USDA
United States Department of Agriculture

APHIS NBAF SCIENTIST TRAINING PROGRAM (NSTP)

KIMBERLY DODD, DVM PHD
DIRECTOR
FOREIGN ANIMAL DISEASE DIAGNOSTIC LABORATORY
U.S. DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE
VETERINARY SERVICES
OCTOBER 20, 2018

National Veterinary Services Laboratories
Foreign Animal Disease Diagnostic Laboratory
Plum Island Animal Disease Center

DIAGNOSTICS SERVICES SECTION

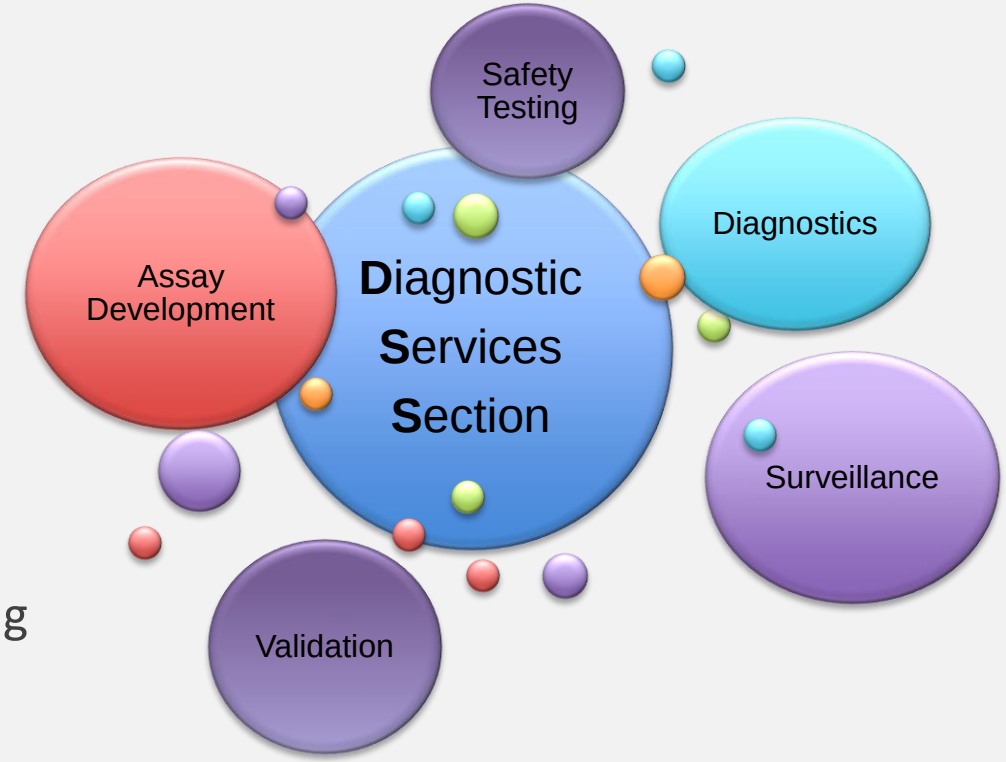
OIE/FAO International Reference Laboratory for foot and mouth disease

National reference laboratory for foreign animal diseases

Supports National Animal Health Laboratory Network (NAHLN)

Ongoing and future priorities

- Assay validation for new sample types
- Comparison of commercially available assays
- Development of new diagnostic platforms
- International and national training



REAGENT AND VACCINE SERVICES SECTION

Characterization and consolidation of TAD biorepository in advance of move to NBAF, including Tier 1 select agents.

