



## **TECHNICAL** REPORT

# Risk assessment guidelines for infectious diseases transmitted on aircraft (RAGIDA)

Influenza

**ECDC TECHNICAL REPORT**

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Influenza



This report of the European Centre for Disease Prevention and Control (ECDC) was coordinated by Cornelia Adlhoc and Katrin Leitmeyer.

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This document reflects the personal views of the experts in their individual capacity and it does not necessarily represent the views of their institutions.

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# Abbreviations

ARI	Acute respiratory infection
IATA	International Air Transport Association
ICAO PANS-ATM	International Civil Aviation Authority Procedures for Air Navigation Services – Air Traffic Management
ILI	Influenza-like illness
PEP	Post-exposure prophylaxis
RT-PCR	Reverse-transcription polymerase chain reaction

# Introduction

In order to assist national public health authorities in the European Union to assess the risks associated with the transmission of infectious agents on board aircraft, and to help in the decision on the most appropriate, operationally possible public health measures for containment, e.g. on whether to contact trace air passengers and crew in case of exposure, the European Centre for Disease Prevention and Control initiated the RAGIDA project (Risk Assessment Guidance for Infectious Diseases transmitted on Aircraft) in 2007.

The RAGIDA project combines evidence retrieved from the literature with expert knowledge for infectious diseases. In 2009 the production of the series of guidance documents for assisting in the evaluation of risk for transmission was initiated for several infectious diseases.

The resulting disease-specific operational documents provide a host of viable options for decision-makers, particularly when faced with the choice of whether to contact trace air travellers and crew that were potentially exposed to infectious diseases during a flight.

Participants in the disease-specific expert panels were selected to include representatives of national public health authorities (particularly those with experience in the investigation and follow-up of incidents involving infectious diseases in travellers), European and international experts for the disease(s) under investigation, experts in microbiology and mathematic modelling, experts from the aviation sector and representatives of ECDC, the European Commission and the World Health Organization. No conflicts of interest were declared by any of the participants.

## Influenza

### Literature review

A systematic literature review was carried out using two databases (EMBASE and Pubmed) to scan for publications on the transmission of influenza viruses on airplanes ('evidence of on-board transmission of influenza viruses'). The date of the initial search was 19 July 2013 with constant updates until 20 January 2014. Of the 402 retrieved articles published from 1960 through January 2014, titles, abstracts and full-text articles were independently reviewed by two experts. As a result, 15 primary evidence articles published from 1979 through January 2014 were identified [1-15]. It appeared that two studies described the same flight [14,15].

All investigations involved retrospective follow-up of contacts after the identification of one or more index cases using either contact tracing of passengers seated within a distance of two rows, contact tracing within the same compartment, or a comprehensive approach that entailed contact tracing of all passengers and crew. Seven articles reported the assessment of multiple events [1,3,5,6,10,12,13]. The time delay for initiating contact tracing after the flight ranged from one day to 47 days [5,12]. The studies applied different primary and secondary case definitions based on variable symptoms only and/or laboratory confirmation (PCR or serology). The proportion of contacts successfully traced ranged from 4% to 100% (for subgroups) [2,4-6,9]. In five studies, travel groups sharing tour activities before or after the flights were analysed [2,3,6,11,14].

Of these studies, 11 described potential transmission of the pandemic influenza virus A(H1N1)pdm2009, and there were single studies describing potential transmission of B/Beijing/184/93-like and human parainfluenza 1 viruses, A/Taiwan/1/86 (H1N1) virus, A/Alaska/18/77 (H3N2) virus, and influenza-like illness (ILI) transmission with an unknown causative agent.

The flight duration was from 45 minutes to 20 hours and 20 minutes (long-distance flight with stop-over but passengers remained seated). Transmission events were described for short and long-haul flights. One study reported a ground delay with malfunction of the engine and of the ventilation system, which led to an attack rate of 72% [1]. Two studies reported evidence of no transmission during flight [5,6].

In addition to the differences in contact tracing, definitions for index and secondary cases as well as confirmatory testing varied between the studies.

