Department of Health Memorandum to the joint Royal Society & Academy of Medical Sciences study on pandemic influenza

Introduction

The Government is giving high priority to improving UK preparedness for both avian and pandemic influenza. Both are evolving fields in which many uncertainties remain. While many decisions related to the contingency plans are ultimately political, it is imperative that plans are informed by the best scientific advice available, and updated as new evidence emerges.

This memorandum summarises the Office of Science and Technology (OST) guidelines on the use of scientific advice in policy making, then outlines how they are being applied in the policy making process for pandemic influenza, and finally explores aspects of the science underpinning the Health Departments' Influenza Pandemic Contingency Plan, including the roles of modelling, risk assessment and management, research and development, academic research, and scientific evidence from the commercial sector.

It focuses on the Department of Health's planning for a possible human influenza pandemic. But the Department is also working with the Department for the Environment, Food and Rural Affairs (Defra) on the human health aspects of possible outbreaks of avian influenza in poultry.

Science in the policy making process

The OST document, *The Use of Scientific Advice in Policy Making: Guidelines,* which was published in 2002 states that Departments should:

- Have procedures in place that can anticipate as early as possible those issues for which scientific advice or research will be needed;
- Ensure that they draw on a sufficiently wide range of the best expert sources, both from within and outside Government;
- Involve the scientists whose advice is being sought in helping them to assess and frame policy options;
- Systematically review priorities to see whether funding needs to be directed to programmes of further research to illuminate outstanding areas of uncertainty that have been identified; and
- Since scientific advice will often involve an aggregation of a range of scientific opinion and judgement, Departments should ensure that the process leading to a balanced view is transparent and consistent across different policy areas.

Policy making structures and procedures

The Department of Health is structured in such a way as to ensure that policy and decision makers have access to a wide range of the best scientific expertise and advice on all aspects of policy making, including pandemic influenza preparedness.

The policy team responsible for developing pandemic influenza preparedness plans is able to draw on a wide range of 'in-house' medical and scientific

expertise, particularly on vaccines and pharmaceuticals, infection control, research and development, mathematical modelling, economic and operational research and communications.

In addition, a number of arms-length bodies, expert advisory groups and academic institutions are closely involved in advising the various pandemic influenza work streams within the Department of Health, both on a day to day basis and through the formal Committee structure. This gives the Department access to a much wider range of independent expertise than is available 'in house'. These arms-length bodies, advisory groups and academic institutions include:-

- The Health Protection Agency (HPA);
- The Medicines and Healthcare Products Regulatory Agency (MHRA);
- The National Institute for Biological Standards and Control (NIBSC);
- The Medical Research Council (MRC) and its National Institute for Medical Research (NIMR);
- Imperial College, London;
- The Joint Committee on Vaccination and Immunisation (JCVI)
- The Advisory Committee on Dangerous Pathogens (ACDP);
- The National Expert Panel on New and Emerging Infections (NEPNEI).

Two advisory groups have been established specifically for pandemic influenza. The UK National Influenza Pandemic Committee (UKNIPC) is the main forum for the provision of specialist advice to the UK Health Departments on the health response during an influenza pandemic. The Health Departments' Influenza Pandemic Scientific Advisory Group (SAG) advises UKNIPC and Ministers on the scientific evidence base for health-related pandemic influenza policies. Membership of SAG includes medical and scientific representatives from across Government, as well as the HPA, NIBSC, the MRC, Imperial College, JCVI, ACDP, the National Expert Panel on New and Emerging Infections (NEPNEI) and the European Centre for Disease Prevention and Control (ECDC). Two sub-groups advise on, and review, work on modelling and surveillance.

These Committees help to formulate, and advise on, all key policy questions. Their minutes, once agreed, are publicly available through the DH website. Cross membership with other Committees ensures consistency across other policy areas.

The Department of Health has also been working closely with Defra on preparedness for a possible outbreak of avian influenza in birds. The Chief Medical Officer's team works closely with that of the Chief Veterinary Officer. The Department of Health has representation on Defra's Animal Diseases Policy Group, and the ACDP has provided advice to both Departments.

Cross government work on pandemic influenza is co-ordinated through the (influenza) working group of officials which supports the Cabinet Committee on Influenza Pandemic Planning which is chaired by the Secretary of State for Health. Through this mechanism, as well as through bilateral links between the Department of Health and other government Departments, scientific

advice and evidence is fed into the cross–government decision making process. The Department also has good international links, both directly and through international bodies such as the World Health Organization (WHO) and the European Union.

Aspects of the science underpinning the UK contingency plans for pandemic influenza

Modelling

In view of the uncertainties surrounding pandemic influenza, mathematical modelling is being used to inform many aspects of the Government's policy making. The Department is working with a number of groups in the UK, including those dealing with infectious diseases and emergency planning in the HPA, Imperial College, London and analysts from the Intensive Care Society. The results of their work are synthesised by the Department of Health's Analytical Team. The Analytical Team also assists in the interpretation of the results for policy makers and carries out further modelling and analysis to aid their conversion into practical policy responses. This process is overseen by the modelling subgroup of the SAG, which also advises on identifying priorities for further work required. The UK is considered to lead the world in this field, although the Department of Health also maintains contact with modellers in other countries.

