Abstract
Mathematical modeling is the only tool to study the potential dynamics of Foot-and-Mouth Disease virus (FMDv) in disease-free countries. Although there are models of within-farm FMDv transmission dynamics, they treat the farm as a homogenous unit. This is unrealistic for large, compartmentalised livestock production units such as a US beef feedlot. Moreover, important management and policy decisions must be made about how to manage infected farms; this requires projecting within-farm outbreaks. We have developed a model of potential FMDv transmission dynamics within a US feedlot. This is an SLIR (susceptible, latent, infectious, recovered) model nested in a meta-population of the home and hospital pens. Parameters were gathered through published experiments, outbreak data, and an expert opinion survey. The model monitors temporal and spatial spread of disease and its clinical manifestation. Spread is via direct animal contact within home pens and in hospital pens, fence-line between adjacent pens, airborne, via water troughs, and indirectly by pen riders. Surveillance was modeled to detect the index infected pen when the proportion of animals with clinical signs reached 3%, 5% or 7%. Detection occurred on day 6-17 post FMDv introduction and the number of infected pens at detection varied from 4-19. Our model underlines the importance of within-farm FMDv infection dynamics, and may serve as a basis for policy and management decisions as well as further research to evaluate disease detection and control strategies such as vaccination.

Keywords: Foot-and-mouth disease, mathematical modeling, beef feedlot, surveillance

Introduction
Foot-and-mouth disease is a highly contagious disease which affects cloven-hoofed animals and some wildlife. There are 7 antigenically distinct serotypes: A, O, C, SAT-1, SAT-2, SAT-3, and ASIA-1 with serotype O being the most widely distributed around the world (1). More than 64 subtypes have been identified and there is no immunological cross-protection between serotypes. Several FMD outbreaks have occurred around the globe in the last 15 years (2) increasing concern of its emergence in previously free countries. In the UK the estimated economic losses due to the 2001 FMD outbreak were $12.3 billion (2). In the US modeling estimates of a $56-$188 billion impact for a central US regional outbreak have been reported (3). It is important that countries with large livestock industries develop control strategies to quickly respond when facing a potential FMD outbreak.

The beef industry in the US is one of the largest in the world. Almost 50% of the total beef finished for slaughter are in large commercial feedlots (one-time capacity >24,000 head of cattle) in the Central US. Approximately 860 million kilograms of beef are exported each year which represents an estimated income of $2.8 trillion US dollars (4). The last time FMD was identified in the US was in 1929. An outbreak of FMD in the central US would have a substantial impact (3,5) and there is increasing realisation that depopulation of large feedlots may not be a practical control strategy (6). Alternative approaches including allowing the feedlot to recover in place with enhanced biosecurity are being considered. This approach raises numerous issues including the impact of surveillance on time to detection and the usefulness of disease spread interventions.

Mathematical modeling is an important tool to predict/represent a potential epidemic of infectious diseases such as FMD in free countries and for specific management systems. While there are several published FMD models (7), they focus on modeling farm to farm transmission and represent the farm as a homogenous unit. This assumption might not be valid for large compartmentalised feedlots in the US when management and policy decisions must be made about how to control disease at the farm level. Although some within-farm FMDv transmission models have been developed (8,9), these models do not consider the typical US feedlot layout and common production management inside the feedlot.

The objective of our model is to project the FMDv transmission dynamics and clinical manifestation within a US beef feedlot, incorporating typical feedlot layout, production management, and animal demographics. Here we use the model to assess FMD spread within the feedlot, estimate the impact of surveillance sensitivity on time to detection based on varying prevalence detection thresholds and estimate the impact of stopping movement of cattle to hospital pens following detection.

Materials and methods
Model structure
We developed a stochastic SLIR (susceptible-latent-infectious-recovered) model nested in a meta-population of home pens and hospital pens in a US beef feedlot. Multiple compartments for infectious animals were considered: Subclinical low infectious, Subclinical high infectious, and Clinical infectious. Two levels of cattle mixing inside the feedlot were modeled: within-pen and between pens.
Within-pen transmission
We assumed that there was homogeneous cattle mixing within the pen and a density-dependent FMDv transmission. The beta transmission parameter value for within-pen FMDv spread was adopted from literature (8).

Between pen transmission
Five different routes of FMDv transmission between the home pens were modeled: direct contact from mixing of cattle from different home pens in the hospital pen, fence-line direct contact, via contamination of water troughs shared between home pens, via environment (dirt/feces) transferred by pen-riders between home pens, and airborne transmission. Morbidity rates for endemic diseases (4) such as Bovine Respiratory Disease were used to account for the probability that cattle move to the hospital pen. We assumed the rate of FMDv transmission in the hospital pen via direct contact was the same as within the home pens. Animals were assumed to move to the hospital pen and come back to their home pens on the same day. We assumed the rate of FMDv transmission via fence-line direct contact was 25% of within pen (0.25 β*). For transmission via water troughs, the quantities of FMDv shed in saliva on a daily basis by animals in the clinical stage were calculated and 30% of that deposited into the water troughs. Daily water consumption by cattle was used to estimate the FMDv transmission probability. The quantities of FMDv shed in saliva, urine, and feces were calculated to account for pen surface contamination (1). A fraction of that contaminated material was assumed to be transported in the hoofs of the horses or boots of pen-riders from pen to pen. For both water trough and pen rider transmission, the ID90 of FMDv via alimentary ingestion was used to model the probability of infection in the exposed cattle. Airborne pen-to-pen transmission was modeled by a modified kernel as a function of the Euclidean distance between centroids of the pens.

