STATISTICAL AND ECONOMIC IMPLICATIONS ASSOCIATED WITH

PRECISION OF ADMINISTERING WEIGHT-BASED MEDICATION IN CATTLE

A Thesis

by

ISAAC DANIEL OLVERA

Submitted to the Office of Graduate Studies of
Texas A&M University
in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

December 2010

Major Subject: Animal Science

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Approved by:

Chair of Committee,   Andy D. Herring
Committee Members,   Jason E. Sawyer
                      David P. Anderson
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ABSTRACT

Statistical and Economic Implications Associated with Precision of Administering Weight-based

Medication in Cattle. (December 2010)

Isaac Daniel Olvera, B.S., Texas A&M University

Chair of Advisory Committee: Dr. Andy D. Herring

Metaphylactic treatment of incoming feedlot cattle is a common preventative action against bovine respiratory disease (BRD). Cattle are dosed based on estimated or actual lot average weights, rather than on an individual basis, to reduce initial processing time. There has been limited research conducted on the effects of accurate weight- based dosing in feedlot cattle. The objective of this study was to evaluate the economic effects of precision weight- based dosing of cattle as compared to dosing the lot average or lot averages plus 50 lb and minus 50 lb. An economic model was created and stochastic simulations performed to evaluate potential outcomes of different dosing scenarios. Economic analyses of the effects of precision weight-based dosing were conducted using SIMETAR$^{©}$ to determine the stochastic dominance and economic effects of different dosing regimens.

Data were obtained from a commercial feedlot for different lots of cattle where individual animal weights were available; for this analysis the minimum lot size was 30 animals, and the maximum lot size was 126 animals. Within lots, individual weight deviations were calculated from the lot mean, the lot mean was rounded up to the nearest 50 lb increment or down to the nearest 50 lb increment to represent mild overestimation and mild underestimation, respectively.

Tulathromycin (Draxxin®, Pfizer Animal Health, New York, NY), an antimicrobial commonly prescribed for treatment of bovine respiratory disease, was used to illustrate the impacts of uniform dosing versus exact dosing per body weight. Based on the dilution space method used to evaluate time of drug effectiveness, it was estimated that Draxxin® administered at the recommended dosage to cattle weighing between 500 and 1000 lb should be provided with 191 hours (7.96 days) of protection from pneumonia-causing bacteria. Due to the pharmacokinetic properties of Draxxin®, an animal that is administered half the recommended dose is only protected from pneumonia-causing bacteria for 8 hours, which is 4.2% of the coverage time of the proper dose. This limits the effectiveness of the prescribed treatment to fully administer therapeutic treatment. In all cases, the correct weight-based dosing strategy cost less than any other dosing technique. Overall, dosing all cattle at the lot average weight costs $6.04 per animal more than dosing at the exact, correct dose. Dosing all animals at the lot average weight plus 50 lb costs $6.24 per animal more; dosing all animals at lot average minus 50 lb costs $4.01 per animal more.

The use of individual animal weights to determine per head dosing of Draxxin® is more cost effective than using lot averages. This concept would appear to extend to all weight-based pharmaceutical products in general, and should be considered a necessary management strategy.

DEDICATION

I would like to dedicate this work to my mother, father and brother for always loving and supporting me throughout my college career. Their unwavering support has always helped me stay on track and keep a goal in my sights. And, to my grandparents for continually praying for me and always remembering and reminding me that God is on my side. Thank you all for always being there for me.

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I would like to thank Dr. Herring for allowing me the opportunity to pursue this degree, for putting up with me and for all the help along the way, Dr. Sawyer for never giving me the right answers, only the right questions and Dr. Anderson for helping to fuel my interest in economics and always having a good story. Thank you all for you time and effort these past two years.

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CHAPTER I

INTRODUCTION

Metaphylactic treatment of incoming cattle in U.S. feedlots is a common method of preventative action against bovine respiratory disease (BRD), particularly with high risk cattle. With 98% of all feedlots already employing a vaccination protocol, drug efficacy needs to be heightened to combat the leading illness, BRD. Upon initial processing cattle are typically dosed based on estimated or actual lot average weights, rather than on an individual basis, to aid in reduction of initial processing time. There are a multitude of drugs on the market for the use in metaphylactic treatments regimens; one of the newest drugs for the prevention of BRD is tulathromycin. This new, unique, triamlide is thought to be far superior to many of the other previous drugs approved for metaphylactic treatment. The heightened movement and dispersion, coupled with the lasting tissue cultures developed aid in making this drug far more efficient, when used properly. There has been limited research done on the effects of accurate weight-based dosing in feedlot cattle and associated drug efficacy.

The dilution space technique has been used to evaluate the amount of water with which a substance equilibrates within an animal's body and used to predict body composition in nutrition research. It appears that this technique is also appropriate to estimate medication dispersion in animals' bodies following injection.

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This thesis follows the style of the *Journal of Animal Science.*

Economic analyses that provide cattle producers tools for risk management are needed. Risk aversion coefficients in conjunction with stochastic models are effective ways to estimate the outcomes based on the probabilities of occurrence and the associated management decision based on risk levels.

The overall objective of this study was to evaluate the economic effects of precision, weight-based dosing in cattle with one specific medication as compared to dosing on the lot average weight or lot average weight plus 50 lb (22.7 kg), and lot average weight minus 50 lb to account for estimation or rounding errors when using lot average weights. The urea dilution space technique was used as a model here to estimate the dispersion and protection time of tulathromycin in the body of live cattle. Based on the resulting estimated protection, an economic model was created and stochastic simulation was conducted to evaluate the potential outcomes of several different scenarios. Economic analysis of the effects of precision weight-based dosing were conducted through simulation using SIMETAR$^{©}$ to determine the stochastic dominance and economic effects of different dosing regimens.

CHAPTER II

REVIEW OF LITERATURE

Introduction

Background information will be discussed pertaining to the use of pharmaceuticals, Bovine Respiratory Disease and its associated management and economic effects in the U.S. cattle feeding industry. The practice of metaphylactic dosing of weight- based medications, the use of the antimicrobial, tulathromycin, as a metaphylactic and its associated pharmacokinetic properties and the concept of urea dilution space to predict pharmaceutical dispersion in the body will be investigated to create a predictive model of efficacy in dosing. A discussion of risk and the use of stochastic models pertaining to economic analysis and the use of the simulation program SIMETAR$^©$ for economic analyses is also included.

Pharmaceuticals

The cattle industry is the largest single sector of production agriculture in the United States with cash receipts totaling more than $49.2 billion (Lawrence and Ibarburu, 2006), made up of approximately 980,000 ranches producing cattle, 85% of which funnel into roughly 2,200 feedlot operations (Abidoye and Lawrence, 2006). With so much influence of animal health on production and profitability in the cattle industry, it is obvious why livestock pharmaceuticals make up a majority of the animal health market. The livestock sector accounts for nearly 70% of all animal pharmaceutical sales, but generally remain steady with no growth (Ahmed and Kasraian, 2002). Despite the low growth in sales, the animal pharmaceutical industry is

consistently undergoing changes and innovations in the areas of drug delivery and the support of efficacy, usually aimed at: (1) enhancing consumer convenience and regulation compliance, (2) increased efficacy and pharmacokinetic properties of drugs, (3) product differentiation, and (4) assurance of target animal and consumer safety (Ahmed and Kasraian, 2002). In 2007 it was estimated that the total added value attributed to pharmaceuticals used throughout the beef production cycle was as high as $524 per animal (Lawrence and Ibarburu, 2007). Obviously in challenging economic times any pharmaceutical that increases production efficiency, weight gain or fights illnesses is highly desired by producers.

There are a multitude of products on the market for proper drug dispensing and more efficient drug delivery. Most common dispensing apparatuses include single dose syringes, multiple dose repeating volume syringes, oral applicators, gun style dispensers, and most recently, a novel, scale driven, automated weight based dose delivery syringe system (Animal Innovations, Inc., www.animalinnovations.com). Drug delivery types, much like the dispensing products, are highly variable and depend mostly on the convenience and value optimization desired, sustainability and stability of drug release, and affected target tissues. Sustained release boluses, oral pastes, pour- on formulas, injectable drugs, controlled internal drug release products (CIDRs), implants and ear tags, and feed premixes are all common types of drug delivery methods. With specific regard to injectable drugs, they can be further classified as intramuscular (IM), intravenous (IV) or subcutaneous (SC). Within the feedlot industry, the majority of drugs are now given via subcutaneous injection. Due to the problem of wasted beef product associated with IM injections in food animals, the Beef Quality Assurance program made a major industry shift towards SC neck injections only in the early 1990's. By early 2000, a BQA audit showed

that 97.5% of top sirloin butts were free of injection site lesions as compared to 78.7% in 1991 (Hilton, 2005). The main animal health products administered to feedlot cattle are parasiticides, and vaccines and antimicrobials associated with Bovine Respiratory Disease complex.

