31st March 06

Royal Society/Academy of Medical Science study on pandemic influenza

Response from Dr Hilary Pickles, Director of Public Health, Hillingdon PCT

I very much welcome the Royal Society's working group in this area. Pandemic influenza is an area that has interested me for some years, partly through the influence of my in-laws (HG and MS Pereira) and partly through responsibilities I used to hold when working in DH (including at various times AIDS and BSE, though not influenza per se). A long-standing interest in the interface between scientific advice and policy making was heightened by taking part in the BSE Inquiry. I have been reflecting on the Government's plans for pandemic flu as I have strived to implement them locally and have commented on the apparent failure to learn all the lessons from the past[1].

For me, scientific understanding has to include all aspects of the evidence base, suitably analysed. I have already corresponded with the chair on the need to take a wide view of science, including the behavioural sciences (annex 1). The working party will be considering 'scientific understanding (basic research to clinical application)', and I hope this will encompass all sorts of reliable evidence. Over-reliance on the medical model based on microbiological/epidemiological/clinical science may lead to failure to appreciate how the populace may behave as a whole. There is much we could learn from medical history as well as behavioural science, aspects touched on in the extract in annex 2.

I comment now under the specific questions being considered by the working group.

What does the scientific understanding (basic research to clinical application) of avian and pandemic influenza, in the short and long term, imply for:

1. Treatment: the use of existing, and the development of, new drugs and vaccines?
Some of my reservations on the practicalities of distribution and the potential unintended consequences of antivirals are covered in my letter to the chair (annex 1) and have been touched on by me elsewhere[2]. This should be as much a part of the 'scientific understanding' as the mode of action, and of course is well understood by the pharmaceutical industry who ditch many promising compounds if the route or frequency of administration would not be marketable. This is a theme being picked up by others[3]. Too much emphasis on antivirals may lead to inadequate attention to the alternative methods of control necessary if the antivirals are less than perfectly applied (which will surely be the case) or have limited effectiveness, say because of resistance. This majority

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[1] Pickles H Using lessons from the past to plan for pandemic flu. *BMJ* 2006;332:783-786
[2] Pickles H and Tailor V. Might oseltamivir be a mixed blessing? 7th Jan 2006. *The Pharmaceutical Journal* 276.11
[3] Bonneux L, Van Damme W An iatrogenic pandemic of panic *BMJ* 2006;332:786-788

of the countries in the world may have to cope with non-pharmaceutical interventions in any case.

2. Clinical care: diagnosis, basic understanding of the diseases; infection control; transmission?

Again, the scientific approach may lead to clinical guidelines which are indeed optimal in terms of expected clinical outcome, but being too far removed from what many clinicians may face in practice in a pandemic. For example, the acute shortage of intensive care and ventilatory facilities is something which was immediately apparent when I first did local planning in 2001, and is being brought out well in the planning which I am now involved with across North West London. It is also being brought up by others[4].

The counsel of perfection that may be possible in infection control in a well-stocked hospital intensive care unit, may disintegrate completely in practice in community settings and with lay volunteers. This is especially so when inadequate attention has been given to the adequacies of the supply chain, and so even the basics may be missing. 'Science' risks doing us a disservice if it does not address the practicalities of life away from the controlled experiment, and that needs to include how healthcare workers and others behave.

There are a range of 'scientific' questions the answers to which may be of real help to those dealing with the practicalities of planning. In annex 3 I list the questions that come up from local work in 2001 which were sent to DH at that time. For some, we still do not have the answers, even best guess expert opinion, although DH and its advisors may be working on them now. This helps demonstrate that leaving researchers to investigate what interests them may leave very important practical questions which are researchable still unanswered.

3. Strategies and preparedness for an outbreak: modelling and surveillance?

My own experience of policy making has been influenced both positively and negatively by modelling. It can be spectacularly wrong, or given with such wide confidence intervals that it is positively misleading, especially as the media always wants to focus on the worst case at the extreme of the range. I have seen some modelling in AIDS and BSE which was biologically implausible, and cried out for a reality check. It may have been understandable from the modeller's point of view working with the data available, but some of the data may be too uncertain to use. In the pandemic flu situation, what is needed in particular is a better understanding of how people actually behave. Annex 4 develops this theme in relation to screening at the ports, a particular interest in Hillingdon since it hosts Heathrow airport.

