Theriogenology Insight: An International Journal of Reproduction of Animals
Citation: Theriogenology Insight: 9(3): 77-86, December 2019
DOI: 10.30954/2277-3371.03.2019.1

Recombinant Bovine Somatotropin and its Role in Dairy Production: A Review

Haben Fesseha*, Saliman Aliye and Temesgen Kifle

School of Veterinary Medicine, Wolaita Sodo University, Ethiopia, P.O. Box 138, Wolaita Sodo, Ethiopia

*Corresponding author: tseyon.h@gmail.com

ABSTRACT

Bovine somatotropin (bST) is a natural metabolic protein hormone produced by the pituitary gland in all cattle and used to increase milk production in dairy cows. Recombinant bovine somatotropins (rbST), that has several amino acids, have been synthesized using recombinant DNA techniques. rBST is administered subcutaneously at day 60 of a cow's lactation cycle when milk production normally begins to decrease and repeated every 14 days. Even though bST has the potential to increase the efficiency of milk production, there is no change in milk composition. In the case of rBST, potentially 10-15% more milk can be obtained from each cow. rBST is biologically inactive in humans and its residues in food products have no physiological effect. Concentration of Insulin-growth factor-I (IGF-1) is no significant difference in bovine growth hormone levels in milk from rBGH-treated and untreated cows. Even if there were a much higher level of bovine growth hormone ingested by humans, our digestive system would break down and inactivate the hormone protein. In addition, the bovine growth hormone does not affect human growth hormone receptors and good management measures should be taken as per manufacturer to ensure a high response in milk yield to bST administration. Thus, the use of rbST to improve productivity within the lactating cow herd allows for a reduction in resource use and environmental impact per unit of milk.

Keywords: Biotechnology, Recombinant Bovine Somatotropin, Milk Production

Globally, there is a rapid increase in the human population particularly especially in developing countries and the demand and supply gap for food is increasing with time. To narrow this gap, multi-dimensional approaches are being carried out. Proponents of a new type of technology biotechnology claim that it will supply more food at less cost to meet this growing demand. One of the major agriculture-related products of biotechnology research is bovine somatotropin (bST) (Addisu *et al.* 2018; Jabbar *et al.* 2009). Bovine Somatotropin (BST) is a natural peptide hormone produced in the pituitary gland of cows. It is produced in small quantities and circulating concentrations of BST are positively correlated with the level of milk production involved in normal growth, development of the mammary gland and normal milk production (Ahmad, 2002; European Food Safety Authority, 2015).

Recombinant bovine somatotropins (rbST), which differ from Bovine Somatotropin by several amino acids, have been synthesized and manufactured using recombinant DNA techniques to increase milk production without adversely affect the health and reproductive performance in dairy cows. The Food and Drug Administration (FDA) approved the rbST product in 1993 after determining that its use would be safe and effective (Burton *et al.* 1994; Lucy *et al.* 1993; Soliman and El-Barody, 2014). Recombinant bovine growth hormone (rBGH) is the synthetic form that is injected into cows to increase milk production. This hormone, both

Received: 11-07-2019 **Revised:** 13-10-2019 **Accepted:** 23-11-2019

the natural and synthetic forms, stimulates milk production in mammals by increasing the production of insulin-like growth factor-1 (IGF-1) (Addisu *et al.* 2018; Collier and Bauman, 2014; Lucy *et al.* 1993).

The use of rbST to improve productivity within the lactating cow herd allows for a reduction in resource use and environmental impact per unit of milk. There is no question that bST use increases milk yield and production efficiency. However, there are many factors that affect the magnitude of the milk production response (Capper *et al.* 2008; Kim and Kim, 2012; Peel and Bauman, 1987). A number of factors have been identified as influencing milk production response in bST research trials: the quality of herd management, including the availability and quality of feed, the dosage of bST, the age of the cow, and the body condition of the cow prior to the start of treatment, and the cow's initial health before and during treatment (Addisu *et al.* 2018). Obtaining a milk yield response to bST did not require special diets or different feed ingredients. However, treated cows did need adequate amounts of a balanced diet that contains all nutrients necessary for supporting expected milk production (Bauman, 1992).

