

# **Influenza Information for Water Professionals**

# **Key Take-Home Messages**

Influenza viruses cause respiratory illness that can be mild or serious enough to lead to hospitalization and death. Because influenza viruses are constantly changing, people can become infected with influenza multiple times in their lifetime. Some types of influenza viruses can cause severe global pandemics.

#### What we know from clinical surveillance

- There are more than 1 billion cases of seasonal influenza (or "flu") worldwide every year.
- In 2010 through 2022, seasonal flu caused 9.3 to 41 million illnesses each year in the U.S. and was consistently one of the leading causes of death.
- Influenza infection can result in complications such as pneumonia and multi-organ failure, especially in people who are older, very young, pregnant, immunocompromised, or have certain chronic conditions.
- Two types of influenza viruses infect humans: "A" viruses cause both seasonal epidemics and global pandemics, while "B" viruses only cause seasonal epidemics. There are many subtypes of "A" influenza, but not all cause human disease.

#### How wastewater surveillance plays a role

- Wastewater surveillance shows promise as a tool for complementing clinical influenza data by providing information on community flu incidence and the timing of flu season onset and peak, possibly serving as an early indicator.
- Many public health labs are already testing wastewater for influenza viral RNA, and data for more than 600 sites are being reported to the <u>U.S. National</u> <u>Wastewater Surveillance System</u>.

# What wastewater workers need to know

- Positive cell cultures of influenza virus from feces have been documented, but not positive cultures from wastewater. Nevertheless, spiked infective influenza virus can persist in water matrices for days, weeks, and potentially longer depending on the nature of the matrix. Therefore, infective influenza virus may be present in wastewater during epidemics and pandemics, but this is not known for certain.
- Wastewater workers are at risk of exposure to flu from infected colleagues, primarily through inhaling or coming into contact with respiratory droplets when the infected person breathes, coughs, sneezes, or talks.
- Staying up to date on seasonal flu vaccines, understanding the effectiveness of disinfectant products, conducting job safety assessments, practicing good hygiene, and wearing appropriate personal protective equipment are important for protecting wastewater worker health and preventing influenza infection.
- Many sodium hypochlorite-, ammonia-, and alcohol-containing products are effective against influenza viruses, including the disinfectants on <u>EPA's "List M"</u>.



# What about "H5N1"?

Although this fact sheet covers influenza viruses most relevant to human health, information specific to influenza A(H5N1) is provided in <u>Box 3</u>.

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# Why It's a Concern

Influenza, or flu, is a mild to severe respiratory illness caused by influenza viruses during seasonal <u>epidemics</u> or periodic <u>pandemics</u><sup>1</sup> (APHA 2015). Although influenza viruses have been circulating among humans for hundreds of years or longer (<u>Taubenberger and</u> <u>Morens 2010</u>), they are constantly changing and can therefore reinfect a person multiple times over their lifetime (APHA 2015). Around the globe, there are about 1 billion cases of seasonal flu every year, resulting in 290,000 to 650,000 associated deaths (<u>WHO 2023</u>). Approximately 5 to 20% of the U.S. population acquires a symptomatic flu infection each year (<u>Tokars et al. 2018</u>). From 2010 through 2022, seasonal flu caused 9.3 to 41 million illnesses per year and 12,000 to 52,000 deaths in the U.S. (<u>U.S. CDC 2024a</u>). When combined with deaths from pneumonia (a common flu complication), influenza represented the 8<sup>th</sup> or 9<sup>th</sup> leading cause of all deaths during the same time period (<u>National Vital Statistics System 2024</u>). Influenza viruses can also cause pandemics, such as the 2009/2010 "swine flu" pandemic, during which the associated disease can be more severe than seasonal flu.

# **About the Virus**

As members of the <u>Orthomyxoviridae</u> family, influenza viruses are <u>negative-sense</u>, <u>single-stranded</u>, segmented<sup>2</sup>, <u>enveloped</u> RNA viruses (<u>Bouvier and Palese 2008</u>). Influenza virus particles (or virions) are usually about 100 to 300 nm in length and either spherical or filamentous in shape (<u>Bouvier and Palese 2008</u>). Four types of influenza viruses are recognized: A, B, C, and D (<u>U.S. CDC 2024a</u>). As shown in **Table 1**, these differ

<sup>&</sup>lt;sup>1</sup> An "epidemic" is the occurrence of an illness (or other health concern) in a community or region above the level that is normally expected (Celentano et al. 2019). A pandemic is a worldwide epidemic.

