



Foot-and-Mouth Disease Vaccination Policy in the United States, October 2020

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Introduction

Foot-and-mouth disease (FMD) is one of the most devastating diseases of livestock. It is estimated that an FMD outbreak in the United States today could cost from \$2 billion to greater than \$200 billion, depending upon its mode of introduction and extent. FMD has not been detected in the United States since 1929; however, the disease is endemic in much of the world. Outbreaks in previously FMD-free countries in the last few decades are an important reminder that introduction remains a salient concern, whether through legal or illegal imports, accidental introduction, or bioterrorism. FMD affects all cloven-hoofed animals, including cattle, sheep, goats, and swine. Mortality rates are not generally high, except in young animals; morbidity rates can reach 90 percent, causing weight loss and reduced milk production in infected animals. While the disease is not a threat to public health, it is easily spread by infected animals and animal products, aerosols, and contact with contaminated articles such as clothing, feed, vehicles, and equipment. The United States must be prepared to respond quickly and effectively should FMD enter the country. Vaccination would be a critical component of a contemporary FMD response in the country.

FMD exercises in the United States and outbreaks in previously free countries such as Japan and South Korea demonstrate FMD vaccine as an effective tool to control, contain, and eradicate the virus. It may also support continuity of business activities, helping to mitigate the disruptive effects to the industry. Stamping-out—the depopulation of infected and exposed animals and disposal of carcasses and materials—is likely to occur to some extent in every outbreak. However, the use of vaccine will limit the number of animals that require depopulation; support the consumption of animal protein for its intended purposes; and be less impactful to the environment. Stamping-out as an exclusive response strategy is not a viable or sustainable emergency response strategy in the United States for anything other than a very small, focal outbreak.

The Animal Health Protection Act (AHPA), 7 U.S.C. 8301 et seq., authorizes the Secretary of Agriculture to carry out operations and measures to detect, control, or eradicate any disease or pest of livestock, and to promulgate regulations and issue orders to carry out the AHPA. This authority has been delegated to the United States Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS), which is thereby responsible for preparing for and responding to an outbreak of FMD in the United States (Title 7 of the *Code of Federal Regulations* [CFR]).

The Agriculture Improvement Act of 2018 (“The Farm Bill”) established a three-pronged program to support animal disease prevention and management. One of the components is the National Animal Vaccine and Veterinary Countermeasures Bank (NAVVCB or “National Bank”). Having a U.S.-only vaccine bank is a concept APHIS officials have long discussed with stakeholders and industry—and it makes a much larger number of vaccine doses available to the United States than was possible through the North American Foot and Mouth Disease (NAFMDVB). APHIS will continue to participate in the NAFMDVB, maintained jointly by the United States, Canada, and Mexico.

In July 2020, APHIS announced a \$27.1 million initial purchase of FMD vaccine for the National Bank. This is the first step toward the goal of acquiring 10-25 million doses of each of the 10-12 highest risk strains of FMD for the NAVVCB.

APHIS continues to prepare the United States for FMD by collaborating with industry, academia, State, and other Federal agencies to identify capabilities and vulnerabilities. This document is intended to add transparency around delivery and administration of FMD vaccine in an outbreak. Many factors impact the role vaccination would play in an FMD outbreak in the United States: the goal is to advance preparedness by facilitating discussion among USDA APHIS' multiple partners.

APHIS believes that an efficient, overall approach to protecting the U.S. livestock industry in an FMD outbreak can be developed. Although the vaccination aspect of preparedness presents unique challenges, these can be overcome with advance planning and collaboration among all stakeholders.

The following statements provide common ground for further collaboration and coordination around FMD vaccine:

- FMD virus strains are sufficiently different so vaccinating against one strain may not protect against different strains, even if they are related.
- The bank holding a matching strain will expect to receive finished vaccine 10-14 days post-order.
- Initial quantities of vaccine received from the NAFMDVB may be limited to 1.75 to 2.5 million doses.
- Initial quantities of vaccine received from NAVVCB will be 2.5 million doses, with subsequent shipments of 2.5 million each 10-14 days, as available. (Note: The desired 10-25 million dose/strain inventory will take several years to build up.)
- Once a decision has been made to vaccinate, APHIS will place the order for the first shipment (ie, the maximum number of doses available, up to 2.5 million).
- The delivery period of 10-14 days will allow APHIS and States to assess the extent of the outbreak and for States to prepare and submit their Emergency Vaccine Requests and Plans.
- The production cycle for vaccine is approximately 14 weeks; thus, there may be a gap in vaccine receipt once initial quantities are exhausted, even if surge capacity production is requested and orders are immediately placed for future vaccine.

USDA APHIS Goals of an FMD Response

The goals of an FMD response have been communicated publicly in the *APHIS FMD Response Plan: The Red Book* since 2010. These goals provide overarching guidance for further capability acquisition or vaccine policy development. The *FMD Response Plan* includes emergency vaccination among the critical activities that would be conducted during an FMD response to achieve these goals.

The goals are to (1) detect, control, and contain FMD in animals as quickly as possible; (2) eradicate FMD using strategies that seek to stabilize animal agriculture, the food supply, and the economy, and to protect public health and the environment; and (3) provide science- and risk-based approaches and systems to facilitate continuity of business for non-infected animals and non-contaminated animal products. In summary, achieving these three goals will allow individual livestock facilities, States, Tribes, regions, and industries to resume normal production as quickly as possible. They will also allow the United States to regain FMD-free status without the response effort causing more disruption and damage than the disease outbreak itself.

Response Strategies and Planning

History of USDA APHIS FMD Response Strategies

The United States responded to FMD outbreaks in the early 20th century by stamping-out (depopulation and disposal). After FMD eradication in 1929, stamping-out remained the preferred response strategy for many decades.