The main biases identified were:

- misclassification due to case identification based on clinical symptoms only
- quality of sampling, and testing
- selection and ascertainment bias
- passive identification of secondary cases using surveillance data
- recall bias.

In most of the studies, alternative source(s) of infection could not be ruled out, e.g. common exposure before (community exposure before travel, mass transit, check-in, departure lounges, entry queues), during (lavatory, pantry), or after the flight (exit queues, baggage areas, border entry and/or security checkpoints). Antiviral prophylaxis provided after flights might have influenced the outcomes.

Due to all these limitations, it remains unclear whether flight duration correlates with a higher secondary attack rate. Low attack rates were described for long-haul flights [7,8] as were high attack rates for short-distance flights [4,7]. It cannot be excluded that the attack rate depends mostly on the number of index cases, with a higher likelihood of susceptible persons being exposed during the flight [2,4,11]. Furthermore, although investigations indicated a likely higher attack rate in close proximity to the index case, secondary cases were also detected in other compartments. Conclusions on extent of transmission are hampered by several factors e.g. the small number of passengers followed-up, number of index cases on board, movement during flight and other exposures before, during or after flight.

Overall, the quality of evidence in the published literature is not adequate to assess the risk for influenza transmission on-board aircraft.

## Objectives and challenges of influenza contact tracing

Contact tracing of passengers possibly exposed to an influenza virus on-board an aircraft might follow different objectives:

- to slow down spread upon introduction into a country/region
- to facilitate timely diagnosis and treatment as appropriate, e.g. to administer post-exposure prophylaxis (PEP) (as appropriate according to national policies)
- to implement other control measures like isolation
- to study the characteristics of the virus
- to assess the epidemiologic situation.

In addition to the limited quality of evidence to assess the risk for influenza transmission on-board aircraft found in the literature, the effectiveness of contact tracing measures remains unclear.

In real life several factors hamper contact tracing and effective public health measures:

- non-specific symptoms
- delayed case identification
- high prevalence of other respiratory diseases clinically similar to influenza
- asymptomatic infections with influenza virus and mildly symptomatic cases
- short incubation period
- high potential for influenza virus introduction by air-travel
- alternative modes of travel/introduction
- lag of decision for immediate action
- difficulties in obtaining passenger contact details in a timely manner
- extensive resource needs
- financial constraints.

Therefore, the feasibility and cost benefit of contact tracing needs to be carefully assessed.

Once the passengers have disembarked, it is challenging to follow-up possible contacts in a timely manner and to implement appropriate intervention.

## Suggested approach for contact tracing of influenza

Taking into account the characteristics of the respective influenza viruses, their spread, and the uncertain effectiveness of contact tracing, three distinct scenarios were defined which are described in the following paragraphs:

- seasonal influenza
- novel influenza virus with pandemic potential OR seasonal influenza virus with increased virulence (emergence of a novel influenza virus in humans with known or suspected sustained human-to-human transmission OR a seasonal virus with increased virulence)
- influenza virus with zoonotic potential (e.g. avian, swine influenza)

# Seasonal influenza

## Suggested approach for contact tracing:

This section refers to human infection with seasonal influenza virus.

During an influenza season, transmission of seasonal influenza virus is likely to take place on-board an aircraft as it does in other enclosed environments (e.g. office buildings, public transportation, theatres). Community transmission of seasonal influenza is likely to be occurring at origin and/or destination, and contact investigations for seasonal influenza are not usually conducted.

Taking all the constraints stated above into consideration, contact tracing of seasonal influenza transmission on board an aircraft is not recommended.

## Novel influenza with pandemic potential OR seasonal influenza with increased virulence

### Suggested approach for contact tracing

This section refers to emergence of an influenza virus that may cause a pandemic such as a novel influenza virus in humans with known or suspected sustained human-to-human transmission OR a seasonal influenza virus with increased virulence.

