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Review on: Effect of using Recombinant Bovine Somatotropin(rbST) Hormone on Dairy Cattle Production

By Dereje Shibru
Gambella University

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rBST is biologically inactive in humans and its residues in food products have no physiological effect, but its injection to cow results in an increase in quantities of IGF-I and becomes one of the leading suspects involved in the development and spread of cancers. There is also suspect of increased human risk for development of anti microbial resistance in exposure to milk antibiotic residues from the use of rbST caused mastitis. This could be managed by practices in use by the dairy industry.

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 (NH3) emissions from livestock production per unit of product produced.

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I. Introduction

Bovine Somatotropin(BST) is a natural peptide hormone produced in pituitary gland of cows. It is produced in small quantities and used in regulating metabolic processes. Circulating concentrations of BST are positively correlated with the level of milk production (EFSA, 2015). In the early stages of a calf's development, it acts as a growth hormone and has a great impact on mammary gland development and subsequent milk-producing capacity in dairy heifers (Soliman and EL-Barody, 2013). During lactation, it serves to mobilize body fat to use for energy and diverts feed energy more toward milk production than for tissue synthesis. The reason of using BST is its potential to increase the efficiency of milk production. Potentially 10- 25% (AHI, 1987) more milk and 10-15% increase in feed efficiency can be from each cow with a cost of implementation of less than 5%. It was discovered in the 1920 and originally called bovine growth hormone (BGH). Experiments in the 1930s revealed that its extraction from the pituitary gland of one cow and injection into another cow, could increase milk production in the recipient cow. In the late 1970s, Dale Bauman, an animal scientist successfully transferred the gene responsible for BGH production in cows to a bacterium. The resulting product was called recombinant bovine growth hormone (rBGH), to avoid the stigma associated with hormones, the industry agreed to change its name to bovine somatotropin (BST). Thus, its synthetic analog would be called recombinant bovine somatotropin (rBST). Simple multiplication of the bacterium meant that it could easily be produced in commercial quantities at a very reasonable cost. Though several pharmaceutical and non pharmaceutical companies became very interested in the product production, monsanto was the first firm to receive approval of FDA to release its products (http://www.agecon.ucdavis.edu/Faculty/Bees/Butler.html). Monsanto licensed Genentech's patent (Keith, 1990) and marketed their products as "Posilac"(Dohoo *et al.,* 2003). Though rBST is used to increase milk yield, it also associates animal health and welfare concerns related with increased production. Therefore, the objective of this paper is:-

- To review the effect of rBST on productive and reproductive performance of dairy cows
- To assess the effect of rBST on animal health and welfare concerns of dairy cows .
- To review the effect of rBST on environment and human health concerns.

Author: Gambella University, College of Agriculture and Natural Resource, Department of Animal Science, Ethiopia.
e-mail: shibrud@gmail.com

II. Sources of BST/BGH and its Biotechnology Production

Recombinant-DNA technology has allowed for the commercial production of rbST 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. The genes responsible for production of BST in bovine tissue cells cause the pituitary cells to produce the biological product BST. These genes were isolated and inserted in to specific bacteria 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 (Crooker, 1993). 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.

