Safety of Bovine Somatotropin in the Dairy Cow

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Introduction

While much has been written and said about bovine somatotropin it is important to remember that this product has not been approved for use in the dairy cow. Approval of any new drug requires stringent testing and proof that the product is effective and safe. The Food and Drug Administration is responsible for determining that the product meets these criteria. Effectiveness simply means that the product will meet manufacturer claims and safety indicating that the product is safe for the target animal, the food product produced by that animal is safe for human consumption, and the product presents no safety threats to the environment. In the case of BST the FDA has determined milk and meat from treated cows is safe for human consumption and that milk from BST research trial sites can be processed and utilized as any other milk. Determinations of efficacy and safety to the target animal and the environment are yet to be made by the FDA.

Animal Safety and Health

Animal safety is an important consideration for any producer. With any new product or technology there is concern that animal health or longevity of production will be compromised. It is not likely that the producer will use a product that is potentially harmful to his livestock regardless of the effectiveness of that product. Numerous studies have been conducted by all of the companies involved in BST research to determine its impact on animal health. These studies have included two lactation trials with animals receiving 0x, 1.5x, 5x, and 7.5x the recommended dose; 25x doses in acute toxicity studies and multiple lactation studies. In each of these studies the test animals were monitored for untoward effects and disease problems related to BST administration. Some of the studies included serum clinical chemistry and hematology during the trial, as well as complete necropsy examinations at the completion of the trial. Perhaps the best indicator of adverse effects of a product on animal health is to measure the animal's productivity. If an animal is stressed or diseased productivity will decline. In the majority of BST trials reported to date there has been a 10–20% increase in fat corrected milk production in cows supplemented with BST as compared to controls.

Animals involved in BST research are closely monitored for evidence of disease conditions and abnormalities. Conditions which are considered common to dairy cattle including mastitis, digestive disorders, parturient paresis, lameness, metabolic disease, periparturient reproductive problems, etc. are all monitored to determine if BST supplementation increases either the incidence or severity of these maladies. Numerous studies[1-6] have shown no significant increase in the incidence or severity of these conditions. Cole et al.[3] reported an increased incidence of digestive distress and lameness in BST treated cows particularly at the 5x dose in one trial but these conditions were not considered to be directly related to BST.

An increased incidence of clinical ketosis, which has been induced by treatment with pituitary BST[7] and postulated to be a potentially harmful side-effect of BST supplementation[8] has not been observed when highly purified rBST is used to treat cows.[9] Studies monitoring levels of serum beta-hydroxybutyrate have been conducted to determine the incidence of subclinical ketosis in rBST supplemented cows.[10-12] No increase in beta-hydroxybutrate levels were noted in these trials indicating no increase in the incidence of subclinical ketosis in BST treated cows.

Evaluation of calves born to dams treated with BST in the previous lactation showed no difference in health, birth weight, or growth rate compared to calves born to control cows.[3,10]

Mastitis and Udder Health

Reported data from most BST trials have not indicated an increase in the incidence of clinical mastitis,[1-3] in the quarter infection rate[13] or in somatic cell counts[6,14-16] in BST supplemented cows. Cole et al.[3] noted a slight increase in somatic cell counts (SCC) in the first year and an increase in the incidence of clinical mastitis in both years of a two year lactation study in animals treated at the higher dose levels. This increase was associated with chronic udder infections which were present at the beginning of the trial.

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Reproduction

While most measures of dairy cattle productivity such as average milk production and milk quality have improved over the years, reproductive efficiency as determined by indices such as services per pregnancy and days open has decreased. While most of this reduction in reproductive efficiency is closely related to management factors such as estrus detection, and artificial insemination technique or environmental factors such as heat stress, numerous studies have shown an inverse relationship between milk production and key reproductive measures.[17-21] Overall impact of production on reproduction appears to be approximately +0.6 days open and +0.01 services per pregnancy for each 100 Kg increase in milk production by 120 days in milk.[22] This reduced fertility is likely due to the partitioning of nutrients toward milk production and an increase in the body energy deficit associated with higher levels of milk production.[23] A similar pattern could be expected from BST augmented increases in milk production in early lactation but reproductive data from various research trials show conflicting results. A number of studies indicate reproduction is not affected by BST supplementation,[2,4,6,10,14,24,25] while others[3,5,15,26,27] indicate days open, calving interval, and/or services per pregnancy were increased by BST treatment prior to breeding.

Periparturient conditions such as dystocia, retained fetal membranes and cystic ovarian degeneration do not appear to be affected by BST supplementation.[3] Although an increased tendency toward multiple births has been reported in BST treated cows,[28] more work is needed in this area.

Any negative impact in reproduction noted in the BST supplemented cow is likely due to an increased energy deficit due to higher levels of milk production and is not a direct BST effect. Reproductive management for the BST cow will be similar to that of the genetically superior, higher producing cow. Accepted standards and goals for optimum days open and calving intervals may have to be reevaluated on an individual farm and individual cow basis.