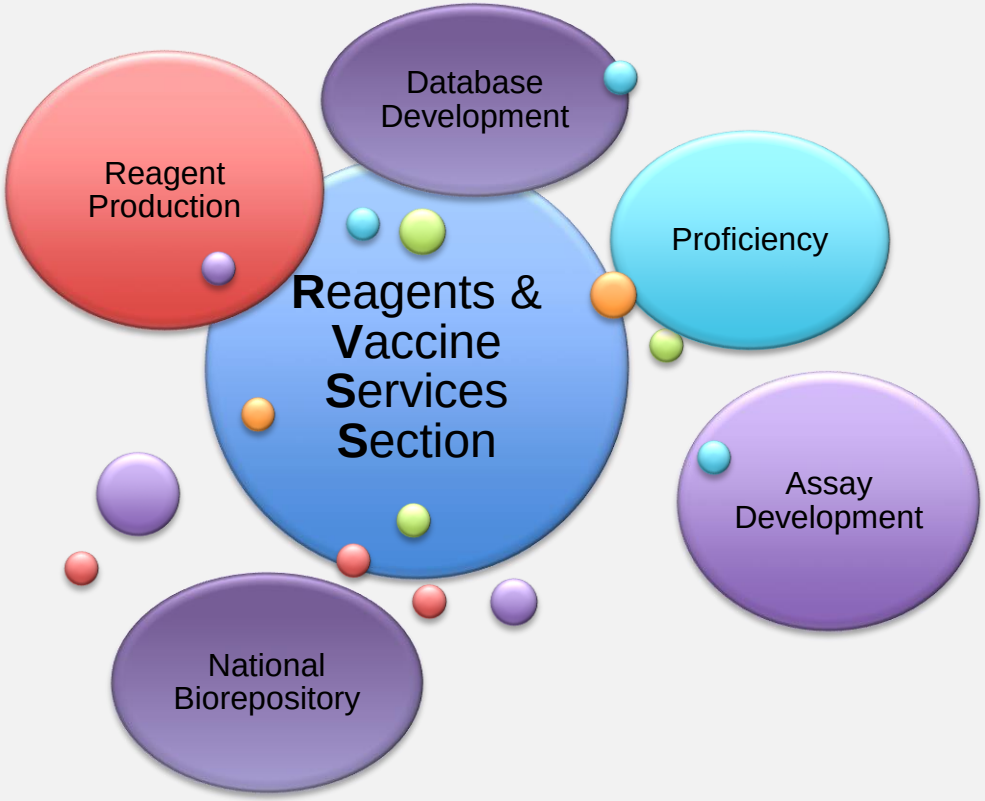
International capacity building:

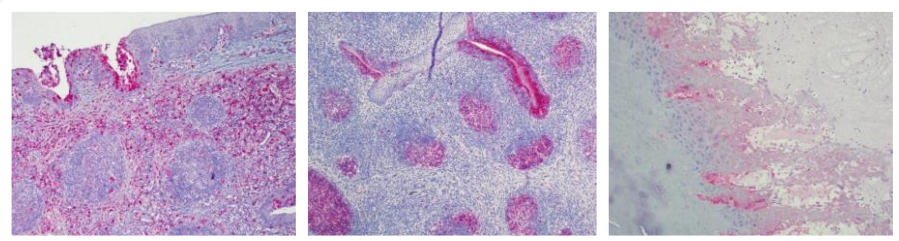
Non-infectious Rinderpest PCR controls and proficiency testing (PT).

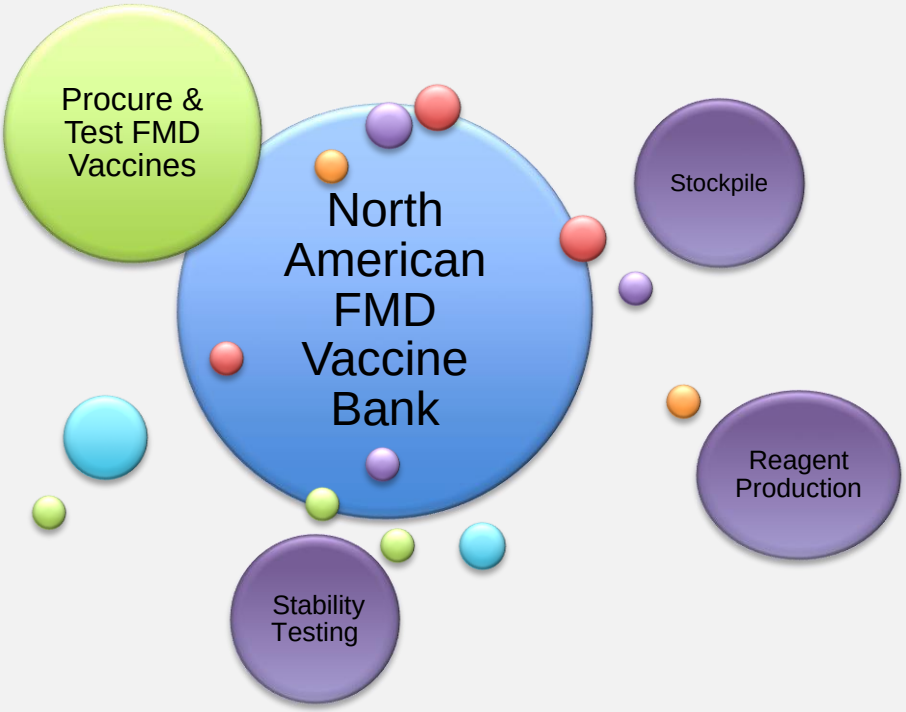
Provide support to the **FADD School**.

