

KEEPING FAD RESPONSE PROGRAMS FROM ERADICATING FARMS

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ABSTRACT

Foreign Animal Disease (FAD) agents, such as Highly Pathogenic Avian Influenza or Foot and Mouth Disease (FMD; a worst-case FAD), are documented threats, whether through accidental or intentional exposures. US policies, as with most countries where FMD is not endemic, follow 'Stamping Out/Eradication' (SOE) protocols: Affected herds are rapidly destroyed to eradicate the agent and quickly resume export trade. While historically effective, SOE goals and techniques no longer apply to US agriculture:

<p>1. <i>Goals are wrong</i></p>	<ul style="list-style-type: none"> ◆ Exports are 10-15% of US animal agriculture; SOE risk majority for a minority; ◆ Eradication is a means, not an end -- Saving farms is the true end.
<p>2. <i>Assumptions are wrong</i></p>	<ul style="list-style-type: none"> ◆ Assume accidental outbreaks & incidental expansion, whereas market-origin or intentional FAD events will likely start at near worst-case magnitude; ◆ Assume the first question is 'will SOE work?' rather than 'Is SOE optimal?'
<p>3. <i>Methods are missed</i></p>	<ul style="list-style-type: none"> ◆ US agriculture is concentrated in regional 'Production Centers' with different needs, strengths, and vulnerabilities than SOE recognize; ◆ Out-of-date concerns force SOE to minimize/disregard immunomodulation.
<p>4. <i>Unintended effects are huge</i></p>	<ul style="list-style-type: none"> ◆ Past FMD SOE saw >1/3rd of animals destroyed for 'welfare' reasons, ◆ Past FMD SOE saw the industries degrade long after the epidemic was over, ◆ Do not consider non-infecteds' production losses as part of FAD impact.

It is evident that FMD eradication by rapid 'stamping out', if applied in a modern concentrated agricultural state, is likely to fail and so damage the affected industries that they will not recover. In short, in our drive to protect agriculture, we may actually destroy it. Stamping Out policies, therefore, can paradoxically enhance FAD agents' sphere of damage and thusly increase their bioterror value, for the policies can accentuate an FAD's breadth of societal damage and augment their economic warfare qualities. A factor that is missing from FMD planning in general is an in-depth consideration of how America's agriculture will cope during an outbreak and how it will recover (i.e., business continuity). We must, therefore, re-evaluate our proposed plans for controlling catastrophic FADs in light of new knowledge. By scientifically addressing the true threats FADs pose to today's agriculture, we will lessen the effects of natural or accidental FAD outbreaks, and will make FADs less attractive as bioterror tools.

INTRODUCTION & GOAL

Lessons learned from the current H5N1 HPAI pandemic and the United Kingdom (UK) 2001 & 2007 FMD experiences, combined with planning efforts in the US, have revealed crippling shortcomings in the Stamping-Out Eradication strategy. Many states have recognized that new technologies must be incorporated into a strategy that would prevent and/or limit large scale outbreaks.

A factor that is missing from FMD planning in general is an in-depth consideration of how America's agriculture will cope during an outbreak and how it will recover (i.e., business continuity). Without totally abandoning current eradication strategies, the revised Strategy will serve as a model not only for North Carolina, but also for states with similar agricultural vulnerabilities.

BACKGROUND

The world before 2001

For most of the 20th century, agriculture was seen as being ubiquitous, small scale, and oriented/marketed locally. In economic terms, agriculture was viewed as an "assumed function". This means that, in most analysts' perspective, agriculture was assumed to be not at risk of massive damage by foreseeable disasters. However, external markets' responses to a localized FAD outbreak was viewed as coming closest to inducing a national disaster, by closing off foreign trade opportunities. So, agricultural protection with regards to FADs was aimed at identifying the affected animals/herds/flocks and destroying them as soon as possible to minimize impacts on national-level trade agreements and markets.

Additionally, the thrust of national and state level agricultural regulations and disease control programs carried unstated presumptions that the only risks agriculture faced were from accidental or natural threats, and these assumptions colored the scenarios against which programs were designed. The idea of massive intentional attacks on US agriculture, or of market-spread outbreaks, was not a serious consideration for researchers or decision-makers.