All the constraints of influenza contact tracing (see page 2) also apply to novel influenza virus in humans with pandemic potential OR a seasonal influenza virus with increased virulence. Contact tracing should not be undertaken by default, but rather in exceptional situations, if indicated by the outcome of the situational risk assessment.

In any case, the assessment of possible transmission of novel influenza virus with pandemic potential OR a seasonal influenza virus with increased virulence on an aircraft needs to be undertaken on a case-by-case basis. This situational risk assessment should take into account how the index case was classified (probable or confirmed), the time of travel in relation to onset of symptoms, the epidemiological situation in the country of destination and in the country of departure, and the purpose of the contact tracing.

The algorithm for contact tracing is outlined in Figure 1.

## Criteria to be considered in the risk assessment

### The index case

The index case is a probable or laboratory confirmed case of novel influenza virus with pandemic potential OR a seasonal influenza virus with increased virulence. As an example, the case definitions are given below. Those would need to be adapted accordingly.

### Infectivity during flight

**Infectivity of the index case:** A case of novel influenza virus with pandemic potential OR a seasonal influenza virus with increased virulence is assumed to be infectious one day prior to symptom onset and up to 14 days after symptom onset.

### Time factor

**Flight occurred less than 10 days ago:** The incubation period for seasonal influenza is assumed to be on average two days (ranging from 1–4) [16]. The incubation period of a novel pandemic or a seasonal influenza virus with increased virulence may not be known. In order to identify potential cases, passenger tracing should only be considered if the flight took place within the last 10 days, which approximately corresponds to two incubation periods of known seasonal influenza strains. Thereafter, a message to raise awareness among medical doctors and public health professionals should be considered.



## Epidemiological situation

### The evidence of transmission in the country of departure and in the country of destination

The decision to perform contact tracing for a laboratory confirmed or probable case on a flight should be based on existing evidence for transmission in the country of departure and in the country of destination (see the following two scenarios).

- **Evidence of ongoing transmission in the country of destination.** Contact tracing is not warranted when local cases without a link to travel or community transmission have been detected in the country of destination whether or not there is ongoing transmission in the country of departure.
- **No evidence of ongoing transmission in the country of destination:**
  - **Evidence of ongoing transmission in the country of departure AND epidemiologic link** (e.g. to an area where novel virus circulates, close contact to a confirmed case, laboratory exposure, health-care-related exposure):  
In this situation, it is suggested that comprehensive contact tracing should be considered without waiting for laboratory confirmation to prevent potential secondary and tertiary cases and for early treatment.
  - **No evidence of ongoing transmission in the country of departure:**  
In countries of departure where no ongoing transmission of novel virus was documented and without another known epidemiologic link, there is a great likelihood that an acute respiratory infection without a laboratory diagnosis is caused by a pathogen other than a novel influenza virus. Contact tracing decision of a suspected case among passengers or crew arriving from such a country should await laboratory confirmation. During the early phase of a novel influenza virus with pandemic potential: comprehensive contact tracing is recommended only for laboratory confirmed cases. .

## Other considerations

### Scale of contact tracing

The existing evidence on influenza virus transmission supports a potential role for transmission through droplets, aerosols and contact. However, the relative importance or predominance of either one of these three possible routes of transmission compared to the other two remains incompletely understood and may depend on the specific setting [17]. In the early phase of a potential pandemic, a narrow window of opportunity might exist to delay or even contain the entry and spread of the new virus into a population or country. However, this can only be achieved through timely contact tracing and comprehensive follow-up of all passengers, allowing the effective use of control measures. Therefore, comprehensive contact tracing is considered to be best practice in the early stages of the emergence of a novel influenza virus with pandemic potential. In addition, a comprehensive approach allows crucial knowledge to be gained about the epidemiological characteristics of such a novel virus.

### Prioritisation

If not all passengers can be contacted, contact tracing efforts should focus on the following:

- passengers seated in the same compartment as the index case OR
- passengers seated two seats in all directions around the index case AND
- all crew members serving in the compartment AND
- persons having close contact with the index case e.g. travel companions or persons providing care.