III. How Does rbST Work and when is it used

In lactating dairy cows, somatotropin is a major regulator of milk production. In biological terms it is referred to as a homoerotic control and acts to coordinate metabolism, thereby allowing more nutrients to be used for milk production. This coordination involves most organs and tissues in the body and includes the metabolism of all nutrients. The bST can act directly on tissues or act indirectly by causing the release of IGF-I (Chase *et al.*, 1998). Indeed, IGF-I levels were increased during rbST administration to lactating cows (Molento *et al.*, 2002). The biological effects of IGF-I are further regulated by specific IGF-binding protein that control access of IGF-I to target tissues and by the abundance of the type-I IGF receptor at the target tissues (McGuire *et al*., 1992). In this respect, Vanderkool *et al.*(1995) showed that rbST similarly increased serum concentrations of somatotropin in cows and they also increased serum IGF-I, liver IGF-I mRNA and serum IGF-binding protein-3, but serum IGF-binding protein-2, number of free binding sites for IGF-I in mammary tissues were decreased. The supplemented rbST working in conjunction with the animal's naturally circulating somatotropin results in an increase in milk production in dairy cattle (Bauman, 1999). Rapidity of onset and cessation of the increased milk yield response suggested that activity rather than number of secretary cells was affected by exogenous bST (Gluckman and Brier, 1987).Total RNA is an index of cell metabolic activity (Butler and Cohn, 2013). Binelli *et al.* (1995) showed that the total RNA, RNA concentrations, RNA accumulation and the RNA to DNA ratio increased in the mammary tissues of cows treated with rbST. Increased metabolic activity of mammary tissue, which is likely effected 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 and Collier, 1985). This increase in mammary blood flow would contribute to a partitioning of nutrients to the mammary gland (Pee1 and Bamnan, 1987) and to an increase in milk component synthesis and secretion, because many key enzymes, notably lactose synthetase, inherently operate below their respective maximum velocity (OKronfeld, 1982).Therefore, mammary cell activity can be increased by exogenous bST, further increases in milk yield requires increase and retention of cell numbers (Tucker, 1987). Involvement of bST, directly or indirectly via growth factors, is likely in regulation of mammary secretary cell proliferation and maintenance (Forsyth, 1989; McFadden *et al.*, 1990 and Politis, *et al.*, 1990). In its administration cows produce more milk and utilize nutrients more efficiently. The net effect is commonly referred to as an improvement in "productive efficiency". Productive efficiency is highest for a dairy producer's best cow and indeed, genetically superior cows make more somatotropin and have greater production efficiency.

The period of rbST supplementation is done in synchrony with a cow's natural lactation cycle. A cow's peak milk yield occurs about eight weeks after the calf is born and thereafter daily milk production gradually declines through the remainder of the lactation cycle. Also small response was found when lactating animals are injected rbST in early lactation prior to peak yield. In addition, bST increases milk yield by 10% when administered in early to mid-lactation and by 40% in late lactation (Bauman and Vernon, 1993). Finding in Thailand, reported that, bST increased lactation performance by 22% during early lactation (Chaiyabutr *et al.*, 2009). Hence, the use of rbST is initiated during the 9th or 10th week of lactation and continues until the end of lactation. From a producer prospective the use of rbST makes all cows more like the best cows in the herd. Milk responses have been observed in all cows regardless of genetic merit and for all breeds of dairy cattle.

IV. Effect of rBST on Productive Performance of Cows

a) Milk yield of cows treated with rBST

Use of rbST treatments has increased milk production in all dairy breeds examined, including Bos indicus cows (Phipps *et al*., 1991). Though management factors have been identified as major source of variation in the magnitude of dairy cows responses to rbST(Bauman, 1992).These factors include dosage of rbST, injection interval and genetic potential and environmental conditions. According to Phillips (1996) cows that are better managed are known to have a

greater response to rbST than poorly managed. In addition to management factors bovine somatotropin (bST) is a major regulator of milk production through coordinating the metabolism of body tissues to use more nutrients for milk synthesis (Etherton and Bauman, 1998). Indeed, a characteristic of healthy, high producing cows is a greater pituitary secretion of somatotropin (Burton *et al*., 1994). In addition to the innate production of somatotropin, for lactating dairy cows, the optimal dose of rbST administration as a galactopoietics agent is between 25 and 50 mg/day (Downer *et al.*, 1993; Phillips, 1996). Similar study by Bauman (1992) reported that the production response increases with increasing dose of BST up to a maximum response at 30-40 mg/day. Given an adequate dosage, increasing the milk yield in response to rbST was maintained by following the rbST administration in daily and every 7, 14 or 28 days (Zinn *et al*., 1993; Chalupa *et al*., 1996). 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). The magnitude of milk yield response to rbST were reported to be increased by 7, 19, 21 and 24% with 5, 10, 15 and 20 mg/day (West *et al*., 1990); 7 and 9% with 10.3 and 25 mg/14 days (Zhao *et al.*,1992); 9, 14 and 12% with 11.4, 22.8 and 22.9/28 days (Laurent *et al.,* 1992) 0, 12 and 25% with 7.1, 14.3 and 21.4 mg/7 days (Zinn *et al.*, 1993), 18% with 250 mg/14 days (Ocampo *et al.*, 1995), 12.2 and 20.0% with 250 and 500 mg/14 days(Abdel-Rahman *et al*., 2010)and 22% with 500 mg/14 days (Thammacharoen *et al.*, 2011). Although, rbST daily injection may produce better response (Bauman, 1992), administration of sustained release formulations of rbST are more practical (Fernandez *et al.*, 1995). However, the increase in milk yield with sustained-release formulations of rbST within a single injection interval will vary (Zinn *et al.*, 1993). That is, following each injection, the milk yield will increase to a peak, approximately at the mid-point of the injection interval and then decline until the next injection (Phillips, 1996).

