



CONSULTATIVE SIGNAL ASSESSMENT  
**PRIMARY RISK ASSESSMENT**  
EVIDENCE BASED RISK ASSESSMENT  
PUBLIC HEALTH EVENT ASSESSMENT

**H5N1 (AVIAN FLU) IN MAMMALS IN SEVERAL EUROPEAN COUNTRIES**

Date of the signal	Date of the PRA	Signal provider	Experts consultation	Method
02/02/2022	04/02/2022		<b>Permanent experts:</b> Karin Cormann (DGOV), Christian Huvelle (AViQ), Romain Mahieu (COCOM), Cecile van de Konijnenburg (FOD), Dirk Wildemeersch (AZG)  <b>Specific experts :</b> Cyril Barbezange (Sciensano), Bart Bautmans (AZG), Nathalie Bossuyt (Sciensano), Pol Gosselin (SPWcu), Sophie Lokietek (AVIQ), Mieke Steensels (Sciensano), Steven Van Borm (Sciensano), Marc Van Ranst (KULeuven), Melissa Vermeulen (Sciensano), Muriel Vervaeke (ANB), crisiscel FAVV	E-mail consultation
Date of update	Closing date			

**RAG persons of contact:**

Tinne Lernout (tinne.lernout@sciensano.be)

Javiera Rebolledo (javiera.rebolledogonzalez@sciensano.be)

[rag@sciensano.be](mailto:rag@sciensano.be)

## Signal

The past year, a number of HPAI H5 strains (both avian and mammalian) were detected in a few European countries, in which markers indicative of mammalian adaptation were found. The most recent report from EFSA concerns the period Sept – Dec 2021 and includes observations of avian influenza A(H5N1) in wild mammal species in Estonia, Sweden and Finland (1).

In January 2022, a H5N1 virus, showing genetic adaptation typical of mammals, was found in The Netherlands in a fox.

## Description

### Cause known?

Outbreaks of HPAI H5N1 occur in poultry. It is likely that mammals can also contract the bird flu virus by biting/eating wild birds infected with avian flu.

In general, contact with high dose can cause accidental spill-over (independent of the current strains), but there is no indication that there will be spread from animals to humans (see EFSA protocol)

### Unexpected/unusual

**Expected:** Outbreaks in poultry caused by HPAI H5N8, H5N5, H5N1, H5N4 and H5N3 viruses since October 2020 in several European countries.

**Unusual:** A few detections of HPAI H5N1 have been observed in mammals in 2020-2021 and early 2022 in Europe. The markers of the mammalian isolates were also found in wild birds and/or poultry. These signals of breach of the avian-mammal host species barrier are more rarely reported than from wild birds to poultry (2).

Up to now, H5N1 has not been detected in mammals in Belgium, but the surveillance (in foxes) was only recently set up, and a first fox is being analysed (see further).

Sporadic infections in canines and felids with Alv strains have been regularly seen in previous epidemics (see feline examples with h5n1 2006 strains in Europe). The exposure usually suspected is the consumption of infected wild bird carcasses. These infections usually do not lead to establishment of the relevant Alvs in the feline or canine population.

Ad hoc genetic surveillance in canine and feline wildlife is perhaps necessary but mainly/only for the benefit of human medicine.

### Severity

Influenza A(H5N1) can cause severe disease in humans. The clinical course of human cases of A(H5N1) is characterised by rapid progression to lower respiratory disease, with possible progression to respiratory failure, acute respiratory distress syndrome (ARDS) and multi-organ failure (3). The CFR from HPAI A(H5N1) is country-dependent, but is overall estimated at 66% (4).

### Dissemination Very low

To date, no symptomatic human infections with the clade 2.3.4.4.b HP H5 virus currently circulating in Europe among birds and now also found in foxes (5), have ever been reported worldwide. Positive swabs from humans have been reported in UK and Russia, and in the case of Russia also a few seroconversions, but no development of symptoms.

The H5N1 virus, which was found in the Netherlands in January 2022 in a fox (with different molecular markers), has a genetic adaptation that is typical for mammals. Additional genetic adaptations are still needed before the bird flu virus can spread to and between humans. However, because influenza viruses can mutate rapidly, it cannot be ruled out that the H5N1 virus will mutate further into a virus type that would become easily transmissible from person to person, while maintaining its ability to cause serious illness. Increased vigilance is therefore necessary.

### Risk of (inter)national spread

Influenza A(H5N1) remains poorly adapted to humans. Transmission from birds to humans is rare and no sustained human-to-human transmission has been observed.

However, the observed infections in mammals are a result of overcoming the inter-species barrier from birds to mammals, which is mostly associated with gene reassortment. If more mammalian species can be infected with these viruses, there is higher risk of genetic evolution of these viruses that may lead to the next human pandemic (6).

## Preparedness and response

### Preparedness

A surveillance system is in place in Belgium for avian flu in poultry: there is a mandatory clinical surveillance (including several defined criteria requesting samples to be send in to Sciensano's NRL Avian Influenza). See at <https://www.favv-afsca.be/professionnels/productionanimale/santeanimale/grippeaviaire/situationbelgique>. At European level, there is also a mandatory serosurveillance in place for the of avi-sector.