Other response strategies were considered starting in the 1970's, particularly for severe outbreaks. Late in that decade, vaccine antigen concentrate (VAC) became an important new technology, as it allowed more cost-effective banking of FMD vaccine. At low temperatures, VAC can be stored for much longer periods than finished vaccine, significantly reducing the costs of keeping vaccine on hand. In 1979, the USDA Secretary's Advisory Committee on Foreign Animal and Poultry Diseases suggested

the creation of a vaccine stockpile. This stockpile was intended to augment the traditional strategy of stamping-out with vaccinate-to-kill, which would delay the immediate need for depopulation and disposal of all infected livestock in the event of a widespread outbreak.

In 1982, the NAFMDVB was created by cooperative agreement. Canada, Mexico, and the United States came together to ensure that some vaccine was available if vaccinate-to-kill was required to assist in the control and containment of a North American outbreak.

For the first time in 2010, the *APHIS FMD Response Plan: The Red Book* explicitly stated that USDA APHIS Veterinary Services (VS) would consider the use of all vaccination strategies, *including* vaccinate-to-slaughter and vaccinate-to-live. Current APHIS FMD response policy states that the use of emergency vaccination strategies would be considered in *any* FMD outbreak. More information about this policy is provided in the *APHIS FMD Response Plan* at www.aphis.usda.gov/fadprep.

Need for Vaccination Strategies

Given that FMD response policy in the United States has evolved to consider emergency vaccination strategies in any FMD outbreak, it is worthwhile to explicitly acknowledge why this change has occurred:

- There is a lack of capacity to depopulate cattle, swine, or other affected animals rapidly enough to control or contain FMD.
- There is not sufficient capability to appropriately dispose of large numbers of carcasses in a manner that is timely, environmentally appropriate, and acceptable to stakeholders and the public.
- There would be severe economic losses for producers due to the loss of production animals.
- There would be further losses to producers from the destruction of genetic stock.
- There could be a lengthy interruption in the food supply chain for key commodities—including milk, meat, and cheese.

Current Response Strategies

As stated in the *APHIS FMD Response Plan: The Red Book*, there are generally accepted response strategies for the control and eradication of FMD in domestic livestock following an outbreak:

- Stamping-out
- Stamping-out modified with emergency vaccination¹
 - to kill
 - to slaughter
 - to live
- Emergency vaccination (to live) without stamping-out.

In anything beyond a very small, focal outbreak where further transmission is highly unlikely, emergency vaccination will become critically important to control and contain FMD virus in the United States. Response strategies may be implemented in any combination and vary by location,

¹ Emergency vaccination to kill or to slaughter intends to remove vaccinated animals from the population, and is most likely used to obtain FMD-free without vaccination status. Emergency vaccination-to-live intends to leave vaccinated animals in a population, and is most likely to be used to obtain FMD-freedom with vaccination status. **Kill:** animals would be depopulated and disposed of (not enter market channels). **Slaughter:** animals would enter slaughter channels based on specific requirements and normal ante- and post-mortem inspection requirements. Animals may move to slaughter prior to their scheduled disposition to reduce or eliminate vaccinated animals in a population, or move to slaughter in accordance with normal production schedules and parameters. **Live:** vaccinated animals intended for breeding, slaughter, milking, or other purposes live out their useful lives.

jurisdiction, industry affected, and size of the outbreak.

World Organization for Animal Health (OIE) FMD Status and International Trade Agreements

Historically, a key justification for the exclusive or predominant use of stamping-out has been that access to foreign export markets would be regained more quickly. However, the time to reapply for FMD-free status to the OIE is the same (3 months) for both stamping-out, and stamping-out with vaccination-to-slaughter or kill (Article 8.8.7 [1a, 1b])². For stamping-out with vaccination to live, the *OIE Terrestrial Animal Health Code* indicates that a country can reapply for freedom after 6 months, as long as surveillance is conducted in accordance with OIE requirements (Article 8.8.7, [1c]).

OIE guidance for reestablishing FMD-freedom is important, but countries that import products from the United States may or may not allow the reestablishment of U.S. exports in accordance with the OIE timelines. While the evidence required by the OIE for FMD-freedom can also support the demonstration of freedom to trading partners, bilateral (and sometimes multilateral) negotiations will occur between the United States and other countries regarding the status of U.S. exports after an outbreak. As such, there may be little or no advantage to withholding vaccine in an effort to reestablish trade more quickly, particularly as the outbreak grows larger. Moreover, given the size of the United States, scope of agricultural production, and resources required for intensive surveillance activities, it may even be difficult to have sufficient evidence to reapply for FMD-freedom in accordance with OIE timelines.

In a large FMD outbreak where premises of many thousands of animals are affected, stamping-out (the depopulation and disposal of all affected animals and, where appropriate, in-contact animals) may not be implemented or may be discontinued as the outbreak continues to grow. In this case, OIE-recognized FMD freedom without vaccination can be reapplied for 12 months after the last case or last vaccination (Article 8.8.2); OIE-recognized FMD freedom with vaccination can be reapplied for 24 months after the last case, if vaccination is continuing (Article 8.8.3).

Continuity of Business

Public-private-academic partnerships have successfully developed Secure Food Supply plans and procedures, which facilitate the movement of non-contaminated animal commodities during an FMD outbreak. These plans are now expanding beyond animal commodities to live animals, due to the just-in-time nature of production systems in the United States which require frequent movements. Live animal movements are obviously a much higher risk than commodity movements and bring with them new challenges for continuity of business planning and diagnostics. Though valuable in overall response planning to engage stakeholders and help minimize disruptions to food supply chains in the United States, these plans do not supplant the need for emergency vaccination strategies to control, contain, and eradicate FMD in an outbreak. These continuity of business plans should be integrated into an overall response effort. For further information on these plans, please see the *NAHEMS Guidelines: Continuity of Business*, as well as the *Secure Milk Supply Plan* (www.securemilksupply.com), *Secure Pork Supply Plan* (www.securepork.org), *Secure Sheep and Wool Supply* (<https://securesheepwool.org/>), and *Secure Beef Supply Plan* (www.securebeef.org).

² OIE. (2019). Article 8. *Terrestrial Animal Health Code: Foot-and-Mouth Disease*. Retrieved from: <https://www.oie.int/en/standard-setting/terrestrial-code/access-online/>

Complexities of FMD Vaccination

The acquisition and use of FMD vaccine is a complicated issue; the types of vaccine available, matters of production, and antigenic diversity of the FMD virus are critical considerations for APHIS.