Resume **production of reagent grade antisera** used for vesicular disease viruses AgELISA.

Validation of inactivation methods







Stockpile of NA FMD vaccine (US, CA, MX)

Testing protocols

- Safety testing
- Potency testing
- Stability testing

Member

- International FMD Vaccine Strategic Reserves Network

FMD outbreak response

- Identification of appropriate VAC for formulation and deployment
- Coupling traditional and NGS methods for vaccine matching

Ongoing studies

- Evaluation of a serotype A trivalent vaccine
- Evaluation of NAFMDVB vaccine in swine

NBAF Mission

The NBAF, a new, state-of-the-art biosafety level (BSL) 3 & 4 facility located in Manhattan, KS, will enable the U.S. to conduct comprehensive research, develop vaccines and anti-virals, and provide enhanced diagnostic and training capabilities to protect our country from numerous foreign animal, emerging and zoonotic diseases to assist in protecting our food supply and the nation's agriculture economy and public health.

A Modern Laboratory Facility for Bio and Agro-Defense to Mitigate Threats

NBAF Drivers

Homeland Security Presidential Directive 9

Over 70% of emerging diseases are zoonotic

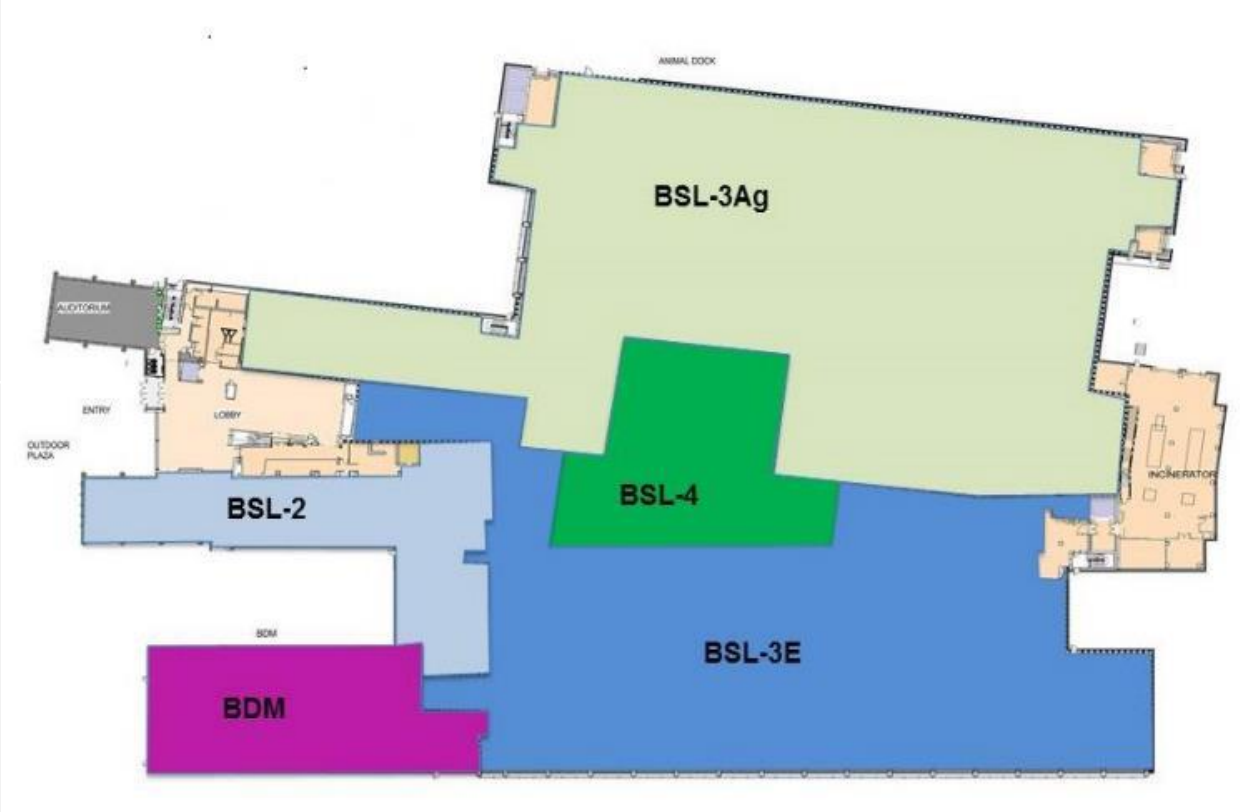
United States has no capacity for large livestock research in a BSL-4 lab and is dependent on use of facilities in other countries