Surveillance is to me like controlled clinical trials. If done well, it can give an excellent reflection of what is happening, but is only directly relevant to those studied. If there are too many exclusion groups, or the data set is so neat and tidy to be atypical of the population as a whole, the value is limited. Practice-based surveillance coordinated by academic GPs has much to commend it. Even so, for populations like those in West

[4] Marsh R. Hard decisions will have to be made: view from intensive care *BMJ* 2006;332:790-791

London where many are transient or not GP-registered, it may not be able to reflect the total picture. That could leave important events uncharted until late.

What lessons can be learnt from other disease outbreaks and more general public emergencies, and the associated emergency planning responses?`
The main lesson to learn from the past is that lessons from the past have not been learned. My recent article in the BMJ touches only a selection of the very many lessons which appear to be being missed. This was written about the October DH guidance, and hopefully there has been some movement since. Potentially the most significant omission appears to be that pandemic flu will affect all society, not just the health service. The disruption to general goods and services may dwarf that from the increased demands on the health service. The virologists and epidemiologists say the UK was relatively unaffected by SARS; the economic scientists will tell you how much it cost the UK plc. The whole system impact matters. Not involving the public in the debate, eg about the inadequacy of the supply chain for antibiotics, food, and lots of other everyday essentials, risks anger later, especially if other nations are urging the public to stockpile.

How do wider ethical, social and regulatory issues, including those associated with the development of new technologies or treatments, influence current policymaking and future preparedness?
I argue that the wider ethical and social issues are not being brought adequately into the thinking, at least in judging policy from the version made public by DH.

On the regulatory aspects, in practical terms on the ground, the likes of me will do what we can with what is available. For example with distribution of anti-virals, as an ex-drug regulator, I would ignore any constraints of the licence if the circumstances demanded and the right PGDs were not ready, being prepared to justify myself later and knowing the risk of challenge was low. Many others with less experience might hold back, unless given a clear green light from on high.

How is the scientific evidence (academic, public or commercial) being incorporated into policy making?
This is for others to judge. From the output seen to date, there has been inadequate involvement of the social or economic sciences. Commercial influence appears to have been dominated by those companies making patentable biomedical products with less attention to those involved with routine manufacture (eg of simple infection control products) or the business sector in general.

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Sir John Skehel
National Institute of Medical Research

3rd March 2006

Dear Sir John

Re: Royal Society taskforce into pandemic flu

I heard of this taskforce with some interest, and wanted to share with you some immediate comments, in case you were tempted to broaden the composition of your group, for example to represent also the economic and behavioural sciences.

The reason for this is the real danger of channelling thinking just along the same lines as those driving government policy, which then might also undervalue the whole system impact. The Science and Technology Committee in its recent inquiry also concluded the Department of Health had too narrow a focus.

I will try to illustrate my point by consideration of antivirals in practice. Like other Directors of Public Health, I have been trying to work out the logistics of local delivery, but unlike most others, I have been trying to plan for the local response to pandemic flu for some years. The established view is that oseltamivir might be expected to have a beneficial effect if taken early in the course of clinical flu, preferably within 48 hours. The national stocks will be enough for one course for a quarter of the population (by September 06). Since that is only just enough for 25% clinical attack rate, and there is concern about encouraging resistance, there will need to be careful control on who gets supplies. Inevitably some of those who might think they deserve oseltamivir will not be able to access it.

That then implies there has to be some vetting of the individual requesting oseltamivir, to check they are ill enough, early enough. The prescribing aspect we can fix, but the vetting creates the dilemma. If everyone is asked to come to pharmacies or specially established flu centres, they are expected to travel when ill and risk spreading infection further. If instead we marshal enough teams to do home visits, these individuals risk acting as vehicles of spread as well as being at personal risk of being assaulted for the oseltamivir, which, by the time of the pandemic, will have an even bigger value on the black market. If we can find enough health care workers and volunteers to run this sort of vetting and distribution system, that reduces our capacity elsewhere, for example for tending the sick who cannot get into overcrowded hospitals. If the modellers tell us 12 hours is better than 48, then there would be even more pressure to have a delivery system working around the clock. If we have to check people are not getting duplicate supplies, then there's a whole new vetting system required, which also risks disadvantaging those that are not

registered with a GP. Already the police are reticent about being able to help us with security, so it feels as if it could be very difficult for anyone trying to deny someone oseltamivir face to face.

