Government
Office for Science

# Pandemic Influenza Guidance Note

## Purpose

This document is intended to assist the Government Chief Scientific Adviser (GCSA) and the Scientific Advisory Group for Emergencies (SAGE) during the 'golden hour' of an emergency involving a Pandemic Influenza. However, it should be noted that a influenza pandemic is a 'rising tide' incident so does not have a conventional golden hour. The document includes:

- A brief introduction to Pandemic Influenza
- A list of the initial impacts that could result and mitigations against them
- Key science questions and contact details of experts at relevant science agencies

## Pandemic Influenza

Seasonal influenza is a recurrent public health problem characterised by winter epidemics of variable size and duration and attributable to one or more of influenza A/H3N2, A/H1N1 and influenzae B. The disease is vaccine preventable and the UK has a well-established programme of vaccinating the elderly, high-risk groups and pre-school and primary school children every autumn. The largest NHS burden results from the hospitalisation of elderly people particularly if H3N2 is pre-dominant. Subtypes H1N1 and H3N2 are fully adapted human viruses and therefore they can easily spread to humans.

An influenza pandemic is an extended global epidemic of influenza caused by a new influenza A virus which has emerged by genetic reassortment, and to which the human population is wholly or partially non-immune. The natural reservoir of influenza A viruses is wild aquatic shore birds though multiple mammalian species other than humans are also susceptible. Most animal influenza A viruses do not cause frequent disease in humans. However, type A viruses circulating in birds and animals have caused sporadic infections in humans, including avian and swine viruses and reassortants (a process in which genes from different influenza viruses combine in new combinations to create a strain with a new complement of genes), notably of the subtypes H5, H7, and more rarely H6, H9 and H10 subtypes. Most of these human infections have been sporadic and the viruses have not transmitted efficiently or at all human-to-human.

Past pandemic influenza viruses have been reported to arise through either (1) genetic reassortment:, as happened in 1957, 1968 and 2009; (2) genetic adaptation: a process in which genetic mutations occur randomly and less abruptly in an animal or avian virus resulting in a sequence of viruses progressively better adapted to infect human and transmit more efficiently human-to-human, which may have been the mechanism of emergence of the 1918 pandemic virus; or (3) some combination of both. Thus, pandemic influenza viruses tend to contain new genetic material derived from animal or avian viruses (or both, as in 2009). As influenza viruses are unpredictable, it is uncertain what combination of changes will allow the next pandemic influenza virus to emerge.

The novelty of a pandemic virus means that there is little or no pre-existing immunity in the human population; consequentially international spread is inevitable and rapid; population attack rates are high with typical clinical attack rates (the proportion of the population becoming ill with symptoms) of 25-35% with at least as many asymptomatic cases, and the illness itself may be (but is not always) more severe than is seen with seasonal influenza.

Depending upon the population immunity profile, the burden of illness is likely to not be as concentrated in the elderly. In general, in all of the known pandemics of the last 100 years there has been a marked downward shift in age specific burden (attack rates); and mortality burden has shifted from the elderly towards younger age adults. In a severe pandemic these changes will give rise to specific problems in terms of temporary or permanent of loss of essential workers, including in the NHS.

There are no practical means of preventing a pandemic virus from entering the UK. Screening at ports is highly inefficient, consumes vast public health resources and will be ineffective because long-haul flight times to the UK are typically 12 hours and the incubation period for influenza is 72 hours. In 2009 screening could not have been established until long after the UK had its first imported pandemic cases.

Previous pandemics have caused between an estimated 0.5million (2009) and at least 50million (1918) deaths worldwide. The case fatality rate has varied between 0.01% (2009) to 2.5% (1918). Compared with highly variable pandemic mortality, the proportion of the population becoming ill with symptoms is more consistent across known pandemics and has tended to be 25-35% (with variability by age).

There have been four pandemics in the last hundred years, most recently in 2009/10; this gives an annualised risk of circa 4%. Influenza pandemics have typically produced up to three sequential waves of activity, each lasting 12-16 weeks, and separated by a few months. For example, the "Spanish Influenza" had 3 major waves in March 1918, Sept 1918 and Feb 1919. The reasons for multiple waves (i.e. peaks and troughs in cases over a period of time) of differing size and severity is not well understood because pandemics happen so rarely. Just as seasonal influenza activity occurs in winter when environmental and social conditions favour virus survival and human-to-human transmission, pandemic waves tend to be more severe if they coincide with autumn or winter, milder in spring, and have not been documented in the summer.

## Consequences

Pandemics have a high level of unpredictability in terms of when they will occur, how many waves there will be, and the precise timing, duration and severity of each wave. The shortest interval between pandemics has been 11 years and the longest interval 41 years. The last pandemic was in 2009-10.