Types of Vaccine Available

Potency

In order to meet the goals of an FMD response, the United States must have access to sufficient vaccine. The OIE recommends the use of high-potency vaccine ($\geq 6PD_{50}$ per dose) in emergency vaccination campaigns. Regular potency, commercial vaccine for use in endemic countries is typically $\geq 3PD_{50}$ per dose. In obtaining access to additional vaccine (beyond existing holdings), APHIS prefers high potency, differentiating infected and vaccinated animals (DIVA) compatible vaccine.

High-potency vaccine can be made from VAC. Historically, VAC held by the NAFMDVB was stored at USDA's Foreign Animal Disease Diagnostic Laboratories (FADDL), Plum Island, New York. Recently, contractual arrangements allow for commercial storage of VAC at the vaccine manufacturer.

Adjuvant

There are two types of common adjuvant for FMD vaccine—aluminum hydroxide and oil. Aluminum hydroxide-adjuvanted vaccines are effective in cattle and small ruminants; however, they are ineffective in pigs. Oil-adjuvanted (water-oil-water emulsion) FMD vaccines can be used in any species.

Purification

Highly purified FMD vaccines have had the non-structural proteins removed. As such, they are considered DIVA compatible. Unpurified vaccines contain low levels of non-structural proteins, and are not DIVA compatible. VAC accessible to the United States will be reformulated into purified vaccine.

Novel Vaccine Technologies

Novel vaccine technologies on a variety of different platforms are currently being pursued both commercially and within Federal-government research institutions. However, they are in various stages of development and licensing; only one novel vaccine (an adenovirus-vectored A24 toptotype) has been licensed by the USDA APHIS Center for Veterinary Biologics for use in the United States.

Antigenic Diversity

Planning for FMD vaccination is complicated, in part, due to the antigenic diversity of different serotypes and strains (also known as toptypes). Vaccination against one serotype of FMD virus does not cross-protect against other serotypes and cannot be relied upon to protect fully or at all against other strains of the same serotype. It is perhaps appropriate to consider FMD vaccine as 20 to 25 different vaccines (covering the high priority toptypes) rather than just a single vaccine. Because of the variance in behavior of some FMD viruses, different quantities of VAC may be required to match virulence potential. In selecting vaccine strains for the United States, antigenic coverage should be carefully considered. Bivalent, trivalent, and multivalent vaccines do exist.

Production Locale

In surveying vaccine choices, it must also be considered that no live FMD virus may be introduced for any purpose into any part of the mainland of the United States, by commercial manufacturers or federal entities (21 U.S.C. 113A). In addition, because current vaccine technology requires live FMD virus for production of FMD vaccine, there is no killed virus FMD vaccine production in the United States. To date, the only FMD vaccine development in the United States is with a genetically modified,

non-infectious version of the FMD virus. The Secretary authorized its movement to the U.S. mainland in 2018 for continued vaccine development and study.

Current Vaccine Capabilities

Vaccine selection technical committees for the two banks consider global FMD virus distribution patterns when making recommendations on which serotypes pose the greatest threat to North America and should, therefore, be banked. These are readily available from quarterly reports of the World Reference Laboratory for Foot-and-Mouth Disease (WRLFMD) at <https://www.wrlfmd.org/ref-lab-reports>.

Vaccine Banks

Governance

The National Bank, a U.S. entity, is managed by APHIS; funding is as authorized by the Farm Bill. Since the establishment of the NAFMDVB, the United States bears 70 percent of the cost of the NAFMDVB, Mexico 20 percent, and Canada 10 percent. Allocation of the vaccine will be in accordance to the contribution ratio to the Bank. Any or all countries may opt to take a portion of their finished vaccine, irrespective of whether they have animals infected with FMD. However, vaccine availability is not strictly limited by this ratio since countries may decide to reallocate all or a portion of their vaccine to the affected country(s). Each country is responsible for replenishing the VAC they use.

VAC Holdings

The NAFMDVB has modernized its operations to mirror those of the National Bank, which include in contractual arrangement 1) stores of VAC at manufacturing production site overseas, and 2) replacement options for vaccine antigen concentrate that would otherwise expire.

Time to Delivery

Between 1.75 and 2.5 million doses of finished vaccine formulated from VAC in the NAFMDVB, and/or 2.5 million if from VAC in the National Bank, would arrive at a U.S. port 10-14 days post-order. For the National Bank, subsequent shipments could arrive every 10-14 days, if available.

If an outbreak is due to an antigenically distinct 'new' FMD strain, or a strain for which there is no VAC, delivery time for finished vaccine would depend on multiple factors: the surplus production capabilities of manufacturers; capacity to produce a suitable vaccine strain; and whether an appropriate seed virus needs to be developed.

Other U.S. Capabilities

For select topotypes, the United States may also have access to indeterminate additional quantities of high-potency ($\geq 6PD_{50}$ per dose) or regular-potency ($\geq 3PD_{50}$ per dose) FMD vaccine. For some vaccine, this could be acquired through the Transboundary Animal Biologics, Inc. (TABI), a not-for-profit corporation that has acquired a permit for the importation, distribution, and sale of the BIOAFTOGEN® vaccine, a killed virus quadrivalent vaccine for FMD, produced by BIOGENESIS BAGO of Argentina. The requirements to become a Permittee for veterinary biologics are listed in 9 CFR 104.5, and in accordance with VS Memorandum 800.101 and 800.50. In an FMD outbreak, this vaccine may be administered as directed by USDA APHIS as part of an official USDA animal disease control program.