While there has been concentration on antiviral stocks, we are not aware of what has been done about protective equipment, so cannot even be sure those health care workers assessing people for oseltamivir can be made to feel safe. The economists would also be able to calculate, I presume, what it would do to the NHS finances if we moved from our efficient just-in-time system to build up local stockpiles of face masks etc. Since whatever system is established is bound not to work perfectly, there will be aggrieved relatives who afterwards will feel they might not have lost their loved one if only they had been able to get that precious antiviral. We might know the value might be pretty marginal in practice, but it has been sold as a life saver, and the public will be seeing it as such.

Out of this, while the virologists and pharmaceutical companies may say oseltamivir will be an important part of the national policy, I see it rather differently on the ground. The system for vetting and distributing oseltamivir risks spreading infection, causing resentment, and taking health care workers away from looking after those with the usual emergencies or complications of flu. Perhaps we just need as much attention to these practical aspects as has been given to the hard sciences, but as it stands at the moment, I'd be hard pressed to say that our antiviral stocks will be beneficial to population health overall.

This is only one example of why the Royal Society may be doing us all a disservice if it concentrates on the laboratory and theoretical aspects, rather than looking at the whole system. I'd be happy to expand on this further, if it would be helpful. I could of course put some evidence in myself, and might well do that (for example sending an advance copy of an article the BMJ will be publishing on the 1st April, if the BMJ don't mind, about lessons not learned from the past in pandemic flu planning). But above all, I am hoping you can expand the horizons of your group to cover a wider range of sciences, including some 'softer' ones.

Best wishes

Yours sincerely

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Director of Public Health/medical director

ANNEX 2. Extract from pandemic Flu: encouraging a positive population response
Hilary Pickles and Robin Goodwin
Eurohealth Vol 11 no 4 (in press, and embargoed until it appears there)

Lay perceptions of illness
How we will deal with any outbreak is likely to depend in part on our existing beliefs about illnesses. We all hold perceptions about disease in, the 'modern world', the types of people most usually at risk, and 'common sense' notions of the best way to cope with illness. Such beliefs help us cope with the threat challenges and threats in our world, including the threats posed by new pandemics. Of course many of these beliefs may bear little resemblance to the advice being given to deal with any pandemic, but they are still likely to be important in informing our behaviour. Such 'common sense' beliefs are rarely, however, taken into account by the medical profession, who tend to approach risks as 'objective' hazards. Unfortunately, at times of crisis, such beliefs can also be deeply divisive for any society.

In the SARS and Ebola virus outbreaks, associations with Chinese or Africans 'others' allowed Europeans to distance themselves from the apparent risks posed[6]. SARS emerged of course in a polluted, crowded, East Asian environment, where, to the Western reader, an almost primitive and medieval alliance persisted between people and their animals. Blaming (usually foreign) 'others' is common when faced with threatening disease, who are often thought as 'bringing it on themselves' perhaps because of their ways or living or outdated practices. So it may be easy to target Chinese populations in Western countries, particularly those that associate most closely with apparently 'risky' professions (e.g. restaurateurs). In Toronto, some Chinese suffered for their association with SARS[7].