If a crew member is the index case, all passengers seated in the area served by the crew member during the flight should be regarded as contacts, as should the other members of the crew.

### How to handle a symptomatic case on-board during flight

If a passenger develops symptoms suggestive of respiratory infection, the passenger should, if possible, be isolated and provided with a surgical face mask. The flight attendant should follow the International Air Transport Association (IATA) guidelines for infection control [18].

When such a passenger is identified during a flight, the flight crew should notify public health authorities at the destination airport via air traffic control, in accordance with the International Civil Aviation Authority Procedures for Air Navigation Services – Air Traffic Management (ICAO PANS-ATM) [19], and follow recommendations issued by health authorities at the destination (if available) regarding the distribution of passengers locator cards. They should request valid contact addresses for the 14 days after the flight in order to facilitate contact tracing of passengers if indicated.

## Q&A sheet contact tracing: novel influenza virus in humans with pandemic potential OR a seasonal influenza virus with increased virulence

### When should contact tracing be considered?

After performing a situational risk assessment and considering the global epidemiological situation and susceptibility of passengers, contact tracing should be initiated:

- if there was a probable or confirmed case on board;
- AND
- if that case was on the flight one day prior to symptom onset OR while symptomatic, up to 14 days after symptom onset;
- AND
- if the flight occurred within the last 10 days (see Figure 1).

### When is a patient infectious?

In the case of a novel influenza virus or seasonal influenza virus with increased virulence, all available information regarding transmission should be studied and the best evidence used for assessment of the infectious period. In adults, virus shedding and communicability is greatest in the first 3–5 days of illness. In young children, virus shedding can occur for 7–10 days, and perhaps even longer in immunocompromised persons. This can be adjusted, as more information becomes available.

The extended time frame for infectivity of the index case should be adjusted after consideration of age, immune status and duration of virus shedding.

### Who should be considered for contact tracing?

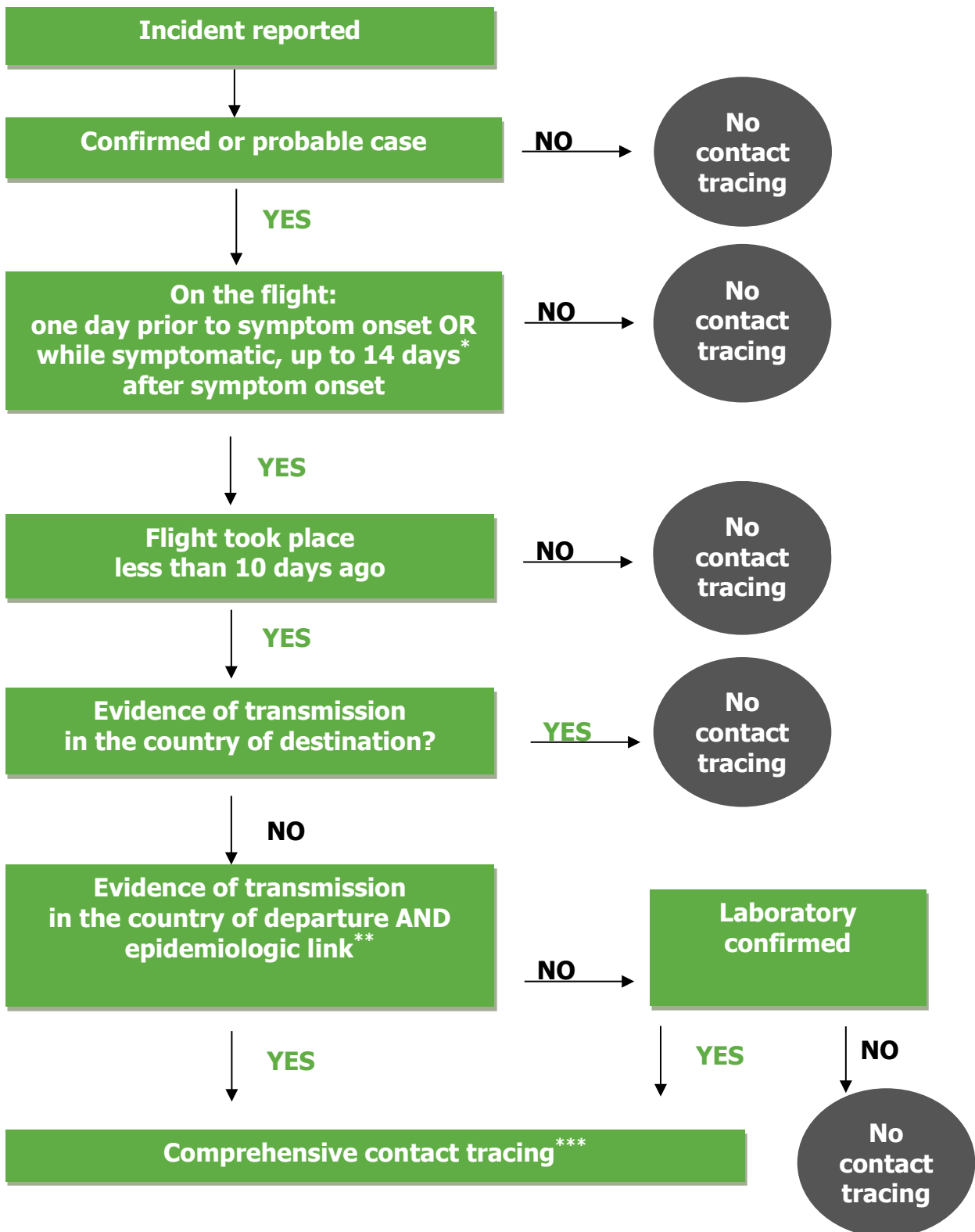
Early in the containment phase following the occurrence of a novel influenza virus or seasonal influenza virus with increased virulence, a comprehensive (aiming to identify every passenger and crew) contact tracing should be considered to prevent potential secondary and tertiary transmission and subsequently slow down the spread upon introduction into a country/region. Cases require timely diagnosis and appropriate treatment and contact tracing facilitates administration of PEP (in accordance with national recommendations or policies) for exposed people.