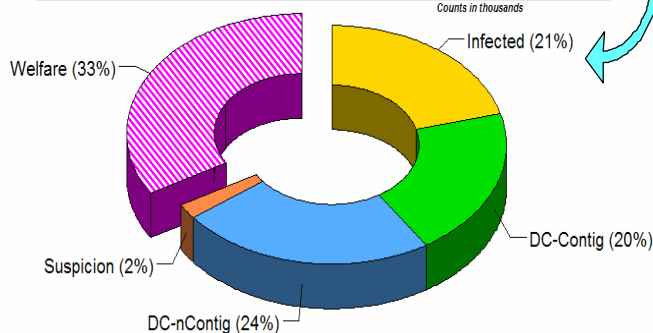
The world since 2001

Today, agriculture is regional, large scale, highly mobile, and interdependent. It is dependent on transportation and just-in-time management.

Biotechnological advances since the start of the century have created new tools -- genomics, proteomics, nanotechnology, to name three -- and options for dealing with catastrophic transboundary diseases. Additionally, in-depth reviews of recent FMD outbreaks [Taiwan (1997), United Kingdom (2001, 2007), South America (2001)], plus similar events dealing with Bovine Spongiform Encephalopathy (BSE) [Canada (2003), USA (2004, 2005)], with added insight from evaluations of Newcastle Disease and Highly Pathogenic Avian Influenza outbreak responses in North America (2003-2004), have uncovered new considerations in regional or state disease control programs.

For instance, the UK experienced near wholesale destruction of its livestock markets starting with the discovery of BSE in 1985, exacerbated by the tie-in to human disease (new variant Creutzfeldt-Jacob Disease) in 1994, and finished with the official destruction of over 6 million animals in the 2001 FMD outbreak – 1/3rd of which were done so for “welfare” reasons (Figure 1). The UK has experienced, as a result, a drop in domestic consumption,

Type of Premises	Cattle		Sheep		Pigs		Other		Weighted Total	
	No.	Pct.	No.	Pct.	No.	Pct.	No.	Pct.	No.	Pct.
Infected	303	40%	952	19%	20	5%	1.3	13%	1277	21%
Danger Contact, Contig	195	26%	983	20%	53	12%	1.6	16%	1233	20%
Danger Contact, Non-Contig	81	11%	1296	26%	69	16%	1.0	10%	1448	24%
Slaughter on suspicion	14	2%	111	2%	3	1%	0.3	3%	128	2%
Welfare Disposal	169	22%	1587	32%	287	66%	5.4	57%	2048	33%
Total	763	100%	4930	100%	432	100%	9.5	100%	6134	100%
Percent of Total	12%		80%		7%		0%		100%	



Rushton, et al. Economic analysis of vaccination strategies for foot and mouth disease in the UK. *Plan Livestock Services, Ltd. Veterinary Epidemiology and Economics Research Unit, Reading University, UK. July 16 2002*

Figure 1. Breakdown of reasons for animal destruction by species. UK FMD 2001. From the Royal Society FMD2001 Review

signaling that severe outbreaks can lead to such changes in demand that our attempts to maintain supply are futile.

In another example, the Taiwan FMD experiences in the late 90's (Figure 2), demonstrate that agriculture is not an assumed function, that it is actually quite fragile in the face

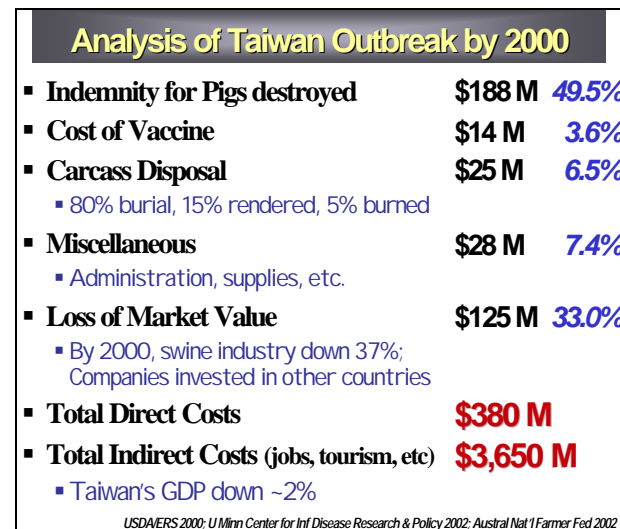


Figure 2. Estimates for the costs of the 1997 Taiwan FMD outbreak through 1999. Market losses comprised 1/3rd of direct costs; indirect costs (tourism, secondary employment, etc.) are nearly 10 times greater than the direct costs. From USDA ERS, 2000; CIDRAP, 2002; Austral Nat'l Farmer Fed, 2002.