The Assessment of Capability-Strategy Match

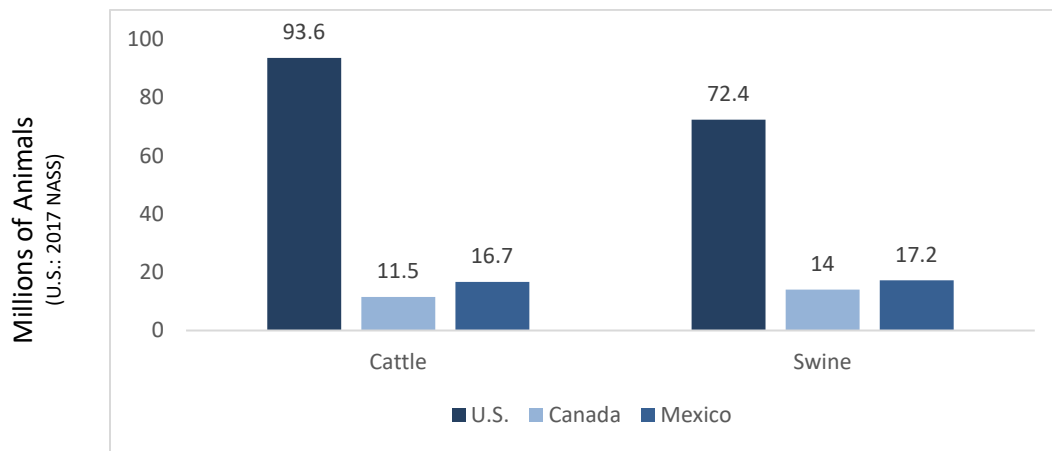
In order to implement emergency vaccination described in the *FMD Response Plan*, there must be sufficient vaccine capabilities to support the execution of the control and containment strategies to combat an FMD outbreak.

Vaccine Quantities

Empirical Estimate

The United States has unique livestock demographics compared to other countries. In 2017, there were over 93.6 million cattle and 72.4 million swine in the United States, significantly more FMD-susceptible animals than in either Canada or Mexico (Figure 1). Seventy percent of U.S. States have susceptible livestock populations in excess of 1 million animals; several States have more than 10 million animals.

Figure 1: North America Cattle and Swine Inventory



In highly animal-populated areas of top agriculture States in the U.S., with both swine and cattle, the current availability of FMD vaccine would be insufficient to vaccinate all susceptible species, even in a moderate outbreak. For example, Figure 2 demonstrates that millions of doses of vaccine would be required to vaccinate swine and cattle—just in the infected zone. If the entire state were to become a vaccination zone, the estimate skyrockets.

Figure 2: Example—State of Iowa with Response Zones and Susceptible Populations



Where	Bovine	Swine	Sheep/Goats	Operations
Infected Zone	209,862	3,585,624	19,189	2,581
Buffer Zone	3,741,058	19,139,426	225,159	33,647
Total	3,950,920	22,725,050	244,348	36,228

Total livestock affected: 26,920,318

The Iowa Infected Zone contains 9 infected counties.
Data—National Agricultural Statistics Service, 2017.

Doses

In addition to the numbers of livestock, it is critical to mention that the number of doses required is likely to be more than the number of animals. With a good vaccine match (to the field strain), cattle should be protected for 6 months with one dose before a booster is required. However, for swine, even if there is a close vaccine match, two doses may be required for full protection, with the second dose being administered within 2–4 weeks of the first dose. This results in significantly more vaccine needed for animals that may not be moved to slaughter within a specific time frame or that are vaccinated to live.

Mismatch

Given the vaccine capabilities available to the United States, and the country’s animal populations, the United States does not have sufficient vaccine quantities to implement an effective emergency vaccination strategy in most FMD outbreak scenarios. Either a vaccinate-to-kill or –slaughter, or vaccinate-to-live strategy might be possible in a moderate regional outbreak, but nothing larger, even given currently available capabilities. Figure 3 illustrates the different types of FMD outbreaks which could occur; Table 2 offers an assessment of current capabilities, including (but not limited to) vaccine quantities.

Figure 3: Proposed Typology for FMD Outbreaks

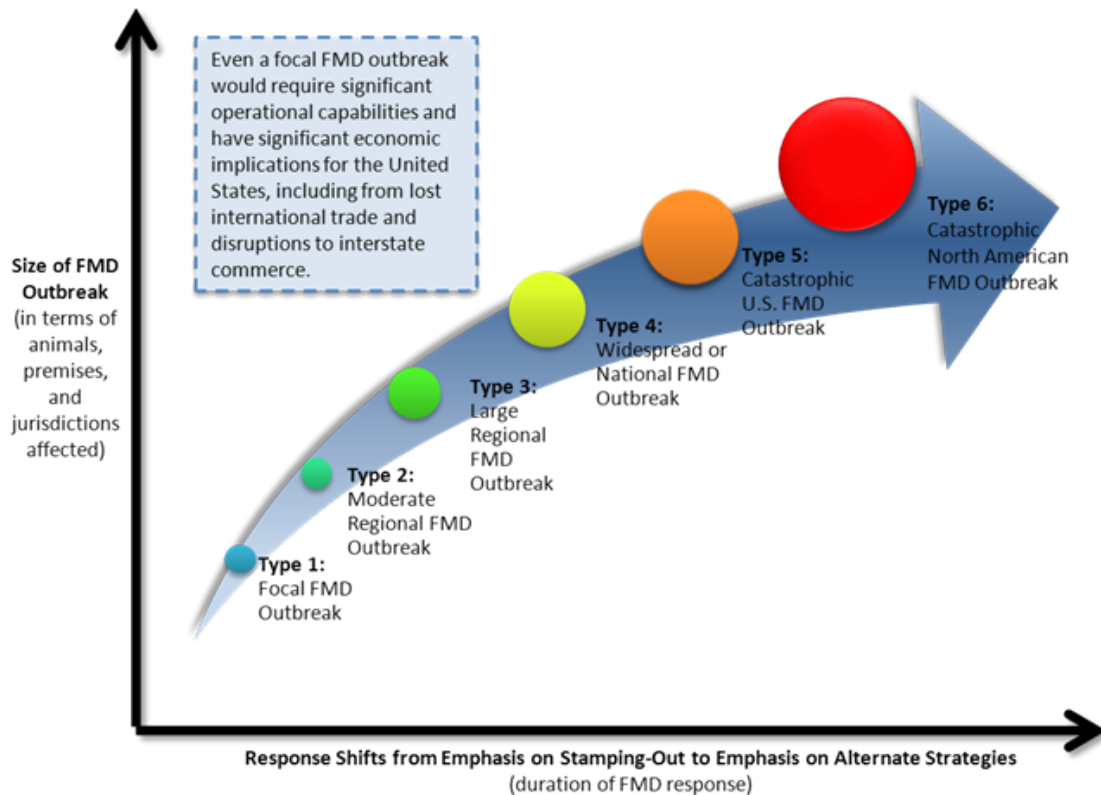


Table 1: Current Capability of the United States to Effectively Implement Vaccination Strategy or Strategies³

