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The effect of trace mineral supplementation on natural and conventionally raised feedlot beef cattle

by

Emma Kay Niedermayer

A thesis submitted to the graduate faculty

in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

Major: Animal Science

Program of Study Committee:
Stephanie Hansen, Major Professor
Daniel Loy
Lee Schulz

Iowa State University

Ames, Iowa

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NOMENCLATURE

ADG	Average daily gain
BF	12th rib back fat
BSC	Bovine satellite cell
BW	Body weight
Ca	Calcium
CP	Crude protein
Co	Cobalt
Cu	Copper
Cu/Zn SOD	Copper zinc superoxide dismutase
d	day
DM	Dry matter
DMI	Dry matter intake
DP	Dressing percent
EBW	Empty body weight
EGF	Epidermal growth factor
E_2	Estradiol
F:G	Feed:gain
Fe	Iron
G:F	Gain:feed
GH	Growth hormone
h	hour

HCW	Hot carcass weight
I	Iodine
IGF-1	Insulin-like growth factor-1
IMF	Intramuscular fat
KPH	Kidney, pelvic, heart fat
LM	Longissimus dorsi
ME	Metabolizable energy
Mg	Magnesium
MMA	Methyl-malonyl CoA
MMP	Metalloproteinase
Mo	Molybdenum
Mn	Manganese
MS	Marbling score
N	Nitrogen
Na	Sodium
NDF	Neutral detergent fiber
NEFA	Non-esterified fatty acid
Ni	Nickel
NRC	National Research Council
REA	Ribeye area
Se	Selenium
SelN	Selenoprotein N
SelW	Selenoprotein W

SEM	Standard error of the mean
TBA	Trenbolone acetate
TM	Trace mineral
TMR	Total mixed ration
T_3	Triiodothyronine
T_4	Thyroxine
VFA	Volatile fatty acid
Vit E	Vitamin E
YG	Yield grade
Zn	Zinc

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“Life will only change when you become more committed to your dreams than you are to your comfort zone.”

ABSTRACT

There are multiple programs producers can market cattle into including certified natural programs. These programs offer premiums for producers as an incentive to raise natural cattle that have slower growth rates because of the inability to utilize growth-promoting technologies. Because of tremendous improvements in genetics resulting in dramatic increases in growth rates of modern feedlot cattle, it is of value to investigate how to maximize the growth potential of these types of cattle. Trace minerals are essential for growth processes throughout the body. The supplementation of trace minerals has produced varying responses in regards to growth performance and carcass characteristics of cattle. However, there are several factors that can contribute to an animal's trace mineral status and response to trace mineral supplementation including initial mineral status, environment, genetics, and stage of production. Thus, the objectives of this research were to: 1) evaluate the growth response and trace mineral status of certified natural Angus steers supplemented with dietary trace minerals and given an injectable trace mineral at different times in the feeding period and 2) evaluate the effect of supplementing dietary trace minerals at NRC recommendations or industry concentrations in non-implanted or implanted steers that receive high potency implant series. Within our first research objective, an injectable trace mineral had no effect on growth performance regardless of injection given at the start of the growing period, start of the finishing period, or at both time points, likely due to the steers having adequate trace mineral status throughout the feeding period. Injectable trace mineral did improve the trace mineral status of natural beef steers by increasing liver Cu, Zn, and Se concentrations during the growing period, as well as Cu and Se concentrations during the finishing period. After completion of our second research objective, we found there was a

implant × trace mineral supplementation interaction during the first 56 days of the experiment on the first implant where growth rates were increased in implanted cattle that received supplemental trace minerals and subsequent body weights tended to follow a similar pattern. But there were no implant × trace mineral supplementation interactions for overall live or carcass adjusted animal performance. Hormone implants improved growth parameters and increased hot carcass weight. Trace mineral supplementation also improved dry matter intake and carcass adjusted final body weight, average daily gain, and improved feed efficiency regardless of implant status. Hormone implants decreased Cu and Mn concentrations 14 days after the implantation of a high dose potency implant. The varying concentrations of trace mineral supplementation increased liver Cu, Mn, Se, and Co concentrations 14 days post reimplantation and at harvest compared to steers receiving no trace mineral supplementation. The combination of utilizing hormone implants and supplementing steers at industry recommended concentrations of trace minerals produced the most favorable breakeven selling price of all costs. The findings of these experiments produced conflicting responses in regards to the effects of trace mineral supplementation on the growth rates of feedlot steers. These variable responses could be attributed to divergent mineral status, dietary concentrations of trace minerals, steer genetics, and growth rates. More research is warranted to better understand which mineral(s) may be responsible for producing a growth response in feedlot steers along with what concentrations are needed to optimize steer growth performance.

CHAPTER I

INTRODUCTION

The economic viability and sustainability of the beef industry in the United States relies on the ability to improve the efficiency of production. Hormonal implants are one tool commonly used in the beef industry, which are currently utilized in nearly 90% of all yearling-fed steers and heifers (Capper and Hayes, 2012). Implants provide an undisputable return on investment by increasing growth rates by 20% and feed efficiency by 15% in beef animals (Schanbacher, 1984; Bartle et al., 1992; Johnson et al., 1996a). The greatest growth rates are often observed with the use of combination implants that contain both estrogen and testosterone analogs. The most common forms of these compounds are estradiol and trenbolone acetate, which have a synergistic relationship that results in a net increase in the accretion of lean tissue (Johnson et al., 1996a).

In today's markets there has also been an expansion of the natural beef niche market, which includes beef that is raised without the use of growth promoting technologies and antibiotics. Unfortunately premiums offered for natural beef products often do not exceed the increased costs due to lost performance by not being able to utilize growth-promoting technologies. This warrants new research in identifying alternatives to growth-promoting technologies.

Trace minerals support the growth and development of animals through numerous cellular processes. For example, Zn has been shown to be essential for nucleic acid and protein synthesis (Hambidge et al., 1986) and serves as a cofactor for metalloproteinases 2 and 9 (McCall et al., 2000), which are thought to increase the rate of proliferation of

bovine satellite cells (Thornton et al., 2015). Copper and Mn exert their roles in growth through the formation of cartilage and the support of the extracellular matrix (Leach and Harris, 1997; Rucker et al., 1998). Selenium also plays a role in the growth and development of animals through selenoproteins, which assist in combating oxidative stress and increase proliferation of muscle tissue. Selenium also supports the conversion of thyroid hormones from the less active thyroxine (T4) to the more active triiodo-thyronine (T3; Wichtel, 1998; Suttle, 2010) in which iodine is critical (Suttle, 2010). Another trace mineral, Co, is essential in vitamin B_{12}, which supports propionate metabolism and the transfer of methyl groups (Suttle, 2010), potentially providing muscle cells with a source of energy to proliferate.

Because NRC recommendations are concentrations of trace minerals at which signs of mineral deficiency are prevented, these concentrations may not be ideal to optimize the genetic growth potential of modern feedlot beef cattle. This research is set to evaluate the potential importance of trace mineral supplementation in cattle fed in natural programs or with the use of hormone implants.

Thesis organization

The following chapter, chapter II, will provide a detailed review of the literature in regards to mechanisms by which trace minerals support the growth and development of feedlot cattle along with the mechanisms of hormone implants. The remaining two chapters, chapters III and IV, present research that is published in the *Professional Animal Scientist* and intended to be published in the *Journal of Animal Science*. More specifically, chapter III examines the effects of injectable trace minerals on the growth response and

mineral status of Angus beef steers raised in a certified natural program. Chapter IV examines the effects of trace mineral supplementation at NRC or industry concentrations on the growth performance, mineral status, and carcass characteristics of beef steers not implanted or implanted with a high potency implant series. Finally this thesis will conclude with overall research findings, conclusions, and suggestions for further research.

.

CHAPTER II

LITERATURE REVIEW

Trace Minerals' Role in Growth

Trace minerals (TM), including Zn, Cu, Mn, Se, Co, and I, are required for biological function, immune function, and normal growth of animals, and deficiencies negatively affect overall production of cattle. Often feed ingredients like forages do not meet all the TM requirements of cattle (Kegley et al., 2016), therefore, supplementation may be necessary. Cattle producers have a variety of mineral sources at their disposal, including inorganic, organic, hydroxy, or injectable TM sources that often vary in bioavailability to the animal. To assess an animals status, the liver is the most representative of the endogenous stores of TM (Kincaid, 2000). Trace minerals exert effects on the growth of animals through a variety of processes (see **Table 1**).

2.2 Zinc

It is well documented that Zn is essential for growth and health of animals and deficiencies of Zn can be characterized by loss of appetite, decreased growth rates, reproductive failure, and even skin abnormalities (Miller, 1970; Suttle, 2010). Not to underestimate the importance of Zn, this critical TM is involved in over 300 enzymes and even more proteins in the body (Suttle, 2010). In livestock species Zn is essential for desired production traits like growth and health that result in economic benefits to those that raise them. For example, Zn is involved in gene regulation involved in nucleic acid and protein metabolism (Suttle, 2010). Diets fed to animals that are low in Zn can cause a decrease in feed intake because consumption of diets containing low concentrations of Zn

can increase the production of cholecystokinin (Cousins et al., 2003). Low Zn consumption also causes a decrease in leptin secretion from adipocytes (Kwun et al., 2007), which both are hormones, cholecystokinin and leptin, play a role in signaling satiety. Phospholipase A2 is also a Zn-dependent enzyme, which aids in the formation of chylomicrons, necessary for lipid absorption in the gastrointestinal tract (Suttle, 2010). In addition Zn plays a role in health and the antioxidant function of animals. For example, Cu/Zn SOD is a Zn-dependent enzyme and Zn also induces metallothionein production, both of which protect cells against free radical damage (Suttle, 2010).

2.2.1 Protein synthesis

The decreased growth rates often times seen with Zn deficiencies (Suttle, 2010) is thought to occur due to Zn being required for many enzymes involved in nucleic acid and protein metabolism (Hambidge et al., 1986). It has also been shown that the Zn-finger proteins are essential for some enzymes to bind to the promoter region of a DNA strand (Chesters, 1991). This exhibits the role that Zn plays in gene expression and activation along with regulation of transcription (Chesters, 1991). To demonstrate the importance of Zn for DNA synthesis Williams and Chesters (1970) conducted an experiment using young rats in which two diets were fed. One contained 0.9 mg/kg of Zn (Zn-deficient) and the second contained 40 mg/kg of Zn from $ZnSO_4$, and these diets were fed for 5 days. Even after a limited time of a Zn deficient diet, deficient rats had decreased DNA synthesis in the liver, kidneys, and spleen with decreases in protein synthesis detected in kidneys and the spleen (Williams and Chesters, 1970). Because of the increased rate of proliferation in intestinal mucosa cells, rate of protein synthesis is also increased, potentially increasing susceptibility to Zn deficiency. Interestingly, in rats fed a diet

containing 2 mg Zn/kg DM for 28 d, Zn had no effect on protein synthesis in cells of the intestinal mucosa (Southon et al., 1985). Another tissue in which low Zn concentrations may inhibit protein synthesis is bone tissue (Ma and Yamaguchi, 2001). Researchers noticed that protein synthesis in diaphyseal and metaphyseal tissues cultured from young rats was increased when 10^{-5} or 10^{-4} M of Zn were added to the culture. This suggests that endogenous Zn has a direct stimulatory effect on protein synthesis in bone tissue, and is important in young growing animals when bone growth is rapid (Ma and Yamaguchi, 2001).

2.2.2 Cell signaling, proliferation and differentiation

The importance of Zn cannot be over looked, with almost every signaling and metabolic pathway in the body requiring one or more Zn-containing proteins (Suttle, 2010) with Zn serving as a structural component, a regulatory element, or both (Beyersmann and Haase, 2001).

Evaluating cell communication and signaling can be conducted through a variety of hormones and proteins. For example, because Zn is stored in vesicles along with insulin in pancreatic β-cells, when both are released into portal circulation, Zn may be functioning by coordinating metabolic processes in the liver (McNulty and Taylor, 1999).

Zinc has also been shown to increase the formation of IGF-1 along with stimulating epidermal growth-factor receptor in cellular signaling pathways (Beyersmann and Haase, 2001), by having hormone-like actions and activating these pathways (Haase and Maret, 2003). Zinc is thought to do this by increasing phosphorylation of insulin and IGF-1 receptors, as demonstrated in rat glioma cells (Haase and Maret, 2005). Because of the involvement of Zn in regulatory pathways of cell proliferation through DNA synthesis

a deficiency in Zn could limit the formation of DNA (Kobusch and Bock, 1990) and can also impair the availability of growth hormones to cells, like IGF-1 (Beyersmann and Haase, 2001). Again, IGF-1 is needed for cells in order to assist in the transition from the G1- to S-phase of the cell cycle (Beyersmann and Haase, 2001). There is also evidence that periods of stress that a beef animal may undergo, like weaning or transportation stress, can decrease serum IGF-1 concentrations, potentially directing IGF-1 away from growth (Graham et al., 2010). A mild stimulation of the immune response, in response to a stressor, can cause an excretion of Zn, decreasing serum concentrations (Graham et al., 2010). Measuring serum IGF-1 and Zn could be used as an indicator of growth for calves (Graham et al., 2010).

A deficiency of Zn has been shown to have adverse effects on the insulin response. Droke et al. (1993) studied decreases of Zn deficiency on glucose tolerance by measuring insulin, IGF-1, and somatotropin concentrations in lambs. There were three treatments classified as severely deficient, marginally deficient, and adequate with the diets containing 3.7 mg Zn/kg, 8.7 mg Zn/kg, and 43.7 mg Zn/kg, respectively. Authors noted the Zn-adequate lambs had the greatest insulin response, with Zn-deficient lambs having lesser circulating insulin concentrations prior to feeding. These authors also noted that deficient lambs exhibited decreased growth, which could be caused by decreased circulating IGF-1 concentrations, even though somatotropin concentrations were greater 45 minutes after a GH-releasing factor infusion in Zn deficient compared with adequate lambs (Droke et al., 1993).

Interestingly, Zn has been shown to promote the transport of glucose into fibroblasts and adipocytes, with a greater glucose uptake response observed in adipocytes

(Haase and Maret, 2003; Tang and Shay, 2001) with an 80% increase in an insulin-like effect of Zn on lipogenesis in lean mice (Chen et al., 1998). When feedlot cattle are reaching finished weight, they could be experiencing a degree of insulin-insensitivity. This insensitivity could be lessened with Zn supplementation by enhancing insulin activity, which was observed in genetically obese mice supplemented with 44 mg Zn/kg from dietary sources and 20m*M* $ZnCl_2$ from water (Chen et al., 1998). With out insulin, cells cannot absorb glucose from circulation (Chausmer, 1998) but the Zn induced uptake of glucose could support the transportation of glucose into myocytes and adipocytes and support the synthesis of protein and marbling.

Reeves and O'Dell (1983) investigated the effect a Zn deficiency would have on glucose metabolism in rats. It was noted that Zn deficiency decreased the adipocyte uptake and utilization of glucose and was thought to be due to the inhibition of insulin to bind to the plasma membrane of adipocytes (Reeves and O'Dell, 1983). With Zn's effect on insulin, it is important to note that adipocytes and skeletal muscle require insulin for the uptake of glucose (Reeves and O'Dell, 1983). A decrease in glucose absorbed from the bloodstream can limit the growth of peripheral tissues. In regards to feedlot cattle this could have detrimental effects on muscle growth if the cells to do not have adequate glucose availability.

Epidermal growth factor (EGF) is also an important factor contributing to cell proliferation. Zn has been shown to phosphorylate EGF receptors in human bronchial epithelial cells (Wu et al., 1999). Though the mechanism of this response is not clear, the authors hypothesize that Zn might interact with the sulfhydryl groups on the EGF receptor, causing activation; or Zn may inactivate phosphatases that dephosphorylate EGF

receptors, resulting in a greater concentration of phosphorylated EGF receptors (Wu et al., 1999). It has also been proposed that the Zn induced phosphorylation of EGF receptors may be conducted with the help of metalloproteinases (MMP-3) in an autocrine or paracrine mode of action (Wu et al., 2004). To support this, Beyersmann and Haase (2001) also noted a stimulation of the EGF receptors in response to extracellular Zn. Cultured primary mouse hepatocytes have been shown to exhibit increased EGF-stimulated DNA synthesis, when adequate amounts of Zn are added to the culture medium (Kobusch and Bock, 1990). Marginal Zn status could be limiting the rates of cell proliferation and amount of DNA synthesized by growing satellite cells or myocytes in rapidly growing beef animals.

In cell culture, the inhibition of EGF receptors decreases TBA-induced protein synthesis (Thornton et al., 2016) and proliferation (Thronton et al., 2015) in bovine satellite cells. This suggests that EGF is extremely important for hormone induced satellite cell growth. This lends the opportunity for Zn to also play a role in the activation of the EGF receptors and have an additive effect on increasing the proliferation and growth of satellite cells in bovine muscle.

2.2.3 Metalloproteinases

The properties and functions of the Zn ion allow it to be present in many tissues serving as a cofactor for metalloenzymes (McCall et al., 2000) with the active site containing Zn (Woessner, 1991). Metalloproteinases are required for the degradation of the extracellular matrix when cellular migration and tissue repair and modeling are occurring (Johnson et al., 1998), for example in the processes of angiogenesis and bone resorption (Woessner, 1991). It has been found that the activity of these enzymes is up

regulated in response to growth factors (Johnson et al., 1998), like IGF-1 or insulin. Zinc is needed to coordinate the timely mobilization of cysteine to the active site of these enzymes (Johnson et al., 1998). Metalloproteinases have been shown to play a role in increasing the rate of proliferation in bovine satellite cells (Thornton et al., 2015). Matrix metalloproteinases 2 and 9 contribute to increased growth of satellite cells by cleaving heparin-binding epidermal growth factor-like growth factor from the membrane of satellite cells, resulting in the activation of EGF receptor (Thorton et al., 2015). These authors also noted that inhibition of metalloproteinases 2 and 9 suppressed TBA-induced bovine satellite cell (BSC) proliferation. Because metalloproteinases are also important for angiogenesis, this could lead to the increased availability of nutritive substrates to myocytes.

2.2.4 Live Animal Performance

Beef cattle that are deficient in Zn may exhibit signs including decreased growth by decreasing feed intake and efficiency, a drop in milk production, increased susceptibility to stress and infections, along with a decrease in reproduction efficiency (Miller, 1970). Growth responses to TM supplementation, including Zn supplementation, are variable. Trace mineral status is an instrumental factor when evaluating responses to TM supplementation, as growth responses from dietary TM supplementation or TM injections are more evident when cattle are mildly or severely TM deficient (Ahola et al., 2005). Research contributing to the establishment of the Zn requirement for growing cattle has determined 30 mg/kg DM of Zn to be adequate in order to prevent signs of Zn deficiency (National Academics of Engineering, Science and Medicine, 2016), though this requirement has not changed in over 40 years.

In several studies, Zn supplementation, regardless of source, has resulted in increased ADG and improved efficiency when control diets do not meet adequate NRC concentrations for Zn (Spears, 1989; Engle et al., 1997). Heifers that were fed diets deficient in Zn (17 mg/kg DM) for 21 days had a 42- 46% decrease in ADG and 40-50% decrease in G:F compared to heifers that were fed a diet containing 40 mg/kg DM (Engle et al., 1997). The results of this may not be indicative of Zn deficiencies due to only a 21 d experimental period, where differences in gut fill could be contributing to these differences in performance. Engle et al. (1997) hypothesized that the reduction in efficiency observed with a Zn deficiency is related to an alteration in the rate of protein turnover. A marginal Zn deficiency contributed to a decrease in the rate of protein turnover but overall did not decrease muscle mass in Holstein steers (Engle et al., 1997). Spears and Kegley (2002) observed a 9.4% increase in ADG when Angus and Angus × Hereford steers (246 kg) were supplemented with 58 mg Zn/kg DM from Zn oxide and Zn proteinate sources compared to a control treatment group that received 33 mg Zn/kg DM for 196 days, which is still greater than the Zn requirement for growing beef cattle (National Academics of Engineering, Science and Medicine, 2016).

In contrast, Gunter et al. (2001) observed no performance benefit to Zn supplementation when supplementing Zn in the forms of Zn sulfate (74 mg Zn/kg DM), Zn polysaccharide (66 mg Zn/kg DM), or a Zn amino acid complex (90 mg Zn/kg DM) to feedlot beef steers (216 kg). This lack of performance response is likely due to the diet and Zn supplementation fed in the feedlot phase being well above adequate concentrations for Zn, ranging from 59-90 mg Zn/kg DM.

2.2.5 Carcass Characteristics

Zinc supplementation can also have variable effects on carcass parameters. For example, Zn supplementation to steers in the form of Zn oxide or Zn proteinate (51 mg Zn/kg DM) increased quality grade and marbling score but had no impact on HCW, DP, REA, KPH, or BF thickness (Spears and Kegley, 2002). While supplementation with a Zn amino-acid complex at a rate of 30, 60, or 90 mg Zn/kg DM in addition to a diet already containing 90 mg Zn/kg DM decreased BF thickness and yield grade, no effect on HCW or DP was noted when no beta agonist was fed (Genther-Schroeder et al., 2016). When ractopomine hydrochloride (300 mg/d) was fed, growth rate of steers linearly increased with the addition of Zn to the diet, suggesting growth responses during β- agonist supplementation may increase an animals Zn requirement (Genther-Schroeder et al., 2016). A lack of response on carcass characteristics was observed when Limousin steers were supplemented with dietary Zn (30 mg Zn/kg DM) and also administered an injectable Zn supplement (provided 381 mg Zn/steer) likely due to steers having adequate Zn status (Niedermayer et al., 2016).

Zinc is a dynamic mineral in the respect that it can affect the growth animals in many ways. Zinc can exert its effects directly by being a component of the structure of enzymes and metalloproteinases but also indirectly through its role in the activation of EGF receptors, IGF-1 and the insulin response. Even though Zn is involved in hundreds of processes in the body it would be beneficial to have a clear understanding of how the supplementation of Zn to beef cattle could increase muscle growth or increase feed intake. It would also be beneficial to determine if the concentration of supplemental Zn can be

changed during different times of a beef animals life where demands for growth may differ.

2.3 Copper

Copper was identified as an essential mineral when ruminants deprived of Cu showed signs of ataxia (Bennetts and Chapman, 1937), depigmentation of hair, growth retardation (Whitelaw et al., 1983), and bone disorders like osteoporosis and widening of the epiphyses (Suttle, 2010). The activities of superoxide dismutase (Cu/Zn SOD) in neutrophils are also decreased with Cu deprivation (Suttle, 2010).