Pandemic influenza preparedness planning is based on a reasonable worst-case scenario that:

- Up to 50% of the population fall ill
- Of which, from 10% up to 25% are expected to have complications, half of these will be bacteriological such as pneumonia with possibly as little as a 35% overlap between the recognised seasonal 'at risk groups' and those who actually get complications).
- Peak illness rates of around 10 to 12% (measured in new clinical cases per week as a proportion of the population) in each of the weeks in the peak fortnight.
- Absences rates for illness reach 15 to 20% in the peak weeks (at a 50% overall clinical attack rate, assuming an average 7 working day absence for those without complications, 10 for those with, and some allowance for those at home caring for children.
- Up to 4% of cases required hospitalisation with an average six day length of stay but, of which 25% could, if the capacity existed, require intensive care for 10 days (i.e. require level 3 critical care).
- Case fatality ratios up to 2.5%.

The reasonable worst-case scenario is **not** a prediction of what will happen but of the worst that might realistically happen. We would expect most pandemics to be less severe and less extensive than this scenario but, by planning for it, planners are assured that they have a high probability of meeting the demands posed by a pandemic should it occur.

The UK strategy to minimise spread of infection and treat individual cases is multi-faceted and evidence-based. It is referred to as 'defence in depth' and includes:

- **Surveillance & modelling** to detect and assess the impact of the virus, identify and quantify the groups most at risk of severe illness, hospitalisation and death;
- **Reducing risk of transmission** through good infection prevention and control practices e.g. hand and respiratory hygiene advice and provision of personal protective equipment for front-line health and social care staff which are held in stockpiles;
- **Minimising serious illness and deaths** e.g. holding stockpiles of antivirals to treat influenza and antibiotics to treat complications such as pneumonia;
- **Reducing pressure on primary care services and hospitals** by activating the National Pandemic Influenza Service, an automated system which enables antivirals to be rapidly authorised for patients without the need to see a doctor;
- **Advanced purchase agreement to guarantee access to pandemic specific vaccines** – likely available 4-6 months after the pandemic has started with current technologies;
- **Pandemic specific vaccination,** when possible and appropriate, to protect the public;
- **Surge plans** to deal with increased demand on health and care services in hospitals and community settings

## Key Impacts

Depending on the severity of the pandemic, the impact will be wide-ranging. The health and social care sector will feel almost immediate impact with increased demand, as may the coronial system (and the equivalents in the Devolved Administrations).

However, all sectors will be impacted by absenteeism due to staff illness and caring responsibilities. This could be an issue for essential services such as emergency services (police, fire and ambulance), transport, energy supplies, water supply and sewerage management, food supply, security, education, communications and financial services. It will also impact on other public services such as the criminal justice system (courts and prisons service) and border security.

