UK Health Security Agency

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Event:	Influenza virological surveillance arrangements, winter 2024/25
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Instructions for Cascade

To be cascaded to the standard UKHSA distribution list, and to:

- **Regional Deputy Directors** to cascade to Regional Acute Respiratory Infection leads
- **UKHSA microbiologists** to cascade to non-UKHSA microbiology labs (NHS labs and private)
- **UKHSA microbiologists** to cascade to NHS Trust infection leads
- **NHS infection leads/NHS microbiologist/NHS infectious disease specialists** to cascade to Infection Prevention and Control teams, Directors of Infection Prevention and Control
- **NHSE National Operations Centre** to cascade to **NHS labs/NHS infection**
- NHS Pathology Cascade

Summary:

UKHSA has updated guidance for influenza virological surveillance arrangements for winter 2024/25. Clinical diagnostic laboratories are asked to:

1. Ensure that influenza subtyping (for H1/H3) is attempted on **all severe influenza A** cases (ITU/HDU/ECMO/fatal cases), either locally or in a UKHSA laboratory.
2. During the winter epidemic period, arrange for a proportion of influenza A positive material to be subtyped - either using validated subtyping assays locally **OR** by referring a locally-agreed proportion of influenza A positive samples to a UKHSA Clinical Network Laboratory (CNL).
3. Forward influenza A positive samples for which subtyping attempts have failed (unsubtypeable samples) to the UKHSA respiratory virus reference unit (RVU Colindale).
4. Forward samples from cases with suspected exposure to avian influenza to UKHSA CNLs for H5 subtyping.

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Background :

National influenza virological surveillance informs the WHO programme for virus strain selection for winter vaccines and monitors antiviral susceptibility and burden of disease caused by circulating strains. Influenza virological surveillance contributes to diagnostic assurance of commercial tests used in the NHS, supports clinical management, and is important for pandemic signalling. There is a **statutory requirement** for UK laboratories to participate in national virological surveillance for influenza which requires the reporting of both positive and negative influenza laboratory test results from all laboratories in the UKHSA Second Generation Surveillance System (SGSS) to provide a comprehensive picture of circulating strains for weekly national and international reporting(1)

Influenza Testing: Typing and Subtyping

There is a diversity of commercial kits in use in England for influenza testing. Most commercial assays detect influenza A and B to provide influenza **type** information, but do not provide the influenza A **subtype** to indicate whether an influenza A H1, H3, or any other subtype has been detected. Hence, the majority of influenza test results determined in a clinical diagnostic laboratory setting do not provide strain information needed for public health surveillance purposes and are unable to identify a novel or zoonotic influenza A. To support national surveillance and identification of zoonotic infections**, subtyping should be attempted on all severe influenza A cases (ITU/HDU/ECMO/fatal cases)**. Subtyping can be performed locally, if validated testing platforms are available, or by a UKHSA laboratory.

As many commercial kits do not disclose the viral target regions, the impact of virus strain sequence variations (in-season virus evolution) on the performance of both typing and subtyping assays cannot be predicted. The characterisation (subtyping and sequencing) of selected samples provides important detail on this issue nationally. It is essential that each influenza testing site has a strategy in place, through the course of the winter epidemic season, for a proportion of influenza A positive material to be subtyped. This can be performed by:

- Using validated sub-typing assays locally and reporting to SGSS, or
- Referring a locally-agreed proportion of influenza A positive samples to a UKHSA CNL (Table 1) for influenza A subtyping, where subtyping cannot be performed locally (2).

UKHSA CNLs should select up to 25 priority samples per week for detailed virological characterisation by the respiratory virus reference unit (RVU Colindale), as detailed in Referral of influenza samples to RVU, UKHSA Colindale, 2024 to 2025(2).

Failure of Subtyping (unsubtypeable samples)

Influenza A positive samples may fail subtyping most commonly if the sample has low viral load, but also due to recent viral evolution affecting assay performance, or if the sample contains a non-seasonal/zoonotic influenza.

Influenza A positive samples for which subtyping attempts have failed should be forwarded to UKHSA RVU Colindale for exclusion of non-seasonal influenza and

review of original test performance, using an E3 referral form with assay information and clinical details provided.

In light of the ongoing worldwide epizootic of H5N1 and diversity of circulating H5 viruses, samples associated with suspected exposure to avian influenza (relevant travel or zoonotic exposure) should be urgently forwarded to UKHSA CNLs (Table 1) for exclusion of H5, using typing/subtyping assays assured for detection of recently-circulating H5 strains, in line with Avian influenza A(H5): laboratory investigations(3)

H5 confirmatory testing, characterisation, and detection of all non-H5 zoonotic influenza viruses is performed in the UKHSA reference laboratory (RVU Colindale), referred using the E73 referral form.

Region/HPT	Seasonal influenza subtyping for A(H1N1)pdm09 and H3N2	Avian influenza H5 subtyping
Midlands	Birmingham	Birmingham
South West South East	Bristol	Bristol
East of England London	Cambridge	Cambridge
North West North East Yorkshire & the Humber	Manchester Newcastle* Leeds*	Manchester

Table 1. Services provided by UKHSA Clinical Network Laboratories and *NHS Collaborating Laboratories, as of 09 December 2024.

Implications & Recommendations for UKHSA sites and services

UKHSA Clinical Network Laboratories (Birmingham, Bristol, Cambridge, and Manchester) should:

1. Ensure that influenza subtyping (for H1/H3) is attempted on **all severe influenza A** cases (ITU/HDU/ECMO/fatal cases).
2. Forward influenza A positive samples for which subtyping attempts have failed (unsubtypeable samples) to UKHSA RVU Colindale using the E3 referral form with assay information and clinical details provided.
3. During the winter epidemic period, select up to 25 priority samples per week for referral to RVU following Referral of influenza samples to RVU, UKHSA Colindale, 2024 to 2025. **Native non-lysed material collected in virus transport medium** should be referred for surveillance purposes.

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Implications & Recommendations for NHS

NHS clinical diagnostic laboratories should:

1. Ensure that influenza subtyping (for H1/H3) is attempted on **all severe influenza A** cases (ITU/HDU/ECMO/fatal cases).
2. During the winter epidemic period, arrange for a proportion of influenza A positive material to be subtyped - either using validated subtyping assays locally **OR** by referring a locally-agreed proportion of influenza A positive samples to a UKHSA CNL
3. Forward samples from cases with suspected exposure to avian influenza to UKHSA CNLs for H5 subtyping in line with Avian influenza A(H5): laboratory investigations

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References/ Sources of information

1. National flu and COVID-19 surveillance reports: 2024 to 2025 season
2. Referral of influenza samples to RVU, UKHSA Colindale, 2024 to 2025
3. Avian influenza A(H5): laboratory investigations
