

# Influenza Risk Assessment Tool (IRAT) - Virus Report

Prepared by the CDC Influenza Division



## North American Low Pathogenic Avian Influenza A(H7N9)

Virus Strain: A/chicken/Tennessee/17-007431-3/2017

Date of Evaluation: October 2017

### Introduction

Human infections with novel influenza A viruses that originate in animals are rare and the risk of such infections overall to humans is generally low. Sporadic infections with novel influenza A viruses do occur, but typically in situations where individuals are exposed to infected animals through direct or close contact. The IRAT is used to examine multiple attributes of novel influenza A viruses that have not gained the ability to spread among humans to assess their potential to acquire this ability and the consequent potential public health impact.

### Situation

The investigation of a highly pathogenic avian influenza (HPAI) A(H7N9) virus detected in commercial poultry in Tennessee by the U.S. Department of Agriculture (USDA) in March 2017 revealed the contemporaneous presence of North American lineage low pathogenic avian influenza (LPAI) A(H7N9) virus. Several commercial and backyard poultry flocks in counties in Tennessee, Alabama, Kentucky, and Georgia were affected. The outbreak in poultry appeared limited and, following mitigation efforts to control the disease, no further LPAI or HPAI A(H7N9) viruses associated with this outbreak were detected in subsequent surveillance [1].

In October 2017, the CDC assessed the pandemic potential of a representative strain of LPAI A(H7N9) virus from the described outbreak using the Influenza Risk Assessment Tool (IRAT).

### IRAT Evaluation

Influenza subject matter experts (SMEs) from the CDC, USDA, and FDA were asked to evaluate influenza A/chicken/Tennessee/17-007431-3/2017 using ten risk elements defined in the IRAT. Each SME scored 1 to 3 elements based on their particular areas of expertise. The point estimate scores for each risk element were averaged, multiplied by predetermined weights, and summed to give an aggregate score for each of the two IRAT risk questions related to potential risk for emergence in humans and potential public health impact if the virus gained the ability to spread efficiently human to human [2].

The summary average risk score was 3.1 for the virus to achieve sustained human-to-human transmission (Table 1), placing the virus in the low risk category. The average risk score for the virus to significantly impact public health if it were to achieve sustained human-to-human transmission was 3.5 (Table 2) and was between the low to low-moderate risk range. Overall, the virus is categorized in the low risk range.

There was little variability in SME point estimate scores for the majority of risk elements. A wider spread in SME scores was observed with the Disease Severity and Pathogenesis risk element; however, none of the individual scores for this element exceeded the lower end of the moderate risk range.

Table 1-Estimated Risk of Emergence

Risk Element	Weight (W)	Risk Score (RS)	W x RS
Human Infections	0.2929	1.71	0.50
Transmission in Lab Animals	0.1929	3.20	0.62
Receptor Binding	0.1429	1.75	0.25
Population Immunity	0.1096	8.50	0.93
Infections in Animals	0.0846	4.17	0.35
Genomic Variation	0.0646	2.60	0.17
Antigenic Relatedness	0.0479	2.33	0.11
Global Distribution in Animals	0.0336	3.00	0.10
Disease Severity & Pathogenesis	0.0211	2.43	0.05
Antiviral/Treatment Options	0.0100	2.00	0.02
Total			3.10

Table 2-Estimated Potential Public Health Impact

Risk Element	Weight (W)	Risk Score (RS)	W x RS
Disease Severity & Pathogenesis	0.2929	2.43	0.71
Population Immunity	0.1929	8.50	1.64
Human Infections	0.1429	1.71	0.24
Antiviral/Treatment Options	0.1096	2.00	0.22
Antigenic Relatedness	0.0846	2.33	0.20
Receptor Binding	0.0646	1.75	0.11
Genomic Variation	0.0479	2.60	0.12
Transmission in Lab Animals	0.0336	3.20	0.11
Global Distribution in Animals	0.0211	3.00	0.06
Infections in Animals	0.0100	4.17	0.04
Total			3.46

The primary drivers of the low risk of emergence score were that there were no human infections, inefficient transmission in laboratory animal model testing, and an avian receptor binding preference for this virus. In the IRAT determination of the risk of emergence these factors are weighted heavily. Humans are not expected to have immunity to this virus which results in a high individual score for population immunity risk, but this factor alone is not sufficient to raise the aggregate emergence risk score out of the low risk category. A similar situation was evident when answering the IRAT question of risk of potential public health impact. The top weighted risk elements in answering this question scored relatively low, although the population immunity score had a slightly greater effect due to its higher relative importance raising the score above 3 to 3.5.