Type of Outbreak	Vaccinate-to-Kill or Slaughter	Vaccinate-to-Live
<i>Type 1: Focal FMD Outbreak</i>	+	- (unlikely strategy)
<i>Type 2: Moderate Regional FMD Outbreak</i>	+ (likely, but depends on response strategy and animal density)	+ (likely, but depends on response strategy and animal density)
<i>Type 3: Large Regional FMD Outbreak</i>	+ / - (possible, but depends on response policies, animal density, and continuous production)	+ / - (possible, but depends on response policies, animal density, and continuous production)
<i>Type 4: Widespread or National FMD Outbreak</i>	+ / - (unlikely, even with continuous vaccine production)	+ / - (unlikely, even with continuous vaccine production)
<i>Type 5: Catastrophic U.S. FMD Outbreak</i>	- (lack of vaccine and resources)	- (lack of vaccine and resources)
<i>Type 6: Catastrophic North American FMD Outbreak</i>	- (lack of vaccine and resources)	- (lack of vaccine and resources)

Capability to Implement Vaccination Strategies

In addition to having sufficient vaccine quantities that can be delivered quickly, effectively implementing emergency vaccination during an outbreak requires other significant resources and infrastructure, including the following:

- Regulatory infrastructure, plans, and processes
- Animal identification (per regulation)
- Communication (strategy and messaging)
- Information management
- Logistics capabilities
- Incident management capabilities
- Resources to simultaneously execute other critical activities, including
 - surveillance,
 - tracing,
 - rapid diagnostics and reporting,
 - quarantine and movement control (including permitting),
 - continuity of business,
 - biosecurity, and
 - cleaning and disinfection.

Important gaps exist in many of the areas listed above. For example, consumers may need to be socialized regarding the consumption of meat and milk from FMD-vaccinated animals. Logistics and information management systems must consider managing resources for vaccination, including specialized equipment and personnel, as well as identification of vaccinated animals. Diagnostic and surveillance systems must be sufficient to provide evidence of disease freedom for non-affected regions. While further discussion of these issues are outside the scope of this paper, the foundation,

³ Includes, but is not limited to, vaccine quantities, time to delivery, and regulatory infrastructure (regulatory issues as well as plans, policies, and processes for activities such as procurement, licensing, permitting, distribution, use, and traceability).

infrastructure, plans, processes, and policies to support emergency vaccination must exist.

Imperative for Additional Capabilities

There is a demonstrated inconsistency between the current FMD response strategies that could be implemented, the susceptible animal populations in the United States, and the resources and infrastructure available to implement those response strategies. This section evidences the need for additional investment in capabilities so emergency vaccination strategies can be effectively implemented.⁴

Economic Estimates of an FMD Outbreak

An outbreak of FMD in the United States would have severe consequences for the multi-billion dollar livestock industry; FMD presents the greatest economic threat to U.S. animal agriculture. However, an outbreak would also have significant economic effects far beyond animal agriculture, threatening critical food and agriculture infrastructure. Over the last decade, economic impact analyses that simulate FMD outbreaks have improved beyond simple cost-benefit analyses.⁵ As a result, these simulations show a wide range of total impacts in the billions of dollars. This estimated impact depends primarily on the following:

- Duration and geographic extent of the outbreak,
- Extent of trade embargoes on U.S. products, and
- Reaction of consumers to the presence of the disease as well as to control measures.

For example, for a moderately sized outbreak lasting less than a year, with trade embargoes of less than 1 year on livestock and livestock products, and limited negative consumer reaction (which reduces losses to livestock and feed producers and processors), losses are estimated in various studies at \$2-14 billion.⁶ However, a prolonged diagnostic delay has been shown to markedly increase costs. For larger outbreaks, with more extended trade embargoes, and negative consumer reactions, economic loss estimates can exceed \$100 billion. A worst-case agroterrorism incident could cost as much as \$228 billion. Given that the 2014–2015 HPAI outbreak—the largest foreign animal disease (FAD) incident in U.S. history—cost nearly \$850 million in direct costs and indemnity, it is likely that an FMD outbreak would be extraordinarily costly. However, there are key factors that impact the direct costs of FMD control, containment, and eradication, including: the primary species affected, the spread of the disease, and which response strategies are implemented. For example, implementing a vaccine strategy over just stamping-out in a simulated accidental release from the National Bio- and

⁴ Please see the Appendix for a list of peer-reviewed articles regarding the use of FMD vaccination in an outbreak.

⁵ Paarlberg PL. 2013. The economics of FMD outbreaks in the United States: Trade impacts, duration of outbreaks, and emergency vaccination. Organization for Economic Cooperation and Development (OECD): *Livestock Disease Policies: Building Bridges between Science and Economics*.

⁶ Modeling estimates vary, and will depend on the factors listed in this section. These estimates are based on information provided in Ekboir, J.M. (1999). Potential Impact of Foot-and-Mouth Disease in California: the Role and Contribution of Animal Health Surveillance and Monitoring Services. *Agricultural Issues Center*. Retrieved from <https://aic.ucdavis.edu/pub/fmd.html>; Oladosu G., Rose A., Lee, B. (2013). Economic Impacts of Potential Foot and Mouth Disease Agroterrorism in the USA: A General Equilibrium Analysis. *J Bioterr Biodef S12*: 001; and Carpenter TE, O'Brien JM, Hagerman AD, McCarl BA. (2011). "Epidemic and economic impacts of delayed detection of foot-and-mouth disease: a case study of a simulated outbreak in California." *J Vet Diag Invest*. 23: 26–33.

