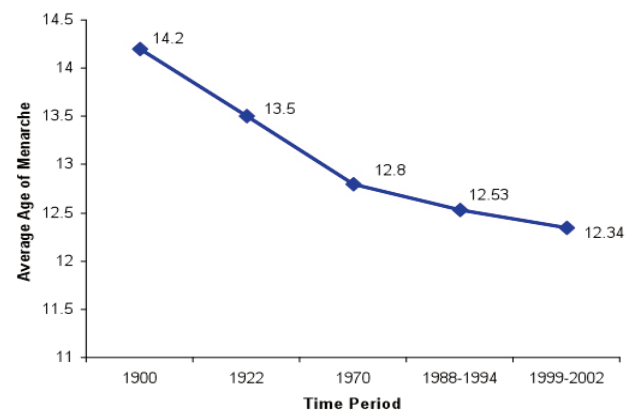
Because of the lack of a difference in the milk, no scientifically proven test exists that can identify the procedures and management systems used in producing the milk.

## 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.<sup>23</sup> 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.<sup>24</sup> [Refer to Figure 2.]

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



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 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 shows a decline again, of two months over approximately one decade.<sup>24,25,26</sup> [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.<sup>26,27</sup>

### 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.<sup>28,29</sup> 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.

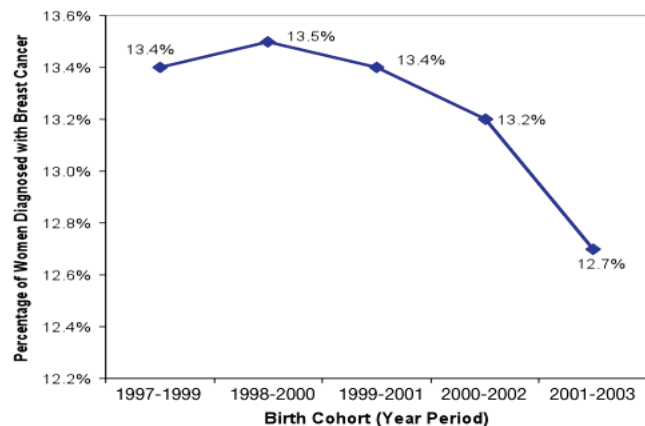
### Q11. What are the breast cancer incidence trends in the United States over the last 30 years or so?

Adjusted incidence rates for breast cancer cases in the United States are lower today than they were in 1994 when rbST commercial use began.<sup>30</sup>

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).<sup>25</sup> [Refer to Figure 3.]

Figure 3. Lifetime Probability of Developing Breast Cancer (Girls Born 1997-2005)<sup>25</sup>



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

The etiology of breast cancer is still largely undetermined, and in 75 percent of women who present with breast cancer, there are no known risk factors other than age and living in Western society.<sup>24,30,31</sup> 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.<sup>32</sup>

### 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.”<sup>32</sup>

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?

It is understandable that questions might arise about whether a growth-promoting substance might somehow cause the growth of cancer cells but there is no evidence that drinking milk from cows supplemented with rbST in any way causes the promotion of cancer. Major reasons include:

1. When bST is consumed orally, it has no biological effect. This has been confirmed in a number of scientific studies.<sup>12,20</sup>
2. bST is not biologically active in humans, even if it were to be injected right into the bloodstream.<sup>12,13,14,17,19</sup>
3. Concern has been raised about IGF-1 in milk since it can stimulate cell growth. Even if the content of IGF-1 in the milk is increased two-fold after rbST, the amount of IGF-1 contained in the daily recommended amount of milk would be less than one percent of the amount that is present in intestinal secretions and less than one ten-thousandth of that produced by the human body.<sup>33,34</sup> (See responses to Q15, “What is IGF-1?” and Q19, “Are the levels of IGF-1 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.<sup>35,36,37</sup> 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 anti-cancer effects – ruminic acid and vaccenic acid.<sup>32</sup>

#### **Q15. What is IGF-1?**

IGF-1 (insulin-like growth factor-1) is a hormone that stimulates growth and maintenance of skeletal tissue in normal people. Humans have IGF-1 in their blood and it is produced in most body tissues. Without adequate IGF-1, humans do not grow normally. They are very short, have weak bones that break easily, have small brains and mental retardation. Therefore, IGF-1 is necessary for normal growth and function. IGF-1 is being discussed in detail in this expert paper because it is present in normal milk and has the potential to stimulate the growth of cells in the stomach and intestines when milk is ingested.

#### **Q16. What is the effect on human health of IGF-1 in milk from cows supplemented with rbST?**

In cows supplemented with rbST, there is a slight increase in the amount of IGF-1 in the milk. The IGF-1 that is in the milk from cows supplemented with rbST is the same IGF-1 that is in non-supplemented cows' milk. The amount of IGF-1 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.<sup>20,34,38</sup> Therefore, there is no evidence that this amount of IGF-1 would pose a health hazard. The amount of IGF-1 that is absorbed by the intestine from milk is negligible. Because the body produces so much IGF-1, the amount that is absorbed, if any, does not cause a detectable increase and body tissues are exposed to no more IGF-1 than if no milk was consumed.<sup>46</sup> For example, the daily intake of milk will provide an amount of IGF-1 that is equal to less than one ten-thousandth (0.0001) of that produced by the human body.<sup>33,34</sup> Additionally, IGF-1 has never been shown to transform a healthy cell into a cancer cell. The digestive secretions, such as saliva, contain IGF-1 which has never been shown to cause intestinal cell transformation.<sup>39,40,41,42,43,44,45</sup>

#### **Q17. How is IGF-1 broken down by the digestive process, and is any of it absorbed intact?**

The majority of IGF-1 is broken down by the digestive process. Because the body produces so much IGF-1 every day, the amount of IGF-1 absorbed by the intestine is minuscule when compared to the amount produced by the body.<sup>34,39,46,47</sup> Therefore, the amount of IGF-1 in milk – either from cows with or without rbST supplementation – does not cause any measurable change in the amount of IGF-1 that is present in a normal healthy human being.