In the main, two kinds of models are being studied in planning responses to a pandemic: epidemiological models consider how the disease will spread, its likely impact and the effectiveness of countermeasures; 'operational' models look at the mechanics of how countermeasures can be implemented. Some economic modelling has also been used.

However, modelling can only be as good as the data fed into the models and the assumptions that are made in the design of the models. Where possible, these assumptions are based on data from previous pandemics, but where this is not possible, information about known influenza viruses is used to provide estimates. In the case of a new pandemic influenza virus there are few data and a wide range in the plausible assumptions because (as far as we are aware) the virus does not yet exist, at least not in its pandemic form.

The role of modelling is to map out the range of possible risks and to suggest which responses are robust over the range of uncertainty. The final advice is based on expert consensus based on a consideration of the results of a number of different models. This consensus is endorsed by the SAG to provide the definitive advice to policy makers.

Department of Health modelling work can be broadly grouped into five work areas:

- The characteristics of a UK epidemic of pandemic influenza without intervention. The results of this modelling have been published in Section 4 of the UK Influenza Pandemic Contingency Plan, which lays out many of the assumptions which underpin policy making.

- The possibilities of containment of a pandemic outside the UK and slowing or preventing its arrival in the UK: Work at Imperial College has shown that it may be possible to halt an incipient pandemic if the initial outbreak was in a rural source, and the infrastructure was in place to facilitate the rapid identification of cases and implement anti-viral prophylaxis and area quarantine measures. The WHO is the organisation that is best placed to implement such a strategy, and the Government has welcomed the WHO's decision to procure a stockpile of antiviral drugs for this purpose. We are also supporting the WHO's continuing efforts to develop an effective implementation strategy for the stockpiled drugs. However, once a pandemic has taken hold, modelling indicates that the imposition of travel restrictions, screening or quarantine at airports would not prevent it reaching the UK nor significantly delay its arrival.

- Antiviral use within the UK: Modelling results indicate that a treatment-only approach is the best use of antivirals, given the current availability of antivirals. (A stockpile of 14.6 million courses of antivirals, enough to treat 25% the population, is currently being established.) Policy makers are however, considering the results of recent modelling which is suggesting a review of the current policy.

- Other possible pre-vaccination preventative measures: Modelling indicates that preventive measures such as the imposition of substantial travel restrictions or cancelling large public events would not have a major impact on the course of a pandemic.

- Vaccination strategies in the UK: A pandemic specific vaccine will probably not start to become available until 4-6 months after the start of a pandemic. Modelling is underway looking at the best targeting of limited quantities of such vaccine. The possible use of a poorly matched pre-pandemic vaccine is also being investigated in combination with both the current and possible alternative antiviral strategies.

- Managing NHS capacity in a Pandemic: Work has been undertaken to establish the ability of the NHS to cope with the possible work load imposed by a pandemic and, where these are in excess of the maximum capacity normally available, to design alternative pandemic measures which can cope with such loadings.

Modelling work in all of these areas is on-going and assists policy makers in refining our planning through a continuous dialogue between analysts and planners. Once a pandemic begins it is envisaged that real-time modelling would be used to inform policy making on a day to day basis and we are working with the HPA to set up systems to make this possible.

Some of this work is published in the academic literature, the Imperial College team for instance have published some of their results in *Nature*, whilst the results of the modelling which underpinned the drafting of the *UK Influenza*

Pandemic Contingency Plan were summarised in the *Plan* itself. The results of other work is used to inform the guidance documents and information leaflets which have been distributed to the NHS and are published on the Department Health website.

Risk assessment and management

The OST *Guidelines* acknowledge that deliberations frequently involve a risk assessment. There is a considerable level of uncertainty surrounding a possible future pandemic, and for this reason the management of risk is a key area of pandemic influenza preparedness planning.

The Civil Contingencies Secretariat (CCS) at the Cabinet Office co-ordinates the UK Government's national risk assessment process, which identifies risks to the UK as a whole over a five year period, and assesses their likelihood and impact. This forms the basis for decisions about emergency preparedness and capability planning. The risk of pandemic influenza is considered within this process, with information about the risk provided by the Department of Health to ensure consistency with the UK Health Departments' UK Influenza Pandemic Contingency Plan.

The Department of Health has a longstanding interest in generic risk issues, and published its *Communicating about risks to public health - Pointers to good practice* in 1998. This document aims to:

- Help identify issues likely to raise risk communication challenges, so that effort can be concentrated on those cases likely to need most care;
- To provide general guidance about risk communication strategies; and
- To suggest forms or further analysis and sources of assistance.

It is impossible to state with certainty that a pandemic will develop, or when, so risk assessment is based on informed expert judgement. Experts believe there is continued risk of pandemic influenza emerging from South East Asia, either from the re-assortment of avian H5N1 and human viruses currently circulating, or through step-wise mutations of the H5N1 virus.