In the United States, 20 years of experience demonstrate that commercial use of rbST by dairy producers is safe, effective, and allows for the production of wholesome dairy products (St-Pierre *et al.* 2014). Thus, this review was organized to review bovine somatotropin hormone and its effect on the productive performance of dairy cows and on the environment and human health concerns.

History of bST and its Biotechnology Production

Somatotropin 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 by coordinating the metabolism of body tissues so that more nutrients can be used for milk synthesis. One characteristic of healthy and high producing cows is the greater pituitary secretion of somatotropin. Modern recombinant DNA technology allows the production of somatotropin in commercial quantities which is biologically equivalent to natural pituitary-derived bST and has the same amino acid sequence plus one extra amino acid (the essential amino acid methionine) at one end (Bauman, 1992; St-Pierre *et al.* 2014).

In 1920, somatotropin was discovered and originally called bovine growth hormone (BGH). In the 1930s, experiments revealed that its extraction from the pituitary gland from one cow and injection into another cow could increase milk production in the recipient cow. In the late 1970s, Dale Bauman, a scientist successfully transferred the gene responsible for BGH production in cows into a bacterium and renamed it as recombinant bovine somatotropin (rbST). The genes responsible for the production of BST in bovine tissue cells cause the pituitary cells to produce the biological product of BST. These genes were isolated and inserted into specific bacteria (*E. coli*) as part of a plasmid, with gene splicing. As these altered bacteria replicate, the new genes are also replicated and passed along to all new bacteria. The presence of these genes causes the bacterial cell to become a little "manufacturing plant" which produces bST in large quantities. Eventually, the bacterial cells are killed and removed, leaving the purified bST. The synthetic analog would be called recombinant bovine somatotropin (rBST) (Addisu *et al.* 2018; Bauman, 1992; Lee *et al.* 1996).

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

 Print ISSN: 2249-6610

body and has no function in humans (Burton *et al.* 1994; National Research Council, 1994).

"Posilac" was the first FDA approved product of the recombinant form of bST distributed by the Monsanto company (Dohoo *et al.* 2003; Molnar *et al.* 1990). BST has been used to increase milk production and given from the 9th-10th week (57-70) after calving until the end of lactation. Dairy cows are usually injected subcutaneously (1.4 ml) in the ischiorectal fossa (either side of tailhead depression) or neck and behind the shoulder (post scapular) and the injection is typically repeated every 14 days. Accordingly, milk production increased from 2.25 litters to 6.6 litter of milk/cow/day in the US (Davis *et al.* 1990).

Effect of RbST on Mammary Gland

The bST can act directly on tissues or act indirectly by causing the release of IGF-I (Chaiyabutr *et al.* 2007; Chase *et al.* 1998). BST increases the activity of the mammary cell leading to higher milk production and some other non-desirable side effects. The rBST has increased milk production in dairy animals. It increases cardiac output and heart rate and this is associated with an increase in the rate of mammary blood flow. Mammary metabolic activity is increased, involving greater subST rate uptake and synthesis of milk components. Resulting in milk yields increase by about 10%-15%. Somatotropin also has a unique effect on stimulating mammary gland development and lactation (Centner, 2016; Chagas *et al.* 2012; Feldman *et al.* 1993).

The total RNA, RNA concentrations, RNA accumulation and the increased metabolic activity of mammary tissue, which is likely affected via bST-mediated insulin-like growth factor-I (IGF-I) could promote local production of vasodilators, which in turn would result in an increased percentage of cardiac output perfusing the mammary gland (Davis *et al.* 1990). This increase in mammary blood flow would contribute to a partitioning of nutrients to the mammary gland and to an increase in milk component synthesis and secretion (Campos *et al.* 2011; Centner, 2016; Peel and Bauman, 1987).