Agro-Defense Facility reduced producer and consumer losses by 70%, and government costs by 90%.⁷

Recent Worldwide FMD Outbreaks

The experiences in both Japan and South Korea support the USDA APHIS VS objective for further FMD preparedness. Their experiences demonstrate the need for appropriate regulatory infrastructure, communication strategies to support vaccination strategies, and sufficient quantity of vaccine in order to effectively control and contain an outbreak of FMD.

In 2010, Japan was able to contain and eradicate FMD using a combination of stamping-out, strict movement controls, and vaccination. Japan has approximately 4.6 million cattle, and 9.6 million swine. Japan initially tried to eradicate FMD by stamping-out infected and suspect animals, in coordination with strict movement restrictions. However, the government modified this strategy because it was not possible to depopulate animals quickly enough to halt FMD transmission in the dense livestock populations in the Miyazaki Prefecture. Approximately 300,000 animals were culled, including about 125,000 vaccinated animals that were depopulated.

South Korea also experienced a severe FMD outbreak from 2010–2011. Like Japan, South Korea initially attempted to stamp-out the outbreak. Officials depopulated approximately 3 million swine, a third of the country's total swine population, and 150,000 cattle. Despite these efforts, problems in quickly and effectively implementing movement restrictions led to the continued spread of FMD. Consequently, South Korea elected to vaccinate the entire national herd, requiring approximately 20 million doses of vaccine. This vaccine was acquired from vaccine banks around the world, including the NAFMDVB. A variety of problems, including farmer/producer resistance to reporting suspect cases, has resulted in South Korea continuing to struggle with FMD eradication: vaccination and culling of affected animals continues to control FMD in the country to the extent that no widespread outbreak occurs, but lingering cases have continued into 2019.

These experiences indicate two critical points. First, the potential need for significant quantities of vaccine in the United States, which has far larger animal populations in a single State or region than either Japan or South Korea. South Korea—with approximately 3.1 million cattle and 9.6 million pigs—could be considered equivalent to a *single* U.S. State; the country had to source significant quantities of vaccine to quell the FMD outbreak. Second, the need to implement vaccination as quickly as possible after FMD detection, if there is any question that the outbreak is not focal. It is clear that for most outbreaks, it will not be possible to depopulate and dispose of animals in a manner that is effective in controlling the spread of disease. Subsequently, emergency vaccination must be implemented as rapidly as possible to work towards containing FMD.

Lessons Learned in FMD Exercises

Palo Duro I, 2007

During the 2007 Palo Duro exercise in the Texas Panhandle, rapidly depopulating 50,000–75,000 head of cattle was deemed a logistical challenge that would not be possible within 72 hours (for depopulation) and 96 hours (for disposal). Additionally, because the Texas Panhandle is a livestock dense region, 75,000 animals constitute only a small portion of the region's total susceptible livestock population (over 3.5 million animals in a 100-mile radius). If FMD spread rapidly prior to detection, it is clear that a stamping-out strategy would not be feasible or appropriate.

Additionally, the Palo Duro I exercise offered an important reminder regarding how fast vaccine can

⁷ Schroeder, Ted C.; Pendell, Dustin L.; Sanderson, Michael W.; and McReynolds, Sara. (2015). Economic Impact of Alternative FMD Emergency Vaccination Strategies in the Midwestern United States. Cambridge University Press. Retrieved from: <https://doi.org/10.1017/aac.2014.5>.

be delivered and distributed in an outbreak scenario. Players in the exercise decided to use vaccine and included the option of vaccinate-to-live. But implementing this strategy was slowed significantly because of the time it could take to identify the topotype, ship the VAC to the manufacturer for formulation of vaccine, and ultimately ship the finished vaccine back to the United States for distribution. Palo Duro I highlighted the critical delay, particularly between the initial doses and secondary doses delivered, that may slow the containment of the outbreak.

FMD Tabletop, 2012

In the June 2012 FMD Tabletop Exercise held in Riverdale, Maryland, the scenario assumption was made that FMD vaccination was not to be considered. Despite this, States requested over 3.7 million doses of FMD vaccine, which exceeds stock held by the NAFMDVB. These requests strongly indicate that States, in an FMD outbreak, would perceive an immediate need for a significant amount of FMD vaccine as part of the strategy to control, contain, and eradicate the outbreak.

This exercise also revealed other resource and infrastructure needs for an FMD response. For example, the number of Incident Management Teams that States reported as ‘needed’ to respond to an FMD outbreak significantly outstripped any current USDA capabilities. Further, the success of Incident Management Teams rests upon implementable and consistent strategic direction. Without this, the actions and decisions of Teams may be disparate and disruptive to overall response goals.

In addition, information management systems—at the time of this exercise—were insufficient to effectively handle the quantity of epidemiological and resource-related data emerging from a large event. Since the exercise, the Emergency Management Response System 2.0 (EMRS2) has made significant strides in meeting the information management needs of an outbreak, including tracing, investigations, diagnostic tests results, and resource requests and management. However, much work remains (and additional resources needed) to ensure that EMRS2 is ready to fulfill its potential in a large FMD outbreak where emergency vaccination is implemented.

Food, Agriculture, and Veterinary Response Exercise (FAVRE), 2013

Hosted in December 2013 by the Department of Homeland Security Office of Health Affairs, in coordination with the Federal Emergency Management Agency Region VII, the FAVRE exercise was designed to improve incident management and response to an agro-terrorism incident. In terms of capabilities, one of the key findings of the exercise was as follows:

FMD vaccine stocks are limited, and processes governing vaccine prioritization and allocation are not clear. Also, there is too little vaccine to support contemporary vaccination strategies.

In addition to Federal planning, FAVRE also highlighted the need for collaborative decision-making on a wide range of strategic and operational issues related to vaccination and the need to develop administrative protocols regarding the implementation of vaccination in an FMD outbreak.