Bauman *et al*.(1999) reported that rbST administration to dairy cows increases milk production and improves the efficiency of milk synthesis. In agreement with this Chilliard (1988a,b) also reported that rbST use significantly increases milk yield in dairy cattle. Its 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 efficient cow does (NRC, 1994; Etherton and Bauman, 1998). According to Phipps *et al*. (1991) report rBST administration significantly increased milk yield in Jersey (+2.9 kg per day), Friesian (+ 3.6 kg per day) and Holstein (+ 2.7 kg per day) cows. Moallem *et al*. (2000) finding strengthen similarly that daily milk yield (DMY) was significantly increased by bST of two different doses of treatment. The commercial preparation in use in the USA is a slow release formulation in which 500 mg are administered every 2 weeks. Similarly administration of rBST increase milk yield in cows, buffaloes and goats (Helal and Lasheen, 2008 as sited by Prasad and Singh, 2010). According to Etherton and Bauman, (1998) in dairy cattle, an increased milk yield after rbST administration is found in all parity dairy cows; however the magnitude of the increase in milk production differs to be due to stage of lactation. Opposing this Abdelrahman *et al*. (2010) reported that primiparous cows showed tiny increases with either 250 and 500 mg, because of not having a well-developed udder, whereas multiparous cows showed significant increases especially cows received 500mg of bST.

b) Milk composition of cows treated with rBST

Milk nutrient density is unaffected by rbST supplementation, thus the quantity of milk required to produce 500,000 t of Cheddar cheese was unchanged compared with that required from populations without rbST supplementation(Barbano *et al*.,1988). There are n o significant differences in milk composition from cows treated with BST and from cows which were not treated as finding of different study summarized in Table 1 showed. All cows produce BST and all milk contains BST. According to Collier and Bauman (2014) and Campose *et al.*(2001) use of rbST has no significant effect on the micro and macro composition of milk. Flavor of the milk is also not affected. Similar studies by Vicini *et al.*(2008) and O'Donnell *et al.*(2010) reported that comparison of retail milks found no meaningful differences in composition of milks labeled as rbST-free or organic(unlabeled). Consumers are not able to pick out the milk from cows treated with BST as compared to milk from control cows. 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. Phipps *et al.*(1991) reported that milk composition in Bos indicus and its crossbreds was unaffected by the administration of bST. 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 (NRC,1994 and Bauman,1992). Contrary to this, results was reported that there was increase for milk fat, somatic cell counts, IGF1 levels and decrease for milk protein percentage was reported (Chilliard *et al.,* 1998; Baer *et al.*,1989 and Kindstedt *et al.*, 1991).

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

Species	Group 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.*,2001
	rbST	22.6	3.16	3.52	4.49	
Cattle	Control	15.6	3.27	3.67	–	Macrina, Tozer and
	rbST	17.9	3.28	3.65	–	Kensinger, 2011
cattle	Control	41.9	2.86	3.65	–	Rivera *et al.,* 2010
	rbST	45.4	2.81	3.30	–	
cattle	Control	36.1	2.90	3.82	–	Liboni *et al*., 2008
	rbST	37.6	2.83	3.78	–	
cattle	Control	12.9	3.45	3.94	4.90	Chaiyabutr *et al.*,2007, 2008
	rbST	14.6	3.51	4.24	4.62	

NOTES: rBST = recombinant Bovine somatotrophin, - not reported

V. Effect on Reproductive Performance

As the Phillips (1996) result indicated, the magnitude of reproductive responses of dairy cows to rbST is variable. High doses of rbST treatment (20.6 mg/day) decreased conception rates, increased days open by 28-30%, days to first estrus and twinning rates and there was a trend for increased services per conception (Burton *et al*.,1990). In addition, increases in days open were observed in cows in which rbST treatment was initiated early in lactation, but not when treatment started at mid or late lactation (McGuffey *et al*., 1991).