Risk assessment is based on the:

- Extent and spread of H5N1 in poultry and migrating birds;
- Extent, severity and incidence of avian influenza in people;
- Extent of antigenic change in current H5N1 viruses, compared to when they first emerged in 1997;
- Historical evolution of influenza viruses and previous pandemics;
- Demography of SE Asia and opportunities for interchange of genetic material between viruses from different species.

Epidemiological and virological information is collected and interpreted by the WHO and World Organisation for Animal Health. The European Commission and the European Centre for Disease Prevention and Control (ECDC) also undertakes assessments. The HPA and Veterinary Laboratories Agency undertake assessments in the UK to inform contingency planning by the

Department of Health, Defra and the Civil Contingencies Secretariat.

Data on the extent to which less severe and sub-clinical infections are occurring in SE Asia - and from ongoing detailed characterisation and analysis of the prevalent viruses to detect antigenic drift or shift - are amongst the most crucial evidence. National and international efforts are co-ordinated by the WHO to ensure that appropriate epidemiological (including serological) studies are being performed and that a suitable range of viruses are sent to specialist virology laboratories for analysis, this will improve assessment and increase confidence.

Research and Development

Policy makers are kept fully appraised of the possible opportunities for managing an influenza pandemic that are afforded by developments in science and technology. As a consequence, research and development (R&D) is fully integrated into the Government's pandemic preparedness programme. The Department of Health's R&D Directorate is represented on the SAG, and works closely with other UK funders, particularly the MRC and the Research Councils.

The MRC has already issued a call for proposals on influenza and has earmarked £10 million for research in this area. The Department of Health will be working with the Council to design research studies in advance and deal with ethical clearance as far as possible ahead of time. The Council has already made provision for proleptic 'readiness' grants: these may be submitted, assessed and awarded before the research can be put into effect, so that expert-reviewed protocols are in place to address important, urgent questions if a pandemic occurs.

The Department of Health is currently finalising a strategy that will ensure that its vaccine, antiviral and diagnosis-related research activities are in line with those of other research funders in the UK, Europe and North America. It is also working closely with the HPA to have in place a research strategy on vaccines and surveillance - which will provide real time data to inform policy making during a pandemic. The Department has for instance, funded clinical trials of novel influenza vaccines which have helped inform vaccine development strategies.

The Department has also met with the MRC, the OST and Defra to discuss the coordination of a cross-government research strategy for pandemic influenza. It has been proposed that a cross-government R&D coordination group be established to ensure that there are no overlaps or gaps in this research.

When this consultation process is complete, we will be in a position to commission further high quality research that is both applicable to the needs of the UK and coordinated with the efforts of other countries, including research ready to be put in place during a pandemic.

Academic Research

A large amount of work on all aspects of pandemic influenza planning has been published in the academic literature. Key papers on pandemic influenza are referred to the SAG for comment and those on vaccines are in general referred to the JCVI. Where appropriate the findings contained in those papers are fed into the policy making process.

However, such publications are only one element of the scientific evidence base, and therefore do not necessarily change policy outcomes. For example, in late 2005 a number of studies on viral resistance to oselatimivir (Tamiflu) were published. The Department of Health is monitoring and supporting research in this area in conjunction with the HPA, as well as receiving information from the Neuraminidase Inhibitor Susceptibility Network which has been set up in collaboration with the WHO to monitor the possible emergence of viral resistance. The assessment was that the available evidence indicates that the clinical significance of oseltamivir-resistant strains of influenza appears to be limited. Nevertheless, the Department is continuing to monitor emerging evidence closely, in conjunction with the SAG.

Scientific evidence from the commercial sector

The Department of Health (with specialist input from vaccine experts) has also been closely monitoring the scientific evidence that has been emerging from the commercial sector, particularly in relation to vaccines. The time that it will take to manufacture and deliver a pandemic vaccine is a key variable in our preparedness planning given its ability to reduce the impact of a pandemic.

The Department regularly meets with the influenza vaccine manufacturers to discuss how it can work with them to develop pandemic vaccines and to shorten the production time as much as possible. This has involved the manufacturers looking at new technologies such as DNA vaccines and cell culture-based production, and researching adjuvanting vaccines. Meanwhile, the Department has been working with NIBSC and others to rationalise the testing process which ensures that a safe vaccine is produced, and to support the industry is ensuring that the research which it commissions on vaccines is in line with that of other research funders.

The outcomes of these discussions with the manufacturers have been a key factor in informing vaccine policy and strategy, particularly the need to prioritise vaccine when it becomes available and the decision to tender for a ‘sleeping contract’ for a pandemic vaccine. This contract will cover finance to support vaccine development and licensing.

CONCLUSION

This memorandum demonstrates how scientific evidence has been one of the key drivers of the Department of Health’s current preparedness planning for an influenza pandemic, and how the Department has ensured that its policy making has been compliant with the principles laid out in the OST *Guidelines.* It is important to remember however that the available scientific evidence has not resolved all of the uncertainties surrounding a future pandemic, and is unlikely to be able to do so, making policy making in this area difficult. For that reason, the Department continues to look at gaps in knowledge and how they

can be filled and all aspects of the Government’s preparedness planning are kept under review. Emerging scientific knowledge is one of the key drivers of that review process.