A pilot production capability is needed to accelerate existing countermeasure development efforts

A replacement is needed for the aging Plum Island Animal Disease Center (PIADC), which is over 60 years old and at the end of its useful life with limited capability

NBAF Laboratory Facility Plan Meets Mission Objectives

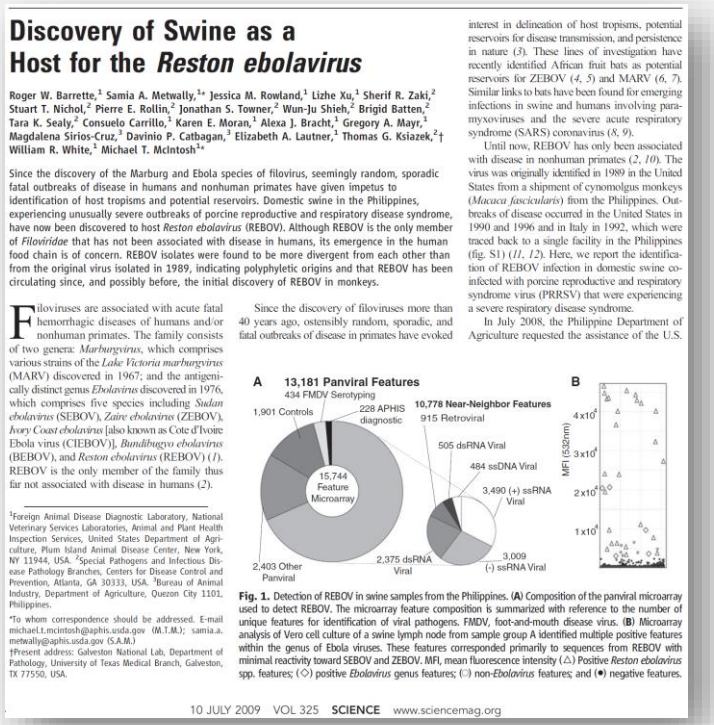
- **BSL-4:** High consequence zoonotic diseases
- **BSL-3E + BSL-3Ag:** Research and Development (R&D), diagnostics, and parallel vaccine trials for Foreign Animal Diseases (FADs), to include Foot-and-Mouth Disease (FMD)
- **BSL-2:** Assay, characterization, optimized throughput, and multi-agency use
- **BDM:** Vaccine development



NBAF will allow for research and operational efficiency gains compared to existing PIADC.

