

JEV Research Gaps Identified

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Immediate preparation/response

- 1. Investigate trade implications of a JEV incursion into the US, including countries where JEV is endemic and countries negative for JEV. Estimate the potential economic losses to the US pork industry due to production losses on sow farms, disrupted domestic and international markets, and trade restrictions if JEV is introduced.
- 2. Investigate the mechanism of JEV spread throughout a single production site, defining the risks or epidemiological factors playing a role in the extent of transmission and variation of clinical signs within a litter and across litters. Goals include identifying mitigation strategies to minimize JEV impact on farm production.
 - a. Define the role of vector-free or direct pig-to-pig transmission in the epidemiology of JEV.
- Design novel or confirm current US diagnostic assays for JEV (PCR and antibody at NVSL, FADDL and NAHLN laboratories) can distinguish between other flaviviruses in the US (WNV, SLEV) and will detect all five genotypes (I-V) of JEV.
- 4. Model spatiotemporal spread of JEV post-incursion to identify mitigation strategies for biocontainment and rapid eradication from the US.
- 5. Determine the most effective consumer and producer messaging on JEV being a "mosquito disease," with the goal of minimizing negative effects on pork production and consumption while maximizing safety and protection of swine personnel in the event of JEV incursion.

Intermediate response

- 6. Investigate surveillance targets (species, high risk locations in US, sample types) and diagnostic assays (PCR, antibody) to develop an effective surveillance plan for earliest detection of a JEV incursion into the US.
 - a. Examples may include feral swine, commercial swine, high-risk backyard swine, mosquitos, water birds, migratory birds, sentinel animal systems such as

chickens, lagoon effluent, bird feces, oral fluids, tonsils, human encephalitis cases.

- 7. Investigate syndromic surveillance for case compatible VDL submissions in the US of reproductive disease from sow farms (abortions, mummified fetuses, stillborns, neonatal tremors) to define the annual or seasonal number of compatible cases, including the percent of cases in which no definitive diagnosis of endemic disease or toxicosis is determined.
- 8. Develop experimental challenge models for JEV to interrogate interventions and their effect on clinical disease severity, pathogenesis in pregnant sows, transmission rates, virus replication, and prevalence within and across litters.

Longer term response

- Develop vaccine candidates for use in US commercial swine to minimize production losses if JEV is introduced, focusing on subunit, vectored, mRNA, or killed vaccines, that could be deployed post-outbreak and would allow differentiation of vaccinated from infected animals (DIVA).
- 10. Determine the extent of JEV cross-protection that is present in US commercial swine after exposure to other flaviviruses (WNV, SLEV) endemic to the US.
- 11. Investigate effective mosquito control measures for swine farms in the US, including recommendations based on site design, ventilation type, and manure storage. Chemical insecticide residues and withdrawal periods should be indicated.
- 12. Investigate and characterize the competence of potential vector host species in the US for JEV, including their geographic proximity to feral and commercial swine populations, and propensity to feed on pigs or ardeid birds.
- 13. Define the risk and mitigation of known wildlife hosts, such as feral swine and ardeid birds, in the role of JEV introduction and spread to commercial swine in the US.
- 14. Investigate and characterize the competence of novel vertebrate host species (nonardeids and non-swine) in the US to act as amplifying or dead-end hosts of JEV, including their geographic distribution and proximity to commercial or feral swine.
 - a. Examples may include non-ardeid bird species, microbats, fruitbats, opossums.
- 15. Investigate the molecular pathogenesis differences between genotype 4 and historical JEV genotypes, including an estimation of virulence factors based on whole genome sequencing.