A prioritised strategy (first, passengers seated two seats in all directions around the index case and second, passengers seated in the same compartment, as well as close contacts (e.g. crew, travel companions, persons providing care)) could be considered based on the situational risk assessment.

### Are there special considerations for individuals of higher susceptibility?

If contact tracing is carried out and the risk assessment identifies passengers at higher risk of severe complications, such as infants or children, special efforts should be made to trace them.

**Figure 1. Algorithm for contact tracing: novel influenza virus in humans with pandemic potential (known or suspected sustained human-to-human transmission) OR a seasonal influenza virus with increased virulence**



Contact tracing should only be undertaken in exceptional situations, if indicated by the outcome of the situational risk assessment. \*can be adjusted by the duration of virus shedding/infectivity (depending on age, immune status)

\*\*epidemiological link e.g. to an area where novel virus circulates, close contact to a confirmed case, laboratory exposure, health-care-related exposure

\*\*\*if indicated by the outcome of the situational risk assessment.

# Influenza virus with zoonotic potential (e.g. avian and swine influenza)

## Suggested approach for contact tracing

This section refers to human infection with an influenza virus with zoonotic potential, which is prevalent in animals, and which has been repeatedly documented to have infected human(s) on a limited scale, usually following close contact with infected animals and without causing sustained human-to-human transmission. Examples include human infections with avian origin influenza A (H5N1) and (H7N9), or swine origin variant influenza A (H3N2v).

All the constraints for influenza contact tracing (see page 2) also apply to influenza virus with zoonotic potential. The assessment of possible transmission of an influenza virus with zoonotic potential on an aircraft needs to be undertaken on a case-by-case basis. This situational risk assessment should take into account the efficiency of transmission, the index case classification, the time of travel in relation to onset of symptoms and the purpose of the contact tracing.

The algorithm for contact tracing is outlined in Figure 2.