Bovine Respiratory Disease and Associated Management

Bovine Respiratory Disease complex (BRD) is a very extensive disease that encompasses both bacterial and viral pathogens; there is much difficulty in differentiating the various entities, so the complex as a whole is commonly referred to as Undifferentiated Fever (UF) or simply BRD (Booker et al., 2007). *Mannheimia* (formerly *Pasteurella*) *haemolytica, Pasteurella multocida, Histophilus somni* (formerly *Haemophilus somnus*), and *Mycoplasma bovis* are the primary bacterial pathogens that are threats and whose infections typically manifest themselves following viral infection. The primary viral diseases that are associated with BRD include infectious bovine rhinotracheitis (IBR, caused by bovine herpesvirus type 1), bovine viral diarrhea (BVD), parainfluenza- 3 (PI3), and bovine respiratory synctial virus (BRSV) (Martin and Bohac, 1985).

Since January of 1992 there have been significant increases in mortality rates within feedlots (Babcock et al., 2006). With the many innovations in preventative medicines and medical treatments for cattle and producer education through BQA programs, this fact is astonishing. The most common and costly disease in feedlot cattle, bovine respiratory disease (BRD), has shown to be a long plaguing issue within the cattle industry as a whole. With BRD accounting for approximately 75% of feedlot morbidity and almost 50% of mortality (Edwards,

1996; Gardner et al., 1999), it is obvious that more in depth research is needed to aid in reduction of BRD related cases (Snowder et al., 2006).

In a study over a six year period spanning from 1994 to 1999 it was shown, using collective NAHMS data, that there was a 38% increase in mortality among feedlot cattle moving from 10.3 deaths per 1000 to 14.2 deaths per 1000 cattle; more than half of those deaths (57.1%) could be directly attributed to BRD (Loneragan et al., 2001). Preventative methods to help decrease the incidence of BRD upon arrival at feedlots have been studied in depth. It has been shown that preconditioning calves prior to arrival may aid in decreased feedlot morbidity by 6% and decrease mortality by 0.7% (Cole, 1985). A study investigating the added value associated with calves prior to shipment from ranch of origin reported that calves weaned and preconditioned 45 days prior to shipment had lower incidents of BRD than calves transported from the same ranch immediately at weaning or calves assembled at auction markets, even when comingled at the preconditioning site (Step et al., 2008). Furthermore, calves marketed through auction barns shipped immediately after weaning had almost double the risk of BRD morbidity incident rates than calves that were weaned prior to shipping (Roeber et al., 2001).

Economic Effects of BRD on Feedlots

The economic effects associated with incidents of BRD are staggering. The economic impact of BRD alone has been reported to cost the cattle industry $800- $900 million annually (Griffin, 1997; Chairase and Greene, 2001). Snowder et al. (2006) estimated that the individual treatment cost per animal was $13.90; therefore the total economic loss associated with BRD in 1,000 feeder calves was approximately $13,895 not including the cost of feed prior to mortality,

labor costs, or associated handling. Research supports that for every 10% increase in feedlot morbidity linked with BRD, medicine cost increase $2 per head for all cattle that are finished (Edwards, 1996). With 11.6 million cattle on feed in 2009 a simple $2 increase could cost the industry more than just increased production costs (NASS, 2010). In markets that compete on costs any additional inputs needed have some corresponding price increase at the retail level. The USDA has stated the own price elasticity of beef as -.621, meaning that for every observed 10% increase in price there is an associated 6.21% decrease in quantity demanded (USDA, 2008). Price fluctuations associated with cost management in the production sector have a larger impact on beef sales and marketability than just profitability of the individual producer, these cost carry through to the consumer level and directly affect the industry at the sales level.

There has been extensive work done on the factors affecting profitability in cattle associated with BRD. Gardner et al. (1999) specifically noted that the disease resulted in consistently lower average daily gains, lighter hot carcass weights, and lower marbling scores; furthermore, the presence of lung lesions associated with respiratory disease could be highly correlated to the reduction in performance. Steers diagnosed with respiratory disease at slaughter, based on pulmonary lung lesions and active bronchial lymph nodes, returned $73.78 less than animals without lesions. Approximately 21% of the deductions were attributed to the cost of treatments and medications, the remaining 79% were attributed to the reduction in hot carcass weight (8.4% less) as well as reduced quality grades (24.7% more US Standard carcasses in group with lesions) (Gardner et al., 1998). It is not uncommon for the cost of morbidity to outweigh the cost of mortality, a death early in the production cycle can save on feed, medications and associated handling costs. If the death occurs early enough in the production

cycle the only loss attributed to the animal is the purchase price. The additional costs of lower average daily gains, lower carcass values and less desirable products can inflate the cost of morbidity to $92.26 for animals that were ill as compared to those that were not (McNeill et al., 1996).

Feedlot Metaphylactic Dosing

In general, feedlots are one of the largest adopters of pharmaceutical technologies. Lawrence and Ibarburu (2006) reported that at initial processing, approximately 98% of all feedlots vaccinated incoming cattle against respiratory disease. One of the more widely practiced time management strategies used in feedlots is metaphylactic treatments. Metaphylaxis, also referred to as mass medication, is a preemptive strike against cattle that may be considered high risk for contracting or spreading illness; dosing all incoming cattle at initial processing with an approved antimicrobial. When administering metaphylactic treatment, feedlots will often process hundreds of incoming cattle at a time so efficient time management is a necessity. Many factors influence the decision to treat incoming cattle metaphylactically, including shipping distance, arrival weight, appearance, BRD incidence from cattle within the same region, source, season, age, etc. With these factors considered, it was shown that larger feedlots, defined as 8,000 head or larger, were 54.4% more likely to employ the use of metaphylactic treatments aimed solely at combating BRD alone within their feedlot compared to smaller operations of 1,000 to 7,999 animals (USDA, 2000).

Upon arrival, cattle may be sectioned into one of two categories, high risk and low risk type cattle (Edwards, 1996). Cattle deemed high risk generally include: calves recently weaned,

cattle that have been trailered long distances, groups of cattle that were purchased and grouped at auctions, cattle that are considered high stress when they arrive, and cattle that have had low exposure to unfamiliar other cattle. Low-risk cattle include: single source cattle, pre- weaned calves, yearling cattle and cattle coming from preconditioning/ stocker operations (Booker et al., 2007; Step et al., 2007; Sanderson et al., 2008).

Tulathromycin as a Metaphylactic

Much research has been completed on the efficacy of metaphylactic treatments for cattle entering feedlots. As stated earlier, 80.9% of large feedlots (54.4% more than smaller feedlots) employ the use of metaphylactic treatments to help prevent BRD outbreaks (USDA, 2000). For the purpose of this research we focused on the use of tulathromycin (Draxxin Injectable Solution, Pfizer Animal Health) as the metaphylactic antimicrobial of choice.

Tulathromycin was developed for the prevention and treatment of respiratory disease in cattle and pigs (Booker, 2007). Due to the pharmacokinetic properties of tulathromycin, compared to other similar macrolides (erythromycin, tylosin, spiramycin and tilmicosin), the long lasting effects and rapid dispersion and movement are thought to make it superior to most other metaphylactic antibiotics. Despite the fact that Tulathromycin is two to three time more expensive than other macrolides, it may be more cost effective for the prevention of BRD. In an economic study of metaphyactics, tulathromycin was shown to have an advantage of $16.43 and $3.67 per animal over oxytetracycline and tilmicosin when administered metaphylactically; this was due to the lower treatment and retreatment rates, lower mortality incidents, improved average daily gain and higher quality grades, despite higher dosing costs and lower yield grades observed

on both antibiotics, lower feed efficiency compared to tilmicosin (Booker et al., 2007). Booker et al. (2007) concluded that through the use of tulathromycin fewer animals are at risk for incident of BRD. By reducing morbidity, the associated treatments are reduced, thus aiding in (1) reduced amount of antimicrobials administered in the beef production industry, (2) increased profit potential for producers, and (3) improved welfare of cattle with reduced handling, stress and isolation.

Pharmacokinetic Properties of Tulathromycin

Tulathromycin was the first product classified as a tribasic macrocyclic antibiotic, now referred to as triamilides (Nowakowski et al., 2004). Triamilides are semisynthetic derivatives of the natural product, erythromycin (commonly used in humans for respiratory ailments), and are characterized by the presence of three polar amine groups (tribasic) that differentiate them structurally from other macrolides (Letavic et al., 2002). Tulathromycin is formulated in an equilibrated mixture of two macrocycles for subcutaneous or intravenous injection as a single dose to provide a full course of treatment against respiratory bacterial pathogens in cattle and swine. It is thought that unique features of the triamlide class enhance penetration of gram-negative bacterial pathogens, resulting in increased drug potency and effectiveness (Evans, 2005).