of major supply and demand perturbations. In 1996 Taiwan was one of the largest pork exporters in the Pacific rim. After FMD, Taiwan became a net pork importer; as of 2006 they had not regained their production or markets.

From documents found in Taliban caves in Afghanistan, through to environmental/animal rights underground websites, it is apparent that agriculture is deemed a large, soft target to damage US infrastructure. Bioterror aimed at agriculture, or agroterrorism, is a prime tool of politically motivated economic warfare - its impacts go far beyond agriculture (Figure 2) – causing severe long-term economic and socio-political damage. Ripple effects of such disruptions, or mere threats of exposures (New Zealand, 2005), are difficult to foresee, forestall, or counter.

PROS AND CONS OF CURRENT FMD CONTROL PLANS

Advantages

In the US, and NC, the current program for controlling FMD is based on the ancient concept of quarantine and slaughter, commonly referred to as a “Stamping Out” policy. In such a program, we stop animal and animal-product movement, identify affected herds/flocks and likely affected herds/flocks, and destroy the animals before they

can spread disease. After a period of strict surveillance and biosecurity regulation, movement permits begin to allow markets to build back. As a tactic, this is highly useful in FMD, for it stops virus replication and shedding – the major means of FMD virus spread in an outbreak – as the UK model in Figure 3 suggests. SOE has been proven multiple times to be effective in breaking an epidemic of FMD (USA 1929, UK 1967). National and international rules and regulations have been developed to precisely characterize and quantify the means of accomplishing such tasks, and of documenting their success in returning a country or region to FMD-free status.

As a result of the very long and proven track record of the Stamping Out strategy, its conceptual and logistical straightforwardness, and its clearly identifiable outcome, throughout the 20th century it was the preferred tactic embraced by FMD-free countries.

Emergency vaccination is a growing tactic in the armamentarium against FMD. A successful ‘ring’ or ‘fence’ vaccination protocol involves identifying an infected premise (IP) and vaccinating herds around the IP to limit opportunities for the agent to spread, analogous to setting backfires to stop forest fires. It is seeing increasing recognition and use in international FMD programs, and the World Organization for Animal Health (WOAH, or OIE; Office International des Épizooties) and the European Union (EU) are changing rules which penalize vaccine using countries. Recently, several US state veterinarians have stated that emergency vaccination will be their state’s primary mode of dealing with FMD.

Disadvantages

To limit scavengers and potential public health concerns, however, stamping out programs also require very rapid carcass destruction, usually by burial or burning. Both carry

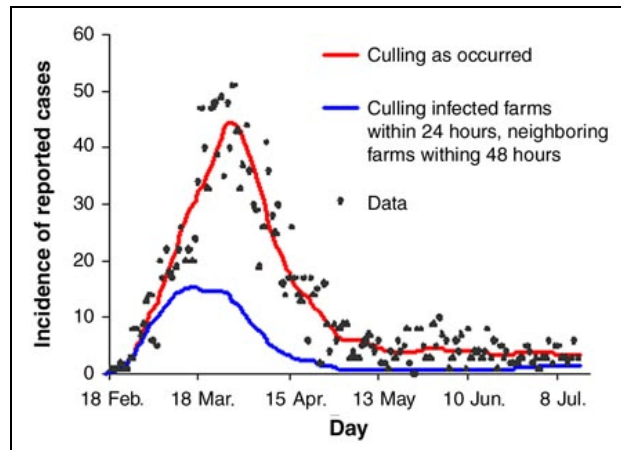


Figure 3. Actual and simulation of FMD response in the UK 2001. Assumes diagnostics, euthanasia, and disposal occur according to program goals: Euthanasia within 24 hr of diagnosis, and disposal within 48 hr. From DEFRA, 2002.

public perception and environmental problems.