## Criteria to be considered for the risk assessment

### The index case

The index case is a laboratory-confirmed case of influenza with zoonotic potential. As an example, the case definition for avian influenza A(H5N1) is given below. The specific case definition should be adapted accordingly.

### Infectivity during flight

**Infectivity of the index case:** a case of influenza with zoonotic potential is assumed to be infectious one day prior to symptom onset and while symptomatic.

### Time factor

**Flight did not occur more than 10 days ago:** the incubation period for seasonal influenza is assumed to be on average two days (ranging from 1–4) [16]. However, the incubation period is slightly longer for avian influenza A(H5N1), ranging from 2–5 days [20], and for A(H7N9) virus infection, ranging from 1–10 days, with a median of six days for A(H7N9)[21]. Since these viruses are known to have limited person-to-person transmission, investigations should be attempted during 10 days (the longest incubation period of currently known strains of influenza A viruses with zoonotic potential). In order to identify potential cases, passenger tracing should only be considered if the flight took place within the last 10 days unless new information becomes available that suggests a longer incubation period. Thereafter, a message to raise awareness among medical doctors and public health professionals should be considered.

## Other considerations

### Scale of contact tracing

Human-to-human transmission of animal influenza with zoonotic potential is usually limited.

In order to acquire information on secondary transmission, a restricted contact tracing strategy focusing on close contacts (e.g. crew, travel companions, persons providing care) and on passengers seated two seats in all directions around the index case should be applied.

If the index case is a crew member, all passengers seated in the area served by this crew member during the flight should be regarded as contacts, as should the other members of the crew.

There might be situations with limited human-to-human transmission, irrespective of severity, in which a more extensive contact tracing strategy would be considered.

### How to handle a symptomatic case on-board during flight

If a passenger develops symptoms suggestive of respiratory infection, the passenger should, if possible, be isolated and provided with a surgical face mask. The flight attendant should follow the IATA guidelines for infection control [18].

When such a passenger is identified during a flight, flight crew should notify public health authorities at the destination airport via air traffic control, in accordance with the ICAO PANS-ATM procedures [19] and follow recommendations issued by health authorities at the destination (if available) regarding the distribution of passengers locator cards. They should request valid contact addresses for 14 days after the flight in order to facilitate contact tracing of passengers following their exposure if indicated.

## Q&A sheet contact tracing: influenza virus with zoonotic potential

### When should contact tracing be considered?

After situational risk assessment and considering the global epidemiological situation for influenza virus with zoonotic potential and the susceptibility of passengers, contact tracing should be initiated if:

- there was a confirmed case on board

AND

- if that case was on the flight one day prior to symptom onset OR symptomatic while on the flight

AND

- the flight occurred within the last 10 days (see Figure 2).

### When is a patient infectious?

In the case of a novel zoonotic influenza virus, all available information regarding human-to-human transmission should be studied and the best evidence used for the assessment of the infectious period. The extended time frame for infectivity of the index case should be adjusted after considering age, immune status and duration of virus shedding.