Generally, antibiotics are classified as bacteriostatic, bactericidal or a both; but typically the macrolides are considered bacteriostatic. This means they inhibit bacterial growth by preventing essential protein biosynthesis through selective binding to bacterial ribosomes and stimulate dissociation of peptidyl -tRNA from the ribosome during the translocation process (Vannuffel and Cocito, 1996), meaning they inhibit cell division and lead to cell death.

Tulathromycin is unique in that it exhibits both bacteriostatic and bactericidal features. The minimum inhibitory concentration (MIC) for 70% (the minimum concentration of a drug necessary to inhibit 70 percent growth, associated with being bacteriostatic) was found to be the same as the minimum bactericidal concentration (MBC) for *M. haemolytica* and *P. multocida* (Evans, 2005). So, along with preventing cell division, tulathromycin's tribasic structure aids in penetrating the gram negative pathogens, the most common cause of BRD, aiding in attacking these pathogens.

Aiding in the movement of tulathromycin and its associated efficacy is the ability of the drug to use phagocytic cells to help store and move the drug. Data suggest that heightened concentrations in infected lungs can be attributed to tulathromycin moving with immune cells to affected areas and being secreted slowly into the extracellular area where it can be used to attack pathogens. As well, evidence supports that the leukotoxins produced by the gram- negative organisms, such as *M. haemolytica,* induce lysis of the phagocytic cells carrying the drug (Evans, 2005).

The ability of the tissue concentration of tulathromycin to remain high for an extended period of time is presumed to be the underlying reason behind the high efficacy rates observed; after tulathromycin is administered, the bioavailability is approximately 91% (Skogerboe et al., 2005). Tulathromycin is metabolized slowly, and a majority of the remaining drug is excreted in feces and urine. Because tulathromycin is absorbed rapidly into the tissue, lung concentration is a better predictor of the pharmacodynamic properties than the use of plasma concentrations for efficacy models based on concentrations (Evans, 2005).

Urea Dilution Space

The urea dilution technique was developed in an effort to adequately and efficiently predict the body composition of cattle in vivo through estimating empty body water concentration as a calculation of a percent of total composition. Because urea is inexpensive, and it is somewhat easy to analyze the plasma urea nitrogen content, the urea dilution technique is more readily applied in both research and industry where measurement of body composition during growth may be necessary (Rule et al., 1986). It was the only method emerging that was time efficient and accurate. Before then, methods included backfat measurement tools, ultrasonic probes, visual appraisal or use of titrated water or deuterium oxide (used in humans) as dilution constants (Bartel et al., 1983). The other dilution constants often required several hours to adequately determine body composition, as well as including a factor known as turnover rate. The turnover rate estimated the body water dilution much the way the urea dilution technique does but required more time, especially during peak lactation and increased during gestation, and required the use of specialized equipment to calculate.

Unlike the other dilution methods, the urea dilution technique was reported to work as quickly as 12 minutes and accurately report the body water percent (Bartel et al., 1983). Soberman et al. (1949) stated that substances to be used in body composition estimates as physiological tracers should "show an even and rapid distribution throughout the body water, should be nontoxic, not foreign to the body and not cause any physiological disturbances." As well, tracer substances should be "accurately and easily measured in either whole blood or plasma and they should not be selectively stored, secreted or metabolized." The urea dilution technique was validated by Bartle et al. (1987) for the estimation of body composition. They concluded

that the technique met all the requirements of a proper tracer in cattle. Urea space was defined by Kock and Preston (1979) as the volume of water with which urea equilibrates. They made the assumption that urea space is correlated with empty body water, therefore urea space measurements could be used as adequate predictors for estimating body composition in cattle.

Risk

Risk is defined as a part of the business decision out of the manager's control (Richardson, 2010). Hardaker et al. (2004) identified six specific areas of risk observed in agricultural production as a whole: (1) production risk (2) price risk (3) institutional risk (4) human/ personal risk (5) business risk and (6) financial risk; the following is a discussion of the areas regarding risk in agriculture. Production risk comes from the unpredictable nature of agriculture as a whole: weather, illness, livestock growth and performance, morbidity/ mortality rates in a given year and pasture quality or availability are all areas of concern in production risk. Additionally, production risk extends to the highly variable prices of farm inputs and outputs that usually aren't certain at a given point in the future. Price risk associated with production usually includes risks associated with the high amounts of commodities needed in livestock production. Market volatility can often cause sudden price changes that a producer may not have accounted for, as well as, the variability in the supply and demand changes of product. Institutional risk is a risk that governing bodies introduce through the implementation of various rules and policies. Institutional risk can be further broken down into: political risk (risk of adverse policy changes), sovereign risk (risk that foreign governments will fail to uphold predetermined agreements and commitments), and relationship risk (risk from issues between partners or other organizations).

Fourth, there is the human/personal risk aspect. This is a risk that develops within the management of the firm. Crises such as death or serious illness of integral team members may interfere with of the processes of normal daily operations.

Business risk is the combination of production, market, institutional, and personal risk. Business risk impacts the firms' business performance in terms of the net cash flow generated or net farm income earned. Finally, financial risk results from financing options of the firm. Bank and loan issues or investor shortcomings are all common issues in financial risk.

It has been stated "the purpose of simulation in risk analysis is to estimate distributions of economic returns… so the decision maker can make better management decisions" (Richardson, 2010). There are two types of simulation models to help analyze economics returns, deterministic models and stochastic models. Deterministic models do not take risk into account and only calculate outputs based on input variables. They are adequate for investigating the outcomes based on managerial changes, but do not assume a risk variable, and are therefore static compared to the business environment.

Stochastic Models

Stochastic models incorporate some sort of uncertainty or, an assigned risk variable. Incorporating risk into a model allows managers to create alternative scenarios and analyze the probabilistic outcomes of the model. Once modeled, a manager must select the most appropriate economic option with the goals of the individual operation in mind. Without assessing risk within a model the simulations for alternative scenarios will not be adequate to base decisions upon. If there was no risk in a business environment, the optimal strategy would simply be that

which has the greatest economic return. With a risk variable included, the decision becomes much more complex. Economic returns associated with the risk of losses may force the selection of a less profitable but more stable alternative based on the assumption of less risk resulting, in the long run, in a more stable economic environment (Hardaker et al., 2004).

The main goal of simulating risky alternatives is to allow for accurate decisions to be made on economic issues that may be too large, complex, costly or lengthy to actually perform. Most models are quite easily adapted to changes within the firm's business environment and can be used to train new management in procedures without exposing the business to actual risk. Although models can be an extremely effective tool for analyzing a given scenario, people will largely discredit the use of simulations based solely on human error, or they will put full faith in the model because "that's just what they're supposed to do" (Richardson, 2010). Models are only as good as they are built, and confined by the data used to create them.

Simulation and Econometrics to Analyze Risk

Simulation and Econometrics to Analyze Risk (SIMETAR$^©$) is a front loaded Microsoft Excel based program developed by Richardson, Schumann and Feldman in the Department of Agricultural Economics, Texas A&M University (Gill et al., 2003). It utilizes Visual Basic programming to work directly in Microsoft Excel. SIMETAR$^©$ was specifically written for analyzing data, simulating risky alternatives and presenting findings. Of the more than 230 functions in SIMETAR$^©$, they can be categorized into seven groups: 1) simulating random variables 2) parameter estimation and statistical analysis 3) graphical analysis 4) ranking risky

alternatives 5) data manipulation and analysis 6) multiple regression and 7) probabilistic forecasting (Richardson, 2010).

Monte Carlo simulations use random sampling of probability distribution functions as model inputs, the simulation process produces possible outcomes based on the stochastic inputs. The results show the probabilities of the occurrence of each outcome given the actual data set. SIMETAR$^©$ gives the user the option to use one of two Monte Carlo simulation methods, Latin Hypercube and Monte Carlo distribution. Richardson (2010) gives an adequate explanation of the two methods, cited in the following discussion. The Latin hypercube procedure is the preferred method of sampling probability distributions. Latin hypercube breaks the distributions into N intervals and randomly selects at least one value from each interval. The number of intervals, N, is the number of iterations used in the model. By sampling from N intervals, the Latin hypercube method insures that all areas of the probability distribution are weighted within the simulation model, making fewer iterations necessary to produce an accurate replication of the data set. The Monte Carlo procedure randomly selects values based on the probability distribution. As a result, the Monte Carlo method samples a greater percentage of random values about the mean, therefore, under samples the areas in the tails. A larger number of iterations must be used to more accurately account for all of the distribution area and minimize the effects of under sampling in the tails of the probability distribution.