Palo Duro II, 2016

Palo Duro II was a follow up to the first Palo Duro exercise held in 2007. The scenario dictated 6 Infected Premises, including dairy, swine, and feedlot operations. Even though this outbreak theoretically involved small numbers of animals, emergency vaccination was implemented by the Unified Incident Command during the exercise. While previous exercises discussed the need for FMD vaccine, in Palo Duro II there was immediate consensus between State, Federal, and industry stakeholders to implement emergency vaccination. Palo Duro II clearly demonstrated that the case has been made for emergency vaccination as a fundamental tool in an FMD response. Recommended future work was to concentrate on additional processes and procedures surrounding the implementation of emergency vaccination strategies, as well as on the acquisition of additional vaccination resources for anything beyond a small focal outbreak.

ARMAR, 2018

In May 2018, APHIS hosted the ARMAR (Agriculture Response Management and Resources) FMD exercise. Six States participated with APHIS in the functional exercise, which had primary objectives of identifying and communicating resource needs. The scenario assumed rapid depopulation and a nationwide standstill, during which the initial extent of infection would be evaluated and virus sequencing and vaccine planning would occur. No State successfully depopulated any animals in the exercise due to a variety of factors: prohibitory injunctions (3 States), high-value animal premises (1 State), large population animal premises (1500-head feedlot, 1 State), lack of trained personnel, and imminent expectation of vaccine receipt.

The combined initial vaccine request for the six playing States in ARMAR totaled 6.5 million doses, and one non-playing State submitted an anticipatory vaccine request for 300,000 doses. If requested today, these orders would not be immediately filled due to the vaccine quantity limitations described in this paper. Further, justifications for the vaccine requests did not always demonstrate a State's ability to handle the requested amount of vaccine appropriately through delivery. In a real event, APHIS will be faced with difficult prioritization decisions—what “qualifies” an affected State to receive vaccine? Is a single industry in one state to be protected at the potential cost of other States' livestock economies? How does limited vaccine get distributed among simultaneous requests from multiple States? These questions can be answered in a science- and risk-based manner; yet, realistically, other influences exist. Vaccine allocation will be a significant political, practical, and logistical challenge, even with a more substantial vaccine inventory.

Modeling FMD Intervention Strategies

USDA APHIS VS Center for Epidemiology and Animal Health maintains a national FMD simulation model to estimate the impact of various outbreak scenarios and compare the effectiveness of disease response measures, including evaluating different vaccination strategies.⁸ Recent analyses of simulated FMD outbreaks starting in different regions and industry sectors of the U.S. demonstrate that a vaccination campaign employed with stamping-out can reduce the size, extent, and duration of a moderate to widespread outbreak.⁹ This is especially observed when vaccination is implemented early in an outbreak. Further, the modeling studies have shown that a State's capacity to effectively and efficiently carry out their vaccine strategy, such as how quickly farms are vaccinated, achieving appropriate coverage in areas targeted for vaccination, and vaccinating based on risk, can reduce the impact of an outbreak even when limited vaccine doses are available.

Recent modeling studies performed in other countries reinforce these observations. FMD modeling studies performed in Australia, Canada, New Zealand, and the United Kingdom also show that a vaccination campaign employed with stamping-out reduces both costs and duration of a moderate to widespread FMD outbreak.^{10,11,11} Rawdon, et al. (2018) also infer that vaccination of cattle farms only “was not inferior to” vaccination of all susceptible species, and this may be a strategy worthy of consideration. Finally, it is clear that initiating vaccine early in an outbreak, eg, at 10-16 days vs. 17-

⁸ USDA APHIS VS CEAH Epidemiologic and Economic Modelling. https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/SA-Epidemiology-AnimalHealth-CEAH/SA_Monitoring_and_Modelling.

⁹ Holmstrom, L. (2020) “Epidemiologic Modeling for FMD Emergency Preparedness.” USDA APHIS VS National Training and Exercise Program Webinar, April 9, 2020. Available at <https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/training-and-development/video-gallery>.

¹⁰ Feng, S., Patton, M., and Davis, J. (2017). Market impact of foot-and-mouth disease control strategies: A UK Case Study. *Front. Vet. Sci.* 4:129. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5585142/>.

¹¹ Rawdon, T., Garner, M.G., Sanson, R.L., Stevenson, M.A., Cook, C., Birch, C., Roche, S.E., et al. (2018). Evaluating vaccination strategies to control foot-and-mouth disease: a country comparison study. *Epidemiology and Infection* 146:1138-1150. Retrieved from <https://europepmc.org/article/med/29785893>.

21 days,^{10,12} promises a better outcome as measured by the ultimate number of Infected Premises. It follows that ordering vaccine and administering it as soon as possible based on risk during an outbreak should be among our collective response goals.

Objectives of Current Planning

Together, the density of animal populations in the United States and the consequences of an FMD outbreak indicate the need for significant planning and capability development for emergency vaccination. The availability of FMD vaccine provided by the 2018 Farm Bill has reignited interest in vaccine policy and procedure development.

USDA APHIS has identified three key objectives for FMD emergency vaccination and vaccination policy, with the recognition that additional response capabilities (such as information management) will also be required:

- Continue engagement of all stakeholders, internally and externally, on FMD preparedness and response issues.
- Increase guaranteed access to FMD vaccine.
- Determine the requirements needed to achieve the response goals. This may include:
 - identifying the types of vaccine (e.g., strains or topotypes);
 - establishing multiple sources (such as manufacturers of suitable vaccine);
 - identifying which vaccines will be used in specified livestock populations;
 - establishing a desired quantity of vaccine;
 - discussing allocation issues and decisions with stakeholders; and
 - preparing States to request, receive, and administer FMD vaccine.