Effect of rBST on Lactating Cow

1. Effect of rBST on Milk Production

Bovine somatotropin (bST) is a major regulator of milk production through coordinating the metabolism of body tissues to use more nutrients for milk synthesis (Addisu *et al.* 2018; Carriquiry *et al.* 2009; Etherton and Bauman, 1998). Administration of rBST increases daily milk yield (DMY) in cows, buffaloes, and goats without altering the gross composition. Though management factors have been identified as a major source of variation in the magnitude of dairy cows' responses to rbST (Bauman, 1992; Prasad and Singh, 2010; St-Pierre *et al.* 2014).

These factors include the dosage of rbST, injection interval, genetic potential, and environmental conditions. Dairy cows that are better managed have a greater response to rbST than poorly managed. (Burton *et al.* 1994; Shibru, 2016). For lactating dairy cows, the optimal dose of rbST is between 25 and 50 mg/day. Low doses of rbST (10.2 mg/day) in the transition period resulted in higher postpartum body weight, quicker recovery of body condition during lactation and significantly more milk during treatment (Gulay *et al.* 2003).

2. Effect of rbST on Milk composition

The complex composition and unique biophysical properties of milk can easily be disturbed by slight deviations in composition. All cows produce BST and all milk contains BST. The use of rbST has no significant effect on the micro and macro composition of milk, Flavor of the milk is also not affected (Collier and Bauman, 2014). The comparison of retail milk found no meaningful differences in the composition of milk labeled as rbST-free or organic. 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. Natural variations occur between cows, but these cannot be related to which treatment the cow received (O'Donnell-Megaro *et al.* 2011; Shibru, 2016; Soliman and El-Barody, 2014). Factors such as genetics, diet, breed of cow, age, stage of lactation, environment, season and milking practices such as milking interval and frequency of milking cause the variability observed in milk quality and composition; however, these factors would have equal effects in rbST supplemented and non-supplemented cows (Macrina *et al.* 2011; National Research Council, 1994, 2005).

The pH, macro and micronutrient, Somatic cell count of milk was not affected by bST injections in different studies (Chaiyabutr *et al.* 2007; Prasad and Singh, 2010). Another protein hormone found in milk, insulin-like growth factor I (IGF-I), is regulated by bST. Because the biological effects of IGF-I are not species-specific, as they are for bST, when bST is administered to dairy cows, the concentration of IGF-I in blood increases about three-fold and the levels of IGF-I in milk can increase up to two-fold. Nonetheless, IGF-I in milk does not pose a safety risk because it is a protein and is digested like all other dietary proteins. Furthermore, IGF-I is present in human breast milk, and at levels as high or higher than the levels in milk from bST-supplemented cows (Firkins *et al.* 1989; Liboni *et al.* 2008; Shibru, 2016).

Public Health, Animal Welfare and Environmental Impact of rBST

1. Public health Importance

(a) Effect of insulin-like growth factor-1 in milk of cows supplemented with rBST

Insulin-like growth factor-I (IGF-1) is a secondary hormone produced by mammals in response to levels of natural growth hormones. IGF-1 circulates in the blood of mammals, miraculously coordinating cellular growth and function. Added synthetic growth hormone's presence stimulates more production of IGF1, which circulates to the milk duct tissues. FDA scientists have reviewed and concluded that rBSH is biologically inactive in humans and therefore, residues of rBSH in food products would have no physiological effect even if

Table 1: Comparing milk yield and composition of cows untreated and treated with rbST