The supplementation of Cu at supranutritional concentrations has been shown to have growth-promoting effects in pigs and poultry through intestinal bacterial control (Suttle, 2010). Interestingly, Cu supplementation to weanling pigs through a Cu-injection (250 ppm Cu as Cu histidinate), stimulated serum mitogenic activity (Zhou et al., 1994). The authors noted, even though it was not significant, that Cu injection also increased GH mRNA slightly (Zhou et al., 1994). In evaluating the response Cu has on bovine pituitary glands, it has been noted that Cu (6×10^{-5} M) caused a 10 to 15-fold increase in the release of GH from pituitary glands collected at slaughter from animals of unspecified age and sex (LaBella et al., 1973). Though the mechanism is unknown, a positive relationship of Cu on GH synthesis and release may help to explain the growth response exhibited in some species. There are a variety of mechanisms by which Cu may positively influence the growth of animals.

2.3.1 Hemoglobin Synthesis

It is well established that hemoglobin in erythrocytes is needed for the effective transport of oxygen throughout the body. It has also been exhibited that there is a complex

relationship between the regulation of metal ions in the body and how they can be involved in biological processes. For example, Cu catalyzes the autoxidation of hemoglobin even when Cu is in very low concentrations (Rifkind, 1974). This is thought to occur through the unique ability of Cu to bind hemoglobin at a specific binding site and allow the oxidation to occur (Rifkind, 1974). It is thought that Cu is uniquely able to affect hemoglobin because of its effective oxidation and reduction of Cu(I) and Cu(II), and explains the reason that some other metals like Zn(II), Ni(II), Mg(II), and others do not have the catalytic effect on hemoglobin synthesis (Rifkind, 1974).

Heme proteins belong to one of the largest classes of metalloproteins (Sigman et al., 2003) and there is evidence that Cu plays a structural role in the heme/Cu terminal oxidase enzymes (Ferguson-Miller and Babcock, 1996). These Cu and Fe proteins process O_2 in the body (Kim et al., 2003) by having a heme-Cu in the center of the protein where O_2 binding can occur (Sigman, 2003). The oxidase enzymes exert their functions by assisting in the continuation of electron transport in respiration (Ferguson-Miller and Babcock, 1996). These enzymes are present in the inner mitochondrial membrane (Einarsdottir and Caughey, 1985) to support the production of ATP for the animal to use (Garcia-Horsman et al., 1994).

In some preliminary experiments conducted with anemic lambs, it was noted that lambs that received supplemental Fe (40 mg ferric chloride daily) and Cu (6 mg $CuSO_4$ daily) had 55% more rapid improvement in hemoglobin compared to lambs that only received supplemental Fe at the same rate (Thomas and Wheeler, 1932). This could be a result of the role Cu plays in the enhancement of Fe absorption. A similar result was seen in chicks that were fed a diet containing 0.2 mg Fe (as $FeCl_3$), where there were increases

in hemoglobin synthesis when 0.01 or 0.02 mg Cu (as $CuSO_4$) was added to their diet compared to chicks that received no supplemental Cu in their diet (Elvehjem and Hart, 1929). Some research has shown the high concentrations of Cu can decrease Fe status along with hemoglobin concentrations; this is likely due to an increase in Cu accumulation in the liver (Dove and Haydon, 1991). To over come the decrease in hemoglobin concentrations in young pigs fed diets containing 250 ppm of Cu, there is a need to increase the amount of dietary Fe supplementation, but diets containing 5 ppm of Cu had no effect on hemoglobin concentrations (Dove and Haydon, 1991). It can be concluded that when Cu and Fe are properly balanced, Cu can aid Fe in the synthesis of hemoglobin (Elvehjem and Hart, 1929; Elvehjem, 1935).

2.3.2 Lysyl Oxidase

With decreased growth rates often observed with Cu deficiency this may be linked to the role of Cu in the lysine 6-oxidase enzyme, also known as lysyl oxidase. This enzyme is essential for the stabilization of the extracellular matrix with collagen and elastin crosslinking (Rucker et al., 1998) through post-translational modification of collagen and elastin (Romero-Chapman et al., 1991). The pro-form of lysyl oxidase, is combined with carbohydrates and Cu, then converted to the lysyl oxidase form which may play a role in the assembly of the extracellular matrix (Rucker et al., 1998). It is hypothesized that Cu and lysyl oxidase are released from secretory vesicles into the extracellular space and may explain why the presence of dietary Cu can increase lysyl oxidase activity (Rucker et al., 1998). When evaluating the effect of dietary Cu supplementation in rats, it was determined that lysyl oxidase may undergo daily turnover when measuring the accumulation and incorporation of ^{67}Cu into lysyl oxidase in rat skin

(Romero-Chapman et al., 1991). The authors also noted that Cu repletion increases the activity of lysyl oxidase (Romero-Chapman et al., 1991), suggesting that Cu deficiency could have detrimental effects on the building of collagen and elastin in extracellular matrix formation. This was illustrated when chicks fed Cu-deficient diets containing <1 mg/kg of Cu had a greater extent of collagen solubility in bone than chicks fed a diet containing 25 ppm of Cu. This would again suggest that Cu deficiency in chicks decreases collagen cross-linking in bone (Rucker et al., 1975).

The effects of Cu on collagen are important because of the large amount of collagen that is present in skeletal muscle (Light et al., 1985) to provide the muscle with strength and stability (Haus et al., 2007). Rates of growth and the influence of hormones can also cause a shift in collagen concentrations in skeletal muscle (McCormick, 1999). For example, testosterone causes an increase in the synthesis and turnover of collagen (McCormick, 1999). Along with growth rates and circulating hormones, as an animal or human ages this causes an increase in the strength of cross linkages in intramuscular collagen (Haus et at., 2007; Hill, 1966).

2.3.3 Live Animal Performance

With most TM supplementation strategies growth responses are variable and can be influenced by a variety of factors. For example there is evidence that there are differences in Cu metabolism between Angus and Simmental breeds of cattle (Ward et al., 1995; Fry et al., 2013). Another major factor that can contribute to a growth response to Cu is the concentrations of an antagonist like Mo in the diet consumed. For example, a growth response may not be seen when Cu is supplemented to cattle but if the balance of Cu and Mo is not accurate, that Cu supplementation may be needed in order to over come

the detrimental effect of Mo on Cu status (Dias et al., 2013). Suggesting that the Cu: Mo ratio of the diet positively affected ADG (Dias et al, 2013).

To examine the impact of Cu supplementation to cows and their offspring, 2 year old cows received no Cu supplementation or were supplemented Cu from inorganic (200 mg Cu from $CuSO_4$) or organic (100 mg Cu from AvailaCu) 45 d prepartum until 60 d postpartum (Muehlenbein et al., 2001). Copper supplementation had no effect on cow BW, body condition, or BW change with calf birth weights and weaning weights also not being affected (Muehlenbein et al., 2001).

In a feedlot receiving study (35 d) conducted by Salyer et al. (2004), utilizing lightweight (average weight approximately 229 kg) heifers examining the effect of supplementing 10 mg Cu/kg DM as $CuSO_4$ or Cu polysaccharide complex, no effects on ADG, DMI, or G:F were observed. The chemical composition of the diets ranged from 20.3 to 23.6 mg Cu/kg DM (Salyer et al., 2004), which could explain the lack of performance response due to this diet meeting the heifers Cu requirements.

Copper supplementation of 10 or 20 mg/kg as $CuSO_4$ in addition to a diet containing 4.9 mg Cu/kg DM to Angus steers had no effect on ADG, DMI or feed efficiency during the finishing period (Engle and Spears, 2000a). In a growing and finishing experiment utilizing Simmental steers, with a basal diet containing 9.8 mg Cu/kg DM, the additional supplementation of 10 or 40 mg Cu/kg DM had no impact on BW, ADG, feed intake or feed efficiency (Engle and Spears, 2001). This lack of response is likely due to the basal diet already meeting the nutritional requirement of Cu for growing steers, which is 10 mg Cu/kg DM (NAESM, 2016). Unexpectedly, in finishing diets containing 4.9 mg Cu/kg DM and 0.58 mg Mo/kg DM, steers that receiving no additional

Cu supplementation had greater final BW, ADG, DMI, and G:F than steers receiving Cu supplementation from various sources (Engle and Spears, 2000b).

In ruminants the literature is in general agreement that growth responses to Cu are not often observed due to diets today are commonly meeting the Cu requirements of growing cattle.

2.3.4 Carcass Characteristics

Copper supplementation to steers at a rate of 10 or 20 mg Cu/kg DM with a basal diet containing 4.9 mg Cu/kg DM, decreased 12th rib backfat compared to steers that did not receive Cu supplementation in addition to the basal diet but had no impact on other carcass measurements (Engle and Spears, 2000a). In regards to fatty acid profile, the authors also noted that Cu supplementation increased the longissimus muscle percentage of unsaturated fatty acids but tended to decrease the percentage of saturated fatty acids (Engle and Spears, 2000a). In a different study comparing concentrations of Cu supplementation and source (20 mg $CuSO_4$, 40 mg $CuSO_4$, 20 mg Cu citrate, 20 mg Cu proteinate, and 20 mg Cu chloride; per kg/DM) and their effects on carcass characteristics it was observed that steers that received no supplementation of Cu had greater HCW and increased 12th rib backfat along with a tendency for Cu to decrease saturated fatty acids in longissimus muscle (Engle et al., 2000a). The authors hypothesize that the changes in fatty acid profile may be a result of changes in microbial biohydrogenation process in the rumen with a greater amount of unsaturated fatty acids being available in the small intestine for absorption (Engle et al., 2000a).

Copper plays an essential role in growth in part due to its function in hemoglobin synthesis and support of lysyl oxidase activity. But the relationship between the optimum concentrations of Cu supplementation to cattle to maximize the function of both of these processes is yet to be determined. Like other aspects of trace mineral nutrition there are a large number of factors that can affect if the minerals are absorbed and actually utilized in the animal. It would be beneficial to evaluate the source of Cu that is fed to a ruminant animal and its impact on how efficiently Cu can get incorporated into the synthesis of hemoglobin and the building of extracellular matrices with lysyl oxidase. Along with the source and concentration of Cu, it would also be beneficial to explore how the rate of growth of an animal can affect the metabolism of Cu. For example, in feedlot operations where growth rates of cattle are often times increased by metabolic modifiers like hormonal implants and β-agonists. For example, hormonal implants have been shown to increase frame size in feedlot steers, which would increase bone growth, and the need for lysyl oxidase activity in order to lay the foundation for the formation of strong bone and skeletal muscle.

2.4 Manganese

In the 1930s, Mn was identified as an essential metal for growth and reproduction of livestock species (Suttle, 2010). Manganese has been found to be present in low concentrations in various tissues and is needed for proper bone development and reproductive function of both male and female animals (Hidrioglou, 1979; Suttle, 2010). Slipped tendon and nutritional chondrodystrophy (dwarfism) along with skeletal abnormalities have been observed in Mn deficient poultry (Gallup and Norris, 1939). In ruminants, Hansen et al. (2006) demonstrated that calves born to Mn deficient heifers

were diagnosed with neonatal chondrodystrophy. With one of the most common symptoms of Mn deficiency being adverse effects on skeletal development resulting in dwarfism (Liu et al., 1994), it is important to understand the role Mn has in skeletal development.

2.4.1 Glycosyltransferases

When young and developing animals are growing under a Mn deficient environment, especially in utero, skeletal development is likely to suffer (Leach and Harris, 1997). Manganese's role in the formation of epiphyseal cartilage appears to be involve proteoglycans, which are a major component of the cartilage extracellular matrix (Liu et al., 1994). Proteoglycans are present in the extracellular matrix and contain proteoglycan monomers, which are made up of glycosaminoglycan side chains (Liu et al., 1994). Proteoglycans play a large role in the strength and integrity of cartilage, by helping to strengthen the cartilage and preventing it from bowing under large weight stress (Leach and Harris, 1997). Glycosyltransferases are enzymes that play a role in the synthesis of glycosaminoglycan side chains and require Mn as a cofactor (Leach, 1986). It has been noted that glycosyltransferases are the enzymes that add carbohydrates (UDP- sugar) to core proteins, which result in the formation of proteoglycans (Leach and Harris, 1997).

Incorporation of sulfate into glycosaminoglycans can serve as a measure of the rate of glycosaminoglycan synthesis, with a lack of glycosaminoglycan synthesis serving as a cause of Mn deficiency induced perosis (Bolze et al., 1985). It has also been noted that decreased concentrations of Mn interfere with in vivo cartilage sulfate synthesis, which results in an increase in the number of incomplete glycosaminoglycan chains (Bolze, et al., 1985). This indicates that a Mn deficiency decreases growth by decreasing

glycosaminoglycan synthesis (Bolze et al., 1985). This can result in a variety of degrees of skeletal problems including lameness, enlargement and stiffness of joints, shortened limbs, along with twisting of legs (Leach and Harris, 1997), due to weak cartilage structure. Often times Mn deficiency can be observed in perosis and slipped tendons in poultry where joints are swollen and tibias are twisted (Leach and Harris, 1997).

2.4.2 Manganese and Carbohydrate Metabolism

There is evidence of a complex relationship between Mn and carbohydrate metabolism through an insulin and glucose response. When rats were fed a diet consisting of 1 µg Mn/g during gestation, their offspring exhibited a glucose tolerance curve similar to what would be seen in diabetic animals (Baly et al., 1984). The authors also noted that in Mn deficient rats, the degree of insulin secretion inhibition worsened as the period of glucose stimulation was extended (Baly et al., 1984). Manganese deficient rats exhibited decreased insulin synthesis and release from the pancreas along with an increased rate of insulin degradation (Baly et al., 1985). In contrast, Baly et al. (1990) noted that Mn deficient rats had decreased glucose transport and fewer insulin receptors per cell but noted no decrease in insulin affinity. These authors hypothesize that the decrease in glucose transport could be due to a decrease in glucose transporters on the surface of adipocytes (Baly et al., 1990). It has been noted that insulin and Mn had an additive effect to increase the rate of oxidation of the carbon-1 of glucose to yield CO_2 for the synthesis of lipids (Baquer et al., 2003). These authors contributed this effect to the role Mn may be playing as having an insulin-like action or it may be increasing the transportation of glucose into adipose tissue by enhancing insulin when insulin concentrations are low (Baquer et al., 2003).

It is obvious that the mechanism by which Mn affects carbohydrate metabolism is still to be determined. When evaluating the effect of Mn on plasma glucose concentrations in feedlot cattle, Legleiter et al. (2005) found that increasing concentrations of Mn had no effect on plasma glucose concentrations but tended to decrease plasma non-esterified fatty acid (NEFA) concentrations (Legleiter et al., 2005).

2.4.3 Live Animal Performance

The decreased growth often seen with Mn deficiency can be contributed to a lack of cartilage formation in epiphyseal growth plates, which ultimately determines the length of bone growth (Leach and Harris, 1997). This is extremely important for the growth and development of young animals. In poultry, Mn deficiency has resulted in the enlargement of hocks and perosis (Bolze et al., 1985). To examine the growth and development of calves experiencing Mn deficiency, Hansen et al. (2006a) used heifers fed diets with no supplemental Mn and diets supplemented with 50 mg Mn/kg DM (basal diet contained 15.8-18.6 mg Mn/kg DM) for 267 days, beginning Mn supplementation prior to breeding and maintaining dietary treatments throughout gestation. There was no effect of Mn supplementation on heifer performance or reproductive efficiency (Hansen et al., 2006b) but the authors noted that calves born to control heifers had lighter birth weights and tended to be dwarves compared to calves born to Mn supplemented heifers. It was also observed that the majority of calves born to Mn deficient dams experienced superior branchygnathism, and combined with the swollen joints and dwarfism also observed, this could indicate decreased glycosyltransferase activity in Mn deficient calves (Hansen et al., 2006a). Dairy calves born to dams fed low Mn diets (7-10 mg Mn/kg DM) also showed signs of weak limbs and tended to have lighter birth weights (Bentley and Phillips, 1951).

Manganese supplementation can have variable effects on ruminant animals. As a point of reference, the current Mn requirement for growing beef animals is 20 mg Mn/kg DM (NAESM, 2016). Manganese supplementation of 10, 20, 30, 120 or 240 mg Mn/kg DM in addition to a basal finishing diet containing 8.1 mg of Mn/kg DM had no impact on finishing performance or carcass quality of Angus feedlot steers (Legleiter et al., 2005). Hansen et al. (2006b) also noted no differences in heifer ADG, DMI or G:F when heifers were fed a basal diet containing 15.8 mg Mn/kg DM with additional supplementation of 10, 30, or 50 mg Mn/kg DM for 196 days. In contrast, sheep supplemented with high concentrations of Mn (250 or 500 mg/day) grazing pastures with 154-160 mg Mn/kg DM, had decreased daily gains compared to sheep that did not receive supplemental Mn (Grace, 1973). It is possible that the concentrations of Mn these sheep were exposed to could have been interfering with Fe metabolism and decreasing the concentration of Fe in the heart and circulation (Grace, 1973). The concentration at which feed intake begins to be decreased is between 3,000 and 4,500 mg Mn/kg DM with the maximum tolerable level set at 2,000 mg Mn/kg DM for small ruminants (NRC, 2007).

Even though Mn is typically present in tissues in extremely low concentrations (Leach and Harris, 1979) the importance of this trace element cannot be over looked. There is a consistent observation that Mn deficiency can have adverse effects on cartilage formation. Calves with structural defects and a lack of strong limbs are not ideal for feedlot production. It will be important for cattle producers to make sure that cows are supplemented with adequate concentrations of Mn to yield calves with correct bone and cartilage structure in order to build breeding herds by keeping heifers or to produce steers

for the feedlot. There seems to be a degree of difference on the effects on Mn and its impact on carbohydrate metabolism in regards to species. The lack of differences in ruminant models could be a result of ruminants having low concentrations of circulating glucose and therefore, Mn deficiency not impairing the transport of glucose into adipocytes, because ruminant adipose tissue has a preference for acetate as its fuel for triacylglycerol synthesis. Because of the role that Mn plays in carbohydrate metabolism, this could be important in the finishing phase of feedlot production. Late in the feeding period when the production of adipose is critical to make a quality beef carcass, insulin resistance could inhibit the deposition of fat, while Mn could be playing a role in encouraging the uptake of precursors for the development of lipids.

2.5 Selenium

Selenium concentrations in soils and plants vary widely throughout the world. In some places Se concentrations can be toxic as well as severely deficient in short geographical distances, which can raise concerns for those trying to raise livestock in those areas. Some signs of Se deficiency may include: unthrifty calves and lambs, decreased milk production, white muscle disease, along with impaired immune function (Wichtel, 1998). On the other hand Se is also toxic at relatively small concentrations and can result in emaciation, loss of hair and dullness of coat, stiffness of joints, lesions and sloughing of the hooves in animals grazing pastures with high Se concentrations (Suttle, 2010). The current recommendation for Se in growing beef animals is 0.10 mg Se/kg DM (NAESM, 2016).

It was originally believed that the role of Se in livestock species was almost solely in the function of glutathione peroxidase and its importance as an antioxidant (Spears et

al., 1986; Wichtel, 1998; Gunter et al., 2003). Recently there has been more of an appreciation for the role selenoproteins are playing not only in immune function but also thyroid hormone metabolism (Wichtel, 1998). In times of Se deprivation the body has a mechanism by which it prioritizes where Se will be incorporated. In the face of Se deficiency, the Se supply is first prioritized to the thyroid gland is prioritized where any remaining available Se could be used for glutathione peroxidase enzyme function (Fairweather-Tait, 2011). It has also been noted that deiodinases get priority to Se availability over other selenoproteins (Fairweather-Tait et al., 2011).

2.5.1 Selenium on Thyroid Hormones

Thyroid hormones, in particular T_4 and T_3, play a role in growth processes because they have been shown to increase the rate of transcription of the GH gene in the pituitary (Koenig et al., 1987). The deiodinase enzymes that are responsible for the conversion of T_4 (L-thyroxine) to its more active form T_3 (3,5,3'-triiodo-L-thyronine) are selenoenzymes (Wichtel, 1998). There are three different types of deiodinase enzymes that are present in different tissues. Type-1 is active mainly in the liver, thyroid, kidney, and brown adipose tissue with Type-2 and Type-3 present in the central nervous system (Wichtel, 1998). In the instance of Se deficiency, the expression of Type-1 deiodinase is decreased in the liver and kidney while Type-2 and Type-3 do not appear to be as sensitive to Se deficiency (Wichtel, 1998). Dietary Se supplementation has resulted in an increase in T_3 and subsequent decrease in T_4 concentrations in the serum (Kumar et al., 2008) because of a increase in Type-1 deiodinase. In other instances, Se supplementation seemed to have no effect on serum T_3 or T_4 concentrations. For example when lambs were supplemented 0.15

mg Se/kg DM in addition to a diet containing 0.19 mg Se/kg DM for 90 days, there was no increase in serum T_3, T_4, or T_4:T_3 concentrations (Kumar et al., 2009).

2.5.2 Selenoproteins

Selenium is a component of approximately 25 selenoproteins (Beckett and Arthur, 2005) and is incorporated into proteins through the amino acid selenocysteine (Loflin et al., 2006; Sun et al., 2011). There have been two major selenoproteins that have been identified as being involved in muscle and liver, selenoprotein W (SelW) and selenoprotein N (SelN). Both SelN and SelW may support major functions such as aiding in cell proliferation along with serving as an antioxidant and assisting with Ca-binding in muscle tissue (Suttle, 2010).

Selenoprotein W was originally found to serve as a catalyst for redox reactions while preventing white muscle disease in mammals (Sun et al., 2011). In early developing embryos, SelW has been shown to have a protective role against oxidative stress during myoblast growth and differentiation (Loflin et al., 2006). Selenoprotein W has been detected in its highest concentrations during proliferation stages of myoblasts but gradually decreased during differentiation of myotubes (Loflin et al., 2006). There has also been some preliminary research finding a link between SelW and its potential effects on the cell cycle. Hawkes et al. (2009) knocked out SelW in breast and prostate epithelial cells and noted an inhibition of G1-phase progression. This would suggest that SelW, in conjunction with numerous other factors like growth factors, are contributing to the entry of the cell cycle. It has been shown that mRNA expression of SelW, along with the enzymes that are involved in it's synthesis, selenophosphate synthetase-1 and selenocysteine-synthase, are sensitive to dietary Se supplementation (Sun et al., 2011). For

example, Se supplementation at concentrations greater than 0.06 mg Se/kg given to rats fed a Se deficient diet showed a marked increase in SelW protein concentrations in muscle (Yeh et al., 1997a). There is a similar response observed in ruminants where there is a positive correlation between muscle SelW and Se concentrations, muscle cytosolic Se, and muscle glutathione peroxidase activity in lambs (Yeh et al., 1997b).