Table 2 : Reproductive performance of primiparous & multiparous cows given 250 &500 mg

	Primi parous			Multi parous		
Parameter	Control	250mg	500mg	Control	250mg	500mg
Days-open (month)	3±0.43	3.5±0.41	3.2±0.32	2.8±0.42	4.4±0.5	4.8±0.52
Conception rate (%)	60	80	90	50	60	80

Abdel-Rahman et al., 2010

According to Abdel-Rahman *et al*.(2010) results effect of administration of bST (250 and 500 mg) on some parameters related to breeding and conception revealed that, the days-open of treated cows have no significant changes in between primiparous group, but there were apparent increase in average days open in multiparous cows(Table 2). Concerning conception rate (%), it revealed an increase in cows given both 250 and 500 mg bST in both groups than control cows. Although rbST increased days-open in multiparous cows, (possibly due to increased milk production), it simultaneously improved conception rate(%). Flores *et al.* (2008) reported that rbST increased growth hormone (GH) in beef cattle and hypothesized that rbST would alter other metabolic hormones and might influence ovarian follicles in postpartum. Meantime, somatotropin treatment increased concentrations of IGF-I in postpartum cows and is at least partly responsible for the increase in diameter of the largest follicle in anestrous post partum cow. Bell *et al.* (2008) results were in agreement with this conclusion. While Silvia *et al.(*2002) reported that rbST had no effect on reproductive performances, which agrees with results of different studies found no differences in days open, services per conception and days to first estrus at 500 mg/14 day (Weller *et al.*, 1990; Pell *et al*., 1992) or at 56-700 mg/14 day (Downer *et al*.,1993). On the contrary, Dohoo *et al.*(2003) mentioned that bST altered the reproductive performance of treated cows. Similar finding by Flores *et al.*(2007) reported that rbST at 500 mg/14 day in Brahman cows increased the first-service conception rate during the first 30 days of breeding and pregnancy rates during the first 3 days of breeding.

VI. Effects of Recombinant Bovine Somatotropin on Animal Health and Welfare

The use of rBST may have significant welfare consequences since unnaturally high milk yields are associated with poorer body condition and increased rates of mastitis, lameness, and reproductive problems (SCAHAW, 1999).

a) Diminished Body Condition

Body Condition (BC) is a term used to describe a cow's energy reserves, which, when excessively depleted, can have welfare implications (SCAHAW, 1999). According to Grandin(2001) the indiscriminant use of recombinant bovine somatotropin and genetic selection for increased milk production are the two reasons for body condition scores of dairy cows decline.

Similar review by an expert panel of Canadian Veterinary Medical Association (CVMA) on the use of rBST reported that using the nutritional management programs that are common on the majority of commercial dairy herds, it would be a challenge to maintain body condition in cows treated with rBST," despite the fact that there is very good nutritional management (CVMA, 1998). Most research papers showed poorer body condition in cows treated with BST mostly at the end of lactation than the control animals. The difference between BC of treated and control animals varied between 0.2 and 0.5 points (Wells, 1995; Chilliard, 1988; Phipps, 1990). Similarly Studer (1998) suggests that high producing cows which are thin, and whose body condition score declines by 0.5 to 1.0 during lactation, often experience anoestrus. On the other hand, rBST treated cows might have an increased voluntary feed intake starting 4-6 weeks after the onset of the treatment (Oldenbroek and Gansen, 1990). Contrary to the BC of cows, the body weight of rBST treated animal has been recorded as approximately 40 kg higher than control animals at the end of the lactation. However, body composition changed and this effect may be largely due to an increase in body water (Oldenbroek, 1990; Wells, 1995; Chilliard, 199l)