Species	Group of treatment	Milk yield (L/day)	Protein (%)	Fat (%)	Lactose (%)	References
Cattle	Control	23.5	3.65	4.29	9.00	(Kim and Kim, 2012)
	rBST	27.7	3.30	3.84	8.89	
Cattle	Control	20.7	3.16	3.50	4.51	(Campos *et al.* 2011)
	RbST	22.6	3.16	3.52	4.49	
Cattle	Control	15.6	3.27	3.67	—	(Macrina *et al.,* 2011)
	RbST	17.9	3.28	3.65	—	
Cattle	Control	41.9	2.86	3.65	—	(Liboni *et al.,* 2008)
	RbST	45.4	2.81	3.30	—	
Cattle	Control	36.1	2.90	3.82	—	
	RbST	37.6	2.83	3.78	—	
Cattle	Control	12.9	3.45	3.94	4.90	(Chaiyabutr *et al.,* 2007)
	RbST	14.6	3.51	4.24	4.62	

absorbed intact from the gastrointestinal tract (Collier and Bauman, 2014) agreed on ideas that oral consumption of IGF-I by humans has no biological activity and concentrations of IGF-1 in digestive tract fluids of humans far exceed any IGF-1 consumed when drinking milk (European Food Safety Authority, 2015).

Milk from cows treated with rBGH has a slightly higher concentration of IGF-1 than milk from untreated cows. However, the variability of IGF-1 levels in milk may also be due to natural factors (Chagas *et al.* 2012; Collier *et al.* 2008). Since higher IGF-1 level is associated with increased cancer risks in humans, especially breast cancer risk (Peyrat *et al.* 1993; Shibru, 2016; Soliman and El-Barody, 2014). In fact, there is no significant difference in bovine growth hormone levels in milk from rBGH-treated and untreated cows. Even if there were a much higher level of bovine growth hormone ingested by humans, our digestive system would break down and inactivate the hormone protein. In addition, the bovine growth hormone does not affect human growth hormone receptors (Zaitlin *et al.* 2013).

The use of rbST has not affected the expression of retroviruses in cattle or posed an increased risk to human health from retroviruses in cattle. Furthermore, the risk for the development of type 1 or type 2 diabetes has not increased in children or adults consuming milk and dairy products from rbST-supplemented cows. Overall, milk and dairy products provide essential nutrients and related benefits in health maintenance and the prevention of chronic diseases (Collier and Bauman, 2014).

Bovine somatropin is a protein growth hormone that increases average milk yield anywhere from 10-15%, which in turn would lead to cows consuming substantially more nutrients in order to keep up with the increased milk production. Most of a cow's energy consumption goes directly towards milk production. In certain areas of the world, like Ethiopia where this was studied extensively, as the cows needed to intake more nutrition to balance out their milk production, there was also an increased level of chemical fertilizers and heavy metal traces found in the milk due to increased exposure to agricultural chemicals. These chemicals can then easily be passed on to humans and lead to a contaminated milk supply (Addisu *et al.* 2018; Centner, 2016).

Over the past few years, there was no FDA-approved test that can differentiate between milk from rbST-supplemented and non-supplemented cows. However, if properly handled, all milk regardless of the production system is naturally pure and safe (Collier *et al.* 2008; Liboni *et al.* 2008). Food supply since rbST approval in 1993 and its use has not been associated with any scientifically documented detrimental effects on human health (Raymond *et al.* 2009). This was associated with the report of 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 the bovine growth hormone had no effect on growth in humans. This means that even if milk had high concentrations of bovine growth hormone, the hormone would not stimulate human cells to grow. Furthermore, when the 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 (Addisu *et al.* 2018; Hammond *et al.* 1990; Shibru, 2016).

(b) The risk of Antibiotic resistance

According to different studies over the last decades, the pattern of percent of bulk milk tank trucks testing positive for antibiotic residues has steadily declined from 0.100% in 1995 to 0.017% in 2012. Therefore, there is no evidence of increased human risk for exposure to milk antibiotic residues from the use of rbST and residues occur when the milk is saved before the antibiotics have fully clear (Addisu *et al.* 2018). Similarly, (European Food Safety Authority, 2015) report also confirmed that the use of rBST don't affect the appropriate withdrawal times for antimicrobial treatments and would not result in a higher risk to human health due to the use of antibiotics to treat mastitis and that the increased potential for the presence of drug residues in milk could be managed by practices currently in use by the dairy industry and by the drug manufacturers' directions for use'.