Parameterisation
A literature review focused on animal-based experiments and outbreak investigation reports was used as the baseline parameter values for the disease and infection stages of FMD from a published meta-analysis (10). An on-line FMD expert survey was conducted to gather data regarding clinical manifestations in diseased animals and to assess the probability of detection of infected pens. Epidemiologists and virologists with FMD experience were the main target population of the survey. Data on farmer based surveillance detection of within herd, animal-level prevalence thresholds for FMD infected cattle were obtained from colleagues in Uruguay involved during the 2001 FMD outbreak in that country (personal communication).

Modeled scenarios: We modeled a medium size feedlot of 12,000 cattle distributed in 60 pens with 200 head per pen, and 1 hospital pen. The index pen of cattle containing 10 FMD-latent cattle were introduced in the central region of the feedlot. Three surveillance detection scenarios were modeled: at 3%, 5%, and 7% prevalence of clinical FMD cattle in the index pen. Two post-detection response scenarios were modeled: Scenario 1 (baseline) continued animal mixing in the hospital pen following FMD detection; Scenario 2 stopped movements to the hospital pen on the day of detection. Each scenario was simulated 1,000 times. The model was implemented in Vensim® PLE Plus software; Ventana Systems Inc., Harvard, MA, USA).

Results
The median time to detection and number of pens infected varied with the modeled prevalence at detection. At 3% prevalence of clinical FMD cattle in the index pen, detection occurred at a median of day 8 following FMDv introduction in the feedlot and a median of six additional pens were infected. Using the 5% threshold, the detection occurred at a median of Day 9 with a median seven additional pens infected. Using the 7% threshold, the detection occurred at a median of Day 10 with a median eight additional pens infected. For the post-detection response Scenario 1, simulations showed that the within-feedlot outbreak took 60-80 days to fade-out and all pens were infected by a median of 20 days post FMDv introduction (Figure 1). For Scenario 2, the outbreak took 85-120 days to fade out (Figure 2) and all pens were infected by a median of 38 days post FMDv introduction (Figure 1). The Scenario 2 results were similar for the detection thresholds at 3%, 5% and 7% clinical prevalence in the index pen (data not shown).

Figure 1. Median cumulative number of infected pens by outbreak day for scenarios where hospital pen movement was stopped or continued following FMD detection at 3% prevalence of clinical FMD cattle in index pen.

Discussion
Management of FMDv infected feedlots to recover in place without depopulation is currently being considered in US management plans. Assessment of these plans will require estimation of the behavior and detection of FMDv within a large feedlot. The potential value of interventions to mitigate disease spread depend on effectiveness of surveillance for detection as well as transmission dynamics. Surveillance for disease is routinely carried out in US feedlots by daily active observation of cattle by feedlot employees trained to detect disease. We modeled a range of detection thresholds based on active observational surveillance by feedlot employees to
estimate the impact of detection day on the outbreak. Stopping hospital pen mixing of cattle decreased the speed of FMDv transmission across the feedlot, but did not prevent eventual infection of all pens. The number of already infected pens in the feedlot increased as the percentage of FMD clinical cattle in the index pen at detection increased from 3% to 7%. This difference did not result in large differences in the speed or duration of the outbreak if hospital mixing was stopped at detection. Delayed detection does increase risk for off farm transmission to a new premise and will be further investigated.

Figure 2. Percentage of clinical FMD cattle in index pen compared to number of clinical cattle in the feedlot, if the disease was detected at 3% prevalence of clinical FMD cattle in index pen and movements to the hospital pen stopped following detection.

While a longer duration of the outbreak is not obviously an advantage, two potential benefits should be further explored. First, the labor demands for the feedlot in managing a rapid outbreak may be overwhelming and result in additional impacts from failure to adequately care for cattle. Second, vaccination in the face of an outbreak to decrease FMD spread and the final outbreak size may be feasible if the spread of infection can be slowed while cattle develop post-vaccination immunity. The possible value of each benefit requires further analysis. Data presented here suggest that active observational surveillance may allow sufficiently early detection of FMD to allow time for targeted feedlot interventions if hospital mixing is stopped.

Stopping all movements to the hospital pen would also be a challenge for management of the cattle on the feedlot and for animal welfare. Morbidity from FMDv infection as well as continued endemic disease morbidity would still require treatment. Alternate management to allow sufficient treatment would be required and the costs and benefits need to be further assessed. Further refinement of this model will help to generate results to inform both policy decisions and best management practices for feedlots in the face of an FMD outbreak.

References