There is also a surveillance in place for wild birds, but mostly passive. E.g. ANB has ongoing surveillance of bird flu in wild bird populations in order to detect avian influenza viruses. In this

<p><b>Specific control measures</b> (surveillance, control, communication)</p>	<p>surveillance, sick and dead wild birds in Flanders are collected and examined for circulating bird flu viruses.</p> <p>There is no active surveillance in place for avian influenza in <u>humans</u>; only syndromic surveillance for people taking part in culling.</p> <p>Sciensano has the diagnostic capacity to isolate this virus.</p> <hr/> <p>In response to the report of mammalian H5 strains in some European countries in 2021 and given that monitoring is warranted because of the risk of virus mutation, Sciensano recently set up a <b>surveillance in foxes</b>, in agreement with the 3 regions. A 1<sup>st</sup> symptomatic fox has been collected this week and is now being tested.</p> <ul style="list-style-type: none"> <li>• In case of a confirmed infection, the sample will be sequenced (WGS) by the NRL Avian Influenza and the samples will be exchanged with the NRC Influenza for virus isolation.</li> <li>• The European Reference Laboratory Avian Influenza (IZsVe) is willing to share protocols. The zoonotic potential will be based on WGS results (first line).</li> <li>• There is a convention with the 3 regions (Flanders, Wallonia, Brussels) on wild bird AI surveillance (mostly passive surveillance, except W also active surveillance in wild birds), Addendums to extend the passive AI surveillance in wild birds to wild mammals feeding on possibly infected carcasses of wild birds are now being written: <ul style="list-style-type: none"> <li>○ ANB Flanders: addendum currently being drafted by ANB;</li> <li>○ DNF Wallonie: agreement in principle to add this within the current agreement, addendum still needs to be drafted there too;</li> <li>○ LB Brussels: must be further developed given the very limited agreement for the birds.</li> </ul> </li> </ul>
<p><b>Public health impact</b></p>	
<p><b>Public health impact in Belgium</b> Low</p>	<p>The risk for zoonotic transmission is considered to be extremely low for the general public and is been estimated mild for occupational involvement (poultry sector, culling of outbreaks, involved in wild birds surveillance/collection of corpses, ...).</p> <p>Given the evolutionary history of the virus, with the HA gene having evolved from the widely circulating A(H5N1) viruses, people in direct contact with/handling diseased birds or poultry, or their carcasses (e.g. farmers, veterinarians and labourers involved in the culling and rendering) might be at risk of infection.</p>
<p><b>Recommendations</b> (surveillance, control, communication)</p>	<p>The surveillance in foxes that has already been set up should be continued.</p> <p>Surveillance of avian flu in humans should be enhanced. <b>A surveillance protocol for humans involved via occupation in the avian sector during outbreaks</b> has been written by Sciensano (in the framework of the One Health approach) and will be submitted to the regions (through the RMG) for discussion.</p> <p>People gathering wild birds and animals should respect minimal protection and hygienic measures (gloves, disinfection hands, clothing, ...): see protocol of agency that collects cadavers.</p>
<p><b>Actions</b></p>	<p>Reinforce the surveillance of avian flu in humans.</p>

## REFERENCES

1. EFSA Scientific report. <https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2021.7108>
2. Fouchier R.A., Guan Y. Ecology and evolution of influenza viruses in wild and domestic birds. In: Webster R.G., Monto A.S., Braciale T.J., Lamb R.A., editors. *Textbook of Influenza*. Wiley; London, UK: 2013. pp. 175–187.
3. ECDC. <https://www.ecdc.europa.eu/en/zoonotic-influenza/facts/factsheet-h5n1>.
4. Wu ZQ, Zhang Y, Zhao N, Yu Z, Pan H, Chan TC, Zhang ZR, Liu SL. Comparative Epidemiology of Human Fatal Infections with Novel, High (H5N6 and H5N1) and Low (H7N9 and H9N2) Pathogenicity Avian Influenza A Viruses. *Int J Environ Res Public Health*. 2017 Mar 4;14(3):263. doi: 10.3390/ijerph14030263. PMID: 28273867; PMCID: PMC5369099.
5. Rijks JM, Hesselink H, Lollinga P, Wesselman R, Prins P, Weesendorp E, Engelsma M, Heutink R, Harders F, Kik M, Rozendaal H, van den Kerkhof H, Beerens N. Highly Pathogenic Avian Influenza A(H5N1) Virus in Wild Red Foxes, the Netherlands, 2021. *Emerg Infect Dis*. 2021 Nov;27(11):2960-2962. doi: 10.3201/eid2711.211281. PMID: 34670656; PMCID: PMC8544991.
6. Lloren KKS, Lee T, Kwon JJ, Song MS. Molecular Markers for Interspecies Transmission of Avian Influenza Viruses in Mammalian Hosts. *Int J Mol Sci*. 2017;18(12):2706. Published 2017 Dec 13. doi:10.3390/ijms18122706.

Protocols of agency that collects cadavers.

- o [https://www.favv-afsca.be/professionelen/dierlijkeproductie/dierengezondheid/vogelgriep/\\_documents/J026\\_wildefa\\_unaverdachtsterfteboodschapburger-v5-20201116\\_nl.pdf](https://www.favv-afsca.be/professionelen/dierlijkeproductie/dierengezondheid/vogelgriep/_documents/J026_wildefa_unaverdachtsterfteboodschapburger-v5-20201116_nl.pdf)
- o <https://www.natuurenbos.be/beleid-wetgeving/overlast-schade/ziekten-bij-het-wild-levende-dieren/wat-te-doen-met-verzwakte-dode>
- o <http://biodiversite.wallonie.be/nl/22-11-2021-vigilance-grippe-aviaire.html?IDC=3421&IDD=6525>