2. Animal welfare

Somatotropin has less effect on the health and reproductive performance of cows. It was reported that the health and reproductive parameters, including clinical observation, physical examination, somatic cell count, conception rate, services per conception and gestation-length were at or better than resident-herd average. According to previous studies, the administration of rbST was performed to increase milk production. Besides, animal health variables such as the incidence of lameness, reproduction, somatic cell count and incidence of mastitis were not affected due to farms where rbST was used to supplement as compared to farms where rbST was not used (Bauman, 1992; Kim and Kim, 2012; St-Pierre *et al.* 2014).

Genetically superior cows and cows supplemented with rbST can increase milk production only when they are well managed and can consume good quality feed. 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 (Addisu *et al.* 2018; Liboni *et al.* 2008; Shibru, 2016).

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 (Collier *et al.* 2001).

(a) Mastitis

Mastitis is an inflammation of the mammary gland, characterized by increased somatic cell counts (SCC) in the milk and by pathological change in the mammary tissue. The disease is usually caused by pathogenic micro-organisms entering the gland through the teat duct. Major factors affecting the incidence of mastitis are related to environmental conditions and management practices. There is also a small increase in mastitis incidence, expressed on a per cow basis, as milk production increases and the FDA reported that the use of rbST was also associated with an increase in the relative risk of mastitis (Hogan and Smith, 2012).

Milk somatic cell count (SCC) is a measure of milk quality and a reflection of mammary health. Macrophages are one type of Leukocytes mostly predominant somatic cells found in the milk of healthy cows. Somatic cells from an infected quarter of the udder predominately contain a much greater number of neutrophils, macrophages, and lymphocytes present in milk. Therefore, SCC values provide insight related to milk quality and subclinical mastitis (Shibru, 2016; Van Schaik *et al.* 2002). To ensure high-quality dairy products, Bulk tank somatic cell count (BTSCC) is monitored in milk shipments using standards outlined in the U.S. Pasteurized

Milk Ordinance. The legal maximum BTSCC for Grade A milk shipment is 750,000 cells/ml. The overall pattern of the average SCC in the U.S milk supply has declined steadily since 2001. More recent data indicate a continued decline of BTSCC averaged 224,000 cells/mL in 2010 and 206,000 cells/mL in 2011. Therefore, SCC for the U.S. dairy herd has not increased over the interval of rBST use (Shibru, 2016; Van Schaik *et al.* 2002).

3. Environmental impact

The use of rbST to improve productivity within the lactating cow herd allows for a reduction in resource use and environmental impact per unit of milk (Capper *et al.* 2008; St-Pierre *et al.* 2014). When evaluated a dairy herd of one million lactating cows supplemented with rbST and calculated the environmental impacts associated with producing the same amount of milk in a herd not supplemented with rbST. The herd supplemented with rBST required 11.8% fewer animals, used 8.5% less feed, 8.1% less cropping land and 8.1% less water. Moreover, the rBST herd produced 9% less nitrogen and 9.5% phosphorus in excreta and 8.1% fewer greenhouse gases. These are subSTantial environmental gains achieved through maximizing production efficiency in dairy cattle. This technology alters nutrient partitioning, which results in an increase in daily milk yield of an average of 4.5 kg per cow. The use of rBST allows each cow to produce an average of approximately 15 percent additional milk. This means, 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 efforts for husbandry (Addisu *et al.* 2018; Capper *et al.* 2008; Shibru, 2016).