Additionally, the stop movement orders (SMO) required by SOE generate their own problems. For instance, many herds and flocks will denude feed resources (whether pasture or stored feed) during an SMO, leaving producers and regulators with a Hobbes’ choice between allowing animals to starve or euthanizing them, the outcomes of which have been shown in Figure 1 for the 2001 UK FMD event: One in three died not from

disease, but from our programs. That is unacceptable and politically infeasible.

Another problem is that SMOs in today’s highly mobile agriculture practicing ‘just-in-time’ animal and resource inventory management create massive food system damage by themselves. Even an optimistically short 72 hour stop movement (and it is more likely to stretch 7 to 10 days even in a very small, localized outbreak) followed by immediate open movement will force some producers to go for days without feed, and markets without products. As of this writing, 4 days after the 2007 UK FMD outbreak, British store shelves are going empty. However, the UK authorities recognize this issue and are trying to allow limited market movements now.

Furthermore, estimates from the dairy industry are that if interstate milk movement is stopped, the entire NC system capacity would be reached within 48 hours – there would be nowhere for milk to go, even if FMD were not in our state. Healthy dairies would have nowhere for milk to go.

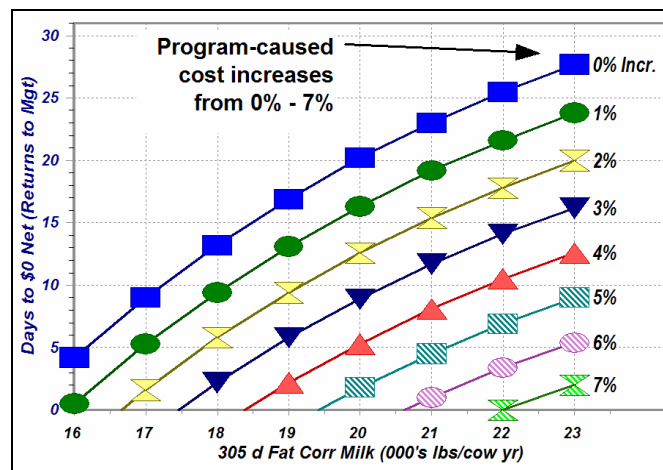


Figure 4. Economic prediction for dairies’ resilience to stop movement orders (using typical NC dairy cost structures and trends), as a function of per cow milk production and across program-induced cost increases from 0% to 7%.

Damage to uninfected farms is inevitable by SMOs. Figure 4 illustrates a simple analysis determining how many non-shipping days a dairy could absorb before its annual profit (measured as returns to management) reached zero. It suggests the average NC dairy producing between 17,000 to 18,000 lbs of

milk per cow, could survive an SMO up to 9-13 days, assuming all else is equal. Should the control and recovery program increase costs (or decrease milk prices) by a mere 3%, these farms will have \$0 returns to management within hours of instituting the SMO. Higher producing farms, assuming similar debt and externals, survive longer, but the trend is relentless: The longer SMOs last, the more of the industry will fail – even though they are doing everything right and remain uninfected.

Another tool in the FAD control kit is ring vaccination, itself a suite of tactics gaining popularity in many state departments of agriculture. Ring vaccination requires a response system that can move extremely rapidly to get the proper vaccine to the animals-at-risk in time, in a useable form, and in the hands of trained personnel. In dealing with FMD, which has 7 serotypes and over 60 subtypes, this is no trivial logistical matter. Furthermore, given that vaccines induce a protective immunity at best 4 to 5 days following inoculation, that window is available for the virus to 'jump' the firebreak.