### Resources Available to SAGE

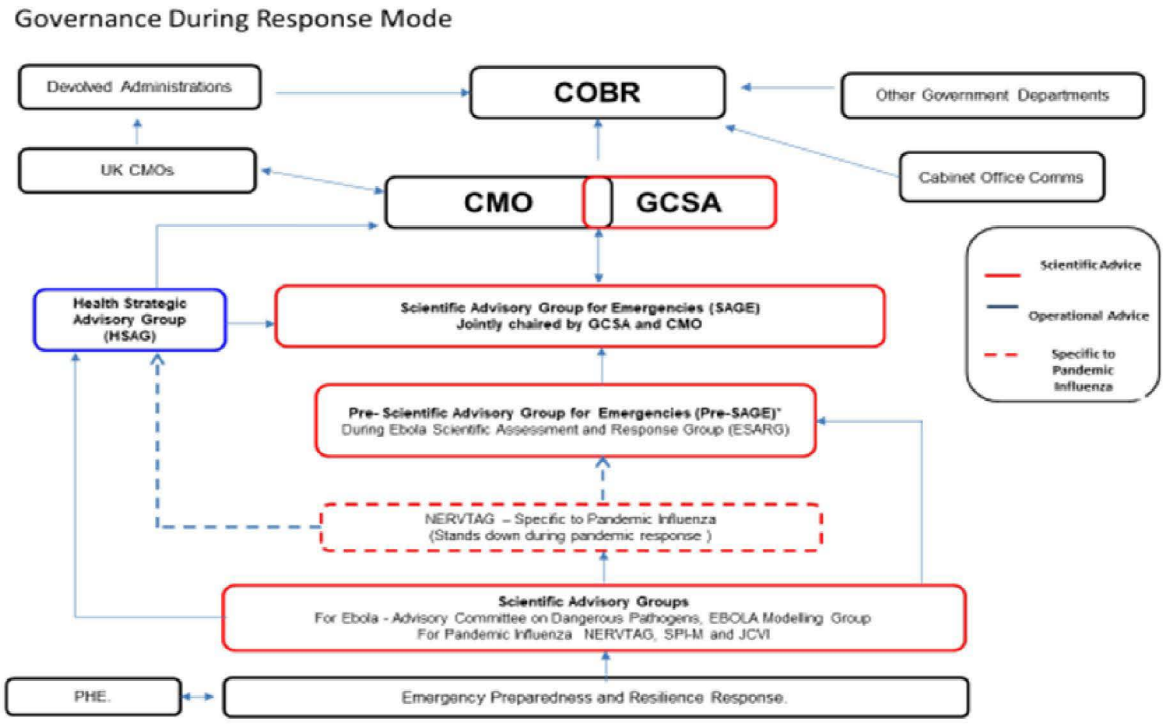
*Surveillance and Modelling*

- During the initial detection and assessment phase (including before the pandemic is officially declared by WHO), an initial rapid assessment of the epidemiological, clinical and virological features of the earliest cases of the novel influenza virus will be undertaken in particular estimating the infection-severity, transmissibility and other key parameters. This information will be used to undertake real-time modelling to predict the future course of the pandemic and identify optimal interventions e.g. pandemic vaccination strategy.
  Key data collections at this stage will be individual level data on the first cases and their close contacts (Case Register and First Few 100) and ad-hoc outbreak studies of clusters of cases in closed settings.
  During the escalation and treatment phases of the pandemic, key objectives will be to monitor the spread and impact of the pandemic virus on the population and health care system and to measure the uptake of antivirals and pandemic vaccine. Data (mainly aggregate) from a range of surveillance systems will be used to meet these requirements and will be used to make "nowcasts" of the current state of the UK epidemic at any time. The data can also be used to make forecasts of the numbers of cases and deaths including demand for secondary care and absence or assess the possible future demand for health services. Safety signals on use of

pandemic specific vaccine will be monitored using Medical and Healthcare products Regulatory Agency's yellow card scheme in the same way as they are for any vaccine. Information on effectiveness of antivirals and vaccines is unlikely to be available until a long time after the pandemic has concluded. Its value will be in informing lessons learnt rather than managing the actual pandemic.

- **Scientific Pandemic Influenza Group on Modelling (SPI-M)** – this group provides expert advice to DHSC and wider UK Government on scientific matters relating to the UK's response to an influenza pandemic based on infectious disease modelling and epidemiology. SPI-M works between pandemics to review evidence and provide support and assurance for mathematical models that may be used during pandemics. It maintains a 'modelling summary' to ensure the latest evidence and model outputs are readily available to policymakers. It is accountable to DHSC, which determines its programme of work. During a pandemic SPI-M provides advice to SAGE as and when required, it plots the course of the pandemic and the range of potential outcomes in response to different policies, working in real-time to analyse and incorporate new data and situations to adapt mathematical models. The executive chair is Dr Paul Allen, DHSC and the academic chair is Prof. Graham Medley, London School of Hygiene and Tropical Medicine.

- **New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG)** – this advisory group provides the CMO, DHSC and other UK Government Departments with scientific risk assessment and mitigation advice on the threat posed by new and emerging respiratory viruses and on options for their management. It meets twice a year (June and December) the flow of information is shown in the diagram below. It is chaired by Peter Horby (Director of the Epidemic Diseases Research Group at the University of Oxford) and has specialist members including a Consultant Respiratory Physician, Virologist and Behavioural Scientist. DCMO and members of the Pan Influenza Policy Team attend the meeting as observers. NERVTAG sets up sub-Committees to consider issues in more detail as needed. NERVTAG is formally dissolved upon declaration of a pandemic but it is expected that a significant proportion of members will join SAGE and/or the CMO's Health Advisory Group.




## Key Questions

- DHSC/PHE/NHS England and Improvement:
  - What do we know about this new strain of influenza?
  - When does a confirmed case start and stop being infectious?
  - What is the incubation period and serial interval?
  - What is the R and R0 value?
  - What does the epidemic curve look like?
  - What is the current geographical spread of the outbreak?
  - What is the likely impact on UK population and the health service?
  - What are the treatment options and how might they mitigate spread?
  - What analysis of epidemiological and clinical data from the early cases has occurred?, notably:
    - What is the cumulative clinical attack rate?
    - What is the case-fatality rate?
    - What is the case-hospitalisation rate?
    - What is the hospitalised case fatality rate?
    - What proportion of cases require ICU?
    - What is the median length of hospital stay?
    - What proportion of cases develop complicated disease?
  - Is there a known preventive countermeasure like a vaccine and what are the timelines for pandemic specific vaccine?
  - Is there evidence of anti-viral resistance?
- DHSC,PHE, HO, DfE, FCO: What is the recommended use of non-pharmaceutical interventions(NPIs) such as school closures, cancellation of mass gathering?

- What is the timeframe for activation of the pre-approved National Institute for Health Research/Health Technology Assessment pandemic influenza projects in hibernation?

## Contacts

- **PHE:** *Yvonne Doyle* Irrelevant & Sensitive
  *Emergency Response Division* Irrelevant & Sensitive
  *DD Immunisation via Colindale Duty Doctor* Irrelevant & Sensitive
- **DHSC:** *Chris Whitty (CMO & CSA)* Irrelevant & Sensitive
  *Jonathan Van Tam (DCMO)* Irrelevant & Sensitive
- **Home Office:** *John Aston (CSA)* Irrelevant & Sensitive
- **DEFRA:** *Gideon Henderson (CSA)* Irrelevant & Sensitive
- **HSE:** *Andrew Curran (CSA)* Irrelevant & Sensitive
- **Independent experts:** *Jim McMenamin (Health Protection Scotland)* Irrelevant & Sensitive
  *John Edmunds,* (London School of Hygiene and Tropical Medicine) awaiting contact details