It is also important to note the role that SelW plays in an animal's gastrointestinal tract. The gastrointestinal tract of livestock species is extremely muscular. The transcription of SelW has been shown to be extremely sensitive to dietary Se in the gastrointestinal tract of chicken, and may play a role in protecting the tract against oxidative damage (Li et al., 2011). This could be playing an underlying role in keeping the health and viability of the gastrointestinal tract in livestock species in order to absorb nutrients from their diet. Selenoprotein W has also been shown to have antioxidant capabilities in other tissues. For example, SelW serves as an antioxidant in embryonic myoblasts of chickens by preventing reactive oxidative species induced apoptosis (Yao et al., 2013).

The definitive function of SelN is not as clear as that of SelW. Castets et al. (2012) found detectable concentrations of SelN transcripts in somites that contain embryonic muscle precursors during mouse embryogenesis. The authors hypothesize that the SelN is present in other types of satellite cells like fibroblast and adipocyte precursors (Castets et al., 2012). In mice, a SelN deficiency leads to a decrease in the pool of satellite cells available for muscle regeneration and repair (Castets et al., 2011). There has been a possible link drawn between SelN and the regulation of Ca homeostasis in skeletal muscle. This is thought to be through SelN acting as a protein chaperone for a Ca channel

involved in the excitation - contracting coupling in muscles (Castets et al., 2012). Selenium supplementation regulates the SelN mRNA concentrations in chicken skeletal muscle and shows preferential sensitivity to Se supplementation between different skeletal muscles and cardiac muscle tissue (Zhang et al., 2012).

Selenoprotein N could serve in optimizing the function of satellite cells in the growth of muscle in animals. It is also well documented that satellite cells are involved in the TBA- induced growth of myocytes, leading to a possible additive effect of SelN and TBA triggered muscle growth. This could also be of particular importance in the growth and development of animals when SelN may be playing a role to prevent oxidative damage to myocytes (Arbogast and Ferreriro, 2010).

2.5.3 Live Animal Performance

Like most of the other trace minerals, growth responses to Se supplementation are extremely variable. Some early research done by Burroughs et al., (1963) selenium supplementation at a rate of either 0.05 or 0.10 ppm to a ground corn based finishing diet containing 0.1 ppm of Se, increased final BW of finishing beef steers by approximately 20 kg when fed for 141 days. Lambs fed a basal diet containing 0.19 mg/kg of Se with an additional 0.30 mg/kg of Se had increased ADG and total gain during a 90 d study compared to lambs that only received the basal diet (Kumar et al., 2008). Spears et al. (1986) wanted to determine the effect Se-Vitamin E injections would have on cows and their offspring when fed a diet marginally deficient in Se. Selenium injections given to cows bimonthly decreased the amount of weight that was lost during mid-late gestation and at time of calving compared to cows that did not receive a Se-Vitamin E injection (Spears et al., 1986). Calves born to these cows also received the same treatment as their

dams and calves receiving the Se-Vitamin E had greater gains during the summer months and greater adjusted weaning weights compared to calves that did not receive Se-Vitamin E injections (Spears et al., 1986). Se-Vitamin E injections also decreased calf death loss from 15.3% to 4.2%, in calves that did not receive an injection vs. calves that did, respectively (Spears et al, 1986).

Selenium supplementation to lambs in addition to a basal diet containing 0.13 mg Se/kg DM in the forms of Na selenite (0.30 mg Se/kg), or Se-yeast (0.30 mg Se/kg, or 0.45 mg Se/kg) had no effect on growth rate, feed intake or feed conversion (Vignola et al., 2009). Grazing beef cow growth performance, reproductive performance, or their calves was not affected by free-choice Se supplementation at a rate of 26 mg Se/kg as-fed through sodium selenite or seleno-yeast (Gunter et al., 2003). Nicholson et al. (1991) also saw no growth response to Se supplementation from a variety of sources, at rates ranging from 0.03- 1.2 mg Se/kg DM with a basal diet containing 0.02 mg Se/kg DM, when given to growing beef steers and Holstein heifers for 112 days. Droke and Loerch (1989) conducted a series of 5 experiments aimed to determine the effect of Se and Vit E injections on performance of receiving beef steers. The use of various concentrations of Se and Vit E injections with a basal diet ranging from 0.036-0.076 mg Se/kg, resulted in no performance enhancement compared to cattle that did not receive Se and Vit E injections.

Various growth responses or lack of responses could be due to the previous Se status of the animals used in these trials. Some results could also be a function of the length of the trial and duration of Se supplementation.

2.5.4 Carcass Characteristics

Though data on carcass response are limited, in the experiment described above by Vignola et al. (2009), there was no effect of Se supplementation on carcass characteristics of lambs. But as dietary concentration of Se increased, the concentration of Se in lamb longissimus dorsi increased (Vignola et al., 2009). Authors also noted that with Se supplementation through Se-yeast sources, the total amount to Se containing amino-acids were increased compared to controls and Na selenite lambs (Vignola et al., 2009). Even supranutritional concentrations (2.80-2.86 mg Se/kg DM) of dietary Se over a 126 d feeding period had no impact on beef steer carcass characteristics (Lalwer et al., 2004).

It seems that the literature is in agreement that Se plays a large role in antioxidant protection for animals, with Se deficiencies resulting in oxidative damage to muscle tissue along with occasional decreases in growth. Even though growth responses to Se may be variable, whether that be through selenoproteins or thyroid hormones, Se may be playing an underlying role in the development of muscle in beef cattle. More research needs to be done to determine if selenoproteins are playing a role in building muscle of finishing animals or if the function of selenoproteins is purely embryonic. There is also a greater need for a deeper understanding in the relationship between enzymes converting T_4 to T_3, which may be affecting the release of GH.

2.6 Cobalt

Cobalt is a unique mineral because there is no known requirement for inorganic Co; rather it serves its biological function as a component of vitamin B_{12} (Kincaid et al., 2003). Microbial populations in the rumen are responsible for incorporating Co into the

structure of vitamin B_{12} (Stangl et al., 1999; Schwarz et al., 2000). Thus, a Co deficiency in ruminants results in the symptoms of a vitamin B_{12} deficiency, such as decreased feed intake, overall unthriftiness, and loss of body weight (Bentley et al., 1954).

Globally, Co concentrations in feedstuffs are variable, and are often a reflection of Co concentrations in the soil and soil pH (Suttle, 2010), therefore altering the feed value of feedstuffs (Bentley et al., 1954). Because ruminants rely solely on Co intake to support microbial synthesis of vitamin B_{12} (Tiffany et al., 2003), with certain feedstuffs being variable in Co concentration, supplementation may be necessary. The current dietary Co requirement for growing beef cattle is 0.15 mg Co/kg DM (NAESM, 2016).

Cobalt plays a role in energy metabolism through adenosyl-cobalamin, by supporting methylmalonyl-CoA isomerase in converting propionate to succinate for gluconeogenesis (Suttle, 2010). Vitamin B_{12}, in the form of methyl-cobalamin, is responsible for transferring methyl groups from 5-methyltetrahydrofolate to homocysteine for the ultimate regeneration of methionine (Suttle, 2010). In instances of Co, and subsequent vitamin B_{12} deprivation, there is often an increase in the accumulation of methylmalonyl CoA (MMA) and homocysteine in the blood because of the decrease in vitamin B_{12} dependent enzyme activity.

Several factors can be measured in order to assess the vitamin B_{12} status in ruminants, these include: serum B_{12}, liver B_{12}, serum homocysteine, and serum MMA (Suttle, 2010).

2.6.1 Cobalt's Role in Propionate Metabolism and Carbon Transfer

When young male German Simmental (207 kg) calves were fed a corn-silage based diet containing 0.083 mg Co/kg DM (deficient) and supplemented with 0.20 mg

Co/kg DM (adequate) for 43 weeks, an increase in liver vitamin B_{12}, and a decrease in serum B_{12} and plasma MMA concentrations in adequate calves compared to deficient calves was noted (Stangl et al., 1999). While the reason behind the decrease in serum B_{12} is unknown, Co supplementation increased liver vitamin $B_{12,}$ which agrees with the decrease in plasma MMA with vitamin B_{12} available to support methylmalonyl CoA isomerase in the conversion of propionate to succinate in the liver. Tiffany and Spears (2005) evaluated the addition of Co to corn- (0.04 mg Co/kg DM) and barley-based (0.02 mg Co/kg DM) finishing diets fed to steers weighing 316 kg at a rate of 0.05 or 0.15 mg Co/kg DM for 146 or 160 days. There was a 28% and 35% increase in plasma B_{12} and an 18% and 22% increase liver B_{12} in the 0.05 and 0.15 supplemented steers, respectively, compared to cattle receiving no supplemental Co (Tiffany and Spears, 2005). In contrast, Kincaid et al. (2003) noted no effect of Co supplementation on serum vitamin B_{12} concentrations in primiparous and multiparous lactating Holstein cows when fed diets containing 0.37, 0.68 or 1.26 mg Co/kg DM, 21 d before their expected calving date until 120 days into milk. This could perhaps be a result of the diets containing high concentrations of Co, where a lack of vitamin B_{12} production is unlikely.

Vitamin B_{12} has been shown to be essential for propionate metabolism, which is a critical gluconeogenic volatile fatty acid (VFA) for ruminant animals. Tiffany and Spears (2005) suggested that low Co concentrations could limit gluconeogenic precursors because of the decreased circulating vitamin B_{12} concentrations leading to a decrease in methylmalonly-CoA isomerase activity, which is needed to convert propionate to succinyl-CoA in the liver. This would explain why, in progressive stages of vitamin $B_{12,}$ deficiency an increase in circulating MMA in the blood and urine can occur (Clark et al.,

1986). When various concentrations of Co was supplemented to Angus steers (274 kg) as $CoCO_3$ and Co propionate at rates ranging from 0.10 to 1.0 mg Co/kg DM for 112 or 127 days, Co supplementation resulted in a decrease in plasma MMA concentrations in growing and finishing phases of the feeding period, indicating a decreased activity of methylmalonyl-CoA mutase (also known as methymalonyl-Co isomerase; Suttle, 2010).

Folate and homocysteine metabolism also rely on vitamin B_{12} as a co-factor in methyltetrahydrofolate methyltransferase (Fisher and MacPherson, 1991). This is needed for the transfer of one carbon (especially methyl) units from 5-methyltetrahydrofolate to homocysteine, which is needed to regenerate methionine for use by the rumen microbes and for the animal to subsequently absorb (Suttle, 2010). Kincaid et al. (2003) measured the Co composition of cellular fractions in bovine liver and found the greatest proportion of Co to be present in the cytosolic space where the regeneration of methionine from homocysteine occurs.

In early research with rats, Smith and Monty (1959) used vitamin B_{12} deficient rats that were born from vitamin B_{12} depleted dams and bred them to measure growth, blood and liver characteristics of the offspring. There was no difference in BW 4 weeks after birth between the vitamin B_{12} deficient and vitamin B_{12} supplemented rats, but at 6 and 9 weeks vitamin B_{12} supplemented rats had 28% and 29% greater BW, respectively, compared to vitamin B_{12} deficient rats (Smith and Monty, 1959). In the vitamin B_{12} deficient rats, there was also a severe decrease in the rate of the conversion of MMA to succinate. Marston et al. (1972) pair fed ewes, 2 to 5 years of age, and gave one of the paired animals an injection of 50 µg vitamin B_{12} per day, in order to determine the effect of Co-deficient diet of wheaten hay chaff and wheat gluten (Co content of diet was not

reported) on the production of VFAs in the rumen along with how those VFA are metabolized in the body under a Co-deficient state. An injection was administered to insure the accumulation of vitamin B_{12} in the tissues and avoid the lack of appetite often times observed in animals suffering from a vitamin B_{12} deficiency. It was observed that blood clearance of propionate was 72% slower in B12-deficient sheep compared to those with greater status and contributed the observed decreased feed intake in deficient sheep to this altered propionate availability (Marston et al., 1972). The hindering of propionate metabolism is likely a function of the decreased activity of methymalonyl-Co isomerase in the liver available to metabolize propionate.

2.6.2 Live Animal Performance

As with other trace minerals, growth responses due to Co supplementation are variable and depend on numerous factors. One of those important factors when evaluating studies in regards to Co supplementation is the type of diet fed to the animals, species, and growth rates. Because there are different microbial populations present in the rumen when animals are fed forage vs. concentrate based diets, this could affect the amount of Co that may need to be supplemented to ruminant animals (Schwarz et al., 2000). It has been suggested that Co supplementation may be more beneficial for high concentrate diets because of a shift in the microbial population and a decrease in the synthesis of Vitamin B_{12} (Schwarz et al., 2000). Tiffany and Spears (2005) suggested that when cattle are fed barley-based diets microbial production of B_{12} may be lesser when compared to cattle fed corn-based diets because of the increased rate of fermentation of barley, compared to corn, by the microbial populations. Cobalt supplementation also decreased the acetate: propionate ratio measured in rumen fluid of a subset of the steers, 84 days after the

beginning of Co supplementation (Tiffany and Spears, 2005). This decrease in acetate: propionate ratio indicates an increase in efficiency of these steers as a result of the Co supplementation.

Pope et al. (1947) reported Wisconsin sheep producers experienced decreased lamb crops and wool production. The authors examined trace mineral supplementation as a tool to increase the survival rates of lambs and improve overall health and thriftiness (Pope et al., 1947). Lambs were given access to iodized salt or iodized salt with 1 ounce of cobalt sulfate per 45.4 kg of salt. At the end of the first two months no differences due to Co supplementation were noted, but by the third month of the experiment, ewes and lambs not receiving Co began eating less feed and ultimately losing weight. To prevent the ewes and lambs from dying, Co was given to these animals, and the increase in appetite and weight gain was almost immediate, throughout the next month sheep gained 0.39 kg per day (Pope et al., 1947). Even though this experiment utilized extremely small numbers of animals per treatment, it was one of the first studies to reveal the importance of Co supplementation in ruminant feed intake and growth.

Cobalt is needed for proper growth in all stages of production. In a study conducted in Scotland with Blackface ewes, the authors wanted to determine the effects of Co supplementation during gestation on ewe and lamb performance (Fisher and MacPherson, 1991). The treatments imposed on the ewes were either no Co supplementation to Co deficient diets or ewes were supplemented with Co (orally with weekly doses of 0.7 mg $CoSO_4$) during the first half of gestation, or ewes received Co supplementation (orally with weekly doses of 0.7 mg $CoSO_4$) for the entirety of gestation. The authors noted that even though there were no differences in ewe body weight or

condition score, conception rate, or reabsorption rate was affected (Fisher and MacPherson, 1991). Lambs born to ewes that received supplementation during all of gestation took less time to stand, find the udder, and suckle even compared to lambs born to dams that received Co supplementation during the first half of gestation (Fisher and MacPherson, 1991). These authors came to the conclusion that inefficiencies in reproductive performance can even occur with animals suffering subclinical deficiencies of Co (Fisher and MacPherson, 1991). Subclinical Co deficiency could explain poor reproductive efficiency in a cowherd as well. Judson et al. (1997) noted that even though Murray Grey cows in South Australia were grazing a pasture with marginal Co concentrations (< 0.05 mg Co/kg DM) for 96 weeks, and no clinical signs of Co deficiency were noted, cows that did not receive one oral dose of slow releasing cobaltic oxide pellets had lesser conception rates than cows that did receive Co pellets (either one, two or four pellets containing 9 g Co_3O_4) during the 96-week experiment.

When young German Simmental bull calves were fed for a 280 day experiment and fed a corn silage and concentrate diet with various concentrations of Co ranging from daily intake rates of 0.42-5.52 mg Co as $CoSO_4$ including the basal diet and supplementation, the authors established a Co requirement for growing bulls (Schwarz et al., 2000). It was noted that to optimize growth the Co requirement is 0.12 mg Co/kg but to optimize feed intake the optimal concentration increased to 0.16-0.18 mg Co/kg DM (Schwarz et al., 2000) with no mention on the effects of feed efficiency. One limitation to this study is the small number of animals per treatment group but the authors noted that the NRC recommended concentrations, 0.10 mg Co/kg DM (NRC, 1996) for Co may not be adequate to optimize growth and feed intake of growing bulls and determined that 0.20

mg Co/kg DM is more appropriate (Schwarz et al., 2000). Interestingly, this work is cited in the updated NRC mineral recommendations, as partial support for the 2016 NRC increased Co recommendation for growing beef cattle of 0.15 mg Co/kg DM (NAESM, 2016).

In agreement to increase the requirement for Co, the addition of Co of 0.05 mg or 0.15 mg Co/kg DM to corn-based diets (0.04 mg Co/kg DM) and barley-based diets (0.20 mg Co/kg DM) increased ADG and G:F during the first 84 of the finishing period and DMI throughout the finishing period (Tiffany and Spears, 2005). It is important to note that as cattle reach mature body weight the percentage of protein decreases and adipose increases per kilogram of weight gain (NAESM, 2016). There are two possible mechanisms to explain this response, one is the shift to fat accretion may be changing the demand the animal has for energy from propionate to requiring lipogenic precursors, which could ultimately decrease the effect of Co deficiency later in the finishing period (Tiffany and Spears, 2005). The second being that because DMI increases throughout the finishing period, the amount of total dietary Co could also be increasing making Co intake high enough to meet the animals Co requirements (Galyean et al., 1999).

In some situations, a growth response may not occur. For example Clark et al. (1986) gave 2000 μg injections of vitamin B_{12} monthly to Angus crossbred heifers (8 months of age, weighing approximately 185 kg) grazing pastures for 10 months with an average Co concentration of 0.05 mg Co/kg DM, and observed no differences in BW between heifers that did or did not receive the vitamin B_{12} injections.

2.6.3 Carcass Characteristics

The evaluation of Co supplementation on carcass characteristics is limited and variable. Supplementary dietary Co at rates of 0.05 or 0.15 to diets containing 0.02 or 0.04 mg Co/kg DM for 146 or 160 days to steers weighing 316 kg was shown to increase HCW (by 15 kg and 20 kg in 0.05 and 0.15 mg Co/kg DM treatments, respectively, compared to non-supplemented controls) but had no effect on other carcass characteristics (Tiffany and Spears, 2005). When various concentrations of Co was supplemented to Angus steers (274 kg) as $CoCO_3$ and Co propionate at rates ranging from 0.10 to 1.0 mg Co/kg DM for 112 or 127 days, there was no effect of Co supplementation on MS, DP, HCW, backfat, KPH, YG, REA, or USDA quality grade (Tiffany et al., 2003).

It is well established that when one wants to determine the role of Co in biological processes in the body, vitamin B_{12} is key. Even though the essentiality of Co for proper health and growth has been known for some time the requirement for growing cattle may be different than what is recommended currently. In conclusion, 0.15 mg Co/kg DM may not be adequate in order to optimize growth for today's type of cattle. Research done by Schwarz et al. (2000) along with Tiffany and Spears (2005) exhibited growth responses to Co supplementation at concentrations greater than current NRC recommendations. Even though the microbial population factor in Co metabolism may be a challenge it would be extremely beneficial for the beef industry to determine the ideal Co concentration to supplement in order to optimize growth.

2.7 Iodine

Similar to Co, iodine (I) has one known function in the body, which is to serve as a component of thyroid hormones (Meyer et al., 2008; Suttle, 2010). The thyroid hormones thyroxine (T_4) and triiodothyronine (T_3) are important for energy metabolism, growth, and brain development (Meyer et al., 2008). A deficiency of I in pregnant ruminants has lead to impaired growth and neurodevelopment of the offspring, goiter, weak calves and even abortions (Paulikova et al., 2002; Guyot et al., 2011). This transfer of I from dam to offspring has been shown to be through placental transfer rather than through colostrum (Guyot et al., 2011), leading to detrimental effects on the offspring when dams are I deficient. The current requirement for I is 0.50 mg/kg DM for growing and finishing cattle (NAESM, 2016). These requirements may be increased if there are goitrogenic substances present in feeds. For example, some forages and soybean meal contain goitrogens that prevent I from being taken up by the thyroid gland (Miller et al., 1975; NAESM, 2016). This could be of particular importance in receiving or growing cattle diets that typically contain higher proportions of forage.

2.7.1 Iodine hormones and growth

To show how important the thyroid gland and hormones are to the growth of ruminants, Erenberg et al. (1974) conducted thyroidectomies on ovine fetuses in the last third of gestation and did necropsies on fetuses 19 to 43 days post-thyroidectomy to measure the growth of organs, RNA, DNA, and protein concentration of tissues, and brain lipid content. Within 1 week after the thyroidectomies were conducted circulating T_4 concentrations had fallen to less than 0.7 µL/100 mL, with the normal range being between 4.5 and 12 µL/100 mL (Erenberg et al., 1974). An I deficiency resulted in a 12-

fold increase in iodothyronine deiodinase in the thyroid glands of cows and their calves on a diet containing 0.06 mg I/kg diet, from mid-gestation to parturition compared to cows receiving a diet containing 1.4 mg I/kg diet (Zagrodzki, 1998).

Grisby and Trenkle (1986) wanted to determine the effect of estrogen implants on T_4 and T_3 in Simmental, Limousin, and Angus steers. A Compudose implant (25.7 mg E_2) was administered to these steers and caused no differences in plasma T_4 due to implant or breed and across all breeds the E_2 implant also had no effect on T_3 concentrations 30 days after implantation (Grisby and Trenkle, 1986). Another factor that is important to consider when evaluating T_4 concentrations is that they hardly respond to the short term supplementation of dietary I and are generally relatively stable (Hemingway et al., 2001). This may be an indication that because T_4 concentrations are usually relatively stable they may have limitations in truly reflecting the I status of an individual.

Even though thyroxine is important for the growth of animals, it is also important to note that thyroxine stimulates metabolic rates and heat production resulting in an increase in the animals maintenance requirement (Post, 1963). Higher plasma thyroid concentrations and the increased oxidation of brown adipose tissue in young animals demands higher rates of O_2, which ultimately leads to metabolic inefficiencies (Symonds and Clarke, 1996). This could be of particular importance if an animal does not have access to an adequate food supply and thus could result in a loss of body weight (Post, 1963). Interestingly, there has been an in vitro study finding that thyrotropin directly affects adipocytes and causes a release of leptin from human adipose tissue (Menendez et al., 2003). In vivo, O'Connor et al. (2007) demonstrated that on d 144 of gestation, perirenal adipose tissue leptin mRNA and plasma leptin was greater in ovine fetuses that

were thryoidectomized in utero compared to fetuses where thyroid glands were not removed. It was also noted that thyroidecotmized fetuses had decreased concentrations of T_3 and T_4 and weighed less on d 144 of gestation (O'Connor et al., 2007). In conclusion it is apparent that thyroid hormones have inhibitory effects on the perirenal adipose tissue gene expression of leptin, though the mechanism is unclear if thyroid hormones are directly decreasing the amount of leptin protein synthesis or if it is exerting effects through other modes of action.