b) 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. Many different bacteria cause mastitis, some being considered as specific udder pathogens, others being merely opportunistic organisms that cause disease when there is an increased susceptibility of the udder for some reason. Among the common bacteria causing clinical mastitis are Staphylococcus aureus, Streptococcus spp., E. coli, as well as other pathogens (Bramley, 1992; Wilesmith *et al*., 1986). Major factors affecting the incidence of mastitis are related to environmental conditions and management practices (Hogan and Smith, 2012).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. Similar finding was also reported by Soliman and EL-Barody (2013) that the incidence of mastitis in rbST-treated cows is due more to increased milk yield than to any direct effects of rbST. Similarly meta-analyses by Dohoo *et al.(*2003) reported that nearly 25% increase in the risk of clinical mastitis resulted due to rBST using.

Research trials prior to registration of rbST for commercial use indicated that there may be a slight increase in somatic cell count (SCC) with its use, which can be a reflection of milk quality or mammary health status (FDA, Veterinary Medicine Advisory Committee, 1993).

Milk somatic cell count (SCC) is a measure of milk quality and a reflection of mammary health. Macrophages is one type of Leukocytes mostly predominant somatic cell found in the milk of healthy cows, but neutrophils, lymphocytes and epithelial cells are also present (van Schaik *et al.*, 2002). Somatic cells from an infected quarter of the udder, predominately contains much greater number of neutrophils, macrophages and lymphocytes present in milk (van Schaik *et al.*, 2002). Therefore, SCC values provide insight related to milk quality and subclinical mastitis. 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 (APHIS Veterinary Service, Centers for Epidemiology and Animal Health, 2011). The legal maximum BTSCC for Grade A milk shipments is 750,000 cells/mL. Maximum allowable BTSCC for other countries include 400,000 cells/mL in the European Union, Australia, New Zealand, and Canada and a maximum BTSCC of 1,000,000 cells/mL for Brazil(Norman *et al.,* 2011). The overall pattern of the average SCC in U.S milk supply has declined steadily since 2001. More recent data indicate a continued decline of BTSCC averaged 224,000cells/mL in 2010 and 206,000 cells/mL in 2011(Norman *et al.*, 2013). Therefore, SCC for the U.S. dairy herd has not increased over the interval of rBST use. Rather, SCC has declined over the last decade indicating an improvement in milk quality and mammary health. Van Schaik *et al*. (2002) demonstrated that high SCC is a generic predictor of poor milk quality. Herds with 200,000 cells per mL of milk or less had the lowest incidence of antibiotic residues. Therefore, the inference from SCC data over the period of 15 years is that the potential human threat from milk antibiotic residues has declined dramatically. Contrary to this the CVMA and the European Commission's Scientific Committee on Animal Health and Animal Welfare (SCAHAW) found that rBST use increases the risk of both mastitis and lameness (Grandin, 2001 and CVMA, 1998). As CVMA,(1998) reports rBST use may increase the frequency of clinical mastitis by approximately 25% and prolong recovery. It is concluded that BST causes a substantial increase in the risk of mastitis on most farms and this risk, with associated poor welfare, would not occur if BST were not used (Grandin, 2001).

c) Recombinant Bovine somatotropin (rBST) use increases lameness rates

Given the pain associated with foot and leg problems, "welfare will be seriously and adversely affected as a consequence of the BST treatment" and the CVMA did not feel that existing dairy cattle management techniques would be able to control or eliminate the increased risk of lameness (CVMA, 1998).

Studies found that the risk of lameness approximately 50% higher for rBST-injected cows (CVMA, 1998) while SCAHAW found a 220% increase in foot problems with injected cows suffering twice as long (Grandin, 2001). In agreement with this Cole *et al.* (1992) and Zhao *et al.*(1992) reported that there was increased incidence of lameness in rbST-treated cows. Dohoo *et al.*(2003) meta-analyses review reported that 55% increased risk of developing clinical signs of lameness as a result of using rBST.