For most people, the similarities between the recent SARS outbreak and avian influenza may also make them unwilling to follow official health guidelines. SARS was also presented by the media as a disease that could kill millions, yet it virtually disappeared in a few short months. Leading commentators in national newspapers across Europe have already began to question whether this is just 'another' false alarm, and have placed considerable suspicion on leading politicians[8]**.** Already low levels of trust, particularly in the former Communist nations of Eastern Europe, make a suspicious public sceptical of official health warnings, leading them to wonder "why are they telling us this?" We saw this following the Chernobyl nuclear disaster, when official advice about what was and was not suitable to eat often conflicted with both widely held beliefs about food safety - and the real everyday practicalities of poor societies. As a result, such advice was often disregarded[9]. Fatalistic attitudes, particularly amongst the elderly and the poor, as well as a generalised mistrust of any who work in a 'selfless' health sector, may make important behaviour changes difficult to achieve. It may be necessary to ensure that health messages come from respected international (European, rather than US-based) agencies, rather than apparently 'compromised' national governments. The power of the internet to challenge the accuracy of any such proclamations needs to be recognised, but the internet could be actively mobilised too to provide vital information and counter unproductive rumours.

Planning for an alternative scenario
A preferable approach to pandemic planning might be to appreciate that this as a major and general disruptive challenge, rather than a largely medical problem. Society as a whole will be stressed, and society will need to respond, based on the core response to any major disaster, with specific flu elements added on. Sickness rates mean few businesses will be unaffected, so all need to prepare for managing through a lean period, concentrating on the essentials. Some, like those involved in health and social care, will face the double challenge of increased pressure from their patients and clients and a reduced number of staff. With the right encouragement and advance

planning, volunteers from less essential industries should be able to help out. The pandemic will be a real opportunity for whole communities to pull together, to be encouraged to go beyond self-help to neighbour help.

As with all emergency planning, the best way to develop this model may well be to build on existing structures and relationships, building up from the neighbourhood and commune. Nationally and internationally there may need to be action to remove barriers to cooperation, and to the extreme effort needed in a pandemic situation (like the restricted hours of the working time directorate). The final judgement may well come how any community looked after the most vulnerable, such as those with learning disability or mental illness held in residential institutions, where transmission is likely to be exceptionally difficult to control. For this high ideal of a truly civilised response, the basis needs to be a better understanding of the likely population response, wider then just the direct reaction to the influenza virus.

While attention is focussed on the pandemic situation, there will be other urgent business that needs to continue. The economic impact will be very considerable, and some individuals and businesses will need sympathetic handling[10].

The end game

The pandemic is inevitable, although it may prove to be a damp squib. What really matters is the recovery phase and thereafter. If all goes well, we will have a society at peace with itself, looking back in pride at surviving a terrible time, together. In spite of the shortages and rationing and loss of life, the aim is a lack of recriminations. The internet means it will not be possible to conceal mistakes, so instead we need to seek to learn from them, not forgetting the cover up is always worse than the original error. For this we need leadership at international, national and local level.

Good planning for this need not cost much, except in time. We need to get the attitudes right, with society understanding about its vulnerabilities and the need for prioritisation. Brave policy makers will be planning for openness and trusting the public. Together we will rise to the challenge.

Conclusion

It is important to keep this pandemic in proportion. Even if it proves as bad as 1918, the majority of the world's population will survive with full physical health. The onus is on us to ensure society as a whole comes through well too.

References

1. See www.who.int/csr/disease/avian_influenza/en/index.html for the latest position
2. WHO global influenza preparedness plan (Apr 05) on www.who.int/csr/resources /publications/influenza /WHO_CDS_CSR_GIP_2005_5/en
3. WHO writing group. Nonpharmaceutical Interventions for Pandemic Influenza, National and Community Measures. *Emerging Infectious Diseases* 2006;12: 988-94
4. Tolomiczenko, G.S., Kahan, M., Ricci, M., Strathern, L., Jeney, C., Patterson, K., & Lynn, W. (2005). SARS: coping with the impact at a community hospital. *Journal of Advanced Nursing, 50,* 101-110.
5. Forster P W & Tang Y 2005. The role of online shopping and fulfillment in the Hong Kong SARS crisis. Proceedings of the 38th Hawaii International Conference on System Sciences
6. Washer, P. (2004). Representations of SARS in the British newspapers. *Social Science and Medicine, 59,* 2561-2571.