### Individual Risk Element Summaries

**Human Infections:** No human disease was reported for this virus; this is a different lineage of virus than the A(H7N9) causing zoonotic infections in China. Without any human disease detected, this risk element scored in the low range.

**Transmission in Laboratory Animals:** Studies in the ferret direct contact model demonstrated inefficient transmission with this virus similar to other LPAI viruses, indicating a probable low risk in humans [3].

**Receptor Binding:** Sequence analyses did not indicate adaptation of the virus to mammalian receptors; similar to other LPAI viruses that preferentially bind to  $\alpha$ 2,3 galactose-linked sialic acids.

**Population Immunity:** Although there were no serological studies available for this specific virus, it is anticipated that overall population immunity to this virus will be very low. Consequently, this risk element ranks high.

**Infections in Animals:** This lineage of virus appears to be endemic in wild birds [4]; this virus was isolated from a poultry outbreak which was limited. This risk element scored in the low-moderate range.

**Genomic variation:** This LPAI virus meets the criteria for low risk in that it is very closely related in all gene segments to wild bird H7N9 viruses. Reassortment only with closely related viruses and lacks molecular signatures of importance for human infections.

**Antigenic relatedness:** Risk was ranked low for this element based on its similarity to the HPAI A(H7N9) that was isolated from the same outbreak. The HPAI showed that ferret antisera raised to existing candidate vaccine viruses A/turkey/Virginia/4529/2002 (H7N2) and A/Canada/rv444/2004 (H7N3) inhibited this virus at titers equivalent or within 2-fold of homologous virus titers.

**Global Distribution in Animals:** Surveillance during the outbreak investigation revealed that the virus was present in a limited number of commercial or backyard flocks in four states. However, following eradication efforts, surveillance has been negative which suggests very limited distribution and only in wild birds at the time of the IRAT evaluation.

**Disease Severity & Pathogenesis:** No evidence of human disease was detected with this virus and animal model studies (mouse and ferret) demonstrated mild disease suggesting the potential risk is low for humans.

**Antivirals and Treatment Options:** No known markers associated with antiviral resistance were identified resulting in a low risk score for this element.

#### [Comparison to Other Viruses Scored with IRAT](#)

The scores for the emergence risk and potential public health impact for the LPAI A/chicken/Tennessee/17-007431-3/2017 were plotted along with a selection of other viruses previously scored using the IRAT (Figure 1). The LPAI A(H7N9) virus aligns with other North American lineage avian viruses in a category of low risk. Viruses with higher IRAT risk scores are included for comparison.