APHIS
NBAF Diagnostic Enhancements

- Ensure facilities capable of **24-7-365** operations to meet emergency response diagnostic testing needs
- Provide needed capabilities for **diagnostic testing of emerging, zoonotic and BSL-4 agents** including Nipah, Hendra and Rift Valley fever virus
  - Ability to work with samples of unknown zoonotic potential
  - Ability to move seamlessly from BSL-3 to BSL-4 when risk to laboratory personnel requires this biosafety level
    - ➢ *Ebola Reston diagnostic case*
  - Ability to meet international reference laboratory responsibilities and **maintain protection of U.S. from FADs and emerging diseases including zoonotics** – currently unable to accept samples from some countries due to known or unknown zoonotic disease risk of situation



Discovery of Swine as a Host for the *Reston ebolavirus*

Roger W. Barrette,[1] Samia A. Metwally,[1]* Jessica M. Rowland,[1] Lizhe Xu,[1] Sherif R. Zaki,[2] Stuart T. Nichol,[2] Pierre E. Rollin,[2] Jonathan S. Towner,[2] Wun-Ju Shieh,[2] Brigid Batten,[2] Tara K. Sealy,[2] Consuelo Carrillo,[1] Karen E. Moran,[1] Alexa J. Bracht,[1] Gregory A. Mayr,[1] Magdalena Sirios-Cruz,[3] Davinio P. Catbagan,[3] Elizabeth A. Lautner,[1] Thomas G. Ksiazek,[2]† William R. White,[1] Michael T. McIntosh[1]*

Since the discovery of the Marburg and Ebola species of filovirus, seemingly random, sporadic fatal outbreaks of disease in humans and nonhuman primates have given impetus to identification of host tropisms and potential reservoirs. Domestic swine in the Philippines, experiencing unusually severe outbreaks of porcine reproductive and respiratory disease syndrome, have now been discovered to host *Reston ebolavirus* (REBOV). Although REBOV is the only member of *Filoviridae* that has not been associated with disease in humans, its emergence in the human food chain is of concern. REBOV isolates were found to be more divergent from each other than from the original virus isolated in 1989, indicating polyphyletic origins and that REBOV has been circulating since, and possibly before, the initial discovery of REBOV in monkeys.

Filoviruses are associated with acute fatal hemorrhagic diseases of humans and/or nonhuman primates. The family consists of two genera: *Marburgvirus*, which comprises various strains of the *Lake Victoria marburgvirus* (MARV) discovered in 1967; and the antigenically distinct genus *Ebolavirus* discovered in 1976, which comprises five species including *Sudan ebolavirus* (SEBOV), *Zaire ebolavirus* (ZEBOV), *Ivory Coast ebolavirus* [also known as Cote d'Ivoire Ebola virus (CIEBOV)], *Bundibugyo ebolavirus* (BEBOV), and *Reston ebolavirus* (REBOV) (*1*). REBOV is the only member of the family thus far not associated with disease in humans (*2*).

Since the discovery of filoviruses more than 40 years ago, ostensibly random, sporadic, and fatal outbreaks of disease in primates have evoked interest in delineation of host tropisms, potential reservoirs for disease transmission, and persistence in nature (*3*). These lines of investigation have recently identified African fruit bats as potential reservoirs for ZEBOV (*4*, *5*) and MARV (*6*, *7*). Similar links to bats have been found for emerging infections in swine and humans involving paramyxoviruses and the severe acute respiratory syndrome (SARS) coronavirus (*8*, *9*).

Until now, REBOV has only been associated with disease in nonhuman primates (*2*, *10*). The virus was originally identified in 1989 in the United States from a shipment of cynomolgus monkeys (*Macaca fascicularis*) from the Philippines. Outbreaks of disease occurred in the United States in 1990 and 1996 and in Italy in 1992, which were traced back to a single facility in the Philippines (fig. S1) (*11*, *12*). Here, we report the identification of REBOV infection in domestic swine coinfected with porcine reproductive and respiratory syndrome virus (PRRSV) that were experiencing a severe respiratory disease syndrome.

In July 2008, the Philippine Department of Agriculture requested the assistance of the U.S.

Fig. 1. Detection of REBOV in swine samples from the Philippines. **(A)** Composition of the panviral microarray used to detect REBOV. The microarray feature composition is summarized with reference to the number of unique features for identification of viral pathogens. FMDV, foot-and-mouth disease virus. **(B)** Microarray analysis of Vero cell culture of a swine lymph node from sample group A identified multiple positive features within the genus of Ebola viruses. These features corresponded primarily to sequences from REBOV with minimal reactivity toward SEBOV and ZEBOV. MFI, mean fluorescence intensity (△) Positive *Reston ebolavirus* spp. features; (◇) positive *Ebolavirus* genus features; (○) non-*Ebolavirus* features; and (●) negative features.