7. Schram J How popular perceptions of risk from SARS are fermenting discrimination. *BMJ* 2003;326: 939
8. Jacek Zakowski, Krowy, ptaki i dziennikarze (Cows, birds and journalists). Lead article, *Gazeta Wyborcza*, 12/03/2006,
9. Allen, P.A. (1999). Countermeasure response among residents of Chernobyl-Contaminated Regions : Analysis of Twelve Focus Groups from Belarus and Ukraine. EC Nuclear Fission Safety Research Programme: Research Area E Contract n°: F14C-CT96-0010
10. Brahmbhatt M. Avian and Human Pandemic Influenza – Economic and social Impacts 2005 on www.who.int/mediacentre/events/2005/World_Bank_Milan_Brahmbhattv2.pdf

17th August 2001

ANNEX 3

Areas where DoH and its expert advisors should be asked to give advice, or where it is felt decisions will need to have taken place at a national level, to enable more appropriate local planning for flu pandemics. These are in addition to areas already identified for national action, like definition of the priority groups for any vaccine

1. Advice needed on practical **infection control** steps which could be taken to prevent possible nosocomial transmission both in hospital and community settings, assuming vaccines are not yet available and there are only limited supplies of antivirals. This advice could include:
   - The value if any of face masks
   - Whether the practicalities of wearing fresh gloves for each new patient contact mean this is unrealistic advice, but were this to still recommended whether less stringent advice would be offered to home carers (and if so how this could be justified).
   - What disinfection routine to use for all sorts of hospital and community equipment, advice on use of detergents and dish washing and other measures effective at disinfecting hard surfaces
   - Whether there is anything of value that could be done to air conditioning systems to reduce droplet spread, or whether drawing curtains round hospital beds might be expected to help or hinder transmission
   - If there are any additional protection measures to protect staff undertaking post mortems

2. Are there any measures, say the right air filters, that could be taken to reduce the chance of flu being transmitted during a **long-haul flight**?

3. What is the best clinical management of fulminating **viral pneumonitis**? If either oxygen or ventilation has a place, are there any indicators that could be used to suggest when the chance of a successful outcome is low? Are there any particular additional precautions that need to be taken to prevent further spread from such cases?

4. What is the best advice about the management of post-flu **staphylococcal pneumonia** in adults, and what estimates are there for the likely time a typical patient might require the sort of care usually done in hospitals, and the expected mortality assuming antibiotics are available. What is the best guess for the proportion of any staph pneumonias being mrsa?

5. What is the best and most expert advice about having **segregated** "known infected" and "not known to be infected" wards/hospital floor/hospitals/residential homes/residential institutions? What advice would there be about the introduction of a patient known to have flu into a setting, such as an ITU, where others are thought non-infected? If one resident in a residential home goes down with flu symptoms, is the best advice: (1) to leave the others residents in place and remover the infected person, (2) remove the other residents and leave the infected resident, or (3) leave all in together assuming transmission is inevitable and may already have happened. Would the same advice apply to any domestic setting, assuming hospitalisation was neither possible nor appropriate?

6. What estimates could be put on the chance of anyone being both infected and infectious to others but being personally unaware of this? Are there any simple measures, say body temperature, which could be used to help reassure staff they are not **sub-clinically infected** (and so not likely to infect others including their own families)?

7. Are any groups of people, say certain HLA groups, thought less likely to get severe flu than others because of **relative immunity**? What advice is there about the most appropriate way of confirming that staff who claim to have had flu already in the pandemic have actually done so and are now **immune** from further infection?

8. Advice will be needed on the most appropriate use of **test-kits** were the availability of these limited at first, say whether for clinical diagnosis or for confirmation of immunity in HCWs who would be encouraged to be in the front line with those ill with flu.

9. What information is there on the national NHS staff-mix in relation to **domestic commitments** and how staff might be expected to cope in circumstances of national disruption, including to schools? Is this something where sociological research would be possible and helpful to the planners?

10. What does research tell us of the pressures to **stockpile** essentials and what public information and other strategies would be expected to be effective to limit this happening? Are there any legal measures that could be used to limit stockpiling of essential goods? What information is there on the likely additional hazards from stockpiling (poor food storage conditions, fire hazards etc) and what planning for these are local economies expected to undertake?