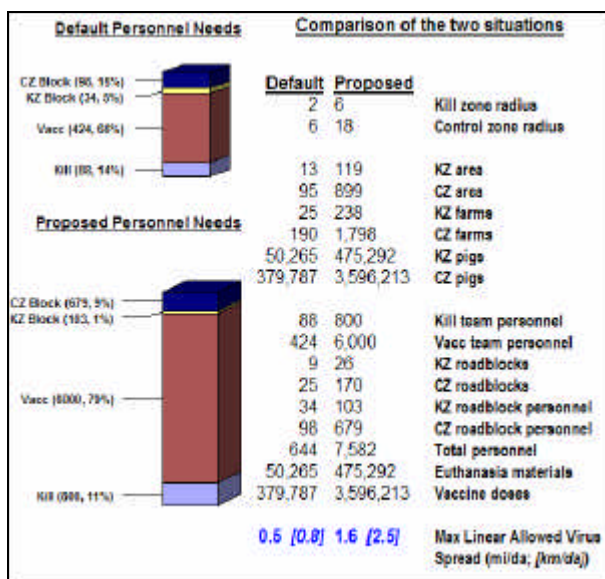


Figure 5. Comparison of hypothetical ring vaccination programs (in swine, typical eastern NC conditions): **DEFAULT**- a 2 mi 'Kill Zone' (KZ) with a 6 mi 'Control Zone' (CZ) vs **PROPOSED** - a 6 mi KZ with an 18 mi CZ. Vaccination occurs within the CZ. A ring expansion of 3x increases personnel and resource needs by 9-11x.

One strategy to combat this moving viral 'front' is to expand the diameter of the control ring, in which vaccination occurs. However, increasing the diameter causes a much larger increase in the required supplies and personnel (See Fig 5 for an example of how this works), which are likely to be an already limiting factor at the smaller ring approach.

Another problem for emergency vaccination-based control is that most current vaccines for FMD limit clinical signs, but allow something on the order of 50% of vaccinated

animals to become infected and to shed the virus – for all intents potentially turning vaccinates into subclinical disease carriers that can confound efforts to control disease spread. The literature is ambivalent about the danger these animals may pose.

A logistical difficulty with emergency vaccination programs relates to likely availability. Currently FMD vaccine stockpiles are actually viral stockpiles that are not in vaccine form, though plans for the Emergency Veterinary Stockpile might change that somewhat. Today, however, they would need to be removed from storage and made into vaccines. Estimates vary, but it is likely that vaccines would take at least a few weeks to arrive, and that full production (in millions of doses) could take more than 4 to 6 weeks. That time lag could make ring vaccination a moot point given how rapidly FMD can spread.

Additionally, until very recently, our diagnostic tests could not differentiate a vaccinated and FMD-free animal from a naive-infected animal, or from a vaccinated-carrier animal, forcing such programs to have to destroy vaccinates within a certain time frame.

Finally, in large-scale modern agriculture, where animals and products are transported nearly on an hourly basis from farm to farm, and from state to state, stamping out and ring vaccination policies are very likely to fall behind the advancing epidemic. Simulations suggest that an FMD outbreak starting in eastern NC swine could be in 5-7 states, affecting +/- 500 herds in the first 10 days following exposure. Worst case scenarios suggest an FMD outbreak could require destroying between 30-50 Million animals, and would take more than 9 months (+/- 280 days) to get under control. Few workers believe that US society would tolerate that level of animal waste and destruction. Fewer still believe the US could stand up the necessary personnel to successfully execute and complete such a massive campaign.

Combined, these post-outbreak vaccination negatives result in after-the-fact simulations suggesting that Ring/Fence vaccination would not have significantly impacted the 2001 UK epidemic.

Whether we combine SOEs and emergency vaccination, or not, our current plans generate numerous unintended consequences beyond the direct market effects mentioned above. Two especially vexing issues include

- (1) that our programs induce paradoxical motivation for producers to seek ways for their herds/flocks to become infected or to bypass control measures in last-ditch efforts to avoid individual financial ruin by either gaining indemnities or selling product; and
- (2) that we ignore the socio-economic and political impacts on non-agricultural facets of communities and economies; impacts that are often several fold greater than the direct impacts on agriculture.

INTERNATIONAL 'THINKING' REGARDING FAD CONTROL

Following the economic, social, animal welfare, and political outcomes of the UK 2001 FMD outbreak and the current H5N1 HPAI outbreak, many nations and trade blocks have reconsidered their FAD programs. The WOAHOIE has increased its interest in, and work with, regionalization within a country, of changing the time-to-trade-resumption penalties that countries practicing FMD vaccination face following an outbreak, and of updating their rules and policies regarding testing and vaccination technologies. The UK and the European Union have, in recent years, pushed for similar changes in international rules, and to have vaccination be a preferred part, if not the primary part, of countries' FMD response programs.