<sup>&</sup>lt;sup>2</sup> <u>Segmented viruses</u> are those whose genomes are divided into separate parts, not all of which necessarily need to be present for the virus to be infective.

with respect to the species they infect and the severity and type of disease they can cause in humans. Types A and B are the most relevant for human health, although not all influenza A types circulate in humans (APHA 2015). Types A and B cause seasonal flu epidemics, while only A is known to cause pandemic flu (U.S. CDC 2023c). Influenza A viruses are categorized into subtypes according to the surface glycoproteins hemagglutinin (H) and neuraminidase (N). The current influenza A virus subtypes circulating in humans are A(HINI) and A(H3N2) (U.S. CDC 2023c), although there are sporadic human infections with H5, H6, H7, H9, and H10 subtypes (U.S. CDC 2024b). Many more A subtypes circulate in animals, most of them in birds (see **Box 3** for information on A(H5NI) infections in birds and cows). A global pandemic can occur when a new influenza A virus subtype that can infect humans emerges for the first time (U.S. CDC 2023c), either when a subtype that circulates in animals mixes with a human virus, or when an animal subtype crosses directly to humans (Wigginton and Ellenberg 2015). It is possible that wild aquatic birds, because they serve as the natural reservoir for influenza A viruses, are the original sources for all human pandemic flu viruses (Taubenberger and Morens 2010).

| Influenza<br>type | Species infected  | Associated human disease   |
|-------------------|---|--|
| А                 | Birds (both wild and domesticated),<br>bats, humans, pigs, horses, dogs, cats,<br>cows, and other mammals | Seasonal epidemics and global<br>pandemics causing mild to severe<br>disease in all ages |
| В                 | Humans, ferrets, pigs, seals  | Seasonal epidemics causing mild to severe disease in all ages                            |
| С                 | Humans  | Sporadic outbreaks of mild disease in children   |
| D                 | Cattle, pigs  | None known   |

| Table 1. | Types | of influen: | za viruses |
|----------|-------|-------------|------------|
|----------|-------|-------------|------------|

Sources: Bouvier and Palese (2008); APHA (2015); U.S. CDC (2023c)

# **Disease Overview**

**Clinical features:** Flu is an acute viral illness of the upper respiratory tract characterized by a sudden onset of symptoms and usually fever, myalgia (muscle aches), chills, cough, chest discomfort, fatigue, weakness, and headache (APHA 2015; <u>U.S. CDC 2024a</u>). Other symptoms may include sore throat, runny or stuffy nose, and sneezing. Gastrointestinal symptoms (nausea, vomiting, diarrhea) have been reported in up to 25% of children during school outbreaks of influenza A and B (APHA 2015), but are uncommon in adults (<u>U.S. CDC 2024a</u>). A cough can last for two weeks longer, but fever and other symptoms typically improve within 5 to 7 days (APHA 2015). Flu complications may include: bronchitis (inflammation of the bronchial tubes), pneumonitis (inflammation of the lungs), bacterial pneumonia or sinusitis (infection of the lungs or sinuses), otitis media (ear infection), febrile seizures, encephalitis (inflammation of the brain), myocarditis (inflammation of the heart), myositis or rhabdomyolysis (inflammation of muscle tissues), and exacerbation of underlying chronic conditions (such as asthma or heart

disease) (APHA 2015; <u>U.S. CDC 2024a</u>). Flu infections can also cause an extreme inflammatory response that results in <u>sepsis</u>, potentially leading to tissue damage, multiorgan failure, and death (<u>Florescu and Kalil 2014</u>).

**Transmission**: In general, pathogen transmission can be either *direct* (such as via direct contact with an infected person or spread of large respiratory droplets) or *indirect* (such as <u>fomite</u>-borne, vector-borne, or airborne). Flu can be transmitted directly and indirectly, with direct contact, droplet spread, fomites, and airborne routes having been documented (<u>Cowling et al. 2013; Killingley and Nguyen-Van-Tam 2013</u>). In most cases, influenza viruses can be detected in infected individuals starting one day before symptoms appear and continuing for 5 to 7 days (<u>U.S. CDC 2024a</u>). The period of peak viral shedding and communicability by an infected person occurs over the first 3 to 5 days of the illness for adults but may last 7 to 10 days in children (APHA 2015).

*Incubation period*: The average incubation period for person-to-person transmission of seasonal flu is 2 days, with a range of 1 to 4 days (APHA 2015). The incubation period for pandemic flu may vary according to the strain. Somone infected with influenza can be contagious during the incubation period.

**Diagnosis:** Because flu can be difficult to distinguish from other respiratory diseases based on symptoms alone, diagnostic testing is needed for a definitive diagnosis (APHA 2015). While rapid tests (sometimes called "point-of-care", or POC, tests) that detect flu virus <u>antigens</u> or viral RNA are available, the most accurate diagnostic tests are laboratory-based tests using PCR, viral culture, or <u>immunofluorescence</u> assays (<u>U.S. CDC</u> 2024a). <u>A multiplex PCR assay</u> can be used to simultaneously detect influenza A, influenza B, and SARS-CoV-2 viral RNA. For both rapid and laboratory tests, a throat, nasal, or nasopharyngeal swab is obtained for analysis.