#### **Q18. Is IGF-1 broken down by pasteurization of the domestic milk supply, and other heat methods used in infant formula processing?**

IGF-1 is not broken down by pasteurization of cow milk. Sterilization of liquid formula completely denatures IGF-1 and other similar protein hormones. Processing of the dry milk powder does not denature IGF-1 and 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. Whatever IGF-1 remains in the powder, the amount is inconsequential compared to the amount of IGF-1 the infant itself produces in secretions (such as saliva, bile and pancreatic secretions). It

should also be noted that IGF-1 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 cows' milk because the concentration of nutrients is not optimal to support growth and development.

#### **Q19. Are the levels of IGF-1 in the milk of rbST-supplemented cows elevated?**

In cows supplemented with rbST, there is a slight increase in the amount of IGF-1 in the milk. However, if several lots of milk are examined from several different farms, generally the range of concentrations of IGF-1 is so broad that even following injection of rbST it is impossible to tell a difference among milk from individual cows or farms of rbST-supplemented cows compared to those not using rbST.<sup>20,34,38</sup> However, taking into account that there is some small increase in IGF-1 in milk from rbST-supplemented cows this degree of increase is very minor compared to the total amount of IGF-1 produced daily by intestinal secretions. Therefore, it does not contribute to any measurable change in total body IGF-1 levels in blood or in intestinal secretions. For instance, the daily IGF-1 level in human saliva and other digestive secretions is equal to the amount of IGF-1 in 270 glasses of cows' milk.<sup>34</sup>

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

The levels of antibiotics in the milk of rbST-supplemented cows are not elevated. It is noteworthy that, in the United States, while dairy cows are being treated with antibiotics for any 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 would 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.<sup>48,49,50,51,52,53,54</sup> 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.<sup>49</sup>

#### **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 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.

## 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).<sup>55</sup>

## Q23. Why has Codex not 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 standards regarding rbST reached Step 8 (final step) of the Codex process in 1999 and has been held there since that time.<sup>34</sup>

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 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 Intakes (ADIs) 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 and Contaminants (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.”

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 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 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 vote.

If an rbST policy approving its universal use was adopted by Codex, that approval 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 over 200,000 lactation cycles for cows on several hundred farms, have indicated cows receiving rbST are of normal health.<sup>48,49,50,51,52,53,54,56,57</sup>

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.<sup>21</sup>

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 both 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.<sup>9</sup>

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.<sup>9,48,53,58</sup>

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 for farms where the quality of management is good and particularly where cows are fed and managed properly.

When farm management is inadequate, including when health and nutrition 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.<sup>59,60,61</sup>

## **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 in 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.<sup>48,51,52,53,54,56,57</sup>

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.”<sup>62</sup> In 15 years, over 30 million cows in the United States have been supplemented with rbST.

## **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 the following lactations.

The biology of this response has been well investigated and is well understood by animal physiologists.<sup>9,10</sup> Naturally occurring hormones, including ST, 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.<sup>18,58</sup> 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 ingest 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, 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.<sup>9</sup>

The somatic cell count (SCC) is also a measure 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.<sup>63</sup>

## **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 somatotrope (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 somatotrope (rbST) in dairy cows will not result in an increased risk to human health due to the use of antibiotics to treat mastitis.”<sup>63</sup>

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 antibiotics.<sup>48,49,50,51,52,53,54</sup>

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.<sup>48,49,50,52,53</sup>

The prevalence of mastitis in any dairy herd is dependent on the husbandry practices employed to 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. Other factors associated with mastitis of which producers have less management control are season of the year, parity, stage of lactation and cow age.<sup>64</sup>



### **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 that was 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.<sup>65</sup>

### **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 for commercial use of rbST in the United States. In the 15 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 show an increased milk production when rbST supplements are used but there were no differences in cow health, culling or longevity.<sup>48,51,52,53,54,56,57</sup>

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 cull rates pre- and post-approval.<sup>66</sup> 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, pre-approval years for 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 over 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.<sup>2</sup>

## **Environmental Aspects of rbST**

### **Q33. What is the environmental impact of using rbST?**

The use of rbST allows each cow to produce an extra 10 pounds, or approximately 1.2 gallons, of milk per day. This translates to mean 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 and that

represents one cow less 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 milk production equal to taking approximately 390,000 cars off the road each year or planting approximately 290 million trees annually.<sup>8</sup>

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 that produced on 540,000 acres of farmland, a reduction in enough fossil fuel to heat over 15,000 homes and a reduction in water sufficient to supply about 10,000 homes.<sup>8</sup>

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 of conventional milk per day would reduce their annual carbon footprint 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 gallon 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. Thus, innovative food production practices like rbST 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.<sup>11</sup> 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 governments. Current estimates are that approximately six percent of the total economic impact of rbST is secured by the technology supplier, 12 percent by dairy producers, 10 percent by various levels of government (taxes); the balance, or 72 percent of the total benefits, has moved downstream to processors, retailers, and consumers. Given the state of competitiveness in dairy processing and food retailing, it is likely that most, if not all, of this 72 percent has been passed to consumers. In the long run, the withdrawal of rbST would increase milk prices by \$0.75 to \$1.50 per hundredweight, or \$0.06 to \$0.12 per gallon of milk, and \$0.075 to \$0.15 per pound of cheese.

Using nine cents per gallon as the average savings passed on to consumers by using rbST supplementation, 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.

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**Kristen Sejrson, 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 effect 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. 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.

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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.

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