[1]Foreign Animal Disease Diagnostic Laboratory, National Veterinary Services Laboratories, Animal and Plant Health Inspection Services, United States Department of Agriculture, Plum Island Animal Disease Center, New York, NY 11944, USA. [2]Special Pathogens and Infectious Disease Pathology Branches, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA. [3]Bureau of Animal Industry, Department of Agriculture, Quezon City 1101, Philippines.

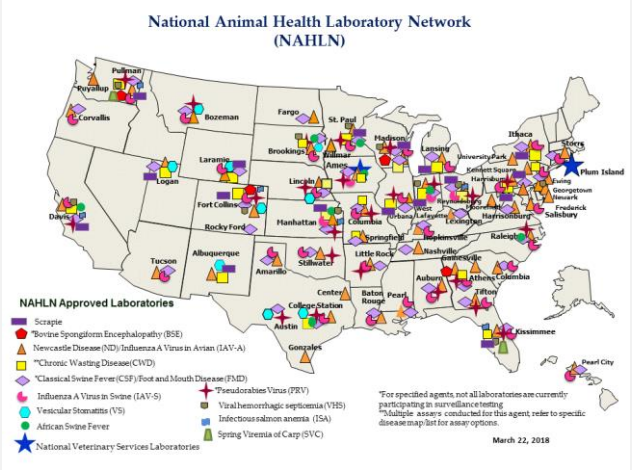
*To whom correspondence should be addressed. E-mail michael.t.mcintosh@aphis.usda.gov (M.T.M.); samia.a.metwally@aphis.usda.gov (S.A.M.)

†Present address: Galveston National Lab, Department of Pathology, University of Texas Medical Branch, Galveston, TX 77550, USA.

Integrate state-of-the-art high throughput diagnostic testing facility to meet high volume testing needs in outbreaks and to validate assays for NAHLN deployment

APHIS
NBAF Diagnostic Enhancements

- Improve training/necropsy facilities for **training increased number** of veterinarians to detect FADs
- Expand capability to meet the **increasing needs of the NAHLN**
- Expand ability to develop and validate **diagnostics for new and emerging diseases**
- Increase **epidemiologic capacity** to monitor worldwide disease trends and prioritize threats to prepare for
- Establish a **robust reagents program** and stockpile – using as needed the Biologics Development Module



PIADC

Current Mission

- ❑ Foot and Mouth Disease
- ❑ African Swine Fever
- ❑ Classical Swine Fever

Diagnostics for Foreign Animal Diseases

Foreign Animal Disease Training

North American Foot and Mouth Disease vaccine bank

NBAF will have expanded capabilities and allows for a dynamic and flexible scientific program to be responsive to threats.

NBAF

Proposed Mission

<u>BSL-3-Ag</u>

- ❑ Foot-and-Mouth Disease
- ❑ African Swine Fever
- ❑ Classical Swine Fever
- ❑ Japanese Encephalitis
- ❑ Rift Valley Fever
- ❑ Others TBD