**Risk groups**: While flu affects people of all ages, children younger than 2 and adults 65 and older are at the highest risk for complications (APHA 2015). In addition, pregnancy, pre-existing chronic conditions (such as asthma, heart disease, diabetes, blood disorders, and chronic kidney disease), and immunocompromised status all increase the risk of complications from flu (U.S. CDC 2024a).

**Mortality**: In the U.S., the proportion of seasonal flu cases that are fatal (or the case fatality ratio [CFR]) has consistently been <0.2% since 2010 (U.S. CDC 2024a). However, the CFR can be higher during a flu pandemic and isn't uniform for all age groups. For example, the CFR for children (ages 0 to 19 years) was usually < 0.1% vs. up to 5% for older adults (ages >65 years) during the 2009/2010 A(H1N1) pandemic (Wong et al. 2013).

**Clinical surveillance**: In the U.S., influenza illness is monitored through multiple public health surveillance systems. These include: virologic surveillance through the <u>National</u> <u>Respiratory and Enteric Virus Surveillance System</u> (NREVSS), outpatient surveillance of "influenza-like illness" (ILI) through <u>ILINet</u>, laboratory-confirmed influenza-associated hospitalizations through the Influenza Hospitalization Surveillance Network (<u>FluSurv-NET</u>), and others. <u>FluVIEW</u> provides a summary of the data from these sources.

# **Presence in Wastewater**

**Shedding:** Some people infected with influenza shed viral RNA in feces (To et al. 2010; Yoo et al. 2010; Arena et al. 2012; Wootton et al. 2014; Hirose et al. 2016; Lowry et al. 2023). Based on pooled results from 10 studies, Minodier et al. (2015) estimated that 21% (95% CL 8.9 to 36%) of people infected with flu shed fecal viral RNA. In a systematic review and meta-analysis, Lowry et al. (2023) calculated that, on average, 35% of people with confirmed influenza A or B infections shed viral RNA in feces (based on data from 30 studies) vs. 98% in mucus (13 studies), 86% in sputum (23 studies), and 82% in saliva (14 studies). Fecal shedding can occur in the absence of respiratory symptoms (Arena et al. 2012) and for a longer duration than sputum shedding (2 weeks or more in feces vs. 7 to 10 days in sputum; Hirose et al. 2016). Fecal viral concentrations analyzed with PCR analysis have ranged from 10<sup>2.0</sup> to 10<sup>7.0</sup> copies per gram of feces (<u>Chan et al. 2011a</u>; <u>Arena</u> et al. 2012; Hirose et al. 2016) vs. 10<sup>5.5</sup> to 10<sup>7.0</sup> copies per mL in sputum (Hirose et al. 2016). Although detecting viral RNA via PCR does not necessarily mean infective virus is present, some studies have demonstrated positive cell culture from feces, indicating potentially infective virus (Dilantika et al. 2010; Tamura et al. 2010; To et al. 2010), while others have conducted cell culture experiments for influenza virus from stool but without a positive result (Wootton et al. 2006; Chan et al. 2011b). It is unclear whether the presence of influenza viral RNA in feces is due to direct intestinal infection or swallowing viruscontaining nasopharyngeal secretions (Pinsky et al. 2010; Chan et al. 2011a).

Similarly, some people infected with influenza shed viral RNA in urine, although fewer studies have examined this compared to fecal shedding. Urine viral RNA was detected by <u>To et al. (2010)</u> in 1 out of 14 pediatric patients (7.1%) and by <u>Ho et al. (2013)</u> in 1 adult patient (out of 1 studied)—all infected with 2009 A(H1N1) pandemic influenza. <u>Zhu et al. (2015)</u> detected viral RNA in urine from 17 out of 18 patients (94%) infected with avian-origin influenza A(H7N9). Urine shedding duration (21 days) was comparable to fecal shedding duration (22 days) and throat swab shedding duration (20 days) (<u>Zhu et al. 2015</u>). To our knowledge, no data are available on viral RNA concentrations in urine or on whether the virus present in urine is infective.