11. There needs to be discussions with the **private sector**, maybe leading to a Concordat, to limit them draining staff from or potentially available to the NHS, if at the same time the private sector are offering clinical services rationed out from the NHS because of the national crisis. Might new legal powers be needed here?

12. The most difficult decisions about **rationing** of clinical services on the NHS, over and above the stopping of elective surgery, will need to be taken at national level and seen to have the endorsement of Ministers. It will be important that this is done, but it is inevitable that some aspects will fall to local decision-making. It would help to have a national checklist summarising the known data on relative effectiveness in providing health gain, in order to guide any of such decisions that fall to local economies. This needs to be structured in a way to be helpful to those making difficult local decisions about deploying limited resources. An example might be the health gain opportunity costs from diverting for a period of say 3 months a trained nurse into another area, assuming the nurse would be replaced in the main job by a volunteer with limited skills.

13. Those required to take difficult local decisions about relative priorities in times of national emergency will need to be provided with national support, including **indemnity** from subsequent challenge, provided decisions are overt and within a legal framework. Central advice will be needed on this.

14. Agreement may be needed for relaxation of the usual arrangements for **post-mortems** for those dying without medical attention in the last days of life. This could empower local officials to permit death certificates to be issued on the assumption of a flu-related death, or after only some limited form of post-mortem examination without dissection which need not be undertaken by a doctor.

Suggestions from Hillingdon Health Authority

ANNEX 4

Screening for pandemic influenza at the ports

The conclusion of academic modellers is that screening for pandemic flu in travellers returning to the UK on long haul flights would be without value[5]. The numbers of detected cases were calculated to be so small so as to make virtually no impact on a potential domestic epidemic. However, some of the assumptions behind this modelling can be challenged leaving this as an incomplete and hence potentially misleading policy evaluation.

Only the new emergence of clinical symptoms during the flight duration was considered. It was assumed that a potential traveller with symptoms would volunteer this and/or the check-in system would be able to detect this in exit screening: neither is likely to be the case, especially with the uncertainty of early symptoms. A traveller who has started the journey to the airport well is likely to want to complete the journey. Airline tickets may not be valid were the journey delayed, or the traveller not want to risk that this would be the case. The pressures on those caught overseas as the pandemic starts would be such that they would want to return home, especially those wanting to return to the (free) NHS with its supplies of oseltamivir. Symptoms could well be denied if need be to get on the flight. Whatever the WHO recommendations, there is little incentive for affected countries to apply much effort to exit screening. A determined traveller should be able to evade exit controls.

The modellers were looking at entry screening in relation to preventing or delaying an epidemic resulting from the importation of SARS or influenza. However, the benefits from entry screening could go much wider than just on the spread of the epidemic[6] and these were not considered in this policy evaluation. This could be especially relevant in WHO phases 4 to 5, targeted at those coming from affected areas of the world. Knowledge that there would be entry screening could act as deterrent to evasion to any exit controls and would reassure airline staff and fellow passengers and enable the planes to continue to fly. It would also enable information to be provided to those from at-risk countries about the early symptoms to assist early presentation. Those that were found to be ill could be directed to early treatment and advised on how to prevent further spread. For the many who transit at airports such as Heathrow, it would also act as exit screening.

Even though the scientific case is likely to remain borderline, the political case – to be seen to be doing something – could come to dominate and enable a complete travel ban to be avoided. Without at least action to help those who volunteer their illness on arrival, those responsible for onward travel – such as airline, tube, train, bus or taxi – may refuse to cooperate in carrying travellers from affected countries. The resultant congestion at the airport could enhance transmission: congestion may be a problem anyway as some nations may chose to ignore the WHO and close their borders and/or carriers fail in anticipation of the forthcoming downturn in business.

These issues are now being considered further with the HPA and DH.

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[5] Pitman R J, Cooper BS, Trotter CL, Gay NJ, Edmunds WJ. Entry Screening for severe acute respiratory syndrome (SARS) or influenza: policy evaluation. *BMJ*, 2005; doi:10.1136/bmj.38573.696100.3A

[6] Pickles H. Screening international travellers in China for SARS. *Commun Dis Public* Health 2003; 6(3): 216-20