BIOMEDICAL- AND TECHNOLOGY-RELATED DISEASE CONTROL OPPORTUNITIES

Following are but a few of the disciplines and technologies that have recently advanced greatly. They bring new tools and opportunities for prevention, response, and recovery.

Vaccinology

Vaccine creation methods are no longer limited to simply isolating the pathogen, killing it, and then exposing the target animal to the antigen. Current vaccine techniques include functional genomics and gene alteration techniques that produce live vector-based vaccines exploiting important gene expression and genetic recombination techniques to increase the safety of derived immunostimulant products as well as to create readily identifiable genetic markers for differentiation from wild virus. Subunit vaccines – products that never involve the use of live agents – can take vaccine safety margins to levels unattainable by standard killed/attenuated techniques. Novel methods of vaccine delivery -- through feed, aerosols, or the previously mentioned vectors -- promise to improve the ability to cover disparate populations. Finally, manufacturing process improvements in lyophilization and sterilization have improved vaccine shelf life and stability, making long-term stockpiling of these tools in ready-to-deploy forms more feasible.

Immune system enhancements

Our expanding knowledge of general animal health, nutrition, and stressors improves the ability of any vaccine to cause a strong immune reaction. Non-vaccine-based opportunities have increased as well. Direct oral or mucosal delivery of interferons (IFN) have demonstrated themselves to be an effective and fast therapy against viruses, including FMD – without vaccine use. The ability to include such products in feed during an outbreak has experimentally shown efficacy in protecting swine from FMD infection, even without concomitant vaccines. Long-term, genetic techniques and expanded genome maps promise new opportunities to create resistant livestock.

Finally, developments in understanding and manipulating different parts of immune systems (e.g., cell mediated vs humoral) to optimize responses to different agents also show highly specific potentials for control applications.

Detection and differentiation

Modern materials science, biochemistry, nanotechnology, mathematical pattern-recognition, spectroscopy, and molecular imaging systems have recently been combined to optimize approaches to rapid, high-resolution, accurate, and efficient diagnostic methods such as oligonucleotide microarrays, aptamer technologies, and nanotube biosensors. Environmentally stable automated systems that can combine sampling and detection technologies have, in the past 5 years, been commercialized and adapted to business, environmental, and military applications as well. Combined with previously mentioned genetically altered vaccines, these technologies potentially allow rapid and repeatable differentiation of vaccinated, recovering, and recently exposed animals.

Information systems

Government and private industry field personnel now access and create information at speeds and distances unheard of only a decade ago. Global positioning systems incorporated into mobile wireless devices (e.g., laptops and palm-held information managers) are currently in-field for military and state-level users. With the advent of national animal identification systems and shared multi-hazard data structures, these systems will create new avenues for planning and executing trace-in/trace-out work, for monitoring animal flow, and for serving as the basis for syndromic surveillance systems, distributed data bases, and 'network aware' activities and coordination, where central decision makers and in-field workers have access to real-time updated data. In the military this is known as offering 'full battlefield awareness'. The analogy to fighting fast moving epidemics is evident.

NEW OPPORTUNITIES OFFER NEW SOLUTIONS

In the time since the 2001 Foot-and-Mouth Disease (FMD) pandemic and the terrorist attacks of 11 Sept 2001, our concepts of biosecurity, risks, threat agents, disease control program effectiveness, and agriculture's value within society have changed. The past several years have also witnessed an explosion in biotechnology, genomics, immunology, simulation algorithms, and surveillance systems. Furthermore, recent catastrophic FAD outbreaks from all parts of the globe, have highlighted policy areas we need to improve (e.g., the lack of state or national consideration of business continuity issues for primary production, secondary handling/processing, and support industries) while designing and executing FAD control and eradication programs.

The combination of this new knowledge has given rise to new considerations for disease control programs. It is now evident that the current concept of FMD eradication by strict 'stamping out' (See Figure 6) in order to maintain agricultural trade, if applied in a North Carolina situation, is likely to not only fail to contain the epidemic, but could so damage the industries that they will not recover. Furthermore, given the concentration of production seen in NC swine, California dairies, Alabama poultry, or High Plains' feedlots, emergency ring vaccination strategies are likely to consume vast amounts of resources to achieve minimal results.

