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The CEIRR Risk Assessment Pipeline Executive Report:

Assessment of the Pandemic Potential of H9N2 B4.7.2 and B4.7.4 Influenza A Viruses

Prepared by The CEIRR Risk Assessment Pipeline
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Priority for Risk Assessment and Risk Mitigation: Moderate

Executive Summary: H9N2 influenza A viruses are prevalent in poultry on multiple continents. Occasional spillovers occur and three were reported recently in China. Viral evolution does not appear to be a driver of the recent cases. Human sera cross-react with but do not block infection by H9N2 viruses. These viruses replicate and transmit in ferrets with prior exposure to seasonal influenza A viruses. While risk does not appear to have increased recently, monitoring of H9N2 virus prevalence and evolution is a priority due to their demonstrated zoonotic potential and the limited functional immunity to these viruses in the human population.

Background: H9N2 influenza A viruses are prevalent in poultry in most of Asia, the Middle East and parts of Africa. Human infections are reported on a rare but consistent basis, are typically associated with exposure to poultry, and result in mild disease. These viruses often co-circulate with other poultry-adapted lineages, including highly pathogenic avian influenza viruses. This co-circulation has enabled frequent genetic exchange. Of note, H9N2 viruses contributed gene segments to H5N1, H7N9 and H10N8 lineages associated with repeated zoonotic infection and human fatalities. The documented zoonotic spread of H9N2 viruses and their reassortants raises concern that these poultry adapted viruses could contribute to an influenza pandemic.

Properties of the Virus | Genetic diversity

- Recent human cases fall within the diversity of H9N2 viruses circulating in China for decades and are similar to viruses sampled from the environment and poultry, consistent with spillovers linked to poultry exposure.
- This lineage has several HA and PB2 mutations that have been linked to human adaptation. However, most of these have been circulating in this lineage for at least 10 years.
- HA 198V and PB2 389R are unique to viruses sampled within this cluster.
- It appears that there is no obvious reassortment immediately prior to this cluster.

Properties of the Virus | Pathogenesis

- A B4.7.4 H9N2 virus caused mild disease in ferrets transient weight loss in a subset of animals.
- A B4.7.4 H9N2 virus was not detected in the brain of infected ferrets
- A B4.7.2 H9N2 virus replicates to low titers in the lung and does not induce severe disease in C57BL/6 mice
- Replication is reduced in the presence of mouse Mx, indicating susceptibility to Mx antiviral function

Properties of the Virus | Transmission

- A B4.7.4 H9N2 virus transmitted efficiently among ferrets housed in direct contact
- In directly challenged ferrets, immunity resulting from prior infection with either H1N1 or H3N2 virus did not alter peak viral loads but accelerated H9N2 viral clearance from the upper respiratory tract.
- Immunity to either H1N1 or H3N2 did not reduce susceptibility of ferrets to infection with H9N2 virus via direct contact exposure.

Attributes in the Human Population | Human Infection

- 195 instances of human infection with H9N2 viruses have been reported to WHO since 1998.
- In April 2025, three human cases were reported in Hunan province, China.
- 80% of 173 human H9N2 cases for which relevant metadata are available involved individuals under 20 years of age, with the 0–9 age group most affected.
- Mild respiratory disease is typical.

Attributes in the Human Population | Population Immunity

- Analysis of human sera from individuals living in the United States revealed antibodies that bind to H9N2 HA and NA proteins, indicating the presence of cross-reactive immunity.
- Antibodies that block H9 HA function were not detected at appreciable levels.
- Antibodies that block N2 NA function were generally low but detectable and showed variation with birth year, consistent with effects of lifetime influenza exposure history.