2.7.2 Protein-bound iodine

Iodine is typically bound to the amino acid tyrosine (Fawcett and Kirkwood, 1953) and the serum concentrations of protein bound I have been established to be indicative of thyroid activity (Burns et al., 1952). In an experiment conducted by Fox et al. (1974), Hereford steers (364 kg) were used to determine how compensatory growth affected thyroid hormone secretion rates. It was noted that steers experiencing compensatory growth had lesser plasma protein bound I and thyroid hormone secretion rates, and is hypothesized that these cattle had a lesser maintenance requirement, thus contributing to the compensatory growth (Fox et al., 1974).

Protein-bound I concentrations have also been measured in Hereford and Hereford × Angus steers and heifers during the finishing phase in conjunction with receiving stilbestrol and melengestrol acetate (MGA; Trenkle, 1970). Stilbestrol and MGA had no effect on protein-bound I concentrations in either steers or heifers (Trenkle, 1970). There was an observed gradual increase in protein-bound I during the finishing period in steers that received and did not receive stilbestrol (10 mg per head per day) (Trenkle, 1970).

2.7.3 Iodine and Selenium

As previously outlined, there are interactions that occur in animals between Se and I. It has been demonstrated that the enzymes that convert T_4 to T_3 are selenoenzymes (Wichtel, 1998). It is also important to note that hydrogen peroxide is used to oxidize I prior to its incorporation into thyroid hormones, which is considered the rate-limiting step in de novo thyroid hormone synthesis (Zagrodzki et al., 1998). With Se's role as a structural component of glutathione peroxidase, this may play a role in regulating thyroid hormone concentrations through controlling hydrogen peroxide in the lumen of thyroid cells (Zagrodzki et al., 1998). Iodine deficiency has been linked to weak calf syndrome and it is hypothesized Se could also play a factor in its cause (Zagrodzki et al., 1998).

2.7.4 Live Animal Performance

As previously outlined with many of the microminerals, growth responses due to supplementation are extremely variable and are dependent on a large number of factors. For example, I supplementation at rates of 0.5, 4, or 10 mg I/kg DM in addition to a diet containing 3 mg I/kg DM, to German Holstein bulls starting at 223 kg until they were 550 kg, linearly increased blood, serum, plasma, and bile I concentrations but had no impact on bull growth rate (Meyer et al., 2008). Even though there was no growth advantage, the highest concentration of I supplementation (10 mg I/kg DM) did increase the weight of the thyroid gland to be greater than the 0.5 and 4 mg I/kg DM treatments (Meyer et al., 2008). In young Holstein bull calves fed 0, 10, 25, 50, 100, or 200 mg I/kg in addition to a basal diet containing 1.58 mg I/kg for 104 – 112 days, a decrease in ADG with 200 mg I/kg supplementation was noted (Newton et al., 1974). Feed intake also decreased in calves fed

100 and 200 mg I/kg, along with several of the calves exhibiting signs of I toxicity such as chronic coughs and excessive nasal discharge (Newton et al., 1974).

The biological role of I in the body is characterized by its role in thyroid hormones. Thyroid hormones are essential for the proper growth and development of animals, but over activity of the thyroid hormones can increase rates of metabolism and cause unnecessary inefficiencies. This could be of particular importance in the production of meat animals where the efficiencies of growth are a main focus. Research is needed to explore the role that thyroid hormones may have on other circulating growth factors in the body to determine how thyroid hormones influence the growth and development of skeletal muscle, both pre and postnatally. The effects of proper dam nutrition and I supplementation could postnatally affect the growth of calves and their ability to express their full genetic potential for growth and muscle deposition.

Table 1. Trace mineral roles in growth processes.

	Role in Growth Processes							
Trace Mineral	Skeletal Development	Protein Synthesis	Cell Signaling	Carbohydrate Metabolism	Antioxidant Function	Extracellular Matrix	Hormone Synthesis	Hemoglobin Structure
Zinc		X	X	X	X	X		
Copper	X		?		X	X		X
Manganese	X	?		X	X	X		
Selenium		X			X		X	
Cobalt				X				
Iodine		X					X	

X indicates known mechanism
? indicates possible influence on mechanism

Mechanisms of Hormonal Implants

Growth in meat animals is a major priority for food production and economic viability of the animal agriculture industry, particularly the accretion of lean tissue or muscle deposition. Growth has been defined as the production of new cells (Owens et al., 1993). Growth is not only limited to muscle, it encompasses adipose and bone tissue growth as well. In utero, a tissue develops through the process of hyperplasia (increase in cell number) but as an animal begins to mature their means of growth becomes limited to the cells ability to grow through hypertrophy (increase in cell size) (Allen et al., 1979) and the integration of satellite cells (B.J. Johnson et al., 1998; Owens et al., 1993). An animal is considered to reach its full size when the ability to produce muscle mass is maximized (Owens et al., 1993) which can be illustrated in a growth curve.

Beef cattle are born with a set number of muscle fibers (Owens et al., 1993) meaning that post-natal muscle growth in cattle is through hypertrophy. Hormone implants are one way to increase the efficiency of muscle cell hypertrophy and the efficiency of satellite cell incorporation into muscle fibers. Hormonal implants have been used commonly in the beef cattle industry since the 1950s to enhance production efficiency and profitability (Reinhart, 2007; NAESM, 2016). They can be used in almost all stages of production and are available in a wide range of potencies to meet producers desired production goals (see **Table 2**). Hormonal implants can be administered to suckling calves, grazing stocker cattle, and to finishing feedlot cattle (Duckett and Andrae, 2001; Platter et al., 2003).

The products currently available that contain estrogen-like compounds can be from natural, synthetic, or plant-based sources. These estrogen compounds include estradiol (E_2) and estradiol benzoate (NAESM, 2016). The synthetic androgen compound often used in implants is trenbolone acetate (TBA). Trenbolone acetate has been shown to increase androgenic activity 3 to 5-fold and anabolic activity 5 to 8-fold compared to natural testosterone (Thornton et al., 2016). Androgenic and estrogenic hormones seem to have different modes of action to result in muscle accretion, even though the exact modes of action have yet to be determined.

2.8.1 Estrogenic Hormones

Research findings indicate estrogen and progesterone type hormones exert their effects by up regulating gene expression in the nuclei of cells of target tissues, including the ovaries, uterus, and liver (Heitzman, 1979). Unlike androgens that are able to compete with glucocorticoids for binding sites, it is known that estrogens do not compete for these receptors in skeletal muscle (Muir, 1985). Thus, they are unable to inhibit the catabolism of protein which glucocorticoids are known to cause (Muir, 1985). The precise effect of estrogen compounds on skeletal muscle is still to be determined.

Estrogen encourages the release of GH from the pituitary gland (Hayden et al., 1992; Grigsby and Trenkle, 1986; Muir, 1985; Trenkle, 1997) but has no effect on the amplitude or frequency of secretory GH peaks (Grigsby and Trenkle, 1986). Growth hormone can either act directly on muscle cells or it can increase the pancreas' production of insulin and signal glucose uptake by myocytes to support their growth. Investigating the effect of estrogens on protein accretion, Loy et al. (1988) found that estrogen implants increased the percentage of gain that was muscle and decreased the percentage of gain that

was fat accretion in Charolais-crossbred steers. The same experiment also found that estrogen implants increased the efficiency of nutrient use, where implanted steers used less metabolizable energy (ME) of their intake to produce one gram of empty body protein gain (Loy et al., 1988).

Estrogen implant strategies have shown positive responses on growth performance and can vary on the dosage rate along with days on feed, and whether or not cattle were reimplanted during the feedlot phase. For example, Loy et al. (1988) exhibited increased overall daily gain, DMI, and nonadjusted feed conversion in Charolais-crossbred steers implanted with mild and strong estrogen implants (Ralgro and Synovex-S) compared to non-implanted controls. It was also noted estrogen implants that were given on d 0 and again on d 84 led to greater hip heights and body lengths of Charolais-crossbred steers (Loy et al., 1998).

2.8.2 Androgenic Hormones

Testosterone has been shown to increase the diameter of muscle fibers, number of satellite cells, and number of nuclei in muscle fibers (Thornton et al., 2016) this ultimately increases the efficiency at which muscle cells can grow.

Because prior to the arrival to the feedlot bull calves are generally castrated they are no longer able to produce testosterone naturally. Steers also have lesser circulating concentrations of somatotropin, also known as growth hormone (GH). Hayden et al. (1992) demonstrated that Charolais steers administered an implant with 300 mg of TBA had 300-fold greater circulating concentrations of 17β-trenbolone, 31 and 72 days post-implantation compared to steers not treated with TBA. Exogenous androgens that are present in hormonal implants increase GH concentrations. Research has determined that

when steers are implanted with E2 and TBA, their GH secretion pattern more closely mirrors the GH secretion pattern of intact male cattle (Trenkle, 1997). Growth hormone has been shown to increase the production and secretion of insulin-like growth factor-I (IGF-1), which ultimately results in increased muscle protein accretion (Florini, 1985). Insulin-like growth factor is produced in skeletal muscle and is needed to stimulate protein synthesis and inhibit the rate of protein degradation in muscle cells (Dayton and White, 2008). It is also well established that IGF-1 facilitates the anabolic effects of GH on muscle and bone tissue (Dayton and White, 2008).

The mode of action of androgen hormones has yet to be completely elucidated, but multiple plausible mechanisms have been explored. Florini (1985) suggested that upon release on androgen hormones into circulation they can travel directly to muscle cells where they bind to receptors on the cell walls of myocytes, triggering the movement of the hormone-receptor complex to the nucleus, which causes the activation of RNA synthesis, ultimately resulting in the building of muscle proteins. An indirect mechanism by which TBA appears to exert its effect is competition for corticoid receptors, which limits the degradation of muscle protein (Preston, 1999). Decreased protein turnover could be the explanation for improved performance efficiency when androgenic hormones are utilized in implants (Muir, 1985). Testosterone has also been linked to a positive N balance, which also ultimately leads to increased protein content of the carcass along with decreased fat content of the carcass (Schanbacher et al., 1980). The decrease in fat content of the carcass can be demonstrated by decreased 12th rib fat, KPH, and intramuscular fat (IMF) compared to animals that were not implanted (McPhee et al., 2006).

2.8.3 Combination Implants

Combination implants are used to describe single implants that contain both androgenic (often TBA) and estrogenic (estradiol) compounds. Combination implants have additive effects resulting in a 20% increase in growth performance and 15% improvement in feed efficiency, when compared to cattle not receiving implants (Schanbacher, 1984; Bartle et al., 1992; Johnson et al., 1996a).

2.8.4 Circulating Hormone Concentrations

Hormonal implants can have varying responses on circulating concentrations of steroids. When Johnson et al. (1996a) implanted yearling crossbred steers (394 kg) with a combination implant containing 120 mg of TBA and 24 mg of E_2, circulating trenbolone concentrations of steers started from a baseline of 8.57 pg/mL, peaked by d 2 (283 pg/mL), dramatically declined by d 40 (113 pg/mL) and steadily decreased through d 143 (70 pg/mL) after 1 implant dosage. That same experiment also measured E_2 concentrations, but found that unlike the dramatic decrease in circulating concentrations of trenbolone, E_2 concentrations of implanted steers were sustained throughout the experiment (Johnson et al., 1996a). Combination implants also increase circulating concentrations of IGF-1 up to 120 d after implantation with 120 mg TBA and 24 mg E_2 (Johnson et al., 1996b).

Sex of the animal and whether they are intact or not will differentially affect response to hormonal implants. For example, when bulls were administered a combination implant (200 mg TBA and 24 mg estradiol-17β) and 95 days later reimplanted with a TBA implant, there was a decrease in plasma testosterone concentrations, suggesting that steroid implants inhibit the secretion of testosterone through negative feedback (Lee et al.,

1990). Lee et al. (1990) noted that anabolic implants eliminated the differences in circulating IGF concentrations between bulls and steers. These results again suggest that hormonal implants are a way for producers to maintain growth rates more similar to that of intact males, while finishing steers with less aggressive behaviors. Reponses to implants also vary between steers and heifers. When Herschler et al. (1995) compared the responses between steers and heifers to variable hormonal implant dosages they noted that regardless of sex animals that received two implants during the finishing period, had greater ADG and lesser feed conversion (FG) than nonimplanted controls. Herschler et al. (1995) also reported that steers that were implanted with Synovex-S and estradiol benzoate had greater gains than steers receiving only TBA, with a differing response in heifers. Heifers that received TBA did not have gains different from heifers that received either estradiol benzoate and Synovex-H implants (Herschler et al., 1995). This could be contributed to the different naturally produced hormone profiles between steers and heifers.

2.8.5 Effects on Myocyte Growth Factors

Satellite cells in muscle fibers are responsible for donating DNA to muscle fibers and thus their proliferation and ability to fuse with muscle fibers is the rate-limiting step in muscle growth (Frey et al., 1995; B.J. Johnson et al., 1998). Some work by B.J. Johnson et al. (1998) has shown that combination implants (Revalor-S) play a role in activating satellite cells in muscle fibers and that cultured cells from implanted steers contained more activated satellite cells than nonimplanted steers. B.J. Johnson et al (1998) also hypothesize that Revalor-S implanted steers have increased concentrations of IGF-1

locally produced which is explaining the enhancement in satellite cell proliferation and ultimately muscle growth.

The effects of TBA + E_2 implants have induced various responses on myocyte growth factors. These differences are often reflected by source of myocytes, in vivo or in vitro experiments, along with the conditions under which cells are harvested. Growth factors that are often measured in an attempt to determine steroidal implant mechanisms include IGF-1 and basic fibroblast growth factor (bFGF). Basic fibroblast growth factor has been shown to be important in embryonic development and could play a role in tissue repair (Abraham et al., 1986). These growth factors have been linked to satellite cell proliferation. Satellite cell cultures grown from steers implanted with a combination (120 mg TBA + 24 mg E_2) implant were more responsive to the addition of IGF-1 and bFGF as demonstrated by a 19% increase in proliferation and larger myotubes formed by satellite cells when compared to satellite cell cultures grown from nonimplanted steers (Frey et al., 1995). In vivo effects of hormonal implants on myocyte growth factors determined by muscle biopsies comparing steers implanted with estradiol (25.7 mg), TBA (120 mg), or the combination (120 mg TBA + 24 mg E_2) 28 days after implantation showed an increase in the relative longissimus muscle (LM) IGF-1 mRNA concentrations in steers receiving an E_2 and TBA/E_2 implant compared to steers receiving the TBA or nonimplanted steers (Pampusch et al., 2008). This increase in LM IGF-1 mRNA expression can be as much as 69% when compared to nonimplanted steer counterparts (L.L. Johnson et al., 1998) Interestingly, no effects of implant type on relative LM IGF-1 receptor mRNA level, estrogen receptor mRNA level, or androgen receptor mRNA level 28 days after implantation has been observed (Pampusch et al., 2008). Some work has indicated that the

source of increased serum IGF-1 concentrations could be partially due to an increase in total IGF-1 mRNA concentration in hepatocytes (B.J. Johnson et al., 1998).

2.8.6 Feedlot Growth Performance

The benefit to using combination implants is additive growth performance. Steers implanted with TBA + E_2 had greater body weight (BW) gains than steers that received TBA or E_2 alone (Duckett and Andrae, 2001; Hayden et al., 1992). Two combination implants can increase ADG by 20% and reduce feed conversion by 13.5% (Duckett and Pratt, 2014). Hayden et al. (1992) compared estradiol (24 mg of estradiol-17β), TBA (300 mg of trenbolone acetate), and the combination, TBA + E_2, in Charolais, crossbred steers weighing approximately 300 kg. Along with the TBA + E_2 group having the greatest BW gain and ADG, they also had increased deposition of lean tissue accretion (measured by urea space dilution) by 25 and 60% when compared to E_2 and TBA treatments respectively, during the 80 day experimental period (Hayden et al, 1992). When net energy of gain (NEg) was calculated, steers implanted with TBA have the greatest NEg values indicating that they use dietary energy more efficiently for live weight accretion (Foutz et al., 1997).

2.8.7 Carcass Characteristics

Along with improved growth rates and increases in efficiency, combination implant administrations have also resulted in economically desirable improvements in carcass characteristics. Most often this is increased HCW (Bruns et al., 2005; Foutz et al., 1997; López-Campos et al., 2013). But other carcass responses observed can be a reduction in carcass fat by 5 to 8% and a 4% increase in REA compared to nonimplanted cattle (Duckett and Pratt, 2014). Although the implant response in HCW is relatively

consistent, the impact on other carcass trait parameters is often variable. Johnson et al. (1996a) saw an 6.5% increase in LM area 115 d after implantation and 10% decrease in KPH 143 d after implantation in a serial slaughter experiment after implanting with a combination implant (120 mg TBA + 24 mg E_2). Similarly, Foutz et al. reported an increase in HCW with combination implants when compared to nonimplanted or cattle that just received an 20 mg estradiol benzoate + 200 mg progesterone implant. But reported no differences in 12th rib fat thickness, KPH or marbling score (Foutz et al., 1997).

There is some concern with hormonal implants and their impact on carcass quality grade. This response is variable and dependent on several factors including body composition when implanted, implant timing, particularly timing relative to harvest, along with implant potency. Duckett and Pratt (2014) demonstrated that one estrogen implant can decrease marbling score by as much as 3.75% and a estrogen followed by a combination implant can decrease marbling score by 11.49%, in relation to nonimplanted controls. Along with finding that the use of a single combination implant only decreased marbling score by 4.62% and two combination implants resulted in a 9.34% decrease (Duckett and Pratt, 2014). Bruns et al. (2005) found that the timing of a Revalor-S (24 E_2 + 120 mg TBA) implant can influence the marbling and maturity scores of Angus and Angus × Limousin steers. With cattle that were implanted at the start of the finishing period (early implant) had the greatest maturity scores, with cattle that received a delayed implant (d 56 of finishing) intermediate and nonimplanted control steers having less advanced maturity scores (Bruns et al., 2005).

Bruns et al. (2005) also noted that early implanted steers had decreased marbling scores compared to nonimplanted but did not differ from steers that received a delayed implant (Bruns et al., 2005). Steers receiving a medium potency estrogen implant on d 0 (Synovex S; 20 mg estradiol benzoate/200 mg progesterone) and then a higher potency combination implant on d 63 (Revalor S; 24 mg E_2 + 120 mg TBA) during a 140 d finishing period had decreased marbling scores compared to nonimplanted counter parts with a tendency for less of the implanted steers to grade average choice or above (Sawyer et al., 2003). Timing and how total number of implants a beef animal receives in its lifetime has been shown to impact the quality of the carcass as well. Platter et al. (2003) examined the effect that life long implant strategies have on carcass quality and observed 550 crossbred steers from five different ranches, finding that lifetime implant programs have detrimental effects on carcass quality. Not implanting until the backgrounding or feedlot phase may be the most ideal time to implant cattle if marketing carcasses for quality grade is a priority.

Since implants increase the proportion of protein in a beef carcass it is important to evaluate how fat is also being deposited in the carcass. Johnson et al. (1996a) measured carcass protein gain by taking a sample from 9-10-11th rib sections and using daily carcass protein and fat accumulation calculations from Andersen et al. (1998). Andersen et al. (1998) demonstrated that from d 0 to 40 after implantation of TBA + E_2 (120/24 mg), there was an increase in carcass protein gain of 82% compared to a nonimplanted controls, along with a 34% improvement in carcass protein gain compared to nonimplanted cattle from d 0-115 after implantation. In contrast, Bruns et al. (2005) found that fractional growth rates for protein and fat did not differ between nonimplanted, early implanted, or

delayed implanted steers, but early implanted steers tended to have lesser fractional growth rates of IMF compared to nonimplanted steers. Because implants increase frame size (Loy et al., 1988), implanted cattle may need more days on feed to reach 27.8% empty body fat and an empty body weight of 478 kg, as noted in NRC as the point at which a small degree of marbling, or U.S. Choice, will be achieved (NAESM, 2016). Bruns et al. (2005) reported implanted steers reaching 28% empty body fat at 33 (early implant) and 51 (delayed implant) kg of empty body weight (EBW) greater then their nonimplanted counter parts. Using overall reported ADG of these cattle, this would result in 19-29 extra days on feed needed to reach the desired body composition of 28% EBW at the end of the finishing period. A large retrospective study conducted by Guiroy et al. (2002), suggests that the range at which finished BW is achieved might be slightly different with an additional weight of 14 to 42 kg for steers and 30-39 kg for heifers dependent on the implant strategy utilized in order to reach a similar body composition to non-implanted animals. The type of cattle, dosage of implant(s) given, and the performance potential of the cattle will determine the variation in additional weight and extra days on feed.

2.8.8 Dietary Impacts on Implant Response

Though estrogen and androgen implants may have different modes of action, the end result is increased lean tissue accretion. If cattle do not have an adequate plane of nutrition the response to implants may be limited. Dietary protein concentration is an important consideration when formulating diets for implanted cattle. For example, implantation with E_2 can increase the percentage of N retention as much as 17% compared to nonimplanted controls (Cecava and Hancock, 1994). Galyean (1996) suggests that

increasing dietary crude protein (CP) may be most beneficial for large-framed, aggressively implanted yearling cattle, with the greatest potential for compensatory gain. Even though cattle may receive a more potent implant in the later part of the finishing period, there is a decreased amount of total muscle gain as finishing progresses and the need for metabolizable protein will be met by an increase in feed intake (Trenkle and Barrett, 2005). Galyean (1996) also suggested that as days on feed increase, increased DMI will offset any potential need for increase in dietary CP, but 10% or less dietary CP may limit a proper growth response.

2.8.9 Conclusion

As a whole, anabolic steroids have been shown to enhance circulating IGF-1 and improve the sensitivity and proliferation of myocyte satellite cells (Preston, 1999). This seems to be the most plausible mechanism by which implants exert their effects either directly, through increasing the release of GH or by increasing the GH receptor activity in the liver and perhaps skeletal muscle, which may lead to increased IGF-1 mRNA (Preston, 1999).