**Detection and quantification**: Culture-independent methods are commonly used to detect and quantify influenza virus RNA in wastewater. These have included droplet digital PCR for influenza A (Wolfe et al. 2022; Boehm, Wolfe, et al. 2023) and both A and B (Boehm, Hughes, et al. 2023; Wolken et al. 2023); digital PCR for influenza A (Markt et al. 2023) and both A and B (Nadeau et al. 2024); and quantitative PCR for influenza A and B (Mercier et al. 2022; Toribio-Avedillo et al. 2023; Vo et al. 2023; Germano et al. 2024). The detection of influenza virus RNA with PCR-based methods does not necessarily mean that infective virus is present. To our knowledge, no studies have attempted to culture influenza virus from wastewater. However, it is reasonable to assume—based on the presence of infective virus in feces—that infective influenza may also be present in untreated wastewater, although this isn't known for certain.

Wastewater influenza concentrations are being tracked as part of multiple programs, including the North Carolina Wastewater Monitoring Program, the Wisconsin Wastewater Surveillance Program, and others. The largest dataset for influenza A and B RNA concentrations in wastewater is available from <u>WastewaterSCAN (2024)</u>. Between January 2022 and April 2024, the program detected influenza A in 19,300 out of >38,700 samples, and influenza B in 10,227 out of >34,400 samples, across 194 water resource recovery facilities (WRRFs). Positive PCR detections ranged from 10<sup>3</sup> to 10<sup>7</sup> gene copies per gram (dry weight) of wastewater solids for both influenza A and B. Detections were more common from October through March (72% and 40% of samples were positive for influenza A and B, respectively, during this time period) than from April through September (22% and 13% positive for A and B, respectively), consistent with influenza seasonality in the U.S.

In addition to quantification, influenza has been subtyped in wastewater through PCRbased approaches (<u>Boehm, Wolfe, et al. 2023</u>; <u>Germano et al. 2024</u>), Sanger sequencing (<u>Wolfe et al. 2022</u>), and tiled amplicon sequencing (<u>Vo et al. 2023</u>).

Survival and viability: Although influenza virus cannot replicate in water (Wigginton and Ellenberg 2015), spiked infective influenza A virus has been shown to persist in water matrices for days to weeks and potentially longer, depending on water temperature, salinity and pH. Based on their systematic review of 19 published studies, Irwin et al. (2011) concluded that the half-life of influenza A virus is longer in water with lower temperature (7 to 12°C vs. ≥ 27°C) and lower salinity (0 to 1 ppt vs. ≥ 30 ppt), and that its half-life in water is significantly longer overall than in air. Most of the included studies considered avian influenza A-which is known to be transmitted via the fecal-oral route in birds (Wigginton and Ellenberg 2015)—rather than subtypes known to circulate in humans. Dublineau et al. (2011) showed that infective A(H1N1) virus survived in water with neutral pH (~6.9) for 300 to >600 days at 4°C and 0 to 5 parts per thousand [ppt] salinity but 12 to 16 days at 35°C and 0 to 5 ppt salinity. This was consistent with Shigematsu et al. (2014), who found that A(H1N1) viruses initially grown on mammalian cells remained infective in distilled water (0 ppt salinity) at 35°C for 25 days (pH not reported). No information is available for persistence of influenza B in water, and no studies have considered the survival of infective influenza A or B virus in wastewater. However, it is conceivable that infective influenza A virus may persist in untreated wastewater for the hours to days typical of collection system and treatment process residence times.

Compared with survival in water, influenza virus survival on surfaces is expected to be much shorter. <u>Greatorex et al. (2011)</u> demonstrated that A(H1N1) virus survived a few hours on household surfaces but rarely more than 9 hours. Persistence may be longer on metallic (especially stainless steel) surfaces, relative to nonmetallic non-porous or wood surfaces (<u>Noyce et al. 2007; Greatorex et al. 2011</u>).

**Fate in treatment processes**: Most of the research on the fate of viruses in wastewater treatment has focused on non-enveloped enteric viruses<sup>3</sup> (Katayama et al. 2008; Kitajima et al. 2014; Schmitz et al. 2016). Enveloped viruses, such as influenza (and SARS-CoV-2), are thought to be more susceptible to inactivation than their non-enveloped counterparts although both demonstrate some level of persistence in water (Wigginton and Ellenberg 2015). Research has shown that UV disinfection (at a dose of 10 to 25 mJ/cm<sup>2</sup>) and chemical disinfection with ozone, chlorine, and chlorine dioxide are all effective at inactivating A(H1N1) and A(H5N1) subtypes during drinking water and wastewater treatment (Lucio-Forster et al. 2006; Lénès et al. 2010). Additional research is needed to understand the fate of influenza viruses in wastewater treatment more fully.