Summary

The economic effects associated with the use of precision dosing in metaphylactic treatments need much investigation. With more than 11 million cattle on feed, any amount of

monetary changes in the industry can cause a drastic change in economic returns within the industry as a whole. Much work is needed to investigate what the social and economic effects directly associated with precision dosing of weight-based medications; therefore, the objective of this study was to evaluate the economic effects of precision weight-based dosing in cattle as compared to dosing on the lot average. The general concepts associated with the urea dilution space equation used to measure in vivo body composition were utilized to estimate antimicrobial concentrations in animal tissues. An economic model and stochastic simulation was constructed to evaluate the outcomes of exact weight dosing, lot average weight, lot average weight plus 50 lb and lot average weight minus 50 lb. Economic and statistical analyses of the effects of precision weight based dosing were conducted to determine the outcome effects of different dosing regimens.

CHAPTER III

STATISTICAL AND ECONOMIC IMPLICATIONS ASSOCIATED WITH PRECISION OF

ADMINISTERING WEIGHT-BASED MEDICATION IN CATTLE

Introduction

The use of metaphylactics to treat incoming cattle in U.S. feedlots is a common method of

preventative action against bovine respiratory disease (BRD). Upon initial processing cattle are

typically dosed based on estimated or actual lot average weights, rather than on an individual

basis, to aid in reducing the initial processing time necessary. There are a multitude of drugs on

the market approved for the use as metaphylactics; one of the newer drugs recently approved for

the prevention of BRD is tulathromycin. This new, unique, triamlide is thought to be far superior

to many of the other drugs previous used in metaphylactic treatments. There has been limited

research done on the effects of accurate weight- based dosing in feedlot cattle and associated drug

efficacy.

The dilution space technique was has been used to evaluate the amount of water with

which a substance equilibrates within an animal's body. This technique was used here to

estimate the dispersion and coverage of tulathromycin. Based on the estimated coverage, an

economic model and stochastic simulation were created to evaluate the potential outcomes of the

different scenarios. Economic analysis of the effects of precision weight based dosing were

conducted using SIMETAR$^{©}$ to determine the stochastic dominance and economic effects of

different dosing regimens. Risk aversion coefficients in conjunction with stochastic models are

effective ways to estimate the outcomes based on the probabilities of occurrence and the associated management decision based on risk levels.

Materials and Methods

Data were obtained from a commercial feedlot for different lots of cattle that were delivered from 2007 to 2009 where the feedlot had individual animal weights upon arrival (all weights herein are denoted in common U.S. industry standard notations i.e. 50 lb, 100 lb and 1000 lb increments). This is not the case for most commercial U.S. feedlots. For this analysis, the minimum lot size considered was 30 animals, and the maximum lot size evaluated was 126 animals. Summary statistics of each lot are shown in Table 3.1. Skewness (the relative inequality of weighting in the tails of the distribution) and kurtosis (a measure of the pattern of dispersion) were calculated. The percent of animals falling within ten percent of the lot mean also were calculated to examine the relative average lot dispersion. Within lots, individual weight deviations were calculated from the lot mean for each animal. Additionally, because mean lot weights are often estimated at arrival rather than calculated overtly, the lot mean weight was rounded to the nearest 50 lb increment to represent mild overestimation and mild underestimation, respectively. For example, if the lot mean weight was 642 lb, then the overestimated mean was projected at 650 lb and the underestimated mean was projected at 600 lb, etc.

Tulathromycin (Draxxin®, Pfizer Animal Health, New York, NY), an antimicrobial commonly prescribed for treatment of respiratory disease, and also often applied en masse for control therapy strategies, was used to illustrate the impacts of uniform dosing versus exact

Table 3.1 Summary statistics of lot weight, variation, and distribution in regard to normal distribution assumptions and weight-based medication efficacy.

	Lot									
	A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**
Mean, lb	1006.97	639.395	661.658	631.285	329.3	973.636	584.602	470.185	1128.90	475.710
St.Dev., lb	104.796	68.5685	75.8332	40.7709	57.6237	112.848	77.0361	103.564	112.674	87.5241
95 % LCI	979.295	621.995	646.333	615.145	304.476	934.155	563.19	441.831	1093.55	451.566
95 % UCI	1034.65	656.794	676.984	647.425	354.124	1013.11	606.015	498.540	1164.26	499.853
CV	10.4070	10.7239	11.4610	6.45839	17.4988	11.5903	13.1775	22.0263	9.98088	18.3986
Min	804	490	472	540	245	820	360	310	920	300
Median	1000	640	670	630	320	936.5	578.5	460	1118	460
Max	1350	775	825	740	500	1315	800	790	1425	740
Skewness	0.69420	-0.0706	-0.19031	0.51703	1.11306	1.03767	0.12527	1.11230	0.55927	0.73142
Kurtosis	0.93274	-0.5829	-0.32885	1.29276	1.78500	0.87316	0.99925	1.35153	-0.10762	0.84060
10% of mean	0.66338	0.6484	0.61752	0.87803	0.43212	0.59083	0.55259	0.34993	0.68354	0.41355
Count	75	81	126	35	30	44	68	70	54	69

dosing per body weight on product usage and cost overruns in arriving feedlot cattle. Other drugs were examined for use as metaphylactics in this study, but tulathromycin offered the most complete label information. It has become widely used in the industry as a metaphylactic and is the most cost influential medication based on price per mL of the labeled dose. Table 3.2 shows the break down of the various BRD treatment medications investigated. The labeled dosage for tulathromycin is 1.1 ml per 100 lb BW, and per unit product cost was set at $4.43 per ml. Product prices reflect reported retail prices from January 2009.

Table 3.2. Similar medications investigated for use as metaphylactics in feedlots.[1]

Chemical Name	Product	Company	Price	Price/ mL	Dose Rate	MIC90 (µg/mL)
ceftiofur crystalline free acid	Excede	Pfizer	$163.95/100mL	$1.64	1.5mL/100lb	*M. haemolytica* .025 *P. multocida* 0.004
tulathromycin	Draxxin	Pfizer	$2213.60/500mL	$4.43	1.1mL/100lb	*M. haemolytica* 2 *P. multocida* 1
enrofloxacin	Baytril	Bayer	$194.95/250mL	$0.78	3.4 - 5.7 mL/100 lb	*M. haemolytica* .06 *P. multocida* .03
oxytetracycline	Tetradure	Merial	$125.00/500mL	$0.25	13.6mg/lb (300mg/mL)	
tilmicosin phoshate	Micotil	Elanco	339.95/250mL	$1.36	1.5mL/100lb	*M. haemolytica* 3.12

[1] Prices relative to January 2009.

Three specific methods were employed to evaluate the effectiveness of administering the weight-based product: (1) estimation of product dispersion through the animal's body in order to provide protection against pneumonia-causing bacteria using the dilution space evaluation, (2) estimation of the level of protection against illness provided to animals that receive varying percentages of recommended dose of weight-based , and (3) estimation of changes in expected illness and correlated costs associated with dosing animals at varying levels of their recommended weight-based dose. These are described individually below.

(1) Estimation of product dispersion in animal's body from injection

Below are the drug properties, assumptions and description of the methodology used to estimate the time associated with the effectiveness of the weight-based medication Draxxin[®].

Concentration: 100 mg/mL

Dosing: 1.14 mL/cwt (1 mL/40 kg)

Lung Capacity of Draxxin[®] (from label description and Pfizer web site):

T_{max} (hours):   24

C_{max} (µg/mL): 4.1

$T_{1/2}$ (hours):   184

MIC 90: 2 (µg/mL)

The procedure used to estimate diffusion of the medication through the body in order to predict the concentration in the tissue is referred to as dilution space evaluation. Kock and Preston (1979) used the urea dilution technique to estimate an animal's body composition in vivo. In that study, urea was used as the chemical marker to determine how it diffused in the water of the animal's body. Urea space was defined by Kock and Preston (1979) as "the volume of water

with which the urea equilibrates." The formula they used to determine the dilution space is provided below.

Volume infused (mg) ÷ [Known Peak (mg/100mL) * LW(kg)] = Dilution Space (DS)

This equation was used to estimate the area, as a percentage of body weight, that a drug is allowed to diffuse into. The peak concentration reported for Draxxin® was 4.1 µg/mL; therefore, concentration of the medication was assumed to be 0.41 mg/100 mL of product. Volume infused and live weights were both calculated on an individual animal basis. The following weight classes of cattle were evaluated to derive a dilution space constant that could be used to predict medication concentration relative to recommended weight-based dosage:

1000 lb = 1140 mg/(.41 mg/100 mL*453.59 kg) = 6.1300

900 lb = 1020 mg/(.41 mg/100 mL*409.09 kg) = 6.0812

800 lb = 912 mg/(.41 mg/100 mL*363.64 kg) = 6.1170

700 lb= 798 mg/(.41 ml/100 mL*318.18 kg) =6.1171

600 lb= 684 mg/(.41 ml/100 mL*272.73 kg) =6.1170

500 lb= 570 mg/(.41 ml/100 mL*227.27 kg) =6.1182

As a result, the dilution space constant of 6.1 can be used across all weight classes of cattle for tulathromycin. The dilution space equation was modified to calculate the maximum tissue concentration. The equation below incorporated the dilution space value to estimate the

maximum concentration of the medication in the tissue when varying percentages of weight-based medication were administered to a 1,000 lb animal.

