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Dear Pandemic Influenza Preparedness Team:

I wish to present information on issues that warrant further consideration for the *UK influenza pandemic preparedness strategy 2011: strategy for consultation* document. The current strategy document focuses on planning and responding to the demands of an influenza pandemic in the UK. Since 2007, there has been a growing scientific debate¹⁻³ over the nature of the hazards posed by pharmaceutical use in a pandemic on the critical infrastructure (i.e., wastewater treatment plants) and the aquatic environment. This concern led to the formation of the NERC Knowledge Transfer Initiative, *Pharmaceutical Release into the Environment during Pandemics and Regional Epidemics (PREPARE; NE/F009216/1)*, which I lead (<http://www.prepare.org.uk/>). On behalf of the PREPARE team, I wish to take this opportunity afforded by the public consultation to recommend the acknowledgement and inclusion of these issues in the 2011 strategy document.

The issue is that during the course of an influenza pandemic, large quantities of drugs are projected to be used to treat cases of influenza and influenza-associated complications⁴. With few exceptions, a large proportion of the ingested pharmaceuticals are excreted from the human body in a biologically-active form to ultimately enter wastewater treatment systems (WWTPs) and rivers²⁻³.

The antibiotic-component of the pharmaceutical response can be expected to challenge and non-uniformly inhibit the growth of microorganisms within WWTPs⁵ on which their treatment effectiveness depends. Whilst this is predicted to reduce the overall organic removal of a WWTP, the greatest risk is the loss of nitrifying microorganisms that are responsible for the removal of ammonia from wastewater influent. Nitrification is a two-step process, with the second step, i.e., oxidation of nitrite to nitrate, particularly sensitive to antibiotics⁶⁻⁷. Inhibition of the microorganisms responsible for this step may lead to accumulation of nitrite nitrogen in the WWTP effluent, a form of nitrogen which is particularly toxic⁸.

A loss in WWTP functioning during an influenza pandemic would result in insufficiently treated wastewater entering the receiving rivers, leading to eutrophication, loss of aquatic life, and fish kill. In the case of those rivers which serve as abstraction points for drinking water, as the Thames River does for London, there are immediate implications for the quality of source water for human consumption.

Several factors will mediate the impact of a pandemic on the aquatic environment:

- Disease characteristics: transmission potential of the new virus, its pathogenicity, and the rate of occurrence of mild to severe illness and complications.
- Drug usage pattern: necessarily dependent on the nature and extent of the UK pharmaceutical stockpiles, and how it is going to be used.
- Vulnerability of WWTP microorganisms to pharmaceuticals: current models suggest that WWTPs are vulnerable to high concentrations of bioactive pharmaceuticals, such as antibiotics. The literature is much less certain about the potential impact of antivirals, but limited evidence does suggest it may pose a risk towards disrupting biofilms within WWTPs¹, which are critical to structuring and protecting the microorganisms within WWTPs.
- WWTP Staffing: the staffing challenges faced during a moderate to severe pandemic will inevitably impact upon the capacity to deliver a fully functioning wastewater treatment and drinking water infrastructure and service.
- WWTP design: There are several different designs for WWTPs within the UK. Some designs are expected to be more robust to the challenge than others, but there is very low confidence about such predictions owing to the lack of empirical data.
- WWTP recovery: As a matter of standard practice, functioning WWTPs are used to 'seed' failing WWTPs. In the event of a pandemic, it might be difficult to find a WWTP that is not impacted which can be used to seed the (many) failing WWTPs.
- Timing: the risk of WWTP failure and river pollution is partly dependent on the timing of the peak of the pandemic within the UK. A winter peak may present a higher risk owing to the decreased efficacy of WWTPs during cold months.
- Precipitation: Periods of increased rainfall will be expected to dilute the pharmaceuticals in WWTPs and rivers. In contrast, a pandemic peaking during a dry period will result in even higher concentrations of drug in wastewater and rivers (existing ecotoxicity models used annual mean river flows¹). The concentration of river pollutants could vary by nearly 2 orders of magnitude when comparing the wettest to the driest period on record⁹. The influence of precipitation can, thus, potentially greatly increase the ecotoxicologic risk.

Summary of planning assumptions for pandemic preparedness

A pharmaceutical intervention in response to an influenza pandemic is inevitable and indeed vital. It is expected that the medical response during a moderate or severe influenza pandemic will result in very high concentrations of antimicrobials in WWTPs as well as, in large part, the rivers into which they discharge. The effects of these drugs on WWTPs and the environment will inevitably lead to a reduction in some 'essential' functions, with loss of nitrification being a particular concern. Consideration should be given to how regulatory authorities and WWTPs and drinking water industries plan their response to this challenge. In the event that WWTPs begin to fail, it is essential that systems be in place to recover them taking into account the added challenge of limited staffing. Efforts towards protecting essential staff in the water industry (wastewater and drinking water) with early vaccination might alleviate some of the risk associated with staffing shortages. In addition, a system needs to be in place to recover a failed WWTP in the absence of any suitably functioning WWTPs nearby.

In summary, even if we accept the environmental hazards, it is necessary that we be aware of, and plan a response to a pandemic situation where very high drug use is prescribed. The UK pandemic preparedness plan should be able to address many of these risk given the available knowledge base, or with some additional

coordination of stakeholders (as demonstrated through the PREPARE Initiative). However, several of the issues raised will need to be tackled at a more fundamental level, which would require additional scientific research during the inter-pandemic period to provide an adequate scientific foundation for informing policy.

Kind regards,



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