Livestock metabolism-use of rBST in lactating cows decreases the quantity of energy and protein needed in comparison to conventional dairy operations along with reducing the total feedstuff used. Fossil fuel consumption-targets atmospheric pollution and resource sustainability environmental concerns. With cows treated with rBST, producing a higher milk yield reduces the feed requirement which in turn decreases with electricity for milk production and the energy required from fossil fuels for cropping. In addition, the global warming potential is reduced equivalent to removing 400,000 family cars from the road. When conventional, conventional with rBST, and organic dairy operations are compared, 8% fewer cows are needed in an rBST-supplemented population, whereas organic production systems require a 25% increase to meet production targets. This is due to a lower milk yield per cow due to the pasture-based system which is attributed to a greater maintenance energy expenditure associated with grazing behavior (Dohoo *et al.* 2003; National Research Council, 2005; Raymond *et al.* 2009).

CONCLUSION AND RECOMMENDATIONS

RBST is a technology that allows a liter of milk to be produced using fewer nutrients and a lower carbon footprint. The administration of rbST to dairy cows effectively increases milk production with no adverse effects on cow well-being and also with normal milk composition. Commercial use of rbST by dairy producers is safe, effective, and allows for the production of wholesome dairy products. Generally, the utilizing of the bST hormone can alleviate the demand for milk due to an increment of the human population. Being a metabolic hormone, cows supplemented with bST increases feed intake, it also increases the treated cow's body weight without effect on animal health and welfare. In addition to this, it has no effect on human health a person who is consuming milk from BST hormone-treated cow. Therefore, the use of rbST reduces the resource used and environmental impact per unit of milk production. That is why increased animal performance is suggested as one of the most effective mitigation strategies to decrease greenhouse gas (GHG) and ammonia (NH_3)

emissions from livestock production per unit of product produced. The human demand for animal protein will double by the year 2050 whereas resources like water and arable land are limited to produce extensively. On the other hand, livestock production emits carbonaceous and nitrogenous compounds that contribute to air and water pollution as well as climate change. Therefore, it is advisable to be aware of using rbST to enhance the efficient utilization of resources and reduce environmental impact.

REFERENCES

Addisu, S., Tegenaw, K. and Tesfa, A. 2018. Review on the role of bovine somatotropin hormone for dairying. *Online Journal of Animal and Feed Research,* **8**: 90-96.

Ahmad, T. 2002. Effect of bovine somatotropin on the lactational and reproductive performance of lactating dairy cows-A review. *Commission on Science and Technology for Sustainable Development in the South,* **8**: 36.

Bauman, D.E. 1992. Bovine somatotropin: review of an emerging animal technology. *Journal of Dairy Science,* **75**: 3432-3451.

Burton, J.L., McBride, B.W., Block, E., Glimm, D.R. and Kennelly, J.J. 1994. A review of bovine growth hormone. *Canadian Journal of Animal Science,* **74**: 167-201.

Campos, B., Coelho, S., Quintão, A., Rabelo, E., Machado, T. and Silper, B. 2011. Use of bovine somatotropin (BST) 500 mg in crossbred *Bos taurus* × *Bos indicus* cows every 12 or 14 days. *A Hora Veterinária,* **30**: 8-13.

Capper, J.L., Castañeda-Gutiérrez, E., Cady, R.A. and Bauman, D.E. 2008. The environmental impact of recombinant bovine somatotropin (rbST) use in dairy production. *Proceedings of the National Academy of Sciences,* **105**: 9668-9673.

Carriquiry, M., Weber, W.J., Dahlen, C., Lamb, G., Baumgard, L. and Crooker, B.A. 2009. Fatty acid composition of milk from multiparous Holstein cows treated with bovine somatotropin and fed n-3 fatty acids in early lactation. *Journal of Dairy Science,* **92**: 4865-4875.

Centner, T.J. 2016. Efforts to slacken antibiotic resistance: Labeling meat products from animals raised without antibiotics in the United States. *Science of the Total Environment,* **563**: 1088-1094.

Chagas, C.E., Rogero, M.M. and Martini, L.A. 2012. Evaluating the links between intake of milk/dairy products and cancer. *Nutrition Reviews,* **70**: 294-300.

Chaiyabutr, N., Thammacharoen, S., Komolvanich, S. and Chanpongsang, S. 2007. Effects of long-term exogenous bovine somatotropin on water metabolism and milk yield in crossbred Holstein cattle. *The Journal of Agricultural Science,* **145**: 173-184.