Volume infused (mg) ÷ [DS * Live Weight (kg)] = Max Concentration (N_0)

Correct Dose = 1140 mg/ (6.1 *453.59 kg) = .41

10% reduction = 1026 mg/ (6.1*453.59) = .3708

20% reduction = 912 mg/ (6.1*453.59) = .3296

30% reduction = 798 mg/ (6.1*453.59) = .2884

40% reduction = 684 mg/ (6.1*453.59) = .2472

50% reduction (half-dose) = 570 mg/(6.1*453.59) = .2060

(2) Protection of animals receiving different levels of the weight-based recommended dose

The equation: $T_{1/2} = \ln2 \div \lambda$ describes the half-life of a medication with a logarithmic decline in concentration; the half life of tulathromycin is reported to be 184 hours. As a result:

184 = .693 ÷ λ   **λ = Decay Constant = .003766**

And, the quantity remaining in the tissue at time t (N_t) can be estimated as:

$N_t = N_0^{-\lambda t}$ where

N_0 = initial quantity to be decayed

λ = decay constant

t = time in hours

As a result, the effective number of hours that animals would be protected from the correct weight-based dose of tulathromycin was calculated where the tissue MIC 90 value was maintained; the number of hours of protection were also calculated for animals receiving 90%, 80%, 70%, 60% and 50% of the recommended weight-based dose. The distribution is displayed in Figure 3.1.

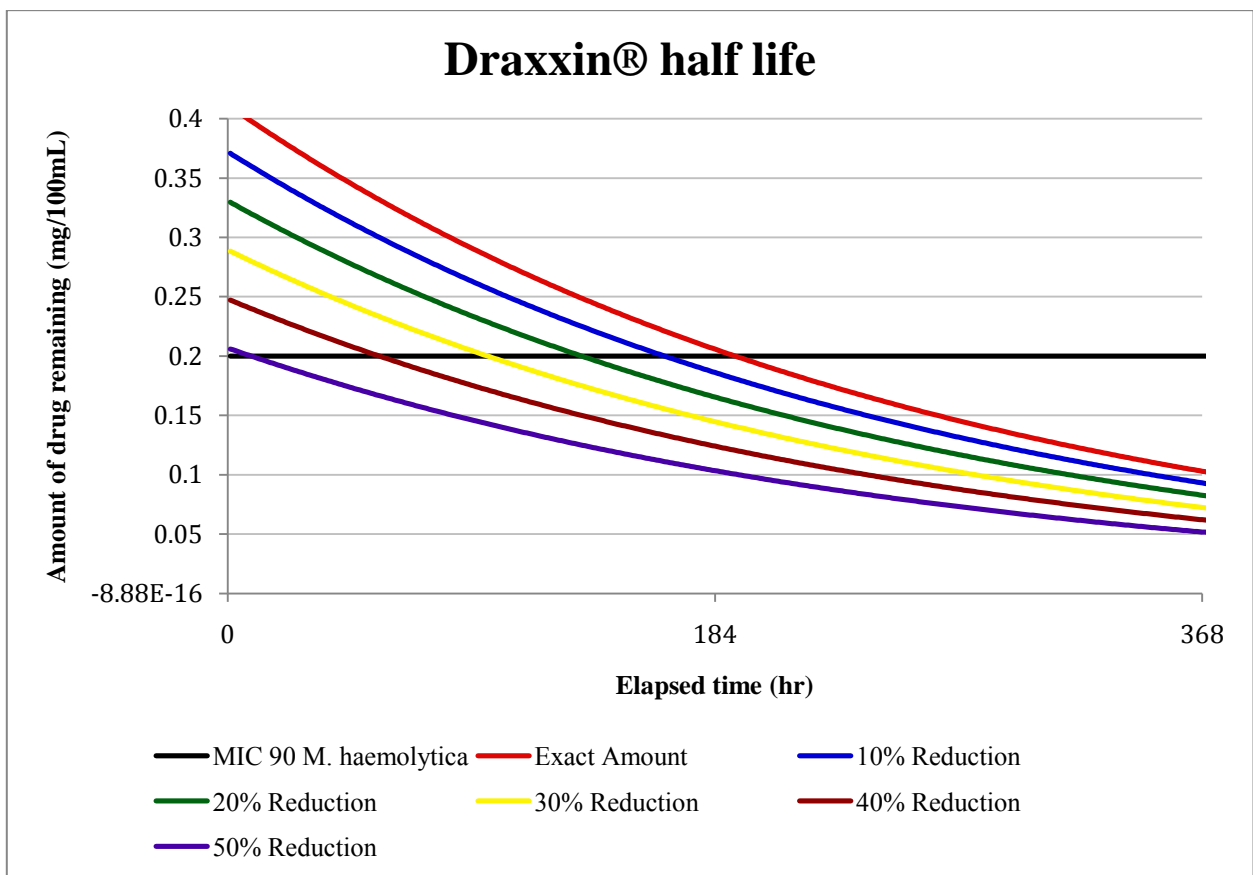Figure 3.1. The decrease in effectiveness of the medication Draxxin® through 368 hours following administration of a correct, weight-based dose and 90%, 80%, 70%, 60% and 50% of the correct, weight-based dose. The dark blue horizontal line is the concentration of Draxxin® that provides tissue minimum inhibitatory concention of 90% (MIC 90) for *M. haemolytica* (causative bacteria of pnuemonia).

(3) Estimation of economic costs due to not using recommended weight-based dose

The total economic loss associated with BRD in 1,000 feeder calves was estimated to be

$13,895, not including feed prior to death, labor or handling costs (Snowder et al., 2006). With a

stated morbidity rate of 14.4%, or 144 calves in the lot, the per incidence cost of sickness

($13,895/ 144) came to $96.49 per sick animal; as a result $96.49 was the value assigned to

represent the cost of a sick animal. Cattle were assumed to be in processing chutes, presumably

with a weigh scale in or directly attached to the head gate; the additional cost to collect the weight

and dose the animal correctly would be minimal if any. Therefore, the costs to collect weight data

were not associated with the total economic input cost.

Based on the reported pharmacological values and morbidity rates for Draxxin[®], the

variation from individual animal weights from a commercial feedlot, and the described economic

assumptions, a simulation model was developed that compared the costs associated with (i) exact,

weight-based dosing, (ii) dosing where each animal received the dose associated with the average

weight of the lot, (iii) dosing based on the lot average weight plus 50 lb, and (iv) dosing based on

the lot average weight minus 50 lb.

Economic analyses utilized the actual weight distributions for the individual lots as well

as an overall (all lots combined) distribution along with the previously described assumptions for

costs and morbidity to randomly simulate 500 different lots of cattle with the same average and

standard deviation of each individual lot. The data analysis package Simulation and

Econometrics to Analyze Risk (SIMETAR[©]) was used to create an economic simulation model

 to evaluate the cost of the different dosing regimens. Each individual animal's specific weight

within the lots was created to be a stochastic variable, being empirically distributed between the

lot maximum and minimum, around the actual lot means and standard deviations. The animals were assigned a uniformly distributed number, designated the sickness variable, to be the variable that would denote sickness at the end of the model. An incoming sickness variable was assigned to designate cattle that were sick upon arrival to the feedlot, with the assumption that cattle that were not sick when they arrived and were treated initially would not become sick. The coverage rate and adjusted coverage rate variables account for the amount of time the animal was covered from the given dose of Tulathromycin. Animals in the "Exact Dosing" lots were always assigned a perfect coverage rate of 1 or full coverage for their respective weight. Animals that were overdosed were adjusted to a maximum of 1. It has not been shown that there is an additive effect of overdosing in coverage time. The morbidity index is the adjusted coverage rate multiplied by the sickness variable to account for the effects of drug on the animals. The morbidity rate is the determinant of which animals remain sick after treatment within the lots. For the purpose of this analysis, the morbidity rate was set at 0.25, in other words, if the morbidity index was below 0.25 then the animal was determined to be sick. The threshold value of 0.25 was based on estimated morbidity rates found by Pfizer in field studies of tulathromycin. It was considered to be an adequate assumption of morbidity based on other research estimates as well. As discussed earlier, the cost of sickness was assigned a value of $96.49 per incident. Each animal designated as sick was assessed the cost of sickness, and all animals were assigned treatment costs based on the amount of Tulathromycin administered. Each lot was simulated 500 times using a Latin Hypercube simulation to observe the distributions and probabilities associated with each cost incidents. Based on the simulation output, the 500 iterations run in SIMETAR$^©$ were graphed into cumulative distribution functions (CDF graphs) to show graphically the cumulative

probability of a specific price event occurring. A Stochastic Efficiency with Respect to a Function chart (SERF chart) was used rank the dosing options. A relative risk neutral assumption was used when creating the SERF charts. Table 3.3 gives an example of the SIMETAR$^©$ simulation created to analyze the cost of sickness.