d) Recombinant bovine somatotropin use may introduce reproductive problems

Rates of pregnancy drop in rBST-injected cows, which may be a sign of how "severely affected by metabolic demands" cows are, and the frequency of multiple births increases substantially, which can lead to further welfare problems (Grandin, 2001). SCAHAW conclusion on the effects of rBST on reproductive problems is failure to conceive which an indicator of poor welfare is. Similar study reported that reproductive problems in dairy cows have become very common resulting with large numbers of cows being culled because of failure to get in calf (Esslemont and Kossaibati, 1997). Dohoo *et al*.(2003) meta-analyses reported supporting results where 40% reduction in fertility of cow as a result of using rBST's. Contrary to this idea Soliman and EL-Barody (2013) reported that rbST did not adversely affect reproduction and the observed decreases in reproductive performance in rbST-treated cows may be attributed more to the increases in milk yield than to direct effect of rbST. Studies showing that milk yield is positively correlated with the extent of fertility problems have come from a range of different countries (Pryce *et al*., 1998).

The increased metabolic activity associated with BST-induced galactopoiesis also involves an increase in heat production by the body, which challenges thermoregulatory processes. As Elvinger *et al*.(1992) reported that, of 18 cows receiving BST and subjected to heat stress, two cows died and four suffered from ataxia, whereas no such responses were observed in 16 control cows. Therefore rBST may also lower the ability of cows to cope with heat, increasing the risk of heat stress.

In general, rBST-treated cows are culled at a higher rate than non treated cows, which likely demonstrates poorer welfare overall (Grandin, 2001). Cows have a natural lifespan of about 20 years, but the stress caused by the conditions on farms renders cows worthless to the dairy industry by the age of 4 or 5 years (USDA, 2007). According to USDA (2007) report, 26.3% of permanently culling in dairy cows from the United States dairy herd was due to reproductive problems. Both the CVMA and SCAHAW recommend against using rBST for welfare reasons which would not occur if it were not used. The conclusion which should be drawn is that avoidable actions which result in poor welfare, such as BST usage, should not be permitted (Grandin, 2001). Contrary to this other studies did not reveal a high culling incidence of BST treated animals compared with control animals (Oldenbroek, 1990).

e) The Human Health Concerns of rBST

i. *Effect of Insulin-like growth factor-1 in milk of cows supplemented with rBST*

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 absorbed intact from the gastrointestinal tract.

Insulin-like growth factor-I(IGF-1) is a secondary hormone produced by mammals in response to levels of natural (synthetic) 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, where a tremendous concentration of IGF-1 receptors exist. IGF-1 is structurally identical in both cows and humans. The injection of rBGH into animals could temporarily increase quantities of IGF-1 in milk; however, these increased levels are within the naturally occurring range of IGF-I found in untreated milk or human breast milk. 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 (JECF, 1998). Therefore, there is no evidence that this amount of IGF-I would pose a health hazard (Juskevich and Guyer, 1990; FAO/WHO Expert Committee on Food Additives, 1998 and Elwood, 2008). Contrary to this IGF-1 is not destroyed by normal pasteurization and if cow's milk sourced IGF-1 entered the human blood stream; the IGF-1 would be active in humans. However, FDA scientists argued that digestive acids in the human gut would break down any IGF-1 consumed through milk. On the other hand, Collier and Bauman (2014) agreed on ideas that oral consumption of IGF-I by humans has little or no biological activity and concentrations of IGF-1 in digestive tract fluids of humans far exceed any IGF-1 consumed when drinking milk. Subsequent research has widely discounted FDA's mistaken notion that stomach acids denature milk-borne IGF-1.Opposing with FAD result, in 1995, the Journal of Endocrinology cited work by researchers in Australia who demonstrated that milk proteins protect IGF-1 from digestion. Therefore, IGF-1 became one of the leading suspects involved in the development and spread of cancers. The IGF-1 hormone already exists in humans; it is usually bound to protein and thus has less of an effect than unbound IGF-1 in milk. Therefore, IGF-1 is biologically active in humans and behaves as a cancer accelerator being associated with breast, prostat e and colon cancers(http://www.ejnet.org/bgh/nogood.h

tml). IGF-1promotes cell division. As cells divide, at some point they are instructed (by their genes, in combination with hormone signals) to stop dividing or they are instructed to die so that the creation of new cells is matched by the death of cells and no net growth occurs; this is called "programmed cell death."If" programmed cell death" is prevented and then cells don' t die at the right time, causing out of control growth of ce lls, which is another way of saying cancer. Cancer is unc ontrolled cell division (http://www.ejnet.org/bgh/nogood. html).