From a systems' perspective, then, the unavoidable conclusion is that current ideas and rules on control & eradication of FADs, in general, and FMD, in particular, are counterproductive and could well cause more harm to agriculture, to rural communities, and to regional economies, than they will alleviate.

Finally, in these days of heightened concern for terrorism, we must face the fact that if we can show that even a simultaneous multi-site outbreak could be controlled with minimal disruption to production and markets, we will have gone a long way to making these pathogens low-yield tools for terrorism. Hence, our control programs that aim to prevent mistakes must now also consider deterrence, and the complications of shifting targets, transposition, and redundant, partial solutions this new perspective brings with it. This requires changing the culture of animal and public health aimed at keeping people from making mistakes, not from keeping people from intentionally doing damage, and changing law enforcement to not always assume every event is enemy action. Combining animal/public health model with the crime control model will require long term education of both groups.

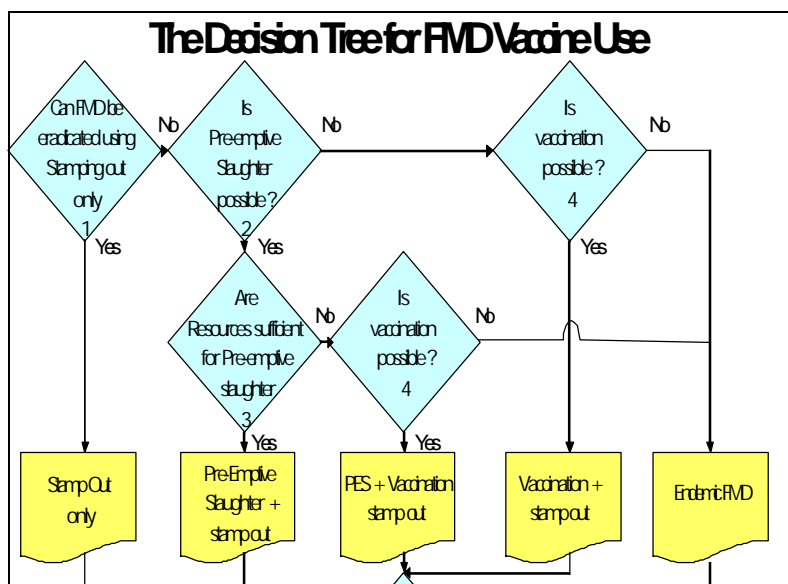


Figure 6. Typical western decision tree addressing FMD assumes SOE is the preferred course of action. Such assumptions do not belong in decision trees.

CONCLUSIONS

We must reevaluate plans for controlling FMD (or other catastrophic transboundary diseases) in light of new knowledge and lessons learned from past outbreaks.

Five characteristics of such a new perspective include:

- 1 The goal should not be eradication at any cost, but to best assure farms' survival. We exist to protect agriculture, not stamp out diseases. Eradication is but one tool we have available. We must allow business continuity tools to drive our efforts; and keep relatively small export markets from driving programs.
- 2 Today's concentrated production centers should utilize coordinated, facilitated, biosecurity and population health programs, potentially including preventive vaccination. If we protect these production centers (regions with high concentrations of dairies, feedlots, hog farms, poultry operations, etc.) , ahead of time, research has shown we will greatly decrease the chance of an uncontrolled epidemic damaging them and the rest of agriculture.
- 3 We should exploit new means to augment animals' immunities, with or without vaccines (such as oral interferons and other innate immune modulators which can be included in standard feeding programs), decreasing demands on specially trained personnel who will always be in limited availability during early parts of any outbreak.
- 4 We must minimize Stop Movement Orders, through genetically altered/vector vaccines and risk-based differential testing methods,— that is, we must allow likely negative herds and products to move through markets. Differential testing and movement permitting was effective in Pseudorabies control across multiple states' production/marketing systems only a few years ago,. This, however, requires greatly increasing and diversifying our laboratory capacity and authorities.
- 5 We must change our formal decision processes to incorporate the new technologies, methods, and opportunities. The decisions cannot presuppose a method as being optimal, such as we currently do with SOE. The decisions cannot carry implicit assumptions of cause or criminality. It is only by promoting transparency and embracing the uncertainties and options available to us will we achieve full buy-in from all the stakeholders.