Access to Additional FMD Vaccine

In 2014, APHIS VS set a preliminary goal of having access to sufficient vaccine (of the most prevalent topotypes) for the United States to vaccinate livestock in either a) the most livestock-dense State (Iowa, with 24 million FMD-susceptible animals), or b) most of the livestock in the two next most highly populated livestock States (Texas and North Carolina, with 17 and 11 million FMD-susceptible animals, respectively). Because swine would require two doses for initial protection (unless slaughtered), this could suggest a goal of approximately 35–40 million doses of vaccine (for a single topotype). Since this time, APHIS has stated that 25 million doses for 10 topotypes is an appropriate minimum target for future acquisitions. This is now an attainable goal.

Reaching this level of vaccine availability still amounts to a minimum level of preparedness for FMD, as twenty-five million doses may only be sufficient for the immediate response. In a widespread outbreak, or if vaccination continues with an emergency vaccination-to-live strategy, additional vaccine will be required to manage the outbreak and for booster vaccinations.

Develop a Plan to Control FMD with Limited Vaccine Supplies

Further planning and stakeholder engagement on FMD vaccination should occur alongside the banking mechanisms and assumptions in this paper. In particular, planning should include scenario-based discussions (e.g., protective or containment vaccination strategies), defining triggers for shifting or

¹² Sanson, R.L., Rawdon, T., Owen, K., Hickey, K., van Andel, M., Yu, ZD. (2017). Evaluating the benefits of vaccination when used in combination with stamping-out measures against hypothetical introductions of foot-and-mouth disease into New Zealand: a simulation study. *New Zealand Veterinary Journal* 65:3, 124-133. Retrieved from <https://www.tandfonline.com/doi/full/10.1080/00480169.2016.1263165>.

modifying response strategies during an incident, and ensuring that barriers to timely administration of vaccine are addressed across both States and industries.

It is unlikely, until further technological advances occur, that the amount of emergency FMD vaccine available in an outbreak will be sufficient to vaccinate all or most animals in the United States. As such, APHIS—in coordination with State, local, and industry stakeholders—should also consider the development of processes, procedures, and strategies for prioritizing the use of currently available vaccine in an outbreak (as suggested during ARMAR). Discussing current thinking openly will help State, Federal, and industry planners develop realistic response plans ahead of an outbreak.

Moving Forward

There are many opportunities and challenges for the country as we look to improve FMD preparedness in the United States, particularly early in an FMD emergency vaccination campaign, to ensure strategic population selection for initial vaccination and proper distribution of vaccine.

How Far We've Come

In the first iteration of this paper, in 2013, we attempted to communicate where we were and where we wanted to be regarding FMD preparedness—it was not a hopeful predicament. Now, with the passage of the 2018 Farm Bill legislation, we have realized additional vaccine capacity and can direct our efforts toward utilizing it.

Where to Go From Here

The management and logistical aspects of FMD emergency vaccination must not be neglected: we must build bank holdings in a responsible, informed manner and be ready to store, distribute and administer vaccine to the farm level in a biosecure manner. In addition, it will be helpful to determine methods to more objectively evaluate State and overall-U.S. FMD preparedness. Transparency and accountability should be central to developing a clear policy framework to ensure our newfound capability can be implemented. Finally, continuing to pursue novel vaccine methods could result in ready availability of efficacious vaccines in a variety of strains and at a lower cost.

Ongoing and sustained communication, collaboration, and cooperation is paramount among stakeholders, particularly on issues related to implementing emergency vaccination strategies in an outbreak. While there is no question that an FMD outbreak would be costly to control and contain, additional analyses may be required on various vaccine issues, whether economic or epidemiologic.

Potential Obstacles

In order for the United States to successfully implement an emergency vaccination strategy, particularly vaccinate-to-live or vaccinate-to-slaughter in a widespread outbreak, intensive collaboration with stakeholders is necessary before an outbreak to make advancements in preparedness. Planning and preparedness efforts earnestly underway now, at least in the swine industry, are being undertaken for a potential outbreak of African swine fever, a disease for which there is no vaccine. This reflects a reality of emergency management that, at any given time, there will be competing priorities requiring diversion of resources. On the one hand, we often find that improvements in FAD response capabilities promote the nation's overall readiness to respond, regardless of disease agent. On the other hand, it serves as a reminder to keep vaccination planning in our sights, or risk it getting pushed aside.

Conclusion

An FMD outbreak of any size in the United States will result in serious economic consequences. Rapid and effective response efforts, to quickly control and contain the virus, can minimize the deleterious effects of an outbreak. Since the shift in U.S. FMD response strategy to include vaccination as a

response option, vaccine availability is much improved. The next milestone is to enhance strategic and operational preparedness to adequately utilize emergency vaccination strategies in a small to moderate FMD outbreak.

This paper has outlined current work on FMD vaccination policy and identified the imperative for further efforts. Effective preparation for an FMD outbreak will require APHIS' continued partnership with State officials, other Federal agencies, industry, international partners, academia, and other stakeholders. Effective and meaningful public-private-academic collaboration will allow the United States to develop an overall approach that will more effectively and efficiently use available resources to protect the nation's livestock industry from an FMD outbreak.

Abbreviations

AHPA	Animal Health Protection Act
APHIS	Animal and Plant Health Inspection Service
CFR	Code of Federal Regulations
DIVA	Differentiating Infected and Vaccinated Animals
EMRS2	Emergency Management Response System 2.0
FAD	Foreign Animal Disease
FADDL	Foreign Animal Disease Diagnostic Laboratories
FAVRE	Food, Agriculture, and Veterinary Response Exercise
FMD	foot-and-mouth disease
HPAI	highly pathogenic avian influenza
NAFMDVB	North American FMD Vaccine Bank
NAVVCVB	National Animal Vaccine and Veterinary Countermeasures Bank
NVSL	National Veterinary Services Laboratory
OIE	World Organization for Animal Health
TABI	Transboundary Animal Biologics, Inc.
U.S.C.	United States Code
USDA	United States Department of Agriculture
VAC	Vaccine Antigen Concentrate
VS	Veterinary Services
WRLFMD	World Reference Library for Foot-and-Mouth Disease

Appendix: Selected References and Literature

These references are not limited to analyses of the United States. This list is not all inclusive, and it includes primarily peer-reviewed literature.

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