Chase, C., Kirby, C., Hammond, A., Olson, T. and Lucy, M. 1998. Patterns of ovarian growth and development in cattle with a growth hormone receptor deficiency. *Journal of Animal Science,* **76**: 212-219.

Collier, R.J. and Bauman, D. 2014. Update on human health concerns of recombinant bovine somatotropin use in dairy cows. *Journal of Animal Science,* **92**: 1800-1807.

Collier, R.J., Byatt, J., Denham, S., Eppard, P., Fabellar, A., Hintz, R., McGrath, M., McLaughlin, C., Shearer, J. and Veenhuizen, J. 2001. Effects of sustained-release bovine somatotropin (sometribove) on animal health in commercial dairy herds. *Journal of Dairy Science,* **84**: 1098-1108.

Collier, R.J., Miller, M., McLaughlin, C., Johnson, H. and Baile, C. 2008. Effects of recombinant bovine somatotropin (rbST) and season on plasma and milk insulin-like growth factors I (IGF-I) and II (IGF-II) in lactating dairy cows. *Domestic Animal Endocrinology,* **35**: 16-23.

Davis, S., Smith, J. and Gluckman, P. 1990. Effects of growth hormone injections on ovulation rate in ewes. *Reproduction, Fertility and Development,* **2**: 173-178.

Dohoo, I.R., DesCôteaux, L., Leslie, K., Fredeen, A., Shewfelt, W., Preston, A. and Dowling, P. 2003. A meta-analysis review of the effects of recombinant bovine somatotropin: 2. Effects on animal health, reproductive performance, and culling. *Canadian Journal of Veterinary Research,* **67**: 252.

Etherton, T.D. and Bauman, D.E. 1998. Biology of somatotropin in growth and lactation of domestic animals. *Physiological Reviews,* **78**: 745-761.

European Food Safety Authority. 2015. EFSA's assistance for the 2015 Codex Committee on Residues of Veterinary Drugs in Food (CCRVDF)

 Print ISSN: 2249-6610

in relation to rBST. *EFSA Supporting Publications,* **12**: 828E.

Feldman, M., Ruan, W., Cunningham, B.C., Wells, J.A. and Kleinberg, D.L. 1993. Evidence that the growth hormone receptor mediates differentiation and development of the mammary gland. *Endocrinology,* **133**: 1602-1608.

Firkins, J., Cleale, R., Clark, J., Rock, D. and Patterson, D. 1989. Responses of dairy cows to sustained-release form of recombinant bovine somatotropin. *J. Dairy Sci.,* **72**: 430.

Gulay, M., Hayen, M., Teixeira, L., Wilcox, C. and Head, H. 2003. Responses of Holstein cows to a low dose of somatotropin (bST) prepartum and postpartum. *Journal of Dairy Science,* **86**: 3195-3205.

Hammond, B., Collier, R., Miller, M., McGrath, M., Hartzell, D., Kotts, C. and Vandaele, W. 1990. Food safety and pharmacokinetic studies which support a zero (0) meat and milk withdrawal time for use of sometribove in dairy cows. *Annales de Recherches Vétérinaires,* **21**: 107s-120s.

Hogan, J. and Smith, K.L. 2012. Managing environmental mastitis. *Veterinary Clinics: Food Animal Practice,* **28**: 217-224.

Jabbar, M., Ahmad, I., Abdullah, M., Pasha, T. and Majeed, F. 2009. Long term use of bovine somatotropic (bST) on reproduction. *South African Journal of Animal Science,* **39**: 266-269.

Kim, Y.H., and Kim, D. 2012. Effects of Boostin-250 supplementation on milk production and health of dairy cows. *Korean Journal of Clinical Veterinary Medicine,* **29**: 213-219.