Anabolic hormonal implants have been a great advancement in cattle feeding that not only improve efficiency of growth but also result in more lean product and ultimately increased profit for producers. Implanting cattle in the finishing phase can increase the value of an animal on average by $51 and could be more if cattle were implanted at all stages of production (Duckett and Andrae, 2001). Duckett and Pratt (2014) calculated that the use of a combination implant would increase profit returns by $163 a head. With the ever-changing markets, over time the prices of feeds and cattle change, likely increasing the profit returns seen recently. Even though the maximum growth rate of a beef animal is

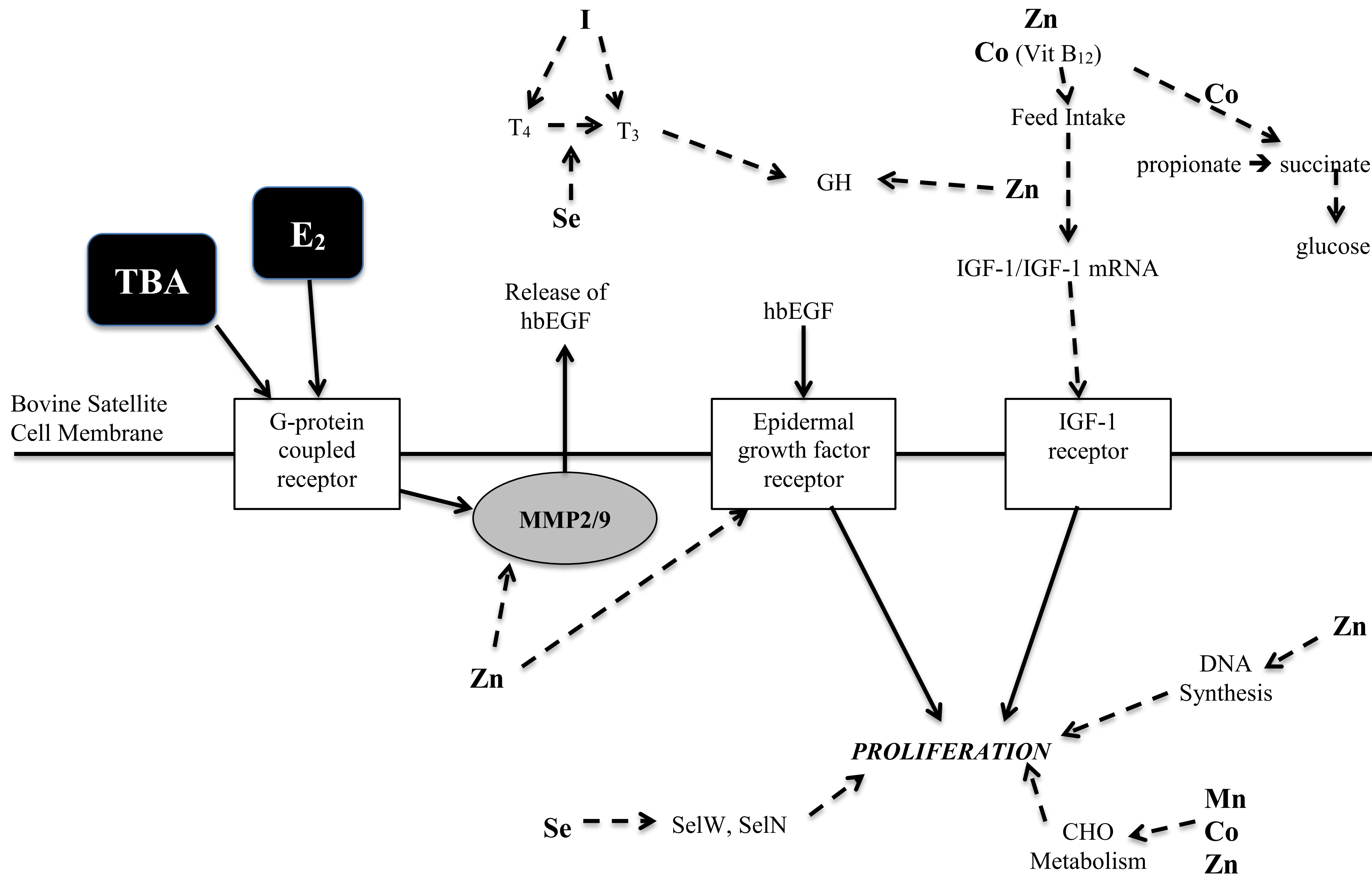
determined by genetics, growth stimulants, like implants, can alter mature body size along with composition of growth to enhance production (Owens et al., 1993). One aspect that needs to be considered is delivery of critical nutrients such as protein, energy, vitamins and minerals needed to support the growth encouraged by technologies such as hormone implants.

Table 1. Available Hormone Implants on the Market, Adapted from ISU Beef Center Publication 113 by D. Loy and E. Lundy. 2016.

Degree of Potency	Active ingredients	Cleared to be administered to	Product Trade Name
Androgen implants	140 mg trenbolone acetate	Feedlot steers	Finaplix-S, Component T-S
	200 mg trenbolone acetate	Feedlot heifers	Finaplix-H, Component T-H
Lower potency estrogen or estrogen-like implants	36 mg zeranol	Suckling calves- steers and heifers, Stockers- steers and heifers, Feedlot- steers and heifers	Ralgro
	10mg estradiol benzoate 100mg progesterone	Suckling calves- steers and heifers	Synovex-C, Component E-C
Medium potency estrogen or estrogen like implants	20 mg estradiol benzoate, 200 mg progesterone	Stockers- steers, Feedlot- steers	Synovex-S, Component E-S
	20 mg estradiol benzoate, 200 mg testosterone	Stockers- heifers, Feedlot-heifers	Synovex-H, Component E-H
	25.7 mg estradiol	Suckling calves- steers, Stockers-steers, Feedlot-steers and heifers	Compudose
	43.9 mg estradiol	Suckling calves- steers, Stockers-steers, Feedlot-steers and heifers	Encore
	72 mg zeranol	Feedlot- steers	Magnum
Lower potency combination implants	8 mg estradiol, 40 mg trenbolone acetate	Stockers- steers and heifers	Revalor-G, Component TE-G, Synovex T40
	16 mg estradiol, 80 mg trenbolone acetate	Feedlot- Steers	Revalor- IS, Component TE-IS, Synovex T80
	8 mg estradiol, 80 mg trenbolone acetate	Feedlot- Heifers	Revalor-H, Component TE-IH
	10 mg estradiol, 100 mg trenbolone acetate	Feedlot- Steers and Heifers	Synovex Choice

Table 1. Continued.

Degree of Potency	Active ingredients	Cleared to be administered to	Product Trade Name
Higher potency combination implants	24 mg estradiol, 120 mg trenbolone acetate	Feedlot- Steers	Revalor-S, Component TE-S
	14 mg estradiol, 140 mg trenbolone acetate	Feedlot- Heifers	Revalor-H, Component TE-H
	28 mg estradiol benzoate, 200 mg trenbolone acetate	Feedlot- Steers and Heifers	Synovex Plus
	20 mg estradiol, 200 mg trenbolone acetate	Feedlot- Steers and Heifers	Revalor-200, Component TE-200
Longer duration combination implants (150-200 days)	40 mg estradiol, 200 mg trenbolone acetate	Feedlot- Steers	Revalor- XS
	28 mg estradiol benzoate, 200 mg trenbolone acetate	Feedlot- Steers and Heifers	Synovex ONE-F
	21mg estradiol benzoate, 150 mg trenbolone acetate	Stockers- Steers and Heifers	Synovex ONE-G



I
T4
T3
Se
Zn
Co (Vit B12)
Feed Intake
Co
propionate
succinate
glucose
GH
Zn
IGF-1/IGF-1 mRNA
TBA
E2
Release of hbEGF
hbEGF
Bovine Satellite Cell Membrane
G-protein coupled receptor
MMP2/9
Epidermal growth factor receptor
IGF-1 receptor
Zn
Zn
DNA Synthesis
PROLIFERATION
Se
SelW, SelN
CHO Metabolism
Mn
Co
Zn

Figure 1. Possible mechanism of trace mineral roles in TBA and estradiol-induced satellite cell proliferation. Adapted from MacDonald (2000) and Thornton et al. (2015). Dashed arrows indicate possible trace mineral impacts on growth factors and metabolic pathways influencing growth and proliferation of bovine satellite cells.

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CHAPTER III

THE EFFECTS OF INJECTABLE TRACE MINERALS ON GROWTH PERFORMANCE AND MINERAL STATUS OF ANGUS BEEF STEERS RAISED IN A NATURAL FEEDLOT PROGRAM

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3.1 ABSTRACT

To evaluate the effects of a injectable trace mineral (TM) on TM status and growth of feedlot steers raised in a Certified Angus Beef Natural system, 168 certified natural Angus steers (359 ± 36.6 kg), blocked by initial BW into pens of 6 head, received a sterilized saline (**SAL**, n = 84) or Multimin90 (**ITM**, n = 84) injection (1.47 mL/100 kg BW). Steers were grown on a corn-silage based diet for 56 d, transitioned, and on d 84 began a dry-rolled corn-based finishing diet. On d 84 steers were assigned equally within treatment, SAL or ITM, to receive a second injection, making four total treatments: 1) d 0 SAL, d 84 SAL (**SAL/SAL**, n = 42); 2) d 0 SAL, d 84 ITM (**SAL/ITM**, n = 40); 3) d 0 ITM, d 84 SAL (**ITM/SAL**, n = 40); and 4) d 0 ITM, d 84 ITM (**ITM/ITM**, n = 42). Liver Cu and Se concentrations were greater ($P \leq 0.01$), and liver Zn concentrations tended ($P = 0.07$) to be greater in ITM vs. SAL steers on d 14. Liver Zn and Mn were not different on d 98 ($P \geq 0.64$). Liver Cu ($P = 0.02$) and Se ($P < 0.001$) concentrations were greater in SAL/ITM and ITM/ITM on d 98. Injectable TM had no effect on growing or finishing BW or G:F ($P \geq 0.14$). Steers had adequate TM status throughout the trial, likely explaining the lack of performance differences due to TM treatment.

Key words: natural, beef cattle, trace mineral, mineral status

3.2 INTRODUCTION

An increasing number of consumers are buying naturally raised animal products, including beef raised without the aid of growth promoting technologies or antibiotics. One difficulty to raising natural cattle is the tendency to have lesser growth rates, demonstrated by a 0.454 kg ADG disadvantage for natural cattle compared to conventionally raised cattle (Cooprider et al., 2011). Premiums often associated with natural beef programs are unable to surpass the increased input costs caused by the slower growth rates of natural cattle compared to conventionally raised cattle. It is well known that trace minerals (TM) are extremely important for numerous biological processes. For example, Cu and Zn are essential for the activity and structure of numerous enzymes needed for growth and immune system function, while Mn is a cofactor for metalloenzymes needed for skeletal structure, and Se is crucial for the antioxidant function of glutathione peroxidase (Suttle, 2010). Trace minerals can improve finishing cattle growth (Genther and Hansen, 2014a) and could help producers minimize the large growth rate and efficiency disadvantages that natural cattle have.

Injectable TM are a unique opportunity to rapidly improve the TM status of ruminant animals (Pogge et al., 2012; Genther and Hansen, 2014b) at times when dietary intake may be decreased. Trace mineral supplementation could alleviate some negative effects of stressful events because TM may have beneficial effects on immune status, disease resistance, and feed intake (Paterson and Engle, 2005). Genther and Hansen (2014a) found that after a shipping event, non-implanted, mildly TM deficient steers that were given an injectable TM had greater ADG throughout the finishing period compared to cattle that did not receive TM injection post-shipping. The investigators also found that

mildly mineral deficient cattle lost more weight after shipping, possibly because they had decreased DMI post-shipping (Genther and Hansen, 2014a). Utilizing a TM injection could help producers rapidly improve the TM status of natural cattle and avoid decreases in performance due to poor TM status and shipping stress when calves enter the feedlot. Therefore, the objective of this study was to determine the effects of an injectable TM product on growth performance and TM status of Certified Angus Beef Natural feedlot steers.

3.3 MATERIALS AND METHODS

Procedures and protocols for this experiment were approved by the Iowa State University Institutional Animal Care and Use Committee (# 11-14-7889-13).

3.3.1 Animals and Experimental Design

One hundred sixty-eight certified natural high percentage Angus, black hided beef steers (359 ± 36.6 kg) were utilized in an experiment conducted at the Iowa State University Beef Nutrition Research Center in Ames, IA. All diets given to the cattle were completely antibiotic, hormone, animal by-product and beta-adrenergic agonist free. Diet compositions are displayed in Table 1 and were formulated to meet or exceed NRC (2000) recommendations. On day -7 steers were dewormed and vaccinated with Eprinex (Merial Limited, Duluth, GA) and Bovishield Gold 5 (Zoetis Inc., Kalamazoo, MI) respectively, and given unique visual and electronic identification tags; all ears were palpated for evidence of hormone implants and none were noted. Steers were weighed on d -1 and 0, blocked by initial BW, into 28 pens with 6 head per pen, and pens were assigned to

receive an initial subcutaneous injection of either sterilized physiological saline (**SAL**, n = 84 steers, 14 pens) or an injectable TM (Multimin90; Multimin USA, Fort Collins, CO; **ITM**, n = 84 steers, 14 pens) at a rate of 1.47 mL per 100 kg of BW on d 0. The Multimin90 product contained 15 mg Cu/mL (as Cu disodium EDTA), 60 mg Zn/mL (as Zn disodium EDTA), 10 mg Mn/mL (as Mn disodium EDTA), and 5 mg Se/mL (as sodium selenite). Steers received a corn-silage-based total mixed ration (TMR) through a 56 d growing phase. Steers were weighed on day -1, 0, and 28 during the growing period. On days 56 and 57 steers were weighed and on d 57 began a series of 3 transition diets for 7 days each until day 84 when cattle began receiving the final corn-based finishing diet.

Body weights were taken on day 83 and 84 to determine initial weights for the finishing period. On day 84, pens of steers were split equally within initial injection treatments to receive an subcutaneous injection of either SAL or ITM, resulting in 4 total treatments with 7 pens per treatment: 1) d 0 Saline, d 84 Saline (**SAL/SAL**, n = 42 steers); 2) d 0 Saline, d 84 Multimin90 (**SAL/ITM**, n = 40 steers); 3) d 0 Multimin90, d 84 Saline (**ITM/SAL**, n = 40 steers); and 4) d 0 Multimin90, d 84 Multimin90 (**ITM/ITM**, n = 42 steers). Steers were weighed on 28 d intervals for the duration of the trial, and consecutive weights were taken on days 161 and 162 to determine final BW. A 4% pencil shrink was applied to all live BW measures, including those used in the calculation of ADG and G:F. Average daily gains were calculated for each individual steer. Steers were fed a probiotic (Bovamine Defend; Nutrition Physiology Company, LLC, Hoersholm, DK) at a rate of 1 $g \cdot steer^{-1} \cdot d^{-1}$ delivered in a dried distillers grains carrier by top dress starting on day 113 until the end of the finishing period.

On d 162, steers were shipped to a commercial abattoir in Lexington, NE (Tyson Fresh Meats), where steers were harvested and marketed under a Certified Angus Beef Natural Program. The USDA quality grade distribution of the steers was 10% prime, 84% choice, and 6% select. The electronic identification reader at the abattoir malfunctioned, failing to record individual animal identification on all animals and thus carcass data were untraceable back to the individual animal.

3.3.2 Sample Collection and Analytical Procedures

Cattle were delivered feed daily at approximately 0700 hours with ad libitum access to both feed and water. Daily measurements of total feed offered and bunk scores were recorded and steers were fed using a modified slick bunk procedure as described by Drewnoski et al. (2014). Ingredient and TMR samples were taken weekly to determine DM content. These samples were dried in a forced air oven at 70°C for 48 h. Dried feed samples were ground through a 2-mm screen (Retsch Zm100 grinder; Glen Mills Inc., Clifton, NJ) and stored in Fisherbrand Sterile Sampling Bags (Fisher Scientific, Pittsburgh, PA). As-fed feed disappearance values were adjusted for sample DM content and pen DMI and G:F were calculated. Total mixed ration samples were composited by month to determine Cu, Mn, and Zn concentration. Composited feeds were digested using trace metal grade hydrochloric acid (catalog number A509-P212; Fisher Scientific, Fair Lawn, NJ) before TM analysis. Feed sample Cu, Mn, and Zn concentrations were determined using inductively coupled plasma optic emission spectroscopy (PerkinElmer, Waltham, MA) as previously described (Richter el al., 2012).

One steer per pen was randomly selected for liver and blood sample collection (n = 28, 7 per treatment) to evaluate TM status in response to treatment throughout the entire

duration of the study. Samples of blood and liver were collected 2 h post-feeding at the beginning of the growing (d -5) and finishing (d 79) phases and 14 days post-injection during each phase (d 14 and 98, for growing and finishing phases respectively.) Liver biopsies were collected using the method of Engle and Spears (2000) and samples were transported to the laboratory on ice and placed in a forced-air oven at 70°C for 7 days. Monthly TMR composites and dried liver samples were digested (CEMS MARSXpress, Matthews, NC) for mineral analysis using trace metal grade nitric acid (catalog number A509-P212; Fisher Scientific, Fair Lawn, NJ) as previously described by Richter et al. (2012). Jugular blood samples for TM analysis were collected into vacuum tubes containing the anticoagulant potassium EDTA (Becton Dickenson, Rutherford, NJ) and were transported to the laboratory on ice and centrifuged at 1,000 × *g* for approximately 10 minutes at 4°C. Plasma was removed and stored at -80°C until analysis. Upon analysis, plasma samples were vortexed, then diluted to a ratio of 1:20 with 1% nitric acid. Liver samples and plasma were analyzed for Cu, Mn, Se, and Zn concentrations using inductively coupled plasma mass spectroscopy (PerkinElmer, Waltham, MA) as described by Pogge et al. (2012).

3.3.3 Statistical Analysis

Four steers had to be removed from the study due to death or treatment with antibiotics, two from the ITM/SAL treatment group and two from the SAL/ITM treatment group, and were not included in statistical analysis. Live animal performance, liver and plasma TM concentration data were analyzed using the MIXED procedure of SAS 9.4 (SAS Inst. Inc., Cary, NC). Animals were assigned to pen and treatment using a randomized complete block design. Fixed effects in growing period analyses were block

and treatment (SAL or ITM) and the fixed effects in the finishing period analyses were also block and treatment (SAL/SAL, SAL/ITM, ITM/SAL, or ITM/ITM). Steers were fed on a pen basis throughout the experiment and pen was the experimental unit for DMI and G:F (n = 14 per treatment for the growing period; n = 7 per treatment for the finishing period). Because treatment was applied to individual animal, BW collected and ADG was calculated on a steer basis, resulting in steer being the experimental unit (n = 83 per treatment for the growing period; n = 40 per treatment (SAL/ITM and ITM/SAL) and n = 42 per treatment (SAL/SAL and ITM/ITM) for the finishing period). The experimental design of the present study allowed for evaluating the timing of administration of injectable TM by utilizing Multimin90 during just the growing or finishing phases, or during the entirety of a natural beef feedlot program. Dry matter intake was averaged on a weekly basis during all feeding periods before statistical analysis and data were analyzed as repeated measures during the finishing period with 28-day intervals (month) as the repeated effect. Liver mineral and plasma mineral data were analyzed as repeated measures across the entire trial using day -5 values as covariates in analysis, using the autoregressive model of covariance structure, selected based on the lowest Akaike information criterion. Degrees of freedom were approximated using the Satterthwaite method. Data were found to be normally distributed and outliers were evaluated using Cook's D (Cook, 1979), no outliers were detected. Mean differences were separated using the PDIFF statement. Data reported are least-squared means with Standard Error of Mean (SEM). Significance was determined at $P \leq 0.05$ and tendencies determined when $0.05 < P \leq 0.10$.

3.4 RESULTS AND DISCUSSION

3.4.1 Plasma and Liver Mineral Concentrations

Liver mineral concentrations provide excellent evidence of the TM status of cattle because many minerals are stored over an extended period of time in the liver (McDowell, 2003). Liver stores contribute to mineral homeostasis by maintaining plasma mineral concentrations. Because plasma mineral concentrations stay relatively constant, unless liver mineral stores have been depleted (state of deficiency), plasma mineral concentrations are not an ideal measurement for mineral status. Based on liver TM concentrations, steers used in the present study were well within the range of adequacy for Cu, Zn, Mn and Se throughout the entire feeding period (Kincaid, 2000; Hansen et al., 2006).

Growing period plasma and liver mineral concentrations measured before initiation of the trial (d -5), 14 d after injection of SAL or ITM, and 5 days before the second injection (d 79) are presented in Table 2. Concentrations of Cu, Zn, Mn, and Se in plasma on d 14 and d 79 were not affected by treatment ($P \geq 0.30$). Trace mineral supplementation can produce varying responses on plasma mineral concentrations. Dietary Cu supplementation of 10 or 40 mg Cu/kg DM as $CuSO_4$ has been shown to increase plasma and liver Cu concentrations compared to steers that received 9.8 mg Cu/kg DM in a basal diet, on d 56 after the start of Cu supplementation through the end of the feeding period (Engle and Spears, 2001). Spears and Kegley (2002) also noted that additional Zn supplementation from various sources (ZnO and Zn proteinate at a rate of 25

mg Zn/kg DM) had no effect on growing (d 56) or finishing (d 140) phase plasma Zn concentrations. In contrast, Pogge et al. (2012) reported an increase in plasma Zn, Mn, and Se measured in Angus and Simmental steers over 15-d following the same TM injection used in the present study, at a rate of 2.22 mL/100 kg BW. Steers that received the ITM in the present study had greater liver Cu and Se concentrations on d 14 than steers in the SAL treatment group ($P \leq 0.01$) but there were no differences in liver Cu or Se concentrations between treatments on d 79 ($P \geq 0.17$). Steers that received the injectable TM tended to have greater liver Zn concentrations ($P = 0.07$) and had greater liver Zn concentrations on d 79 ($P = 0.03$); whereas, liver concentrations of Mn were similar among treatment groups ($P \geq 0.23$) on d 14 and d 79. Some have seen that injectable TM rapidly increases liver Cu and Se concentrations but liver Zn and Mn often vary (Arthington et al., 2014; Genther and Hansen, 2014b), likely because liver Zn and Mn are not consistently reflective of actual status of these two minerals, which are lacking good biomarkers (Kincaid, 2000). Interestingly, a TM injection given to Angus steers of a similar age caused an increase in liver Cu, Zn, Mn, and Se measured over 15 days after injection compared to a saline control treatment group when fed a corn-silage-based diet formulated to NRC (2000) TM recommendations (Pogge et al., 2012).