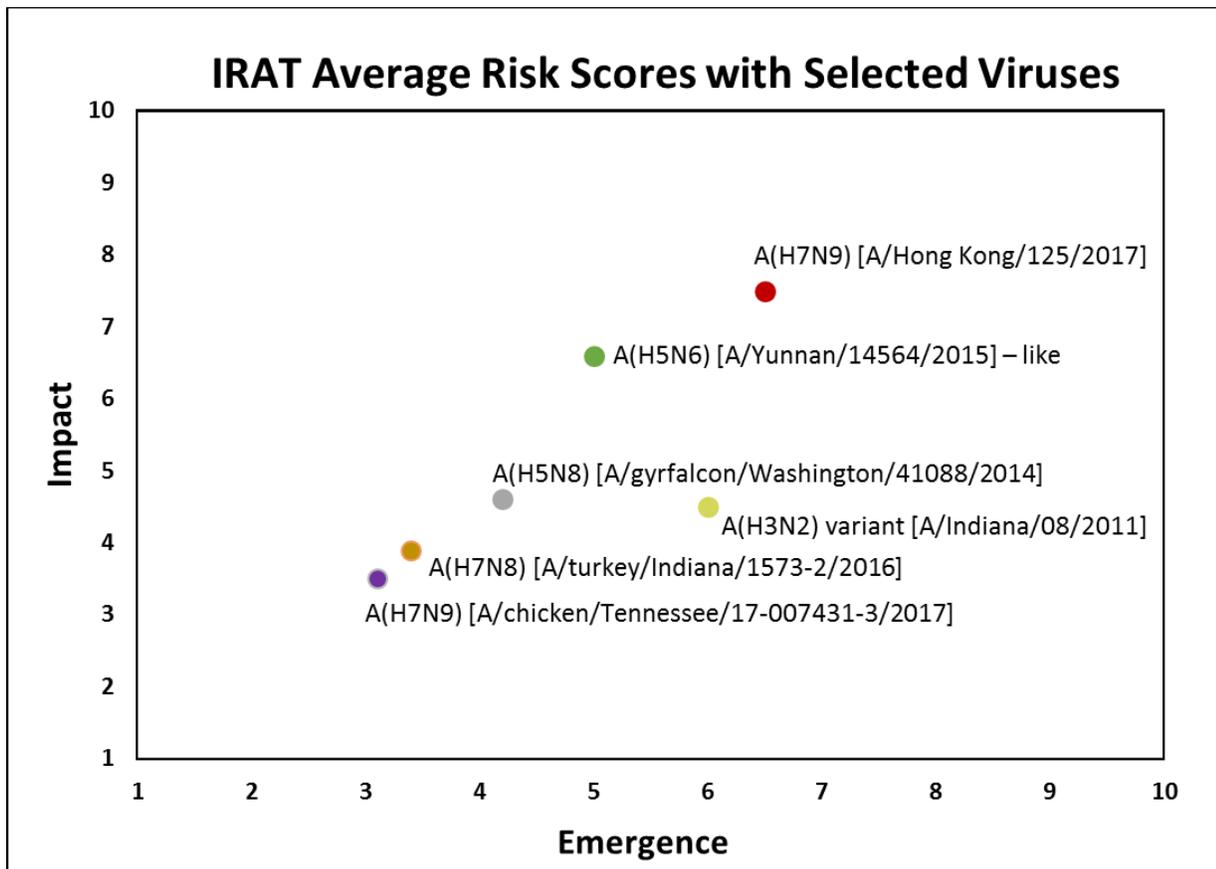


Figure 1: Average IRAT scores for LPAI A/chicken/Tennessee/17-007431-3/2017 plotted by emergence score and impact score. Additional viruses scored using IRAT are displayed for comparison.

Note: IRAT results were generated using information and data known to influenza subject matter experts at the time of the evaluation. Subsequent findings may raise or lower the overall risk scores associated with the virus.

## References

1. USDA-APHIS (2017). Epidemiologic and other analyses of HPAI/LPAI affected poultry flocks: June 26, 2017 Report. USDA:APHIS:VS:STAS:Center for Epidemiology and Animal Health. Fort Collins, CO. June 2017. Doc #391.0317 V2. 39 pgs.
2. Trock SC, Burke SA, Cox NJ. Development of a framework for assessing influenza virus pandemic risk. *Emerg Infect Dis.* 2015;21:1372–8. <http://dx.doi.org/10.3201/eid2108.141086>
3. Belser JA, Brock N, Sun X, Jones J, Zanders N, Hodges E, et al. Mammalian pathogenesis and transmission of avian influenza A(H7N9) viruses, Tennessee, USA, 2017. *Emerg Infect Dis.* 2018 Jan 24(1): 149-152. <http://doi.org/10.3201/eid2401.171574> [Note: manuscript was in preparation during IRAT evaluation, but available to IRAT SMEs for use in virus scoring]
4. Lee D, Torchetti MK, Killian M, Berhane Y, Swayne DE. Highly Pathogenic Avian Influenza A(H7N9) Virus, Tennessee, USA, March 2017. *Emerg Infect Dis.* 2017;23(11):1860-1863. <https://dx.doi.org/10.3201/eid2311.171013> [Note: manuscript was in preparation during IRAT evaluation, but available to IRAT SMEs for use in virus scoring]