ii. *The risk of Antibiotic resistance*

The increased incidence of mastitis experienced by treated cows, which indirectly inducing increased antibiotic use on cows and a resulting dangerous level of antibiotic residue in milk, as well increased pus content in the milk. Though, it is known that major factors affecting the incidence of mastitis are related to environmental conditions and management practices (Hogan and Smith, 2012).There is also a small increase in mastitis incidence, as milk production increases and hence, the use of rbST was also associated with an increase in the relative risk of mastitis. In 1998 the 50th JECFA conference evaluated and concluded that "the use of rbST will not result in a higher risk to human health due to the use of antibiotics to treat mastitis and that the increased potential for drug residues in milk could be managed by practices currently in use by the dairy industry and by following label directions for use (JECFA, 1998). The pattern of percent of bulk milk tank trucks testing positive for antibiotic residues has steadily declined since 1996 and in 2012 was less than one-fifth of the level detected in 1995(0.100% in 1995 vs. 0.017% in 2012). Therefore, there is no evidence of increased human risk for exposure to milk antibiotic residues from the use of rbST. Similarly EFSA (2015) report also confirmed that, assuming that the appropriate withdrawal times for antimicrobial treatments are respected, the use of rBSTs 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 following the drug manufacturers' directions for use'.

VII. The Effect of rbST Supplementation on 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, Dunlap *et al*., 2000 and Johnson *et al*., 1992). Capper *et al*.(2008) 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 (including lactating cows, dry cows, and heifers), 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 (Capper *et al*., 2008). 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 (Capper *et al*., 2008). This increase affects environmental sustainability through the dilution of maintenance concept, the net effect being that rbST use reduces the amount of land required to produce a unit of milk by 9.2%, water use by 10.4%, and the carbon footprint by 9.1%(Capper *et al*., 2008). On an industry basis, rbST supplementation of 1 million cows would therefore reduce the dairy industry's carbon footprint by the annual equivalent of removing about 400,000 cars from the road. The mitigating effect of rbST use on environmental impact has also been noted by other investigators (Bauman, 1992 and Jonker *et al.*, 2002), including Johnson *et al*.(1992), who suggested that large-scale use of *rBST* would reduce methane emissions by approximately 9%. Nonetheless, the political and social acceptability of rbST use within dairy production has been a contentious issue in several countries (Brinckman, 2000).

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. 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(Capper, 2008). Increased animal performance is suggested as one of the most effective mitigation strategies to decrease greenhouse gas (GHG) and ammonia (NH3) emissions from livestock production per unit of product produced (Stackhouse *et al*., 2012)

The use of rBST is a management tool that improves agricultural sustainability and reduces the carbon footprint per gallon of milk(Capper, 2008). 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 mitigati ng the environmental impact will be of even greater

importance in the future for the global production (FAO, 2011).

VIII. Conclusion

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 substrate uptake and synthesis of milk components. Resulting in milk yields increase by about 10%-15%, little effects on the milk composition, processing properties and taste.

rBST treatment have adverse effect on reproduction such as drop in pregnancy rate, the number of days open (failure to conceive) increased in primi-parous cows. It is also a cause for multiple births. This all lead to poor welfare or an indicator of poor welfare.

BST usage increases the risk of clinical mastitis above the risk in non-treated cows. The duration of treatment for clinical mastitis was longer in rbST-treated than in non-treated cows. The welfare of most cows with mastitis is poor, the extent of poor welfare being dependent on the severity of the condition. Which may result in over usage of antibiotics resulting in its residue in milk to be human health concerns of anti microbial resistance?

There is an increased incidence of foot and leg disorders associated with the long term administration of BST which will result in pain and other suffering in these animals. Hence welfare will be seriously affected as a consequence of the BST treatment.

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 green house gas (GHG) and ammonia (NH3) 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 is 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 efficient utilization of resource and reduce environmental impact.

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