Results and Discussion

Based on the dilution space approach to evaluate time of drug effectiveness, it was estimated that Draxxin$^®$ administered at the recommended dosage to cattle weighing between 500 lb and 1000 lb should be provided with 191 hours (7.96 days) of protection from pneumonia-causing bacteria (where the lung tissue concentration should be above the MIC 90 level of protection). Pfizer recommends that animals injected with Draxxin$^®$ should not be given another injection for 7 days, this recommendation supports the basis for the coverage time being 191 hours. Table 3.4 shows the estimated time of coverage that animals receive when dosed at various percentages (100% to 50% reduced in 10% increments) of the recommended weight-based dose. Due to the pharmacokinetic properties of Draxxin$^®$, an animal that is administered a half-dose is only expected to be protected from pneumonia-causing bacteria for 8 hours, which is 4.2% of the coverage time of the proper dose. Therefore, it follows that there is a non- linear relationship between coverage time and dosing, and when using a dosing regimen accuracy can be a key factor in efficacy related problems.

Table 3.3. Example of model input parameters[1] used to evaluate economic costs associated with weight-based medications.

Average(-50) 550 lbs

Weight	Sickness Var	Sick/Not	CovRate	AdjCov	Morb Index	Morb Rate	Morb Cost	Dose Cost	Total Cost
600	0.255950	1	0.9192	0.919	0.2378	1	$ 96.49	$ 27.78	$124.27
550	0.250885	0	1.0027	1	0	0	$ -	$ 27.78	$ 27.78
500	0.260620	1	1.103	1	0.2607	0	$ -	$ 27.78	$ 27.78

[1]This is the model of a lot with an average of 550 lbs.
Weight - empirical distribution based on actual data and weight distributions from commercial feedlot
Sickness variable - a uniformly distributed number used to adjust coverage rates and help add more variability or less consistency between like weights.
Sick/not - 1 = sick, 0 = not sick. A 50% distribution based on Draxxin® studies showing approximately a 50% morbidity rate of a saline substitute.
Coverage rate/Adjusted coverage rate - the coverage of the animals actual weight as a percent of the weight used in the evaluation (lot average, lot average +50 lb, lot average -50 lb) and, if over 1 it is adjusted to reflect only 1. It is unknown if additional dosing aids in prevention.
Morbidity index - the morbidity index (between 0 and 1) is the adjusted coverage rate multiplied by the sickness variable to help account for the change in the percent coverage of the drug.
Morbidity rate - this is a variable that determines what percentage of the morbidity index will be sick. It is currently set a 25%, or if the morbidity index is below .25 then the animal is determined to be sick in the simulation as seen in the first model.
Morbidity cost - this is the cost associated with a sick animal set as a constant of $96.49.
Dose cost - the amount of drug dosed by weight to the animal based on exact, average, average +50 or average -50. In this case, a lot average of 550 lbs
Total cost - morbidity plus the dose cost.

Based on research by Evans (2005), pertaining specifically to the pharmacokinetic

properties of tulathromycin, models using plasma concentration based time dependency

(concentration duration above MIC) fail to adequately predict the observed efficacy due to the

rapid dispersion rates of tulathromycin into tissue.   The time exposure to the pathogens in lung

concentrations are a more adequate predictor of efficacy, but still does not capture the full

advantages of the movement and targeting associated with the triamilide class of antibiotics.

This model is based on the stated maximum lung concentrations related to the MIC 90 for *M.*

haemolytica, and is therefore a conservative estimate of the actual full effective rate of

tulathromycin. In a field trial the expected sickness should be less than that stated in the model

overall, and much less for the exact dosing.

Table 3.4. Amounts of time cattle should be protected from pneumonia-causing bacteria (MIC 90)[1] when administered Draxxin® at recommended, weight-based dosage and varying deviations (90%, 80%, 70%, 60% and 50%) of dose.

% Max concentration reduction	Time above MIC90 (hrs)	% Coverage time vs. recommended	% Less coverage time vs. recommended	Hours of reduced protection vs. correct dose
0 (100% dose)	191	100	0	0
10 (90% dose)	164	85.86	14.12	27
20 (80% dose)	133	69.63	30.37	58
30 (70% dose)	98	51.31	48.69	93
40 (60% dose)	57	29.84	70.16	134
50 (half dose)	8	4.19	95.81	183

[1]MIC 90 = Minimum inhibitory concentration to prevent 90% of bacterial proliferation.

Outputs from the economic simulations are presented in Figures 3.2 and 3.3. This analysis indicates that the correct, weight-based dose cost less than any other dosing technique, showing the real economic incentive for more precise management. The SERF value chart is a stochastic efficiency with respect to a function, or in this case, how much money would it take to match the next best alternative and make someone indifferent to the additional cost. In this output, a reasonably risk neutral manager would always choose to dose at the exact weights, followed by the lot average weight minus 50 lb. The final two would be
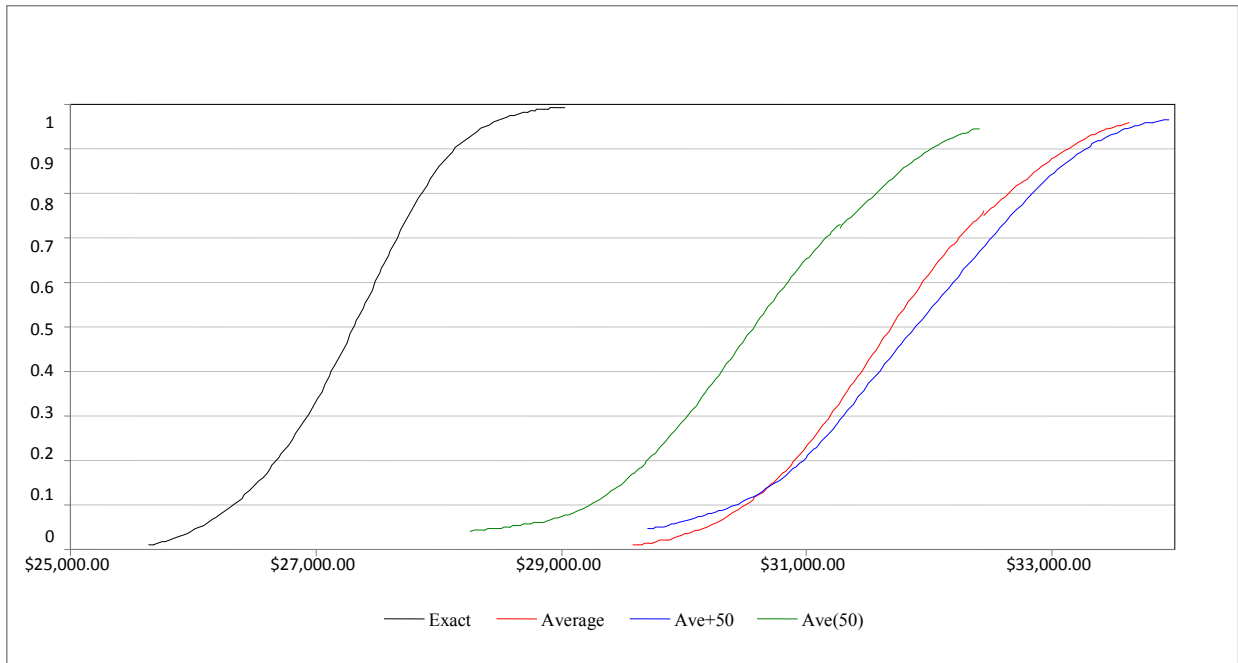

Figure 3.2. Cumulative Distribution Function (CDF) approximations from simulation study that show total costs associated with weight-based dosing scenarios using Draxxin$^®$ for exact weights, lot average weight, lot average weight plus 50 lb, and lot average weight minus 50 lb based on a group of 652 animals.

determined by the preferences of the individual manager since the lines intersect.