Plasma and liver mineral concentrations determined 5 d before the start of finishing (d 79) and 14 d after the injection at start of finishing (d 98) are presented in Tables 2 and 3, respectively. Similar to the growing period, plasma concentrations of all four minerals (Cu, Zn, Mn, and Se) were comparable among the four treatment groups ($P \geq 0.37$) 14 d post-injection (d 98). Similarly, Ahola et al. (2005) reported that dietary supplementation of organic and inorganic sources of Cu, Zn, and Mn did not increase

plasma Cu or Zn concentrations in growing and finishing feedlot steers. But the authors did note that liver Cu concentrations continued to increase throughout the feeding period with dietary supplementation. This would support the results of Pogge et al. (2012) suggesting that plasma TM concentrations are brought back to homeostatic concentrations by d 15 after a sharp increase in TM concentrations immediately following a TM injection. In this situation the evaluation of liver mineral concentrations may be more meaningful in determining the beef animals TM status.

Steers receiving ITM as the second injection had greater d 98 liver Cu and Se concentrations than those receiving SAL as the second injection, regardless of initial injection ($P \leq 0.02$). There were no differences ($P \geq 0.64$) in liver Zn and Mn concentrations among the treatment groups on d 98 of the finishing period. Liver Zn concentrations in response to TM injection have been variable. Pogge et al. (2012) found a slight increase in liver Zn concentrations based on repeated measures analysis of samples taken on d 1, 8, and 15 post TM injection in beef steers. In contrast with the current study, the dietary supplementation of Mn at rates ranging from 10 to 240 mg Mn/kg DM linearly increased liver Mn concentrations with the increasing inclusion of Mn in the diet (Legleiter et al., 2005). Trace mineral injections also increased liver Cu, Zn, and Se concentrations in non-implanted Angus beef steers not fed beta-agonists on TM adequate and TM deficient finishing diets (Genther and Hansen, 2014b). Similar to the present study, Genther and Hansen (2014b) also noted that TM injection had no effect on liver Mn concentrations determined 15 d post-TM injection.

3.4.2 Intake and Growth Performance

Natural cattle are at a disadvantage for growth rates and efficiency because producers are unable to utilize conventional technologies such as ionophores, steroid implants or beta-adrenergic agonists. This disadvantage was well demonstrated by Maxwell et al. (2015) where cattle grown in the natural program had lesser final BW, ADG, and G:F compared to cattle raised in conventional systems. Previous literature has shown improvements in finishing period growth performance, ribeye area, and marbling scores of non-implanted, mildly TM deficient steers treated with Multimin90 at a similar does to that used in the present study (Genther and Hansen, 2014a). Research has also indicated that growth responses from dietary TM supplementation or TM injections are more evident when cattle are mildly or severely TM deficient (Ahola et al., 2005), demonstrating that TM status is a very important factor in the response to supplementation.

There were no differences due to initial ITM or SAL injection on BW, ADG, DMI, or G:F ($P \geq 0.17$; Table 4) measured over the 56 d growing period. Based on repeated measures analysis during the finishing period (d 84 to 161; Table 5) there were no treatment × day effects ($P \geq 0.13$) on BW, DMI or G:F parameters. There was a treatment × day interaction for ADG ($P = 0.01$), where ADG was similar across treatments from d 84 to 113, and was greatest in SAL/SAL cattle between d 113 and 140; however, cattle receiving ITM for the whole trial (ITM/ITM) had the greatest ADG in the final 21 days of the feeding period (d 140 to 161) ($P = 0.01$). Ending BW (d 160, 161) represent consecutive pre-feeding weights, but d 113 and 140 weights were single day pre-feeding weights and therefore treatment differences may be due to slight variation in gut fill of the steers. Based on repeated measures analysis of finishing period performance DMI tended

to be different due to treatment (*P* = 0.07). This was driven by steers in the SAL/SAL group having greater DMI than ITM/SAL and ITM/ITM steers, while not being different from SAL/ITM during this period.

Trace mineral supplementation also has varying effects on cattle growth performance depending on the TM concentration of the basal (control) diet and initial TM status of cattle. Zinc supplementation in the form of zinc proteinate or zinc oxide to a Zn adequate diet increased growing phase ADG of Angus and Hereford × Angus beef steers but had no effect on DMI or G:F (Spears and Kegley, 2002). In basal diets containing 9.8 mg Cu/kg DM during the growing phase and 5.1 mg Cu/kg DM during the finishing phase, supplementing with 10 or 40 mg Cu/kg DM from $CuSO_4$ resulted in no additional performance effects on BW, ADG, DMI and G:F of beef steers (Engle and Spears, 2001). Dietary mineral antagonisms can also affect the growth of ruminants if TM status is sufficiently suppressed. For example, Cu supplementation as Cu sulfate or Cu glycinate at 5 or 10 mg/kg (basal diet containing 8.2 mg of Cu/kg of DM) to Angus and Angus × Simmental steers (277 kg) increased final BW, ADG, and G:F with a tendency to increase DMI when fed a diet also supplemented with 2 mg of Mo/kg of DM and 0.15% S for 120 days and increased to 6 mg of Mo/kg of DM for an additional 28 days (Hansen et al., 2008).

Along with dietary antagonisms, the animals' previous TM status cannot be overlooked when evaluating growth parameters. Engle et al. (1997) found that upon arrival to the feedlot, heifers that were given a Zn depletion diet for 22 days, had lesser ADG and G:F than their counterparts on a Zn adequate diet. When those Zn deficient heifers were supplemented with Zn methionine at a rate of 23 mg Zn/kg DM, feed

efficiency increased to match the Zn adequate counterparts in 3 days after being fed a repletion diet (Engle et al., 1997). Again, performance response to TM supplementation is strongly dependent on the animal's initial status. It has been observed in multiple experiments that animals with adequate Zn status may not have a positive performance response in the feedlot with increased Zn supplementation (Malcolm-Callis et al., 2000 and Gunter et al., 2001). Supplementation of Mn in addition to a growing phase diet containing 29.2 mg of Mn/kg and finishing phase diet containing 8.1 mg of Mn/kg, had little effect on growing or finishing ADG, DMI or G:F (Legleiter et al., 2005). A TM injection given to TM deficient steers two days after transit stress increased DMI and ADG during the subsequent finishing period, but had no affect on ADG of TM adequate steers (Genther and Hansen, 2014a). In another study, Genther-Schroeder and Hansen (2015) found that TM injection had no effect on growing period performance when the injection was given 28 d before a transit stress, in steers that had excellent TM status before injection. It is evident that an animals' response to TM supplementation can be affected by a number of factors including breed, environmental and immune stress, and previous TM status.

3.5 IMPLICATIONS

Trace minerals are essential to support beef cattle growth. Because producers rarely know the TM status of cattle that are entering the feedlot, injectable TM are a viable option to improve the TM status of beef steers to support growth and proper immune function, and prevent the negative consequences of TM deficiency. Representative steers in each treatment group in the present study were well within the range of adequacy for Cu, Zn, Mn, and Se throughout the entire feeding period (Kincaid, 2000; Hansen et al.,

2006). A limited need to improve TM status of steers in the present study may explain why no performance differences were observed due to TM injection. Further research is needed utilizing cattle with varying TM status in order to determine the impact of TM status on growth performance of cattle fed in a natural program.

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Table 1. Composition of growing and finishing diets fed to beef steers raised in a natural feedlot program.

Item	Experimental period[1]	
Ingredient (% DM)	Growing	Finishing[2]
Corn silage	50	-
Cracked corn	15	60
DDGS[3]	33.09	3.09
MDGS[4]	-	25
Bromegrass hay	-	10
Limestone	1.47	1.47
Salt	0.31	0.31
Vitamin A premix[5]	0.11	0.11
Trace mineral premix[6]	0.024	0.024
Calculated composition		
CP, %	14.79	15.20
NDF, %	32.33	20.36
Ether extract, %	5.47	5.46
Se, mg/kg DM	0.15	0.15
Analyzed,[7] mg/kg DM		
Cu	12.1	11.1
Fe	89.3	75.2
Mn	33.6	31.9
Zn	53.0	58.0

[1] The growing period diet was fed d -9 through 56, three step up diets were fed from days 57 through 83, and the finishing diet was fed d 84 through 162.
[2]Bovamine Defend top-dressed during days 113 through 162 at a rate of 1 $g \cdot steer^{-1} \cdot d^{-1}$, along with 0.08 kg of dried distillers grains with solubles (DDGS) as a carrier.
[3] Dried distillers grains with solubles.
[4] Modified distillers grains with solubles.
[5] Vitamin A premix contained 4,400,000 IU vitamin A/kg.
[6] Provided per kg of diet DM: 10 mg Cu (copper sulfate), 30 mg Zn (zinc sulfate), 20 mg Mn (manganese sulfate), 0.10 mg Se (sodium selenite), 0.1 mg Co (cobalt carbonate), 0.5 mg I (calcium iodate).
[7] Analyzed mineral values reflect diet total, including supplemental mineral.

Table 2. Effects of saline or trace mineral injection on growing period plasma and liver mineral concentrations of beef steers raised in a natural feedlot program.

	Treatment[1]			*P* - value
Item	SAL	ITM	SEM	Treatment
Plama[2]				
Cu, mg/L				
d -5	0.94	0.96	--	--
d 14	0.91	0.90	0.039	0.93
d 79	0.88	0.88	0.038	0.96
Zn, mg/L				
d -5	0.94	1.07	--	--
d 14	1.09	1.13	0.037	0.50
d 79	0.99	0.99	0.036	0.98
Mn, µg/L				
d -5	2.79	2.86	--	--
d 14	4.53	4.51	0.688	0.99
d 79	3.42	3.39	0.324	0.95
Se, µg/L				
d -5	94.1	100.1	--	--
d 14	103.6	109.0	3.57	0.30
d 79	107.0	110.2	2.73	0.41
Liver, mg/kg DM[2]				
Cu				
d -5	151.6	164.7	--	--
d 14	159.7	190.9	7.13	0.01
d 79	206.6	230.8	12.91	0.21
Zn				
d -5	100.4	103.3	--	--
d 14	98.8	111.2	4.50	0.07
d 79	85.5	94.1	2.54	0.03
Mn				
d -5	8.48	8.14	--	--
d 14	7.86	8.41	0.459	0.42
d 79	8.13	8.80	0.375	0.23
Se				
d -5	1.62	1.63	--	--
d 14	1.78	2.82	0.141	<0.0001
d 79	2.11	2.27	0.078	0.17

[1] Treatment groups: d 0 Saline (SAL; n = 14) and d 0 Multimin90 (ITM; n = 14).
[2] Plasma and liver mineral concentrations from d -5 used as a covariate in d 14 and d 79 analyses. Day -5 values are shown for reader reference only.

Table 3. Effects of saline or trace mineral injection on finishing period plasma and liver mineral concentrations of beef steers raised in a natural feedlot program.

	Treatment[1]					*P* - value
	SAL/SAL	SAL/ITM	ITM/SAL	ITM/ITM	SEM	Treatment
Plama[2,3]						
Cu, mg/L						
d 79	0.91	0.85	0.93	0.84	--	--
d 98	0.89	0.85	0.90	0.92	0.061	0.88
Zn, mg/L						
d 79	1.03	0.94	1.01	0.98	--	--
d 98	0.95	0.98	1.09	1.05	0.065	0.48
Mn, µg/L						
d 79	3.58	3.20	3.72	3.05	--	--
d 98	3.69	5.03	4.22	3.89	0.558	0.44
Se, µg/L						
d 79	106.4	107.7	110.8	109.8	--	--
d 98	104.9	128.9	122.3	118.5	8.68	0.37
Liver, mg/kg DM[2,3]						
Cu						
d 79	187.8	224.0	234.2	234.8	--	--
d 98	191.5[b]	274.2[a]	204.2[b]	261.0[a]	19.65	0.02
Zn						
d 79	82.6	88.3	98.4	90.6	--	--
d 98	83.3	89.0	88.4	91.7	4.69	0.64
Mn						
d 79	8.07	8.23	8.14	9.32	--	--
d 98	7.67	8.13	7.44	8.15	0.516	0.70
Se						
d 79	2.22	1.98	2.23	2.31	--	--
d 98	1.94[b]	3.16[a]	1.79[b]	3.08[a]	0.124	<0.0001

[a,b] Means within a row, with unlike superscripts differ ($P \leq 0.05$).

[1] Treatment groups: d 0 Saline, d 84 Saline (SAL/SAL; n = 7), d 0 Saline, d 84 Multimin90 (SAL/ITM; n = 7), d 0 Multimin90, d 84 Saline (ITM/SAL; n = 7) and d 0 Multimin90, d 84 Multimin90 (ITM/ITM; n = 7).
[2] Plasma and liver mineral concentration from d -5 used as a covariate in d 98 analyses. Day 79 values are shown by treatment for reader reference only as the second injection had not yet been given at this time.
[3] Day 79 was 5 d before to the second injection, with d 98 being 14 d post second injection.

Table 4. Effects of saline or trace mineral injection at start of growing period on growth and efficiency of beef steers raised in a natural feedlot program.

	Treatment[1]			*P* - value
	SAL	ITM	SEM	Treatment
Initial BW d 0, kg[2,3]	358	358	1.5	0.96
Final BW d 56, kg[2,3]	433	434	1.5	0.76
ADG, kg/d[2,3]	1.33	1.35	0.02	0.65
DMI, kg/d[4]	8.91	8.60	0.156	0.18
G:F[4]	0.109	0.103	0.0030	0.22

[1] Treatment received on d 0, Saline (SAL) or Multimin90 (ITM).
[2] A 4% pencil shrink was applied to all live BW measures as well as in the calculation of ADG and G:F.
[3] Steer was experimental unit, n = 83 per treatment.
[4] Pen was experimental unit, n = 7 per treatment.

Table 5. Effects of saline or trace mineral injection at start of the growing and finishing periods on finishing growth performance and efficiency of beef steers raised in a natural feedlot program.

	Treatment					*P* - value		
Item[2]	SAL/SAL	SAL/ITM	ITM/SAL	ITM/ITM	SEM	Treatment	Day	Treatment x Day
BW, kg[3]					4.1	0.14	<0.0001	0.99
Day 84	483	482	479	479				
Day 113	528	529	523	526				
Day 140	577	573	569	568				
Day 161	600	596	592	594				
Mean BW[3]	547	545	541	542				
ADG, kg/d[3]					0.033	0.77	<0.0001	0.01
Day 84 to 113	1.57	1.63	1.53	1.62				
Day 113 to 140	1.79^{a}	1.63^{ab}	1.70^{a}	1.55^{b}				
Day 140 to 161	1.12^{ab}	1.10^{b}	1.14^{ab}	1.27^{a}				
Mean ADG[3]	1.50	1.45	1.46	1.49				
DMI kg/d[5]					0.099	0.07	<0.0001	0.99
Day 84 to 113	11.96	11.86	11.63	11.67				
Day 113 to 140	11.61	11.41	11.19	11.13				
Day 140 to 161	11.22	11.14	11.01	11.06				
Mean DMI[4]	11.60	11.47	11.28	11.29				
Gain:feed[5]					0.0036	0.68	<0.0001	0.13
Day 84 to 113	0.132	0.138	0.131	0.139				
Day 113 to 140	0.154	0.143	0.152	0.139				
Day 140 to 161	0.010	0.099	0.103	0.115				
Mean Gain:Feed[4]	0.129	0.127	0.129	0.132				

[a,b] Means within a row, with unlike superscripts differ ($P \leq 0.05$).

[1] Treatment groups: d 0 Saline, d 84 Saline (SAL/SAL; n = 7), d 0 Saline, d 84 Multimin90 (SAL/ITM; n = 7), d 0 Multimin90, d 84 Saline (ITM/SAL; n = 7) and d 0 Multimin90, d 84 Multimin90 (ITM/ITM; n = 7). Day 84 was the start of finishing period diets and when steers received the second injection. On day 161 steers were harvested.

[2] A 4% pencil shrink was applied to all live BW measures was well as in the calculation of ADG and G:F.

[3] Steer was experimental unit, n = 40 per treatment (SAL/ITM and ITM/SAL) and n = 42 per treatment (SAL/SAL and ITM/ITM).

[4] Overall means from repeated measures analysis.

[5] Pen was experimental unit, n = 7 per treatment.

CHAPTER IV

EFFECT OF VARYING TRACE MINERAL SUPPLEMENTATION OF STEERS WITH OR WITHOUT HORMONE IMPLANTS ON GROWTH AND CARCASS CHARACTERISTICS

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4.1 Abstract

To determine the effects of trace mineral supplementation and hormone implant strategy on growth and carcass characteristics of cattle, 72 Angus-cross steers (388 ± 17 kg) were blocked by BW (6 steers per pen) to a 2 × 3 factorial. Factors included growth stimulating implant (**GS**): d 0 with Component TE-IS, reimplanted d 56 with Component TE-200 (**IMP**) or no implant (**NoIMP**), and TM supplementation (**TM**): no supplemental TM (**CON**), TM supplemented at 2016 National Academies of Engineering, Science, and Medicine requirements of 10 Cu, 30 Zn, 20 Mn, 0.10 Se, 0.15 Co, and 0.50 I (mg/kg; **REQ**), or TM supplemented at feedlot consultant recommendations of 20 Cu, 100 Zn, 50 Mn, 0.30 Se, 0.20 Co, and 0.50 I (mg/kg; **IND**). Steers received a finishing diet for 124 d in GrowSafe bunks and were harvested on d 125. Data were analyzed in SAS as a 2 × 3 factorial with the fixed effect of block, and steer as experimental unit (n = 12 per combination). Day -7 liver trace mineral concentrations were used as a covariate in analysis. There were no GS × TM effects for liver Zn, Mn, Se, or Co ($P \geq 0.11$) on d 70 or 125. IMP steers had lesser liver Cu and Mn on d 70 ($P \leq 0.05$) on d 125 compared to NoIMP. There was a GS × TM interaction for liver Cu on d 125 ($P = 0.05$) where IMP/REQ, IMP/IND, and NoIMP/REQ had greater liver Cu than NoIMP/CON which had greater liver Cu than IMP/CON. There was a TM effect for liver Cu on d 70 ($P <$ 0.0001) with IND having greater liver Cu than REQ and CON. There was a TM effect (P ≤ 0.01) for liver Mn and Se on d 70 where IND had greater Mn and Se than CON, with REQ being intermediate. There was a TM effect ($P = 0.001$) on liver Mn on d 125 where IND had greater liver Mn than CON and greater ($P < 0.0001$) liver Se than CON and REQ on d 125, while d 125 liver Se was greater in REQ vs. CON. Implanted steers had

greater ($P < 0.0001$) DMI, final BW, overall ADG, G:F, and HCW than NoIMP. Overall DMI was affected by TM ($P < 0.0001$) with REQ and IND being greater than CON. There was a TM effect for carcass adjusted final BW, ADG, and DMI ($P \geq 0.03$) and a tendency for TM to affect adjusted G:F ($P = 0.07$). There was a TM effect ($P = 0.03$) for HCW where IND was greater than CON and REQ. There was a GS × TM ($P = 0.02$) for ribeye area; within IMP, CON were greater than IND, and REQ were intermediate while NoIMP had smaller ribeye area, regardless of TM supplementation. These data indicate REQ trace mineral recommendations might not be adequate for finishing beef steers, irrespective of hormone implant administration.

Key words: beef, implant, trace mineral

4.2 Introduction

Hormone implants can increase the profit returns on finished cattle (Duckett and Pratt, 2014) because of the improved growth rate and feed efficiency commonly seen with combination implants (Bartle et al., 1992; Johnson et al., 1996). With increases in cattle growth rates, supply of critical nutrients such as trace minerals to support growth and development of feedlot animals may need to be increased. Copper and Mn are vital for the development of bone and cartilage (Liu et al., 1994; Suttle, 2010) while Zn plays a role in cell signaling and proliferation (Beyersmann and Haase, 2001). Some selenoproteins function in muscle (Beckett and Arthur, 2005) and both Se and I influence thyroid hormones and subsequently cellular metabolism (Meyer et al., 2008). An essential component of vitamin B_{12}, Co supports propionate metabolism and plays a role in the transfer of methyl groups (Suttle, 2010).

Current trace mineral recommendations are concentrations shown to prevent symptoms of trace mineral deficiency (NAESM, 2016). It is common among consulting feedlot nutritionists to recommend supplementing 125 to 300% of NRC recommended trace mineral concentrations (Samuelson et al., 2016). Unfortunately, very little work has examined these industry recommendations vs. the well accepted national recommendations (Berrett et al., 2015). It is possible that with the superior growth rates resulting from implant utilization there could be a need for increased trace mineral supplementation to the support the muscle and frame growth in feedlot steers. There has been limited research examining the interactions between trace mineral supplementation and hormone implants on cattle performance or mineral status. Therefore, the objective of this study was to determine the effects of national recommendations or industry concentrations of supplemental trace mineral to feedlot steers not receiving hormone implants or receiving a high potency implant strategy on steer growth, carcass performance and mineral status.

4.3 Materials and Methods

All live animal procedures and protocols for this experiment were approved by the Iowa State University Institutional Animal Care and Use Committee (#6-16-8302-B).