Summary of Health and Cow Safety Data from Five Somidobove North American Trials

Significant increases in milk production and improved feed efficiency in Holstein cows from five geographically different trial sites receiving 0, 320, 640, or 960 mg somidobove (rDNA, Bovine Somatotropin: Lilly) at 28 day intervals has been reported.[29] A total of 240 primaparous and multiparous cows entered the study in early, mid, or late lactation and receiving 9, 6, or 3 somidobove treatments, respectively at one of the 4 dosage levels.

Trial animals were monitored closely for health related problems involving the circulatory system, digestive system, feet and legs, mammary gland, nervous system, reproductive system, respiratory system, skin, and urinary system. Also, the incidence of infectious disease, clinical parasitism, metabolic conditions, and mastitis were monitored. Reproductive efficiency was measured in trial animals by calculations of average days to first service, days open, calving interval, first service pregnancy rate, services per pregnancy, and overall pregnancy rate. At the subsequent calving, data was collected on calving ease, calf weight, and sex of the calf. Body condition scores and somatic cell counts were collected for the duration of the trial.

There was no increase in health related conditions involving the digestive, nervous, respiratory, or circulatory systems. There was an increase in the incidence of infectious disease, parasitism, or metabolic conditions in the treated animals. There was no difference in calf weight or the incidence of dystocia among the trial groups.

There was a significant reduction in average body condition scores of BST treated cows which started treatment in the early (8–21 days) postpartum period (Table 1).

TABLE 1. Five Trial Summary: Average Body Condition Score of Cows Receiving Somidobove Beginning in Different Stages of Lactation

	Somidobove (mg/28 days)			
Stage	0	320	640	960
Early	2.62	2.14*	2.17*	2.17*
Mid	2.62	2.57	2.69	2.41
Late	2.79	2.59	2.63	2.68

*Different from control ($P < .05$)

In the trial animals there was no significant difference in the number of cows demonstrating clinical mastitis among the treatment groups but there was an increase in the number of days animals demonstrated clinical mastitis in the 320 mg/28 day and the 960 mg/28 day groups (Table 2). Although BST supplemented cows had an increased number of days with clinical mastitis recorded, the increase was not dose related. With the removal of three chronic mastitis cows from the 320 mg/28 day group and two from the 960 mg/28 day groups there is no significant difference in clinical mastitis days among the groups.

TABLE 2. Five Trial Summary: Incidence and Duration of Clinical Mastitis in Cows Receiving Somidobove

	Somidobove (mg/28 days)							
	0		320		640		960	
	Cows	Days	Cows	Days	Cows	Days	Cows	Days
No. Cows	60	--	61	--	60	--	59	--
Clinical Mastitis	15	104	18	218	16	134	19	199

In the same study there was no increase in SCC in somidobove treated cows compared to controls (Table 3).

TABLE 3. Five Trial Summary: Somatic Cell Counts of Cows Receiving Somidobove Beginning in Different Stages of Lactation

	Somidobove (mg/28 Days)			
Stage	0	320	640	960
Early	79,430	91,200	109,065	95,500
Mid	129,000	97,700*	97,700*	112,000
Late	104,070	93,000	100,000	107,000

*Different from control ($P < .05$)

In this series of trials 113 animals were assigned to the early lactation group and were not pregnant at the initiation of BST treatment. Twenty-seven, 29, 28 and 29 animals were assigned to the 0, 320, 640 and 960 mg somidobove/28 groups, respectively. Pregnancy rates for the 4 groups were; 25/27 (93%) 0 mg, 23/29 (79%) 320 mg, 24/28 (86%) 640 mg, 24/29 (83%) 960 mg. There was no significance or pattern in days to first service among the groups but there was an increase in days open, calving interval, services per pregnancy, and first service pregnancy rate (Table 4).

While these differences are not significant due to the small number of animals in the study, they do indicate a trend toward reduced reproductive efficiency in the BST treated cow. This reduction is likely due to the increased level of milk production and increased energy deficit previously discussed.

TABLE 4. Five Trial Summary: Reproductive Performance of Early Lactation Cows Receiving Somidobove

	Somidobove (mg/28 Days)			
Measures	0	320	640	960
No. Cows	27	29	28	29
Number Preg. (%)	25(93)	23(79)	24(86)	24(83)
Days to 1st Service	83	68	92	78
Days Open	113	120	138	129
No. Calving	23	23	23	23
Calving Interval	393	401	411	399
1st Service Preg. Rate (%)	56	31	36	28
Serv./Preg.	1.8	2.7	2.5	2.6

Summary

From data currently available BST supplementation does not appear to jeopardize cow health or safety. But just as higher producing cows require more conscientious management so will the BST treated cow. Nutritional, reproductive and health professionals will become an even more integral part of the production management team as milk production continues to increase.

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