The risk neutral manager in this case would rather dose at 50 lb below the lot average weight than

50 lb over the lot average weight. While surprising at first, this finding is logical when

examining observed costs. A manager in an attempt to reduce up front processing costs would

under dose, seeing the initial observed costs of medications decrease. The loss of value in

sickness and quality may not be directly observable by the manager, therefore, is an overlooked

loss value associated with the under dosing.
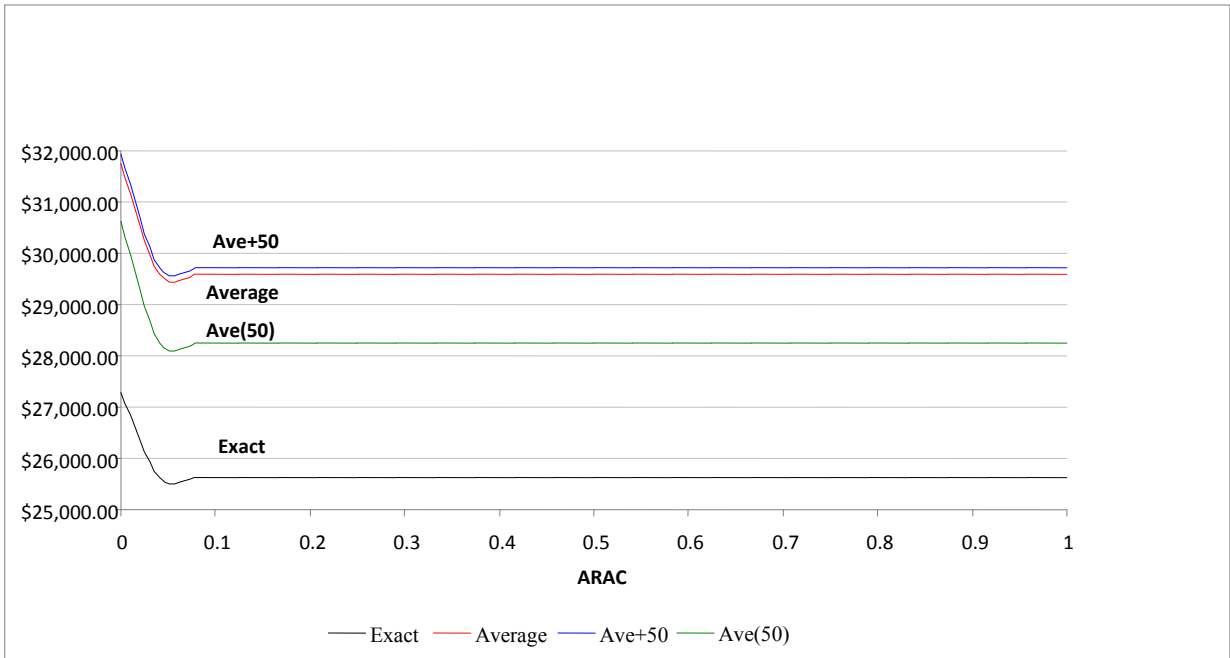

Figure 3.3. Stochastic Efficiency with Respect to a Function (SERF) values associated with
various weight-based dosing scenarios (exact weight, lot average weight, lot average weight plus
50 lb, and lot average weight minus 50 lb) using an Absolute Risk Aversion Coefficient (ARAC)
between 0 and 1 implying complete risk neutrality in decision management for a group of 652
animals.

Table 3.5 shows the costs associated with dosing all animals at the lot average weight, dosing all animals at the lot average weight plus 50 lb, and the lot average weight minus 50 lb, as well as all animals together on a per animal basis. These comparisons are made and interpreted most easily at the 50th percentile, and the results described below are differences at the 50th percentile. Overall, dosing all cattle at the lot average weight costs $6.04 per animal more than dosing at the exact, correct dose. Dosing all animals at the lot average weight plus 50 lb costs $6.24 per animal more; dosing all animals at lot average minus 50 lb costs $4.01 per animal more. These differences can be seen graphically at the 50th percentile on Figure 3.3 for the entire group of animals; the per animal values in Table 3.5 were determined by dividing the total lot costs by the respective number of animals. It is observed, in certain instances, that dosing at a 50 lb increment below the lot average weight can be cost beneficial. The cost savings come from the high cost per mL of Draxxin®. In lots E and F, the skewness aids in under dosing being the more cost efficient protocol. The heightened concentration of animals around the mean in the under-weight class is far outweighed by the large tail of animal weight distributions in the overweight class.

Table 3.5. Differences in cost from exact weight based dosing on (a) lot average weight, (b) lot average weight plus 50 lb, and (c) lot average weight minus 50 lb for Draxxin® on a per lot basis and a per head basis.

Lot #	Lot weight Ave, SD	n		Cost ($) per lot				Cost ($) per animal		
			Exact	(a) Ave	(b) Ave+50	(c) Ave(50)	Exact	(a) Ave	(b) Ave+50	(c) Ave(50)
A	1007, 105	75	--	187.39	350.26	257.37	--	2.50	4.67	3.43
B	639, 69	81	--	322.25	463.74	66.23	--	3.98	5.73	0.82
C	662, 76	126	--	718.61	960.42	642.25	--	5.70	7.62	5.10
D	631, 41	35	--	13.81	141.68	55.50	--	0.18	1.89	0.74
E	329, 58	30	--	113.71	51.00	70.35	--	3.79	1.70	2.35
F	931, 113	47	--	39.76	178.47	(29.12)	--	0.85	3.80	(0.62)
G	585, 77	68	--	211.73	263.24	188.02	--	3.11	3.87	2.77
H	470, 104	70	--	252.82	358.87	(10.87)	--	3.61	5.13	(0.16)
I	1,129,113	54	--	122.35	276.11	236.25	--	2.27	5.11	4.38
J	476, 88	69	--	133.68	313.80	139.57	--	1.94	4.55	2.02
All	693, 242	652	--	3,938.81	4,067.15	2,613.77	--	6.04	6.24	4.01

Implications

Producers many times assume that use of the average weight for a group of animals is good enough for administering weight-based medications. However, whether or not it really is good enough depends upon how much variability exists in the group, and the associated risks from large deviations from the average. Table 3.1 shows that even within small groups of cattle, substantial variation in weight exists, and use of exact weight is cost effective when administering weight-based products compared to other dosing schemes. Under dosage of cattle limits the product effectiveness and increases the costs associated with morbidity.

The differences in economic efficiency are directly related to the cost of the product, and the associated differences in effectiveness as well as the weight distribution. Use of the product Draxxin® (a popular and expensive antimicrobial used in the U.S. cattle industry) at an exact, weight-based dose produced a cost savings of $6.04 per animal was predicted as compared to simply using the average lot weight for each animal's dose. Procedures employed here will work for any weight-based medication where the input parameters are known.

The nature of this economic model is dynamic in that the input parameters can be altered to reflect any individual's respective production setting, new antibiotic or optimal protocol given certain levels of variation. Given known weights and distributions, and the parameters of the drug in question, this method could be used to determine at what point a given dosing protocol becomes interchangeable with respect to lot weights, standard deviations, or distributions.

By reducing the associated costs of production, beef producers can potentially make their products more accessible to consumers. The own price elasticity of beef was said to be -.621, so any cost reductions observed can help to keep beef price relevant as compared to substitutes at

the retail level (USDA, 2008). Producers can often get caught up in the added value of the marketing scheme while losing sight of the costs of production. As with most commodity products, the beef industry is at the mercy of consumer demand. Production costs need to be weighed just as heavily as added or retained value in production.

In order for producers to evaluate and decrease costs of production, all potential impacts that stem from the use of weight-based products must be considered, not just simply cost of product and use of average weights of lots. The use of individual animal weights to determine per head dosing of Draxxin® is more cost effective than using lot averages when there is typical weight variation, but especially when there is heightened variation. This concept would appear to extend to all weight-based pharmaceutical products in general.

CHAPTER IV

CONCLUSIONS

The amount of variation within groups of cattle is the main limiting factor determining whether average dosing or deviations from the average is an appropriate dosing regimen. Off label dosing potentially places limitations on the drugs' efficacy, leading to additional costs associated with increased morbidity or heightens product waste and drives up production costs. The use of individual animal weights to determine per head dosing of Draxxin® is more cost effective than using lot averages when there is typical weight variation, but especially when there is heightened variation.   This concept would appear to be valid with the use of any weight-based pharmaceutical product.

Using the least amount of any pharmaceutical in the most efficient manner in an effort to keep cattle healthy, while minimizing costs, is the ultimate goal in any production setting. By reducing the associated costs of production, beef producers can potentially make their products more accessible to consumers. Increased awareness of the additional benefits of precision dosing in weight- based medications is crucial to avoiding mandated action against producers.

LITERATURE CITED

Abidoye, B. and J. D. Lawrence. 2006. Value of single source and background cattle as measured by health and feedlot profitability. Proceedings of the NCCC 134 Conference on Applied Commodity Price Analysis, Forecasting and Market Risk. Presentation and paper at the 2006 NCCC-134. St. Louis, MO. http://www.farmdoc.uiuc.edu/nccc134.

Ahmed, I., K. Kasraian. 2002. Pharmaceutical challenges in veterinary product development. Adv. Drug Deliv. Rev. 54:871- 882.