4.3.1 Animals and Experimental Design

Seventy-two Angus-cross, black hided beef steers (389 ± 17.2 kg) were utilized in a 2 × 3 factorial design experiment conducted at the Iowa State University Beef Nutrition Research Center in Ames, IA. Following arrival to the research facility cattle were dewormed with Eprinex (Merial Limited, Duluth, GA) and given unique visual and

electronic identification tags. Upon arrival cattle were fed a 40% cracked corn, 30% hay, 25% MDGS, and 5% supplement diet for 7 days. Steers were transitioned over 21 days to a corn-based finishing diet, described in **Table 1**. Nine days prior to the start of the experiment steers were moved to new pens and allowed to adapt to eating out of GrowSafe bunks. On day -1 and 0, steers were weighed and blocked by initial BW into 12 pens containing 6 steers per pen. Pens of steers were assigned to a 2 × 3 factorial, factors included growth stimulating implant (**GS**): either implanted (**IMP**, n = 36 steers) or not (**NoIMP**, n = 36 steers**),** and dietary trace mineral (**TM**) supplementation. The TM treatments included: 1) **CON** that received no additional trace mineral supplementation, 2) **REQ** that received NAESM (2016) recommendations for Cu, Zn, Mn, Se, Co, and I from all inorganic sources, and 3) **IND** which received the mode value from the Samuelson et al. (2016) feedlot consulting nutritionist survey for Cu, Zn, Mn, Se, Co, and I from all inorganic sources. This resulted in six total treatments: **NoIMP/CON, NoIMP/REQ, NoIMP/IND, IMP/CON, IMP/REQ**, and **IMP/IND** with 12 steers per treatment combination. In addition to initial weights, steers were weighed on d 28, 56, 70, 84, along with day 123 and 124 to determine final BW. On d 0 IMP steers received a Component TE-IS implant (16 mg estradiol and 80 mg trenbolone acetate, Elanco Animal Health, Indianapolis, IN) and were reimplanted with Component TE-200 (20 mg estradiol and 200 mg trenbolone acetate, Elanco Animal Health) on d 56. A 4% pencil shrink was applied to all live BW measures, including those used to calculate ADG and G:F. Because individual intake was recorded all performance measures are on an individual steer basis. On day 124, steers were shipped to a commercial abattoir in Tama, IA (Iowa Premium Beef), steers were harvested on d 125 and HCW was collected. After

a 48 h chill, marbling score (MS), quality grade (QG), ribeye area (REA), backfat (BF), and KPH data were collected. Yield grade and dressing percent was calculated based on carcass parameters collected (USDA, 2016). The carcass adjusted performance data calculation of final BW was determined by dividing HCW by the average dressing percentage of 64.66% and overall ADG and G:F were calculated.

4.3.2 Sample Collection and Analytical Procedures

Cattle were delivered feed daily at approximately 0800 hours with ad libitum access to both feed and water. Ingredient and total mixed ration (TMR) samples were taken weekly to determine DM content. These samples were dried in a forced air oven at 70°C for 48 hours. Dried feed samples were then ground through a 2-mm screen (Retsch Zm100 grinder; Glen Mills Inc., Clifton, NJ). Total mixed ration samples were composited by diet within implant period for determination of trace mineral concentrations. Composited feed samples were acid digested using trace metal grade nitric acid (Fisher Scientific, Fair Lawn, NJ) before trace mineral analysis. Three steers per pen were randomly selected for liver and blood sample collection (n = 6 per treatment) to evaluate trace mineral status with the same steers used throughout the study. Liver biopsies were collected 2 h post feeding before the start of the trial (d -7), 14 days after reimplantation (d 70) and liver samples were collected immediately after harvest at the abattoir (d 125). Liver biopsies were collected using the method described by Engle and Spears (2000) and samples were dried in a forced-air oven at 70°C for 7 days. Dried liver samples were acid digested (CEMS MARSXpress, Matthews, NC) with trace mineral grade nitric acid prior to mineral analysis. Feed and liver samples were analyzed for Ca, Cu, Fe, Mg, Mn, Mo, P, K, Se, and Zn using inductively coupled plasma mass

spectrometry (ICP-MS, Analytik Jena Inc. Woburn, MA, USA) in CRI mode with hydrogen as the skimmer gas. Briefly, samples were diluted in 1 % nitric acid, mixed and analyzed by ICP-MS. For quality control, Bi, Sc, In, Li, Y, and Tb were used as internal standards for the ICP-MS. A bovine National Institute of Standards and Technology (NIST) liver sample (US Department of Commerce, Gaithersburg, MD) was used to verify instrument accuracy.

Blood samples were collected on day -1, 70, and 124 into vacutainer tubes containing potassium EDTA or heparin (Becton Dickenson, Rutherford, NJ) prior to feeding. Samples were kept on ice and transported to the laboratory where they were centrifuged at 1,000 × g for 12 minutes at 4°C. Plasma was removed and stored at -80°C until further analysis. Plasma samples were analyzed for glucose according to commercial kit protocols, Wako Autokit Glucose (Wako Pure Chemical Industries, Ltd., Chuo-Ku Osaka, Japan) with an intra-assay CV less than 10% and inter-assay CV of 9.1%. Plasma samples were also analyzed for plasma urea nitrogen (PUN) according to commercial kit protocols, Urea Nitrogen Reagent (Colorimetric Method, Teco Diagnostics, Anaheim, CA) with an intra-assay CV less than 10% and inter- assay CV of 8.3%.

4.3.3 Economic Analysis

Total cost, income, profit, breakeven selling price for variable costs, and breakeven selling price for all costs were collected for steers in this experiment. Budget was utilized from Iowa State University Extension and Outreach Ag Decision Maker File B1-21. Yearling steer purchase price was acquired from the Iowa feeder cattle combined auction the week of August 15, 2016. Feed ingredient prices were averaged from Iowa

markets during the time steers were on feed. Fed cattle value pricing was obtained from USDA AMS National Weekly Direct Slaughter Cattle – Premiums and Discounts (LM_CT155) and grid pricing from USDA AMS 5-Area Weekly WTD Average Direct Slaughter Cattle – Premiums and Discounts (LM_CT169). Interest rates on feeder cattle and variable costs were averaged interest rates from 2012-2016 from the Federal Reserve Bank of Chicago. All costs were held constant among treatments with only the cost of hormone implants and mineral supplementation different among treatments.

Statistical Analysis

Data were analyzed as a 2 × 3 factorial using the MIXED procedure of SAS 9.4 (SAS Inst. Inc., Cary, NC). Animals were assigned to treatments using a completely randomized block design. Fixed effects included block, GS, TM, and GS × TM. The experimental unit for all data was steer (n = 12 per treatment for performance and carcass data except NoIMP/REQ where n = 11; for blood and liver data n = 6 for all treatments except IMP/IND where n = 5). Average daily gain, DMI and G:F were summarized by implant period. Liver mineral from d -7 and plasma glucose and PUN from d -1 served as covariates in analysis. Data were found to be normally distributed and outliers were evaluated using Cook's D. Data from one steer were not included in the statistical analysis due to poor overall performance (from NoIMP/REQ treatment). Data reported are LSMEANS with SEM. Significance was determined at $P \leq 0.05$ and tendencies determined when $0.05 < P \leq 0.10$.

4.4 Results

4.4.1 Live and carcass-adjusted animal performance

Live animal performance data are exhibited in **Tables 2, 3, and 4**. Day 56 BW tended to be (P = 0.10) and d 0-56 ADG was (P = 0.05) affected by the GS × TM interaction, where within IMP, values for steers receiving REQ or IND were greater than CON, all IMP treatments were greater than NoIMP, and no TM effect was noted within NoIMP steers. Steers receiving growth-stimulating implants had greater final BW on d 124 than NoIMP steers (P < 0.0001). There were no GS × TM on d 0 – 56 DMI or G:F (P ≥ 0.16). Day 0 – 56 DMI and G:F was greater in implanted steers than non-implanted steers (P ≤ 0.01). Trace mineral had no effect on d 0 – 56 G:F (P = 0.12). There were no GS × TM interactions for d 56-124 performance or DMI (P ≥ 0.13) or overall BW, ADG, DMI, or G:F (P ≥ 0.66). Day 56 – 124 ADG, DMI, final BW, as well as overall ADG, DMI, and G:F was greater in IMP steers than NoIMP steers (P ≤ 0.03). There was a tendency for trace mineral supplementation to increase overall live ADG (P = 0.07). Trace mineral supplementation also increased d 56 – 124 and overall DMI (P ≤ 0.004). Trace mineral had no effect on d 56 -124 ADG, d 56 – 124 G:F , or overall G:F (P ≥ 0.12).

There were no GS × TM interactions for carcass adjusted live animal performance (P ≥ 0.60). There was a GS effect on carcass adjusted final BW, ADG, and G:F (P < 0.0001), where growth stimulating implants increased these measures over NoIMP. Trace mineral supplementation affected carcass adjusted final BW and ADG (P ≤ 0.03) and tended to effect G:F (P = 0.07). Steers in the IND treatment had greater final BW than

CON steers, with REQ being intermediate, while IND had greater carcass adjusted overall ADG than both REQ and CON steers (*P* = 0.005).

4.4.2 Plasma glucose and urea nitrogen

Plasma glucose and urea nitrogen data are reported in **Table 5**. There were no GS × TM interactions for plasma glucose on d 70 ($P = 0.79$). There was a tendency for a GS × TM effect on d 124 for plasma glucose concentrations ($P = 0.06$) with NoIMP/REQ tending to have greater plasma glucose concentrations than NoIMP/IND will all other treatments intermediate. There was no GS × TM effect for PUN on d 70 or 124 ($P \geq 0.85$). On d 70 steers that received implants had lesser PUN than cattle that did not receive hormone implants, 8.31 and 9.68 mg/dL for implanted and nonimplanted steers, respectively ($P = 0.03$). There was no effect of implant on d 124 ($P = 0.74$), nor was there any effect of TM supplementation on PUN on d 70 or 124 ($P \geq 0.22$).

4.4.3 Liver Mineral Status

There were no GS × TM effects for liver Cu, Zn, Mn, Se, or Co concentrations ($P \geq 0.11$) on d 70 or 124; main effects of GS and TM are shown in **Tables 6** and **7**, respectively. There was no main effect of GS or TM on liver Zn concentrations on d 70 ($P \geq 0.53$). Steers that did not receive implants had greater liver Cu and Mn concentrations on d 70 ($P \leq 0.05$) and lesser liver Zn concentrations ($P = 0.01$) on d 124, compared with IMP steers. On d 70 steers in the IND treatment had greater liver Cu concentrations than REQ and CON ($P < 0.0001$). There was a TM effect ($P \leq 0.01$) on d 70 liver Mn and Se where IND steers had greater liver Mn and Se concentrations than CON ($P \leq 0.01$), with REQ intermediate. There was also a TM effect ($P = 0.02$) on d 70 for liver Co concentrations where REQ steers had greater liver Co concentrations than

CON, with IND intermediate. On d 124 IND steers had greater liver Cu concentrations than CON, with REQ intermediate ($P < 0.0001$). Steers receiving REQ had greater liver Zn concentrations than CON with IND being intermediate on d 124. IND and REQ had greater liver Mn and Co concentrations than CON on d 124 ($P \leq 0.001$). Steers receiving IND had greater liver Se concentrations than REQ and REQ steers had greater liver Se than CON steers on d 124 ($P < 0.0001$).

4.4.4 Carcass Characteristics

There was no GS × TM for HCW ($P = 0.93$). Implants increased HCW by 10.5% compared to non-implanted steers ($P < 0.0001$; **Figure 1a**). There was also a TM effect ($P = 0.03$; Figure **1b**) where IND steers had greater HCW than REQ and CON steers. Carcass characteristics are described in **Table 8**. There were no GS × TM interactions, or main effects of GS or TM for dressing percent, KPH, BF, or marbling score ($P \geq 0.13$). There was a GS × TM ($P = 0.02$) for ribeye area with IMP/CON being greater than IMP/IND, with IMP/REQ intermediate; NoIMP had smaller ribeye area, regardless of TM supplementation. There was also a GS × TM for yield grade with NoIMP/IND steers having a greater yield grade than NoIMP/REQ and IMP/CON with all other treatments intermediate ($P = 0.02$). There was no GS × TM effect on quality grade distribution ($P \geq 0.48$; **Table 8**). There were also no main effects of GS or TM on quality grade distribution of steers ($P \geq 0.18$).

4.4.5 Economic Analysis

The variable cost, revenue, profit, and breakeven calculations for the present study are outlined in **Table 9**. In the present study IMP/REQ and IMP/IND were the only treatments that resulted in a profit ($89.44/steer and $142.67/steer for IMP/REQ and

IMP/IND, respectively). Hormone implants decreased the breakeven selling price for all cost by $0.13/pound. Within implanted steers, supplementing IND concentrations of trace minerals decreased the breakeven selling price for all cost by $0.21/pound compared to CON. Within non-implanted steers, supplementing IND concentrations of trace minerals decreased the breakeven selling price for all cost by $0.07/pound compared to CON.

4.5 Discussion

Implantation is a common practice in the beef industry through all stages of production. Combination hormone implants can increase growth rates by 20% and improve feed efficiency by 15%, compared to cattle not receiving hormone implants (Schanbacher, 1984; Bartle et al., 1992; Johnson et al., 1996). The effects of implants on live and carcass adjusted animal performance in the present study are consistent with previous literature where implanted cattle have greater growth and improved feed efficiency compared to cattle not receiving implants (Johnson et al., 1996; Sawyer et al., 2003). Because of the increase in protein accretion and frame size caused by implants it is critical to supply cattle with adequate nutrients to support optimal growth. Along with macronutrients, micronutrients like trace minerals are essential for growth of beef animals.

In the first 56 days steers that received a moderate potency combination implant (16 mg estradiol + 80 mg TBA) had greater ADG than non-implanted steers, and ADG was further improved by trace mineral supplementation within implanted steers. As expected growth rates were greatly increased due to implant (27% increase during d 0 –

56 and a 25% increase during d 56 – 124). Within the first 56 days trace mineral supplementation more dramatically affected growth rates in implanted cattle compared to those that were not implanted, as shown by the 20% improvement in ADG between IMP and NoIMP CON vs. the 30% improvement in ADG between IMP and NoIMP trace mineral supplemented steers (REQ and IND). The added growth response could be due to a greater need for trace minerals to support growth processes in implanted steers, as the CON diet was marginally deficient in Cu, Zn, Mn and Co.

Blood and liver samples were collected on d 70, fourteen days after reimplantation, because others have suggested that circulating estradiol and TBA concentrations increase rapidly in the days immediately following implantation (Parr et al., 2014) and thus this may be a time of greater need for nutrients to support the rapid growth that accompanies peak circulating hormone concentrations. Similar to the work by others who have shown PUN to decrease after implantation (Heitzman et al., 1997; Loy et al., 1988; Parr et al., 2014), d 70 PUN was lesser in IMP vs. NoIMP steers, suggesting a greater incorporation of N into muscle. In the present study implanted steers had decreased Cu and Mn concentrations in the liver 14 days after reimplantation (d 70), possibly exhibiting the increased need for those minerals to support growth. Copper and Mn exert their roles in growth through the formation of cartilage and the support of the extracellular matrix (Leach and Harris, 1997; Rucker et al., 1998).

One of the earliest examinations of the impact of growth stimulating implants on trace mineral metabolism was conducted by Hufstedler and Greene (1995) in lambs. Lambs implanted with 12 mg of zeranol tended to retain greater concentrations of Zn and had lesser fecal excretion of Mn and Cu compared to non-implanted lambs (Hufstedler

and Greene, 1995), suggesting that trace mineral requirements may be altered when implants are administered to support the demand for increased tissue growth. In the present study a trace mineral response was observed in HCW, increasing with trace mineral supplementation regardless of implant status. Within non-implanted steers, IND steers had a 13 kg advantage in HCW over CON, and within implanted steers, IND steers had a 17 kg advantage in HCW over CON. As the mechanisms by which hormone implants influence cattle growth become better understood, it is possible to see how many trace minerals may support these processes. For example, Zn is essential for nucleic acid and protein synthesis (Hambidge et al., 1986) and increases production of IGF-1 and epidermal growth-factor receptors in cell signaling pathways (Beyersmann and Haase, 2001). Zinc is also a cofactor for metalloproteinases 2 and 9 (McCall et al., 2000), which are thought to increase the rate of proliferation in bovine satellite cells (Thornton et al., 2015).

The CON diet in the present study was deficient in Co, but appeared to be adequate in Se (NAESM, 2016). Cobalt exerts its role in biology as a component of vitamin B_{12}, supporting propionate metabolism and the transfer of methyl groups (Suttle, 2010), which may be necessary to support muscle cell growth. Selenium also plays a role in the growth and development of animals through selenoproteins, which assist in combating oxidative stress and increasing proliferation of muscle tissue, and through the conversion of the less active T4 to the more active T3 (Wichtel, 1998; Suttle, 2010). No research examining the effect of dietary I on implant-induced growth has been reported but, because I is needed for the formation of thryroid hormones (Meyer et al., 2008) which play a role in the transcription of the growth hormone gene (Koenig et al., 1987), a

case could be made for the importance of I in support of growth. Kahl et al. (1978) noted that a Synovex-S implant (20 mg estradiol benzoate and 200 mg progesterone) decreased the T_4:T_3 ratio when measured 60 and 120 days after implantation. This would suggest estrogen is increasing thyroid hormone concentration (Kahl et al., 1978) and subsequently, may also be increasing the steer's requirement for trace minerals, particularly Se and I.

The supplementation of trace minerals to steers in the present study increased liver Cu, Mn, Se, and Co on d 70 and Cu, Zn, Mn, Se, and Co on d 125 of the present experiment. However, CON steers were considered to have adequate status for all minerals examined in this study (Kincaid, 1999; Hansen et al., 2006; NAESM, 2016). The degree of increasing concentrations of trace minerals in the liver in response to supplementation varies, even though for most trace minerals liver is the best indicator of status (Kincaid, 1999). Interestingly, when Berrett et al. (2015) implanted steers with Revalor-XS (40 mg estradiol and 200 mg TBA) and supplemented trace minerals at concentrations similar to those used in the present study (no supplemental trace mineral, NRC (1996) recommendations, or consultant recommendations) to steam-flaked corn-fed feedlot steers, authors did not observe an increase in the concentrations of liver Cu, Mn, or Zn at slaughter. In contrast, in the present study IND supplemented steers displayed greater liver Cu and Zn than CON, and both REQ and IND had greater liver Mn than CON at slaughter. A discrepancy in the response of Zn in the liver may also be contributed to the idea that because Zn is involved in over 300 enzymes (Suttle, 2010) an accurate biomarker to reflect Zn status has yet to be identified. Overall, there is limited understanding of the concentrations of trace minerals in cattle tissues necessary to

support optimal growth, and further refinement beyond a simple definition of deficient, adequate, or toxic, is needed.

The lack of an implant effect on quality grade distribution in this experiment can likely be attributed to the cattle only being on the terminal implant for a short duration. This could also be due to the timing of reimplantation in this experiment. Overlapping the payout times of combination implants can have detrimental effects on marbling deposition (Parr et al., 2011) and high potency combination implants early in feeding period decrease marbling deposition (Bruns et al., 2005).

With the opportunity for increased growth rates and HCW due to implants and increased trace mineral supplementation noted in this experiment, this could be a cost effective practice for producers to implement. It is important to note that the source of supplemental trace minerals utilized in this experiment were from inorganic sources, which are likely to be less expensive, but potentially less bioavailable to the animal, when compared with organic sources. With all variable costs kept constant among treatments except for implant and trace mineral supplementation costs, the use of implants and the supplementation of industry concentrations of trace minerals decreased the breakeven selling price for all costs by $0.21/lb compared to implanted cattle that did not receive supplemental trace mineral. It is also interesting to note that both industry supplemented treatment groups had the lowest breakeven price within implant treatment ($1.87/lb and $1.69/lb for NoIMP/IND and IMP/IND, respectively). In comparison to other treatments, IMP/IND steers acquired the greatest amount of profit at $142.67 per steer. This is lesser than that reported by Duckett and Pratt (2014) who noted the use of one combination implant increased profits by $163 a steer and $219 a steer if two combination implants

were used, compared to non-implanted steers. Variable return on investment can be contributed to the ever-changing market place and demand for beef products.

In the present study, regardless of implant status, trace mineral supplementation resulted in a growth response and increase in HCW. It is important to note that National Academies of Engineering, Science and Medicine recommendations are concentrations shown to prevent symptoms of mineral deficiency (NAESM, 2016) and not necessarily concentrations needed to optimize performance or profit. Further research is needed to investigate which mineral(s) have synergistic relationships with cattle growth and what concentrations are needed to optimize growth of feedlot cattle.

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Table 1. Ingredient and nutrient composition of control diet.

Item	% of diet dry matter[1]
Ingredient	
Cracked corn	62.0
MDGS[2]	25.0
Bromegrass hay	8.0
DDGS[3]	3.0
Limestone	1.5
Salt	0.31
Vitamin A & E premix[4]	0.1
Rumensin 90	0.0135
Calculated composition	
CP, %	14.04
NDF, %	18.30
Ether extract, %	5.02
Analyzed composition[5], mg/kg DM	
Cu	2.0
Fe	53.8
Mn	7.8
Zn	16.8
Se	0.22
Co	0.05

[1] Trace mineral treatments included CON (no supplemental trace mineral), REQ (2016 NAESM requirements of 10 Cu, 30 Zn, 20 Mn, 0.10 Se, 0.15 Co, and 0.50 I; mg/kg), and IND (feedlot consultant recommendations from Samuelson et al. (2016) of 20 Cu, 100 Zn, 50 Mn, 0.30 Se, 0.20 Co, and 0.50 I; mg/kg) all from inorganic sources.
[2] Modified distillers grains with solubles.
[3] Dried distillers grains with solubles.
[4] Premix provided 2,200 IU vitamin A and 25 IU vitamin E/kg diet.
[5] Analyzed mineral values reflect CON diet total.

Table 2. Day 56 BW and d 0-56 ADG of non-implanted or implanted beef steers fed varying concentrations[1] of supplemental trace minerals.

	No IMP			IMP[2]				*P* - value		
	CON	REQ	IND	CON	REQ	IND	SEM[3]	GS	TM	GS ×
Performance	n = 12	n = 11	n = 12	n =12	n = 12	n = 12				TM
BW, kg										
d 56	473[z]	468[z]	478[z]	494[y]	513[x]	509[x]	5.48	0.0001	0.17	0.10
ADG, kg/d										
d 0-56	1.50[c]	1.45[c]	1.61[c]	1.88[b]	2.18[a]	2.18[a]	0.070	0.0001	0.01	0.05

[a,b,c] Within rows, means without a common superscript differ ($P \leq 0.05$).

[x,y,z] Within rows, means without a common superscript tend to differ ($P \leq 0.10$).

[1] Supplemental trace mineral treatments: CON (no additional supplemental trace minerals), REQ (2016 NAESM requirements: 10 Cu, 30 Zn, 20 Mn, 0.10 Se, 0.15 Co, and 0.50; I mg/kg), and IND (feedlot consultant recommendations from Samuelson et al. (2016): 20 Cu, 100 Zn, 50 Mn, 0.30 Se, 0.20 Co, and 0.50 I; mg/kg) all from inorganic sources.

[2] Growth stimulated implanted steers (IMP) received Component TE-IS (16 mg estradiol + 80 mg TBA) on d 0 and were reimplanted with Component TE-200 (20 mg estradiol + 200 mg TBA) on d 56, while NoIMP received no implants.

[3] Reported SEM is greatest of all treatments because of uneven number per treatment.

Table 3. Main effect of implant status on live animal performance and carcass adjusted performance of non-implanted or implanted[1] beef steers fed varying concentrations[2] of supplemental trace minerals.