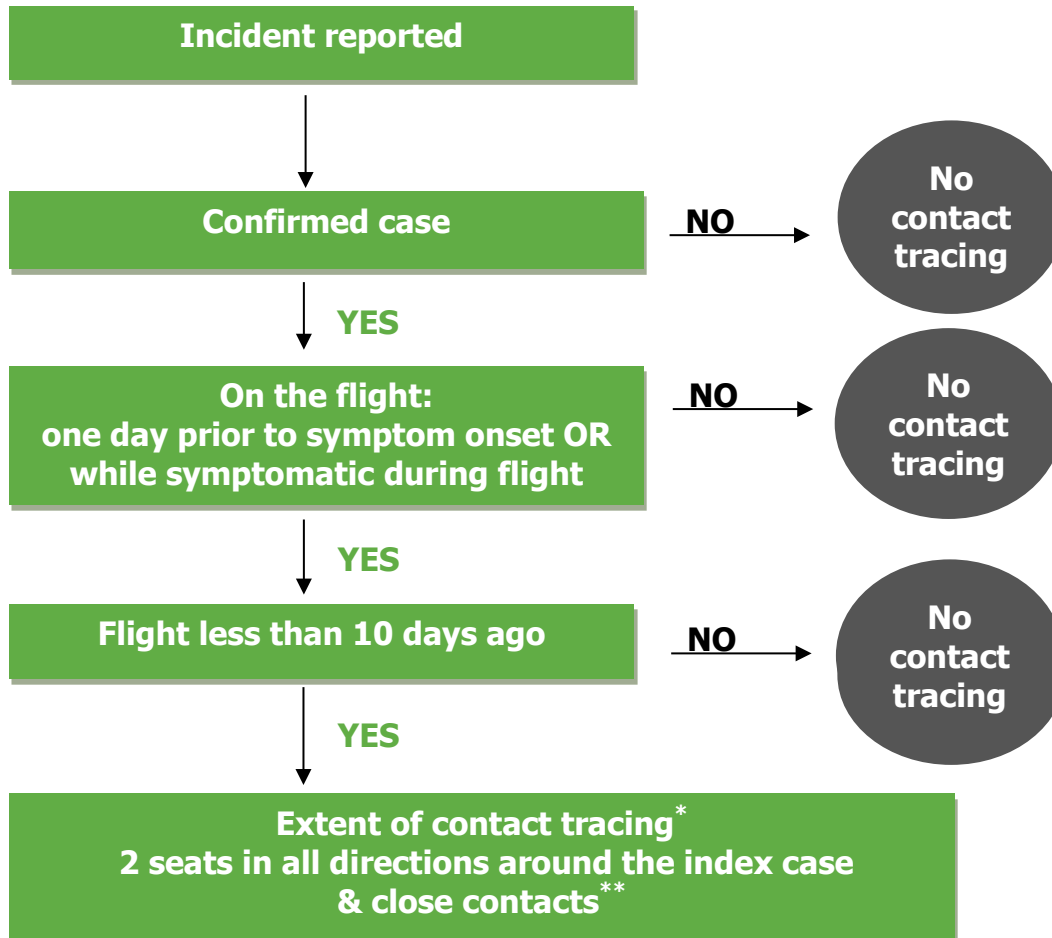
### Who should be considered for contact tracing?

In the event of an influenza virus infection with zoonotic potential, a restricted strategy for contact tracing should be considered: passengers seated two seats in all directions around the index case and close contacts (e.g. crew, travel companions, persons providing care). Cases require timely diagnosis and appropriate treatment, and contact tracing should be performed with a view to administering PEP (in accordance with national policies) to exposed people. There might be situations with limited human-to-human transmission, irrespective of severity, in which more extensive contact tracing strategy would be considered.

### Are there special considerations for individuals of higher susceptibility?

If contact tracing is carried out and the risk assessment identifies passengers at higher risk of severe complications, such as infants or children, special efforts should be made to trace them.

**Figure 2. Algorithm for contact tracing: Human infection with influenza virus with zoonotic potential -prevalent in animals that have been documented to have infected human(s).**



\* There might be situations with limited human-to-human transmission, irrespective of severity, in which a more extensive contact tracing strategy might be considered.

\*\*For close contacts of laboratory-confirmed cases, consider antiviral prophylaxis.

Contact tracing needs to be undertaken on a case-by-case basis and if indicated by the outcome of the situational risk assessment.

## Examples of case definitions (to be adapted accordingly)

The Commission of the European Communities implementing decision of 8 August 2012 amending Decision 2002/253/EC laying down case definitions and the cross-border health decision 1082/2013/EU of the European Parliament and of the Council [22,23]:

### INFLUENZA (Influenza virus)

#### *Clinical criteria*

Any person with at least one of the following clinical forms:

##### **Influenza-like illness (ILI)**

- sudden onset of symptoms

AND

at least one of the following four systemic symptoms:

- fever or feverishness
- malaise
- headache
- myalgia

AND

at least one of the following three respiratory symptoms:

- cough
- sore throat
- shortness of breath

##### **Acute respiratory infection (ARI)**

- sudden onset of symptoms

AND

at least one of the following four respiratory symptoms:

- cough
- sore throat
- shortness of breath
- coryza

AND

A clinician's judgement that the illness is due to an infection

#### *Laboratory criteria*

At least one the following four:

- isolation of influenza virus from a clinical specimen
- detection of influenza virus nucleic acid in a clinical specimen
- identification of influenza virus antigen by direct fluorescent antibody (DFA) test in a clinical specimen
- influenza specific antibody response

Subtyping of the influenza isolate should be performed, if possible

#### *Epidemiological criteria*

An epidemiological link by human to human transmission

#### *Case classification*

##### **Possible case**

Any person meeting the clinical criteria (ILI or ARI)

##### **Probable case**

Any person meeting the clinical criteria (ILI or ARI) and with an epidemiological link

##### **Confirmed case**

Any person meeting the clinical (ILI or ARI) and the laboratory criteria

## INFLUENZA A(H1N1)

### *Clinical criteria*

Any person with one of the following three:

- fever > 38 °C AND signs and symptoms of acute respiratory infection
- pneumonia (severe respiratory illness)
- death from an unexplained acute respiratory illness

### *Laboratory criteria*

At least one of the following tests:

- Reverse transcription-polymerase chain reaction (RT-PCR)
- viral culture (requiring BSL 3 facilities)
- four-fold rise in novel influenza virus A(H1N1) specific neutralising antibodies (implies the need for paired sera, from acute phase illness and then at convalescent stage 10–14 days later minimum)

### *Epidemiological criteria*

At least one of the following three in the seven days before disease onset:

- a person who was a close contact to a confirmed case of novel influenza A(H1N1) virus infection while the case was ill
- a person who has travelled to an area where sustained human-to-human transmission of novel influenza A(H1N1) is documented
- a person working in a laboratory where samples of the novel influenza A(H1N1) virus are tested

### *Case classification*

#### **Case under investigation**

Any person meeting the clinical and epidemiological criteria

#### **Probable case**

Any person meeting the clinical AND epidemiological criteria AND with a laboratory result showing positive influenza A infection of an unsubtypable type

#### **Confirmed case**

Any person meeting the laboratory criteria for confirmation



## AVIAN INFLUENZA A(H5) OR A(H5N1) IN HUMANS

### *Clinical criteria*

Any person with one of the following two:

- fever AND signs and symptoms of acute respiratory infection
- death from an unexplained acute respiratory illness

### *Laboratory criteria*

At least one of the following three:

- isolation of influenza A(H5N1) from a clinical specimen
- detection of influenza A(H5) nucleic acid in a clinical specimen
- influenza A(H5) specific antibody response (four-fold or greater rise or single high titre)

### *Epidemiological criteria*

At least one of the following four:

- human to human transmission by having been in close contact (within one metre) to a person reported as probable or confirmed case
- laboratory exposure: where there is a potential exposure to influenza A(H5N1)
- close contact (within one metre) with an animal with confirmed A/H5N1 infection other than poultry or wild birds (e.g. cat or pig)
- reside in or have visited an area where influenza A(H5N1) is currently suspected or confirmed

AND

at least one of the following two:

- having been in close contact (within one metre) with sick or dead domestic poultry or wild birds in the affected area
- having been in a home or a farm where sick or dead domestic poultry have been reported in the previous month in the affected area

### *Case classification*

#### **Possible case**

Any person meeting the clinical and the epidemiological criteria

#### **Probable case**

Any person with a positive test for influenza A(H5) or A(H5N1) performed by a laboratory which is not a National Reference Laboratory participating in the EU (European Reference Laboratory Network for Human Influenza (ERLI-Net))

#### **Nationally confirmed case**

Any person with a positive test for influenza A(H5) or A(H5N1) performed by a National Reference Laboratory participating in the EU (ERLI-Net)

#### **WHO confirmed case**

Any person with a laboratory confirmation by a WHO Collaborating Centre for H5

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