Babcock, A., R. Jones, and M. Langemeier. 2006. Examining death loss in Kansas feedlots. Pages 46-52 in Beef Cattle Research – 2006, Report of Prog. 959, Kansas State Univ., Manhattan, KS. http://www.oznet.ksu.edu/library/lvstk2/srp959.pdf Accessed June 23, 2010.

Bartle, S. J., J. R. Males and R. L. Preston. 1983. Evaluation of urea dilution as an estimator of body composition in mature cows. J. Anim. Sci. 56: 410- 417.

Bartle, S. J., S. W. Kock, R. L. Preston, T. L. Wheeler and G. W. Davis. 1987. Validation of urea dilution to estimate in vivo body composition in cattle. J. Anim. Sci. 64: 1024- 1030.

Booker, C. W., S. M. Abutarbush, O. C. Schinucht, G. K. Jim, T. Perrett B. K. Wildman, P. T. Guichon, T. P. Pittman, C. Jones and C. M. Pollock. 2007. Evaluation of the efficacy of tulathromycin as a metaphylactic antimicrobial in feedlot calves. Vet. Ther. 8:183-200.

Chirase, N.K and L.W. Greene. 2001. Dietary zinc and manganese sources administered from the fetal stage onwards affect immune response of transit stressed and virus infected offspring steer calves. Anim. Feed Sci. and Tech. 93: 217- 228.

Cole, N. A. 1985. Preconditioning calves for the feedlot. Vet. Clin. North Am. Food Anim. Pract. 1:401-411.

Edwards, A. 1996. Respiratory disease of feedlot cattle in central U.S.A. The Bovine Practitioner. 30:5-7.

Evans, N. A. 2005. Tulathromycin: an overview of a new Triamilide antimicrobial for livestock respiratory disease. Vet. Ther. 6: 83-95.

Gardner, B. A., H. G. Dolezal, F. N. Owens, L. K. Bryant, J. L. Nelson, B. R. Schutte and R. A. Smith. 1998. Impact of health on profitability of feedlot steers. 1998 OSU Animal Science Research Report 102- 108.

Gardner, B. A., H. G. Dolezal, L. K. Bryant, F. N. Owens, and R. A. Smith. 1999. Health of finishing steers: effects on performance, carcass traits, and meat tenderness. J. Anim. Sci. 77:3168-3175.

Gill, R. C., J. W. Richardson, J. L. Outlaw and D. P. Anderson. 2003. An analysis of ethanol production in Texas using three ethanol facilities and their relative optimal subsidy levels. Paper presented at Southern Agricultural Economics Association Annual Meeting. Mobile, AL, February 2003.

Griffin, D. 1997. Economic impact associated with respiratory disease in beef cattle. Vet. Clinics of N. Am. Food Anim. Pract. 13:367–377.

Hardaker, J.B., R.B.M Hurine., J.R. Anderson., and G.Lien. 2004. Coping with Risk in Agriculture, Second Edition. CABI, 2004, Cambridge, MA.

Hilton, W. M. 2005. Beef quality assurance injection sites and techniques. Purdue University

Extension Service. http://www.ces.purdue.edu/extmedia/VY/VY-60-W.pdf. Accessed:

July 7, 2010.

Kock, S. W., R. L. Preston. 1979. Estimation of bovine carcass composition by the urea dilution

technique. J. Anim. Sci. 48: 319-327.

Lawrence, J. D. and M. A. Ibarburu. 2006. Economic analysis of pharmaceutical technologies in

modern beef production. Iowa State University. www.econ.iastate.edu/faculty/lawrence

/pharmaeconomics2006.pdf. Accessed: July 10, 2010.

Lawrence, J. D. and M. A. Ibarburu. 2007. Economic analysis of pharmaceutical technologies in

modern beef production in a bioeconomy era. Iowa State University.

http://econ2.econ.iastate.edu/faculty/lawrence/pharma%202007%20update.pdf. Accessed:

July 10, 2010.

Letavic, M. A., B. S. Bronk, C. D. Bertsche, J. M. Casavant, H. Cheng, K. L. Daniel, D. M.

George, S. F. Hayashi, B. J. Kamicker, N. L. Kolosko, L. J. L. Norcia, V. D. Oberton, M.

A. Rushing and S. L. Santoro. 2002. Synthesis and activity of a novel class of tribasic

macrocyclic antibiotics: the triamilides. Bioorg. Med. Chem. Lett. 12: 2771-2774.

Loneragan, G. H., D. A. Dargatz, P. S. Morley, and M. A. Smith. 2001. Trends in mortality ratios

among cattle in US feedlots. J. Am. Vet. Med. Assoc. 219:1122- 1127.

Martin, S. W. and J. G. Bohac. 1985. The association between serological titers in infectious

bovine rhinotracheitis virus, bovine virus diarrhea virus, parainfluenza- 3 virus,

respiratory syncytial virus and treatment for respiratory disease in Ontario feedlot calves.

Can. J. Vet. Res. 50: 351- 358.

McNeill, J. W., J. C. Paschal, M. S. McNeill and W. W. Morgan. 1996. Effect of morbidity on

performance and profitability of feedlot steers. J. Anim. Sci. (suppl. 1). 74. (Abstr.)

NASS. 2010. Cattle. http://usda.mannlib.cornell.edu/usda/current/Catt/Catt-07-23-2010.pdf.

Accessed: July 26, 2010.

Nowakowski, M. A., P. B. Inskeep, J. E. Risk, T. L. Skogerboe, H. A. Benchaoui, T. R. Meinert,

J. Sherington, S. J. Sunderland. 2004. Pharmacokinetics and lung tissue concentrations of

Tulathromycin, a new triamilide antibiotic, in cattle. Vet. Ther. 5: 60-75.

Pfizer Animal Health. 2005. Comparative efficacy of draxxin or micotil for the control of

respiratory disease in cattle at high risk of developing undifferentiated bovine respiratory

disease. Technical Bulletin. http://www.draxxin.com/pdfs/draxxin/DRX05022.pdf.

Accessed: January 15, 2009.

Richardson, J.W. 2010. Simulation for applied risk management with an introduction

to SIMETAR. Department of Agricultural Economics, Texas A&M University, 2010,

College Station, TX.

Roeber, D. L., N. C. Speer, J. G. Gentry, J. D. Tatum, C. D. Smith, J. C. Whittier, G. F. Jones, K.

E. Belk, and G. C. Smith. 2001. Feeder cattle health management: effects on morbidity

rates, feedlot performance, carcass characteristics, and beef palatability. Prof. Anim. Sci.

17:39-44.

Rule, D. C., R. N. Arnold, E. J. Hentges and D. C. Beitz. 1986. Evaluation of urea dilution as a

technique for estimating body composition of beef steers in vivo: validation of published

equations and comparison with chemical composition. J. Anim. Sci. 63: 1935- 1948

Sanderson, M. W., D. A. Dargatz, and B. A. Wagner. 2008. Risk factors for initial respiratory disease in United States feedlot based on producer-collected daily morbidity counts. Can. Vet. J. 49:373-378.

Skogerboe, T. L., Rooney, K. A., Nutsch, R. G., D. J. Weigel, K. Gajewski and W. R. Kingore. 2005. Comparative efficacy of tulathromycin versus florfenicol and tilmicosin against undifferentiated bovine respiratory disease in feedlot cattle. Vet Ther. 6: 180- 196.

Snowder, G. D., L. D. Van Vleck, L. V. Cundiff, and G.L. Bennett. 2006. Bovine respiratory disease in feedlot cattle: environmental, genetic and economic factors. J. Anim. Sci. 84: 1999-2008.

Soberman, R., B. B. Brodie, B. B. Levy, J. Axelrod, V. Hollander and J. M. Steele. 1949. The use of the antipyrine in the measurement of total body water in man. J. Biol. Chem. 179:31.

Step, D. L., C. R. Krehbiel, H. A. Depra, J. J. Cranston, R. W. Fulton, J. G. Kirkpatrick, D. R. Gill, M. E. Payton, M. A. Montelongo, and A. W. Confer. 2008. Effects of commingling beef calves from different sources and weaning protocols during a forty-two-day receiving period on performance and bovine respiratory disease. J. Anim. Sci. 86:3146-3158.

USDA. 2000. Part III: Health management and biosecurity in U.S. Feedlots, 1999. USDA: APHIS: VS, CEAH, National Animal Health Monitoring System. Fort Collins, CO. #N336. 1200

USDA. 2008. Diet quality and food consumption: food demand analysis. http://www.ers.usda. gov/Briefing/DietQuality/Demand.htm. Accessed: July 28, 2010.

Vannuffel, P. and C. Cocito. 1996. Mechanisims of action of streptogramins and macrolides. Drugs. 51: 20- 30.

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