Item	NoIMP n = 36	IMP n = 35	SEM	*P* - value
Live animal performance[3]				
DMI, kg/d				
d 0-56	9.70	10.27	0.158	0.01
d 56 - 124	9.22	10.91	0.162	0.0001
Overall d 0 - 124	9.46	10.59	0.143	0.0001
BW, kg				
d 0	388	389	1.8	0.82
d 124	559	617	5.9	0.0001
ADG, kg				
d 56 – 124	1.19	1.59	0.055	0.0001
Overall d 0 - 124	1.35	1.83	0.038	0.0001
G:F				
d 0 – 56	0.157	0.203	0.0036	0.0001
d 56 - 124	0.129	0.145	0.0053	0.03
Overall G:F	0.143	0.173	0.0032	0.0001
Carcass adjusted performance				
Final BW[4]	555	619	5.2	0.0001
Overall ADG[4]	1.33	1.84	0.036	0.0001
Overall G:F[4]	0.141	0.174	0.0030	0.0001

[1] Growth stimulated implanted steers (IMP) received Component TE-IS (16 mg estradiol + 80 mg TBA) on d 0 and were reimplanted with Component TE-200 (20 mg estradiol + 200 mg TBA) on d 56, while NoIMP received no implants.

[2] Supplemental trace mineral treatments: CON (no additional supplemental trace minerals), REQ (2016 NAESM requirements: 10 Cu, 30 Zn, 20 Mn, 0.10 Se, 0.15 Co, and 0.50 I; mg/kg), and IND (feedlot consultant

recommendations from Samuelson et al. (2016) of 20 Cu, 100 Zn, 50 Mn, 0.30 Se, 0.20 Co, and 0.50 I; mg/kg) all from inorganic sources.

[3] No GS × TM; $P \geq 0.13$.

[4] Adjusted overall live performance parameters were carcass adjusted with a common 64.66% dress.

Table 4. Main effect of trace minerals on live animal performance and carcass adjusted performance of non-implanted or implanted[1] beef steers fed varying concentrations[2] of supplemental trace minerals.

Item	CON n =24	REQ n = 23	IND n = 24	SEM	*P* - value
Live animal performance[3]					
DMI, kg/d					
d 0-56	9.66	10.14	10.15	0.195	0.13
d 56 - 124	9.42[b]	10.25[a]	10.53[a]	0.120	0.0004
Overall d 0 - 124	9.54[b]	10.20[a]	10.34[a]	0.177	0.004
BW, kg					
d 0	389	389	387	2.34	0.79
d 124	584	585	594	7.24	0.56
ADG, kg					
d 56 – 124	1.35	1.38	1.44	0.069	0.59
Overall d 0 - 124	1.52	1.59	1.67	0.047	0.07
G:F					
d 0 – 56	0.175	0.178	0.187	0.0045	0.12
d 56 - 124	0.141	0.134	0.136	0.0065	0.74
Overall G:F	0.158	0.156	0.161	0.0040	0.67
Carcass adjusted performance					
Final BW[4]	577[b]	584[ab]	600[a]	6.4	0.03
Overall ADG[4]	1.50[b]	1.56[b]	1.70[a]	0.044	0.005
Overall G:F[4]	0.157[ab]	0.152[b]	0.164[a]	0.0037	0.07

[a,b,c] Within rows, means without a common superscript differ ($P \leq 0.05$).

[1] Growth stimulated implanted steers (IMP) received Component TE-IS (16 mg estradiol + 80 mg TBA) on d 0 and were reimplanted with Component TE-200 (20 mg estradiol + 200 mg TBA) on d 56, while NoIMP received no implants.

[2] Supplemental trace mineral treatments: CON (no additional supplemental trace minerals), REQ (2016 NAESM requirements: 10 Cu, 30 Zn, 20 Mn, 0.10 Se, 0.15 Co, and 0.50 I; mg/kg), and IND (feedlot

consultant recommendations from Samuelson et al. (2016) of 20 Cu, 100 Zn, 50 Mn, 0.30 Se, 0.20 Co, and 0.50 I; mg/kg) all from inorganic sources.
[3] No GS × TM; $P \geq 0.13$.
[4] Adjusted overall live performance parameters were carcass adjusted with a common 64.66% dress.

Table 5. Effects of non-implanted or implanted beef steers fed varying concentrations[1] of supplemental trace minerals on plasma glucose and urea nitrogen concentrations.

	No IMP			IMP[2]				*P* - value		
Plasma	CON n = 6	REQ n = 6	IND n =6	CON n = 6	REQ n = 6	IND n = 5	SEM	GS	TM	GS × TM
Glucose[3], mg/dL										
d 0	105	99	98	101	94	114	-	-	-	-
d 70[4]	96	97	95	98	102	103	4.4	0.14	0.88	0.79
d 124[4]	94^{xy}	108^{x}	93^{y}	104^{xy}	98^{xy}	107^{xy}	5.1	0.29	0.72	0.06
PUN[3], mg/dL										
d 0	9.0	8.0	9.4	10.6	10.3	8.2	-	-	-	-
d 70[4]	9.0	9.9	10.2	7.6	9.0	8.4	0.74	0.03	0.22	0.85
d 124[4]	10.0	11.4	10.1	9.7	10.8	10.3	0.85	0.74	0.33	0.90

^{x,y} Within rows, means without a common superscript tend to differ ($P \leq 0.10$).

[1] Supplemental trace mineral treatments: CON (no additional supplemental trace minerals), REQ (2016 NAESM requirements: 10 Cu, 30 Zn, 20 Mn, 0.10 Se, 0.15 Co, and 0.50 I; mg/kg), and IND (feedlot consultant recommendations from Samuelson et al. (2016) of 20 Cu, 100 Zn, 50 Mn, 0.30 Se, 0.20 Co, and 0.50 I; mg/kg) all from inorganic sources.

[2] Growth stimulated implanted steers (IMP) received Component TE-IS (16 mg estradiol + 80 mg TBA) on d 0 and were reimplanted with Component TE-200 (20 mg estradiol + 200 mg TBA) on d 56, while NoIMP received no implants.

[3] Blood samples were collected prior to feeding.

[4] Day 0 concentrations used as a covariate in analysis.

Table 6. Main effect of implant on liver mineral status of non-implanted or implanted beef steers fed varying concentrations[1] of supplemental trace minerals.

Mineral, mg/kg DM[3]	No IMP n = 18	IMP[2] n = 17	SEM	*P*-value GS
Initial (d -7)				
Cu	219	234	-	-
Zn	108	107	-	-
Mn	9.66	9.14	-	-
Se	1.7	1.7	-	-
Co	0.241	0.241	-	-
Day 70[3]				
Cu	228	198	8.2	0.02
Zn	95	98	3.2	0.53
Mn	8.59	7.93	0.228	0.05
Se	2.4	2.4	0.09	0.91
Co	0.182	0.170	0.010	0.36
Harvest (d 125)[4]				
Cu	246	237	15.7	0.67
Zn	125	143	4.0	0.01
Mn	8.70	8.94	0.296	0.59
Se	2.4	2.6	0.09	0.24
Co	0.174	0.158	0.007	0.10

[1] Supplemental trace mineral treatments: CON (no additional supplemental trace minerals), REQ (2016 NAESM requirements: 10 Cu, 30 Zn, 20 Mn, 0.10 Se, 0.15 Co, and 0.50 I; mg/kg), and IND (feedlot consultant recommendations from Samuelson et al. (2016) of 20 Cu, 100 Zn, 50 Mn, 0.30 Se, 0.20 Co, and 0.50 I; mg/kg) all from inorganic sources.

[2] Growth stimulated implanted steers (IMP) received Component TE-IS (16 mg estradiol + 80 mg TBA) on d 0 and were reimplanted with Component TE-200 (20 mg estradiol + 200 mg TBA) on d 56, while NoIMP received no implants.

[3] No GS × TM; $P \geq 0.11$.
[4] Day -7 mineral concentrations were used as a covariate in analysis.

Table 7. Main effect of trace mineral supplementation[1] on liver mineral status of non-implanted or implanted beef steers.

Mineral, mg/kg DM[3]	CON n = 12	REQ n = 12	IND n = 11	SEM	*P* – value TM
Initial (d -7)					
Cu	224	221	233	-	-
Zn	106	104	112	-	-
Mn	9.42	9.25	9.52	-	-
Se	1.8	1.7	1.6	-	-
Co	0.232	0.241	0.249	-	-
Day 70[3]					
Cu	118[c]	233[b]	290[a]	10.0	<0.0001
Zn	97	98	95	3.9	0.89
Mn	7.63[b]	8.25[ab]	8.90[a]	0.276	0.01
Se	2.1[b]	2.3[ab]	2.7[a]	0.11	0.001
Co	0.147[b]	0.192[a]	0.189[a]	0.0117	0.02
Harvest (d 125)[4]					
Cu	137[b]	277[ab]	310[a]	19.0	<0.0001
Zn	126[b]	144[a]	133[ab]	4.9	0.04
Mn	7.61[b]	9.10[a]	9.75[a]	0.359	0.001
Se	2.0[c]	2.5[b]	2.9[a]	0.112	<0.0001
Co	0.135[b]	0.184[a]	0.179[a]	0.0081	0.0004

[a,b,c] Within rows, means without a common superscript differ ($P \leq 0.05$).

[1] Supplemental trace mineral treatments: CON (no additional supplemental trace minerals), REQ (2016 NAESM requirements: 10 Cu, 30 Zn, 20 Mn, 0.10 Se, 0.15 Co, and 0.50 I; mg/kg), and IND (feedlot consultant recommendations from Samuelson et al. (2016) of 20 Cu, 100 Zn, 50 Mn, 0.30 Se, 0.20 Co, and 0.50 I; mg/kg) all from inorganic sources.

[2] Growth stimulated implanted steers (IMP) received Component TE-IS (16 mg estradiol + 80 mg TBA) on d 0 and were reimplanted with Component TE-200 (20 mg estradiol + 200 mg TBA) on d 56, while NoIMP received no implants.

[3] No GS × TM; $P \geq 0.11$.
[4]Day -7 mineral concentrations were used as a covariate in analysis.

Table 8. Effects of non-implanted or implanted beef steers fed varying concentrations[1] of supplemental trace minerals on carcass characteristics and quality grade distribution.

	No IMP			IMP[2]				*P* -value		
	CON	REQ	IND	CON	REQ	IND	SEM	GS	TM	GS x
Item	n = 12	n = 11	n =12	n =12	n =12	n =12				TM
Dress[3], %	63.4	64.7	64.8	64.5	64.4	65.9	5.8	0.26	0.13	0.50
KPH[4], %	2.21	2.00	2.13	2.00	1.96	2.13	0.69	0.24	0.20	0.44
Backfat, cm	1.52	1.34	1.69	1.16	1.46	1.46	0.126	0.13	0.16	0.17
REA[5], cm^2	77.8^{c}	79.8^{c}	81.1^{c}	91.9^{a}	86.6^{ab}	85.1^{b}	1.87	<0.001	0.58	0.02
YG[6]	3.60^{ab}	3.24^{bc}	3.70^{a}	2.84^{c}	3.44^{ab}	3.63^{ab}	0.163	0.09	0.03	0.02
Marbling Score[7]	494	541	550	486	539	483	39.5	0.43	0.46	0.66
% QG Distribution[8]										
Avg Choice or Higher	41.7	58.3	66.7	33.3	58.3	33.3	-	0.23	0.34	0.48
Low Choice	41.7	16.7	25.0	50.0	25.0	41.7	-	0.31	0.18	0.94
Select	16.6	25.0	8.3	16.7	16.7	25.0	-	0.68	0.88	0.49

[a,b,c] Within rows, means with out a common superscript differ ($P \leq 0.05$).

[1] Supplemental trace mineral treatments: CON (no additional supplemental trace minerals), REQ (2016 NASEM requirements: 10 Cu, 30 Zn, 20 Mn, 0.10 Se, 0.15 Co, and 0.50 I; mg/kg), and IND (feedlot consultant recommendations from Samuelson et al. (2016) of 20 Cu, 100 Zn, 50 Mn, 0.30 Se, 0.20 Co, and 0.50 I; mg/kg) all from inorganic sources.

[2] Growth stimulated implanted steers (IMP) received Component TE-IS (16 mg estradiol + 80 mg TBA) on d 0 and were reimplanted with Component TE-200 (20 mg estradiol + 200 mg TBA) on d 56, while NoIMP received no implants.

[3] Dressing percent.

[4] Kidney, pelvic, heart fat.

[5] Ribeye area.

[6] Yield grade.

[7] Marbling scores: small: 400, modest: 500, moderate 600.

[8] Percentage of steers in each treatment by quality grade, within treatment total is 100%.

Table 9. Economic analysis and break-even prices for non-implanted or implanted beef steers fed varying concentrations[1] of supplemental trace minerals.

	No IMP			IMP[2]		
$/steer[3]	CON	REQ	IND	CON	REQ	IND
Total Cost	$1,508.36	$1,509.07	$1,510.07	$1,520.72	$1,521.44	$1,522.63
Income	$1,423.88	$1,463.73	$1,492.86	$1,486.12	$1,610.88	$1,665.30
Profit	($84.48)	($45.34)	($17.21)	($34.60)	$89.44	$142.67
Breakeven selling price for variable costs ($/lb)	$1.90	$1.89	$1.83	$1.86	$1.70	$1.65
Breakeven selling price for all costs ($/lb)	$1.94	$1.93	$1.87	$1.90	$1.73	$1.69

[1] Supplemental trace mineral treatments: CON (no additional supplemental trace minerals), REQ (2016 NAESM requirements: 10 Cu, 30 Zn, 20 Mn, 0.10 Se, 0.15 Co, and 0.50 I; mg/kg), and IND (feedlot consultant recommendations from Samuelson et al. (2016) of 20 Cu, 100 Zn, 50 Mn, 0.30 Se, 0.20 Co, and 0.50 I; mg/kg) all from inorganic sources.
[2] Implanted steers (IMP) received Component TE-IS (16 mg estradiol + 80 mg TBA) on d 0 and were reimplanted with Component TE-200 (20 mg estradiol + 200 mg TBA) on d 56, while NoIMP received no implants.
[3] Budget utilized from Iowa State University Extension and Outreach Ag Decision Maker File B1-21. Yearling steer purchase price from Iowa feeder cattle combined auction of the week of August 15, 2016. Feed ingredient prices were averaged from Iowa markets during the time steers were on feed. Fed cattle value pricing was obtained from USDA AMS National Weekly Direct Slaughter Cattle – Premiums and Discounts (LM_CT155) and grid pricing from USDA AMS 5-Area Weekly WTD Average Direct Slaughter Cattle – Premiums and Discounts (LM_CT169). Interest rates on feeder cattle and variable costs were averaged interest rates from 2012-2016 from the Federal Reserve Bank of Chicago. All costs were held constant among treatments with only the cost of hormones and mineral supplementation different between treatments.

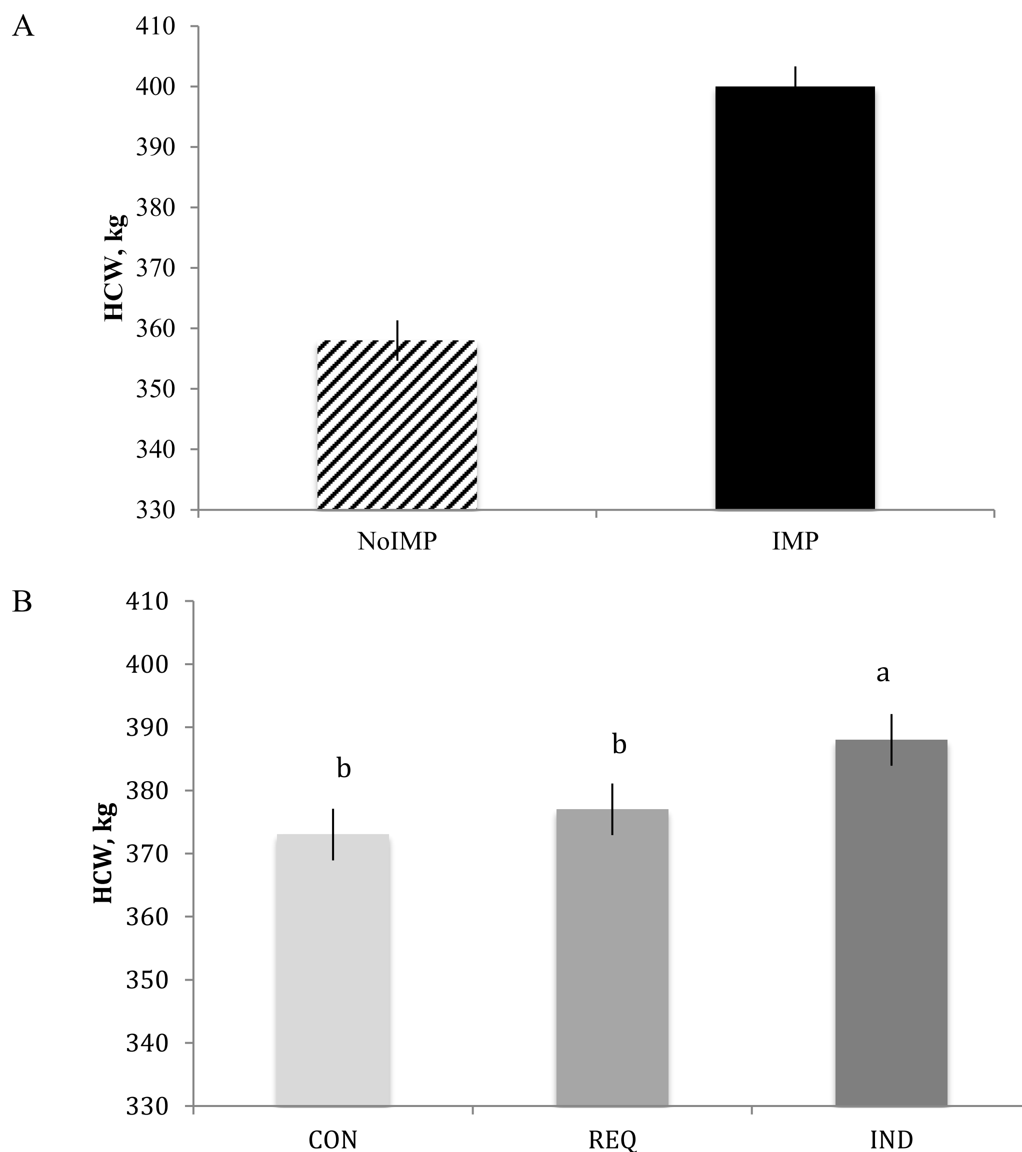

Figure 1. Main effects of implant (panel A; *P* < 0.0001) and trace mineral supplementation (panel B; *P* = 0.03) on HCW of beef steers. [a,b] indicates means within a panel differ (*P* ≤ 0.05). Growth stimulated implanted steers (IMP) received Component TE-IS (16 mg estradiol + 80 mg TBA) on d 0 and were reimplanted with Component TE-200 (20 mg estradiol + 200 mg TBA) on d 56, while NoIMP steer were not implanted. Supplemental trace mineral treatments: CON (no additional supplemental trace minerals), REQ (2016 NAESM requirements: 10 Cu, 30 Zn, 20 Mn, 0.10 Se, 0.15 Co, and 0.50 I; mg/kg), and IND (feedlot consultant recommendations from Samuelson et al. (2016) of 20 Cu, 100 Zn, 50 Mn, 0.30 Se, 0.20 Co, and 0.50 I; mg/kg) all from inorganic sources.

CHAPTER V

GENERAL CONCLUSIONS

Trace minerals are involved in many biological processes within the body of animals, including processes related to growth and development. The purpose of this research was to determine how TM supplementation affects the growth performance, trace mineral status, and carcass characteristics of growing and finishing feedlot beef steers. The studies described in this thesis were designed to evaluate how trace mineral supplementation may influence growth of steers raised in a natural program and steers receiving a high potency implant program.

In the work presented in Chapter III natural cattle were marketed under the USDA Never Ever 3 program and were never allowed to be exposed to antibiotics, growth promoting hormones, or animal byproducts at any point in their lifetime. An injectable trace mineral is a unique way to ensure every animal gets adequate concentrations of trace minerals along with rapidly improving the trace mineral status of the animal. Even though a growth response to injectable trace mineral administration in the particular group of cattle used in this experiment was not apparent, this is likely due to the steers having adequate trace mineral status throughout the duration of the trial. Injectable trace minerals did improve trace mineral status and could be a useful tool to rapidly improve trace mineral status, when the trace mineral status of the animal is unknown upon arrival to the feedlot.

In the study presented in Chapter IV, we found there was a implant × trace mineral supplementation interaction during the first 56 days of the experiment on the first implant where growth rates were increased in implanted cattle that received supplemental trace minerals and subsequent body weights tended to follow a similar pattern. But there were no

implant × trace mineral supplementation interactions for overall live or carcass adjusted animal performance. There was a growth response exhibited by steers in response to trace mineral supplementation, particularly at the industry concentrations. This response was exhibited by increased carcass adjusted final BW, ADG, DMI, and HCW. Interestingly this growth response due to industry concentrations of trace minerals indicates that current National Academies of Engineering, Science and Medicine commendations for trace mineral supplementation may not be adequate to optimize the growth of the current genetics of beef cattle fed today.

Unless cattle are deficient or marginally deficient in trace minerals, growth responses due to trace mineral supplementation may be variable. Because trace mineral status of beef cattle is rarely known, utilizing trace mineral supplementation strategies such as injection or increased dietary concentrations could be used as a risk management tool for producers. Further research is needed to investigate how the administration of injectable trace minerals to calves that are processed and implanted upon or shortly after arrival could provide adequate trace minerals to calves when intake may be marginal. It is also unknown if a rapid increase in trace mineral status might work together with a continuation of increased dietary supplementation of trace minerals to support high growth demands of cattle given hormone implants. It would also be of particular interest to examine the rates of growth by varying implant strategies and at which concentrations of supplemental trace minerals provide the most ideal growth response. This could also be further defined to determine which minerals in particular are working in synergy to produce growth responses to eliminate over supplementation of less crucial minerals. In programs like natural beef programs where losses in performance could reach as much as a 0.45 kg a day decrease in growth rates and a

shift towards undesirable feed efficiency compared to conventionally raised cattle, supplying cattle with the optimum concentration of trace minerals in order to maximize growth is essential for the performance of the cattle and the profit potential for the producers. More research is needed to determine the optimum concentration and timing of trace mineral supplementation needed in order to maximize growth potential of feedlot cattle.