# **Suitability for Wastewater Surveillance**

Influenza concentrations in wastewater have been shown to correlate with clinical data at both the facility/building and city/community scale, as shown in **Table 2**. Influenza A RNA concentrations in wastewater or primary sludge may also provide early warning—relative to clinical surveillance datasets such as hospitalizations—of both the onset and peak of seasonal flu (<u>Schoen et al. 2023</u>). Public health uses of wastewater influenza data may include: more accurate indication of the onset and peak of an influenza outbreak; more complete accounting of influenza illness, including milder cases for which people do not seek healthcare; early identification of seasonal flu strains to assess vaccine effectiveness; help in distinguishing the causes of ILI reported with syndromic surveillance; more complete capture of a population underserved in clinical data; and better information on the anticipated burden on healthcare systems due to emergency department, hospital, and/or intensive care unit visits for flu (<u>Mercier et al. 2022; Wolfe et al. 2022; Boehm, Hughes, et al. 2023; Boehm, Wolfe, et al. 2023; DeJonge et al. 2023; Faherty et al. 2024</u>).

Due to its public health significance and amenability to wastewater-based detection, influenza virus is one of the core pathogen targets included in the National Wastewater Surveillance System (NWSS) Panel 1.0<sup>4</sup> (<u>Kirby 2023</u>). Influenza wastewater data for more than 600 sampling sites are already being reported to NWSS, and the results of an analysis of post-flu-season wastewater influenza A concentrations relative to in-flu-season concentrations is available <u>on the NWSS dashboard</u>. (See Box 3 for a discussion of this analysis.) Utilities should coordinate with their public health partners to understand if and when wastewater testing in their community will be expanded to include influenza, if this expansion hasn't already occurred.

<sup>&</sup>lt;sup>3</sup> Enteric viruses are defined by their habitat, namely, the gastrointestinal tract of mammals. They include viruses in the *Enterovirus* genus (such as coxsackieviruses, echoviruses, enteroviruses, polioviruses, and rhinoviruses), but also adenoviruses, astroviruses, noroviruses, rotaviruses, and others (Flint et al. 2015).

<sup>&</sup>lt;sup>4</sup> The other NWSS Panel 1.0 core pathogens include: SARS-CoV-2, respiratory syncytial virus, adenovirus 40/41, shiga toxin-producing *E. coli, Campylobacter*, norovirus, mpox virus (specifically non-variola orthopoxvirus), and *Candida auris*—as well as four antibiotic resistance genes and laboratory analytical process controls (<u>Kirby 2023</u>).

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#### Table 2. Examples of Correlations Observed Between Wastewater and Clinical Influenza Data at Different Sampling Scales

- This is not an exhaustive list and excludes studies for which a correlation was not explicitly calculated
- Correlations may be moderate or strong; any correlation characterized as "weak" was excluded
- In most cases, influenza B viral RNA was not detected in wastewater, which is why influenza A virus (IAV) is predominantly used

| Sampling Sampling Population |                                     | Population  | Wastewater Data Used for  | Olinia al Data Head for Correlation   |   |  |
|------------------------------|-------------------------------------|---|---|---|---|--|
| Scale                        | Site(s)                             | Captured  | Correlation   | Clinical Data Used for Correlation  | Reference   |  |
| Facility                     | 1 manhole                           | 10,000 students &<br>faculty on<br>university<br>campus | IAV RNA concentrations in primary sludge  | 5-day, centered, smoothed average<br>rate of daily cases in student athletes<br>across entire campus  | <u>Wolfe et al.</u><br>(2022)                           |  |
| Facility                     | 51 pre-K-12<br>schools in 1<br>city | 262 to 2,888<br>enrolled students<br>per school         | Proportion of schools with IAV detected in wastewater   | Citywide rate of visits to healthcare<br>facilities (hospitals, EDs) with influenza<br>diagnosis at discharge                                     | <u>Wolken et</u><br>al. (2023)                          |  |
| Facility                     | 3<br>dormitories                    | ~136 to 211 per<br>dormitory                            | Rate of positive IAV RNA detections at each site  | Number of reported flu cases both<br>within the campus community and<br>the surrounding county  | <u>Germano</u><br><u>et al.</u><br><u>(2024</u> )       |  |
| City                         | 1 WRRF                              | 910,000   | PMMoV-normalized IAV RNA concentrations in primary sludge   | Citywide influenza test positivity rate   | <u>Mercier et</u><br><u>al. (2022</u> )                 |  |
| City                         | 4 WRRFs                             | 35,500 to 93,000<br>per WRRF                            | Pooled raw influent IAV RNA concentrations across all 4 WRRFs   | Number of influenza cases (based on reported positive clinical tests)   | <u>Ahmed et</u><br>al. (2023)                           |  |
| City                         | 8 WRRFs                             | 66,622 to<br>1,480,000 per<br>WRRF                      | Weekly median, PMMoV-normalized<br>IAV RNA concentrations in primary<br>sludge (7 sites) or raw influent (1 site) | State-aggregated weekly clinical<br>sample positivity rates from sentinel<br>laboratories   | <u>Boehm,</u><br><u>Wolfe, et</u><br><u>al. (2023</u> ) |  |
| City                         | 4 WRRFs<br>serving 3<br>cities      | 189,000 to<br>1,085,941 per city                        | IAV RNA concentrations in raw influent  | Number of ED visits in city served by respective WRRF(s)  | <u>DeJonge</u><br><u>et al.</u><br>(2023)               |  |
| City                         | 8 WRRFs                             | ~13,100 to ~2.3<br>million                              | Flow- and population-normalized IAV<br>RNA concentrations   | County-level influenza-associated ICU<br>admissions, percent of ED visits for ILI,<br>and percent of ED visits for flu<br>diagnosis at discharge* | <u>Faherty et</u><br><u>al. (2024</u> )                 |  |