<u>BSL-4 (Zoonotic)</u>

- ❑ Nipah Virus
- ❑ Ebola Virus
- ❑ Emerging pathogens (unknown)
- ❑ Others TBD

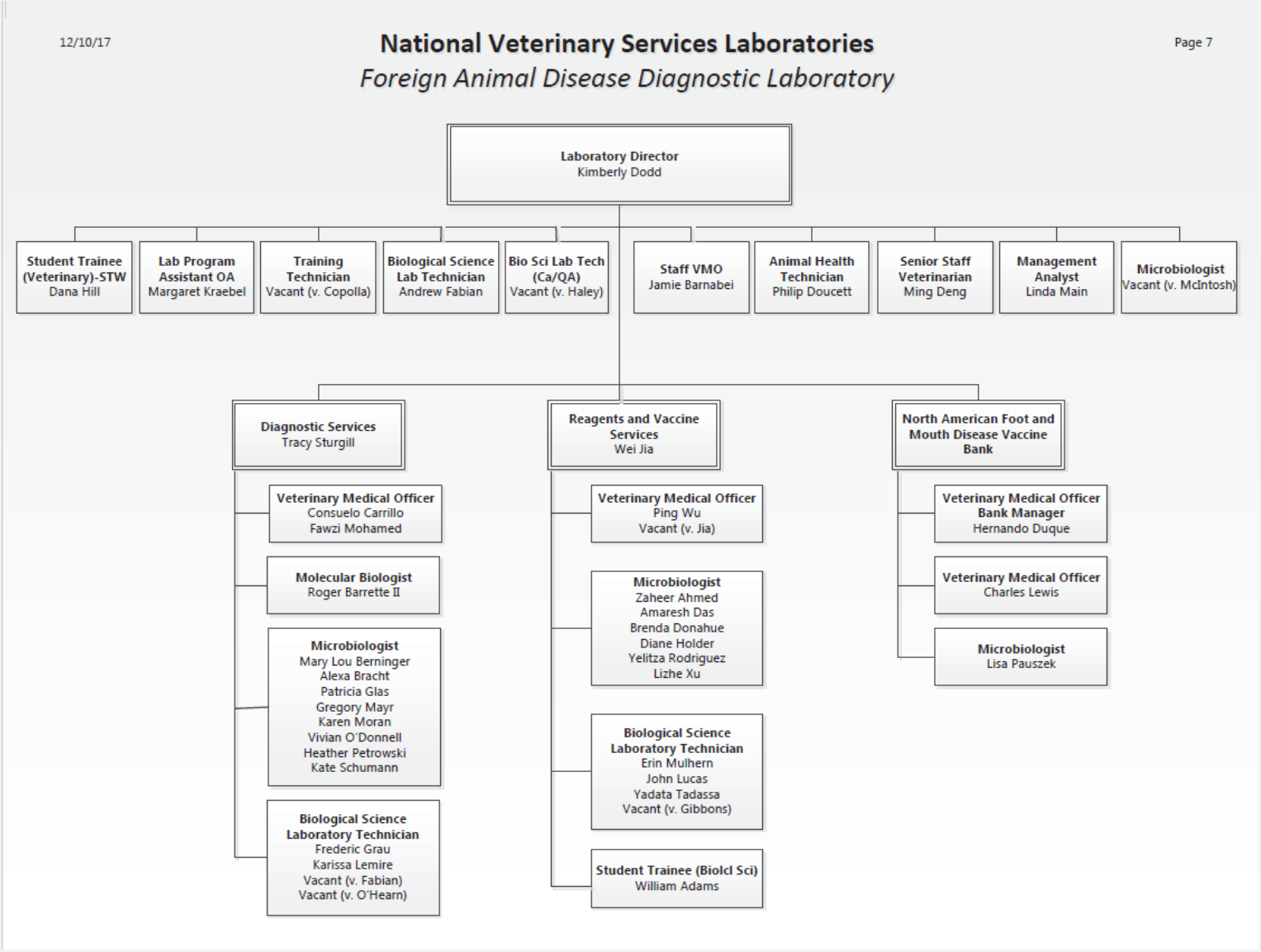
<u>Vaccine Development – Biologic Development Model (BDM)</u>