Lee, B., Lin, G., Crooker, B.A., Murtaugh, M. P., Hansen, L.B. and Chester-Jones, H. 1996. Association of somatotropin (BST) gene polymorphism at the 5th exon with selection for milk yield in Holstein cows. *Domestic Animal Endocrinology,* **13**: 373-381.

Liboni, M., Gulay, M., Hayen, M., Belloso, T. and Head, H. 2008. Supplementation of Holstein cows with low doses of bovine somatotropin (bST) prepartum and postpartum affects physiological adaptations and milk production. *Asian-Australasian Journal of Animal Sciences,* **21**: 404-413.

Lucy, M., Hauser, S., Eppard, P., Krivi, G., Clark, J., Bauman, D. and Collier, R.J. 1993. Variants of somatotropin in cattle: gene frequencies in major dairy breeds and associated milk production. *Domestic Animal Endocrinology,* **10**: 325-333.

Macrina, A., Tozer, P. and Kensinger, R. 2011. Induced lactation in pubertal heifers: Efficacy, response to bovine somatotropin, and profitability. *Journal of Dairy Science,* **94**: 1355-1364.

Molnar, J.J., Cummins, K.A. and Nowak, P.F. 1990. Bovine somatotropin: biotechnology product and social issue in the United States dairy industry. *Journal of Dairy Science,* **73**: 3084-3093.

National Research Council. 1994. "Metabolic modifiers: effects on the nutrient requirements of food-producing animals," National Academies.

National Research Council. 2005. "Animal health at the crossroads: preventing, detecting, and diagnosing animal diseases," National Academies Press.

O'Donnell-Megaro, A., Barbano, D. and Bauman, D. 2011. Survey of the fatty acid composition of retail milk in the United States including regional and seasonal variations. *Journal of Dairy Science,* **94**: 59-65.

Peel, C. and Bauman, D. 1987. Somatotropin and lactation. *Journal of Dairy Science,* **70**: 474-486.

Peyrat, J., Louchez, M., Lefebvre, J., Bonneterre, J., Vennin, P., Demaille, A., Helquet, B. and Fournier, C. 1993. Plasma insulin-like growth factor-1 (IGF-1) concentrations in human breast cancer. *European Journal of Cancer,* **29**: 492-497.

Prasad, J. and Singh, M. 2010. Milk production and hormonal changes in Murrah Buffaloes administered recombinant bovine somatotropin (rBST). *Agriculture and Biology Journal of North America,* **1**: 1325-1327.

Raymond, R., Bales, C.W., Bauman, R.D.E., Clemmons, D., Kleinman, R., Lanna, D., Nickerson, S. and Sejrsen, K. 2009. Recombinant Bovine somatotropin (rbST): A safety assessment. *In* "Joint Annual Meeting of the American Dairy Science Association, Canadian Society of Animal Science, and American Society of Animal Science, Montreal, Canada".

Shibru, D. 2016. Review on: effect of using recombinant bovine somatotropin (rbST) hormone on dairy cattle production. *Glob. J. Inc.*, 18-30.

Soliman, E. and El-Barody, M. 2014. Physiological responses of dairy animals to recombinant bovine somatotropin: a review. *Journal of Cell and Animal Biology,* **8**: 1-14.

St-Pierre, N.R., Milliken, G.A., Bauman, D.E., Collier, R.J., Hogan, J.S., Shearer, J.K., Smith, K.L. and

Thatcher, W.W. 2014. Meta-analysis of the effects of sometribove zinc suspension on the production and health of lactating dairy cows. *Journal of the American Veterinary Medical Association,* **245**: 550-564.

Van Schaik, G., Lotem, M. and Schukken, Y. 2002. Trends in somatic cell counts, bacterial counts, and antibiotic residue violations in New York State during 1999–2000. *Journal of Dairy Science,* **85**: 782-789.

Zaitlin, P., Dwyer, J. and Gleason, G.R. 2013. Mistaken beliefs and the facts about milk and dairy foods. *Nutrition Today,* **48**: 135-143.

 Print ISSN: 2249-6610