**Abbreviations**: IAV = influenza A virus; ED = emergency department; ICU = intensive care unit; ILI = influenza-like illness; PMMoV = pepper mild mottle virus; WRRF = water resource recovery facility

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# Preventing Influenza Infection When Working with Wastewater

**Routes of exposure**: Wastewater workers are at risk of exposure to influenza from infected colleagues, primarily through inhaling or coming into contact with respiratory droplets when the infected person breathes, coughs, sneezes, or talks (<u>Yan et al. 2018</u>; <u>U.S.</u> <u>CDC 2024a</u>). Adults infected with influenza can start shedding the virus 1 day before showing symptoms, making it challenging to identify contagious individuals. The highest transmission likelihood occurs within the first 3 to 5 days of illness.

While uncertainties remain about the persistence of infective influenza virus in wastewater, it is possible that infective influenza virus may be present in untreated wastewater during seasonal epidemics or global flu pandemics. Exposure to virus in wastewater can happen through inhaling aerosols during collection and treatment or splashing of wastewater onto ocular or oral mucous membranes (WEF 2020). Contact with viruses on contaminated surfaces (fomites) followed by touching the face, especially the eyes and nose, is also a potential exposure route. It is important to keep in mind that most surfaces near wastewater collection and treatment equipment are likely to be contaminated with wastewater, and the presence of abrasions, open wounds, and punctures may increase the risk of transmission of any pathogen.

**Infection prevention measures**: The worker safety recommendations of the WEF Blue-Ribbon Panel (WEF 2020) remain relevant for wastewater workers for influenza virus and other infective agents in wastewater. These recommendations are consistent with the CDC's guidance for reducing health risks to workers handling human waste or sewage (U.S. CDC 2023a). Staying up to date on seasonal influenza vaccinations, understanding appropriate disinfectant products, conducting job safety assessments, practicing good hygiene, and using personal protective equipment all play a role in preventing influenza—and other pathogen—infection from wastewater.

#### Vaccination

- While obtaining the annual seasonal flu vaccine may not eliminate the possibility of becoming infected with influenza, it will decrease the likelihood of severe disease. For example, data from the 2012 through 2015 flu seasons in the U.S. showed that, for adults, flu vaccination reduced the risk of hospital admission by 37% and the risk of intensive care unit admission by 82% (<u>Thompson et al. 2018</u>). A 2021 review found that vaccinated adults admitted to the hospital for flu had a 31% reduced risk of death (<u>Ferdinands et al. 2021</u>). For the most recent flu season (2023 to 2024), preliminary data suggest that flu vaccination reduced the risk of flurelated hospitalization in U.S. adults by 41 to 44% (<u>Frutos et al. 2024</u>).
- Flu vaccines can be delivered via injection or nasal spray, neither of which contain active, live virus that can cause an influenza infection. Adverse reactions to the flu vaccines are uncommon. Adverse reactions to all vaccines are tracked in the U.S. using the <u>Vaccine Adverse Event Reporting System</u> (VAERS). Between 2008 and 2023, a total of 155,115 adverse events were reported for all types of flu vaccines in VAERS. During the same period, 2.27 billion flu vaccine doses were given in the U.S. (<u>U.S. CDC 2023b</u>), corresponding to an adverse reaction incidence of <0.01%. The</li>

most common adverse reactions include soreness, redness, and/or swelling at the injection site, headache, fever, nausea, and muscle aches (<u>U.S. CDC 2024a</u>).

• Vaccines can be obtained for free or low cost from a healthcare provider, retail clinic (such as a pharmacy or superstore), public health department, community clinic, or employer. A healthcare provider should be consulted to determine the most suitable vaccine type, best timing, and vaccine availability.