- ❑ Test potential vaccines to shorten development timeline

Diagnostics for Foreign Animal and Zoonotic Diseases

Foreign Animal Disease training

North American Foot-and-Mouth-Disease vaccine bank



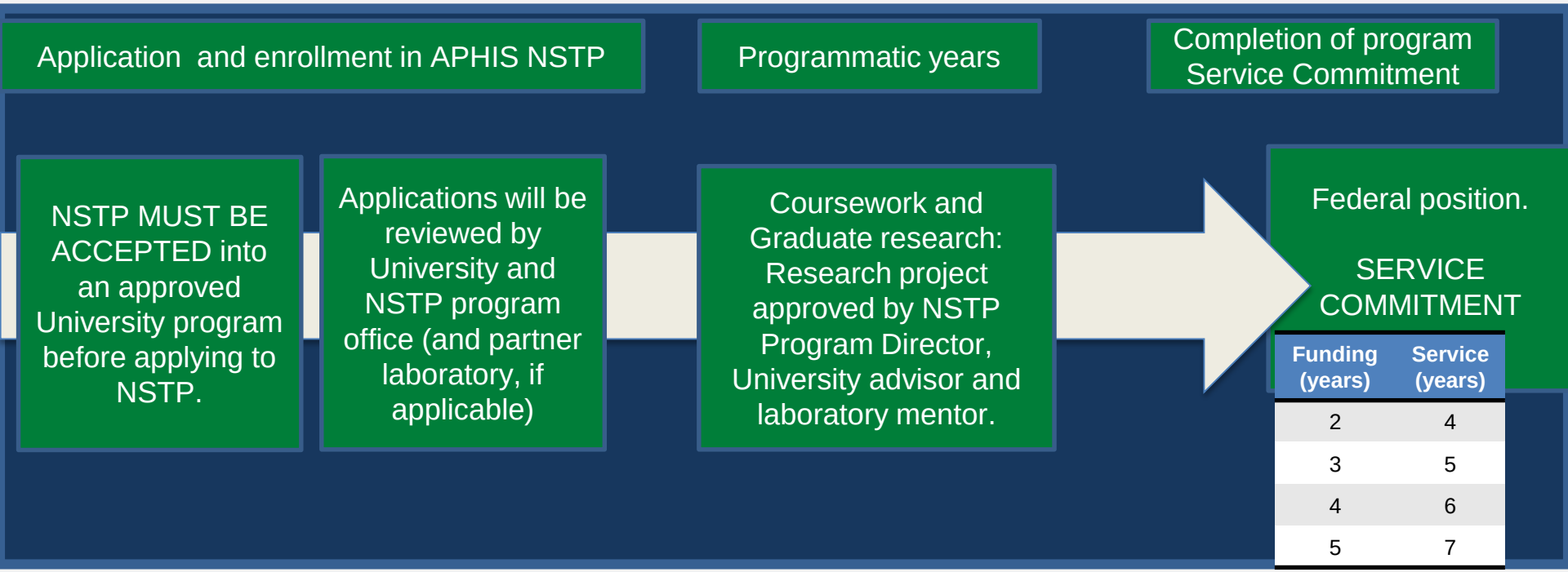
FADDL staff to increase at NBAF to ~78 from ~40 personnel

APHIS NBAF SCIENTIST TRAINING PROGRAM (NSTP)

APHIS NSTP Overview

Goal: mitigate SME gaps as FADDL transitions to NBAF

- Graduate training program to fund highly qualified applicants for up to 5 years
  - MS, PhD, DVM/PhD
  - Laboratory based research: molecular virology, microbiology, bioinformatics, infectious disease
  - Focus on foreign animal diseases and/or emerging BSL-4 agents
  - Funding will include tuition and fees, stipend, health benefits, travel, materials and supplies, publication costs
- Partner laboratories
  - CFIA, CDC, NVSL, K-State/BRI, others TBD
- Guaranteed federal position at completion of program
- Service commitment at NBAF (or PIADC) required



Funding (years)	Service (years)
2	4
3	5
4	6
5	7

- Prospective fellows MUST be accepted to NSTP approved University program before applying to NSTP program.

- All fellows funded through University Cooperative Agreement.
- Covers tuition and fees, stipend, insurance, travel, and some research costs. University covers all indirect costs.

- Maintain minimum GPA.
- Contribute to development of NBAF-related SOPs.
- Biannual progress reports to NSTP program office
- Participate in annual NSTP research symposia.
- Payback required if fellow leaves program for any reason.

- Pending successful completion of program, NSTP fellows offered federal positions.
- Service commitment required
- If fellow fails to complete service commitment, prorated payback required.

Inaugural NSTP class: October 2018

Kimberly Dodd DVM, PhD
Director
Foreign Animal Disease Diagnostic Laboratory
U.S. Department of Agriculture
Animal and Plant Health Inspection Service
Veterinary Services
Kimberly.a.dodd@aphis.usda.gov