Case Definition

Avian Influenza (AI) (Notifiable)

August 2024

Addendum I: HPAI H5N1 clade 2.3.4.4b in Non-avian species

1. **Disease Information General Disease and Pathogen Information:** As of late March 2024, H5N1 clade 2.3.4.4b, genotype B3.13 per GenoFlu, was detected in milk and other bovine-origin samples associated with mild illness in dairy cattle. The virus has been characterized as highly pathogenic per cleavage site analysis and bioassay testing (IVPI per WOAH), and currently the B3.13 genotype is not significantly different from other genotypes affecting wild birds and poultry. Pathways of disease transmission are still being investigated and lateral transmission has been documented. The estimated herd level incubation period in dairy cattle appears variable, from approximately 12 to 21 days. The incubation period for cattle is likely multifactorial and should consider route of exposure, viral dose, production phase of the animal, and likely other factors that are still unknown at this time. The virus is found in high concentrations in milk secretions of lactating cattle

1.1 Clinical Signs: Infections of cattle may be asymptomatic (subclinical) or symptomatic (clinical) and virus is predominantly found in milk and mammary tissue regardless of symptoms. Clinical signs may include a decrease in feed consumption with a simultaneous decrease in rumination and rumen motility; respiratory signs including clear nasal discharge; and subsequent acute drop in milk production. Additional clinical signs may include abnormal tacky or loose feces, lethargy, dehydration, and fever. Severely affected cattle may have thicker, concentrated, colostrum-like milk or produce no milk at all. Other non-avian species may present as primary respiratory cases or with neurologic symptoms.

2. **Laboratory Criteria**
For Bovidae species, milk and mammary tissue are the preferred samples from lactating animals and deep nasal swabs for non-lactating Bovidae. Respiratory swabs/tissues are typical for many mammalian species; brain is recommended for neurologic cases. Other sample types include those listed in APHIS surveillance plan guidance. Serology for serum and milk may be utilized for some species.

2.1 Agent Isolation and Identification: Detect presence of influenza A virus by:

2.1.1 Preferred samples from live or dead animals are tested by polymerase chain reaction (PCR) assays for influenza A and those targeting H5 2.3.4.4b (subtype assays should only be used in conjunction with influenza A detection assays). Virus isolation may also be performed.

2.2 Agent Characterization: Genome sequencing methods are used to determine the amino acid sequence at the hemagglutinin cleavage site to pathotype viruses per the WOAH Terrestrial Manual. Subtyping tools and lineage-specific tools such as pathotyping assays are available at NVSL.

3. **Case Definition and Reporting Criteria for individual animal and single premises herds**

3.1 Suspect Case:

3.1.1 Illness compatible with H5 clade 2.3.4.4b infection; **OR**

3.1.2 Detection of influenza A antigen in milk using a commercially available influenza A antigen test kit (ACIA, approved by USDA); **OR**

3.1.3 Detection of influenza A by PCR at a private laboratory where the host species virus lineage has been ruled out (e.g. swine lineage H1/H3, equine/canine H3).

3.2 Presumptive Positive Case:

3.2.1 Detection of influenza A by PCR at a NAHLN (National Animal Health Laboratory Network) Laboratory where the host species virus lineage has been ruled out (e.g. swine lineage H1/H3, equine/canine H3) with or without the presence of compatible illness**.**

3.3 Confirmed Positive Case:

3.3.1 Identification of HPAI H5 clade 2.3.4.4b at NVSL by molecular assay **OR** genome sequencing.[1]

3.3.1.1 An animal **<u>may</u>** be excluded as a confirmed case after review of all available case information due to:

- An alternative diagnosis can explain the illness or detection fully.[2]
- Test result(s) are poorly or not repeatable and resampling is either not possible or testing from resampling is negative.

For guidance on movement regulations please refer to APHIS Requirements and Recommendations for Highly Pathogenic Avian Influenza (HPAI) H5N1 Virus in Livestock and Herd Status program standards.

[1] Confirmation of a dairy herd in a new state by NVSL requires identification of HPAI H5 clade 2.3.4.4b by PCR for at least two different gene targets with determination of genotype.

[2] Factors that may be considered when assigning alternate diagnoses include the strength of the epidemiologic evidence for HPAI H5 exposure, absence of clinical signs where the potential for environmental contamination cannot be ruled out, and the compatibility of the clinical presentation and course of illness for the alternative diagnosis.