#### Disinfectant products

- Disinfectants on <u>EPA's "List M"</u> are effective against influenza A viruses that normally infect wild aquatic birds (e.g., avian influenza viruses) (<u>U.S. EPA 2023</u>). The products on this list are also effective against the influenza A and B viruses that infect humans and include various readily available products with sodium hypochlorite, hydrogen peroxide, isopropyl alcohol, quaternary ammonia, and other common disinfectants as active ingredients.
- <u>Jeong et al. (2010)</u> demonstrated that both 70% ethanol and 70% 1-propoanol were effective in completely inactivating A(HIN1) viruses after one minute of contact time.
- <u>Zou et al. (2013)</u> demonstrated complete inactivation of avian-origin A(H7N9) viruses with 0.5% or 1% sodium hypochlorite after less than 5 minutes. A more dilute bleach solution (1:50 dilution of 5.25% sodium hypochlorite [0.1%], or about 75 mL [1/3 cup] of household bleach in a total of 1 gallon of water) with a contact time of 1 minute is recommended by the CDC for disinfection of surfaces.

#### Job safety assessments (JSAs)

- JSAs should follow the protocols outlined in <u>WEF 2020</u>. Please email <u>nwbe@wef.org</u> for JSA templates if needed.
- To inform their JSAs, utilities should coordinate with local public health agencies and healthcare institutions to understand the risk of influenza virus in their wastewater.

#### Hygiene

- After handling wastewater or touching surfaces potentially contaminated with wastewater, hands should be washed with soap and water or cleaned with an alcohol-based hand sanitizer (ABHS). Soap and water may be more effective in reducing influenza virus on hands than ABHS alone (<u>Grayson et al. 2009</u>), and <u>should be used if hands are visibly soiled</u>. It is worth noting that, as explained in <u>Weber et al. (2023)</u>, "[w]earing gloves is not a substitute for hand hygiene".
- While working with wastewater and near surfaces potentially contaminated with wastewater, avoid touching the face, mouth, eyes, nose, or open sores or cuts, and do not smoke or chew tobacco or gum. In addition, sores and cuts should be covered with water-resistant band aids.

Personal protective equipment (PPE)

- PPE should be selected to prevent contact with wastewater, either directly (through splashes, contact transfer, or whole-body contact) or indirectly (through touching contaminated surfaces).
- Appropriate PPE may include gloves, boots, coveralls (such as Tyvek suits), face shields, and safety glasses/goggles (<u>LeChevallier et al. 2020</u>).
- Care should also be taken to prevent cuts or punctures when handling wastewater through the use of durable gloves. Gloves should be changed when torn or heavily contaminated.
- Proper procedures for donning (putting on) and doffing (removing) PPE to minimize pathogen exposure should be followed. **Box 1** provides an example of donning and doffing gloves, boots, disposable coveralls, and a face shield or safety glasses/goggles, while **Box 2** provides steps on how to remove gloves when not wearing a disposable coverall.
- Reusable PPE, such as boots, face shields and goggles, should be cleaned after each use. Visibly soiled PPE can be cleaned with soap and water, followed by a dilute bleach solution (1 part 5.25% sodium hypochlorite with 49 parts water) or a disinfectant on <u>EPA's "List M"</u>. For PPE that is not visibly soiled, or not amenable to washing with soap and water, a disinfectant on <u>EPA's "List M"</u> can be used. In addition, PPE should also be inspected before each use.

#### Box 1: Donning and Doffing Personal Protective Equipment

Including gloves, boots, disposable coveralls, and a face shield or safety glasses/goggles

#### Donning

- Wash hands with soap and water, followed by use of alcohol-based hand sanitizer (ABHS)
- Remove shoes and tuck trouser legs into socks
- Step into legs of coverall, pull on boots, and place coverall legs over boots
- Pull coverall over arms and shoulders
- Put on face shield or glasses/goggles and pull up hood
- Zip up garment
- Put on gloves

#### Doffing

- Unzip coverall to waist and roll back hood without touching the inside of the garment
- Pull first arm out of garment sleeve by pulling with the other arm at your back (see <u>this video</u> for a demonstration), pulling your glove off as you completely remove your first arm from the sleeve (see Box 2 for glove removal without a coverall)
- Use your ungloved hand to push the garment off your second arm, only touching the inside of the garment with the ungloved hand, and pull your second arm out of garment, removing your second glove in the process
- Roll garment down body, touching only the inside or the garment with your now ungloved hands, and kick off your boots
- Dispose of the garment, again, only touching it on the inside with your ungloved hands
- Wash hands with soap and water, followed by use of ABHS
- Remove face shield or glasses/goggles from the back by lifting the head band (face shield) or earpieces (glasses/goggles), and discard or clean

#### Box 2: Removing Gloves When Not Wearing a Disposable Coverall

- Remove one glove at a time
- Use one gloved hand to grasp the palm area of the other gloved hand and peel off the glove
- Hold removed glove in gloved hand
- Slide fingers of ungloved hand under remaining glove at wrist and peel off second glove over first glove
- Discard gloves
- Wash hands with soap and water, followed by the use of ABHS

#### Box 3: What to Know About Influenza A(H5N1)

#### Why it's a concern

Since March 2024, the U.S. <u>Department of Agriculture</u>(USDA), <u>Food and Drug</u> <u>Administration</u>, and <u>Centers for Disease Control and Prevention</u> have been investigating outbreaks of highly pathogenic avian influenza (HPAI) A(H5N1) in dairy cows. These outbreaks warrant close investigation because they represent a spillover of avian influenza into a mammalian species not normally infected by this flu subtype.

#### About the virus

<u>HPAI influenza A viruses</u> are those that cause severe impacts to the birds they infect, but not necessarily to cows, humans, or other species. The A(H5N1) currently circulating in cows is Clade 2.3.4.4b, which has been the predominant H5N1 strain circulating in wild birds in Africa, Asia, Europe, and the Middle East since the end of 2021 (<u>Tian et al. 2023</u>). This clade was detected in wild birds in Canada and the U.S. in late 2021 and caused outbreaks in U.S. commercial and backyard poultry in February 2022 (<u>Youk et al. 2023</u>). Outbreaks in dairy cows started in early 2024 and are thought to be due to a single spillover event from wild migratory birds, followed by cow-to-cow transmission (<u>Nguyen et al. 2024</u>). H5N1 RNA has been detected in dairy products, <u>as well as in meat</u>. Clade 2.3.4.4b is related to, but distinct from, the A/goose/Guangdong/1/1996 H5N1 virus that caused poultry and human outbreaks in Hong Kong in 1997 (<u>Chan 2002</u>).

#### Disease overview

A total of 3 human H5N1 cases have been reported in the U.S. in 2024 (for a total of 4 since 2022) in individuals exposed to infected dairy cows, including two mild cases of conjunctivitis (e.g., <u>Uyeki et al. 2024</u>) and <u>a case with respiratory</u> <u>symptoms</u>. The case in 2022 was in a person who had direct exposure to poultry infected with A(H5N1), and <u>fatigue was the only symptom reported</u>. The best place for current A(H5N1) information is CDC's website on <u>H5N1 Bird Flu: Current</u> <u>Situation Summary</u>.

#### Presence in wastewater

Both influenza A(H5) RNA<sup>5</sup> (via ddPCR; <u>Wolfe et al. 2024</u>) and A(H5N1) RNA (via sequencing; <u>Tisza et al. 2024</u>) have been detected in wastewater. Detection of H5 or H5N1 RNA in wastewater does not necessarily indicate people are infected with bird flu in that particular service area. Instead, it seems likely that H5N1 RNA in wastewater is coming from animal sources, especially milk products (<u>which have tested positive for H5N1 RNA</u>), but this is still being investigated.

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<sup>&</sup>lt;sup>5</sup> The assay used detects A(H5) RNA broadly, including A(H5N1) but also potentially other subtypes.

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# Box 3: What to know about influenza A(H5N1) (continued)

#### Presence in wastewater (continued)

Detection of H5N1 RNA in wastewater also doesn't mean that infective virus is present. It is possible that H5N1 virus, like SARS-CoV-2 (another non-enveloped virus), does not remain viable in the sewer, although this is not known for certain. Recent testing of dairy samples (n = 297) showed that 20% were positive for H5N1 RNA using PCR methods but 0% were positive for viable virus (U.S. FDA 2024). If dairy products are the source of the A(H5N1) RNA being detected wastewater, these results suggest the virus may not be infective.

#### Suitability for wastewater surveillance

<u>The CDC NWSS program</u> is comparing recent (that is, outside the normal flu season) influenza A concentrations in wastewater at a given site to levels at the same site between October 1, 2023, and March 2, 2024 (within the flu season). For any site with a particularly high ratio of out-of-season to inseason influenza A RNA in wastewater, CDC is working with relevant partners to understand exactly why the levels are high. Wastewater utilities can help their public health partners in such efforts by identifying potential dairy processing facilities or other potential contributors of dairy products to the wastewater flows in their collection system. Runoff from farms is not expected to be collected in municipal sewer networks. NWSS is not collecting data on the concentration of A(H5NI) RNA in wastewater—only total influenza A.

#### **Preventing infection**

Although the seasonal flu vaccine does not provide protection against A(H5N1), the other infection prevention measures outlined above are sufficient to protect workers from A(H5N1) exposure when handling untreated wastewater. In addition, it is important to avoid contact with any wild birds, but especially those that appear to be ill or have died. Contact with any domestic birds that appear ill or have died should also be avoided. Reach out to your local health department to report any sick or dead birds.

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