

Unlicensed pandemic influenza A H1N1 vaccines

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When WHO's Strategic Advisory Group of Experts (SAGE) on immunisation met on July 7, 2009, they recognised that pandemic influenza A H1N1 vaccines, when they become available, are almost entirely committed under contract to a small number of industrialised countries.¹ SAGE commended WHO for trying to improve real-time access in poor countries, but these efforts will not have substantial effects in the short term.

Currently, about 150 million doses of H1N1 vaccine have been committed to by a few manufacturers. Governments who have their supplies contracted for have made limited commitments to a global stockpile.² Therefore health ministries in countries that do not have H1N1 vaccines face a daunting challenge: how to secure vaccines?

Globally, at least 40 organisations are either developing or already producing seasonal influenza vaccine, with most developing H1N1 vaccines as well.³ Many of these are new start-ups, some of which are located in developing countries.⁴ Some are exploring new cell-based approaches, which might speed development and manufacture.⁵ However, it is unclear when, or if, these vaccines will be licensed and available.

Some countries are shopping for vaccines from these sources. SAGE had an important concern: some national regulatory decisions might reduce global availability, and some developing countries might be reluctant to use a vaccine that has not been licensed in an industrialised country. SAGE encouraged countries to give attention

to emergency provisions for unlicensed vaccines. This encouragement seems to be a green light for countries without access to pandemic vaccines to consider higher-risk strategies to procure and deploy them by emergency use provisions.

Although the US Food and Drug Administration (FDA),⁶ in response to the anthrax scare, established rules allowing licensure of products on the basis of efficacy testing in animals with safety studies in human beings, there is no robust set of guidelines for governments, manufacturers, public health officials, patients' advocacy groups, or the mass media to consider should a public health threat seem to justify making unlicensed vaccines available.

A key requirement is that national and international bodies indicate that a pandemic or public health threat exists with the potential to cause severe adverse consequences. Also, existing methods for responding to a pandemic or public health threat should be regarded as insufficient. Existing supplies of vaccines must be certified as inadequate or lacking in safety or efficacy. Furthermore, existing means for behavioural change, including isolation and social distancing, should be judged as inadequate for substantially reducing the threat of large-scale deaths.

If these conditions are met, data from animal studies should show trustworthy evidence of safety and efficacy of any vaccine proposed for emergency use. If there is a standard animal model for the assessment of vaccine safety, this model should be used before any vaccine is introduced for human use. Clinical trials that show safety of any vaccine proposed for emergency use should also be done before human use. These trials include ensuring the quality of manufacturing processes and the safety of the vaccine itself.

Manufacturers, working with countries where the vaccine is deployed, should appoint data safety and monitoring committees with local representation to assess and provide oversight for emergency release. Timely reports should be made on the safety and efficacy of vaccines being deployed by any nation where emergency release has been started.

In public health emergencies, manufacturers should adjust their financial expectations for sales. The goal of emergency release is to permit the manufacturer to respond to an emergency without taking financial

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advantage of the desperation of nations seeking supplies. Manufacturers should give nations seeking supplies a reasonable opportunity to make their needs known. Public and transparent calls for requests should be part of the process of deciding to whom and at what cost emergency release of vaccine will occur.

Countries seeking emergency release of a novel unlicensed vaccine must show that they have a plan for distributing vaccine in a fair, effective, and transparent manner. Nations must also certify that they will adequately monitor and report on the safety and effectiveness of any vaccine involved to the manufacturer, any oversight board, and appropriate governmental authorities, including WHO. Governments should assure that informed consent processes are robust and that voluntary choice is respected. It is unethical to mandate immunisation with vaccines that have not been fully tested in clinical trials that would normally accompany licensing. Governments should also have a robust plan for communicating about vaccines being made available under emergency circumstances to their populations.^{6,7} Countries seeking emergency release should create a plan for handling any adverse events from vaccination.

These broad principles should provide a starting point for countries seeking unlicensed pandemic vaccine. More work must be done to further refine public health policy for emergencies.

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- 1 Strategic Advisory Group of Experts on Immunization. Report of the extraordinary meeting on the influenza A (H1N1) 2009 pandemic. *Wkly Epidemiol Rec* 2009; **84**: 301-08.
- 2 MSNBC. U.S. to share swine flu vaccine globally. Sept 17, 2009. http://www.msnbc.msn.com/id/32896769/ns/health-swine_flu (accessed Sept 22, 2009).
- 3 WHO. WHO supports fair access to influenza A (H1N1) vaccine. An interview with Marie-Paule Kieny. *Bull World Health Organ* 2009; **87**: 645-732.
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- 7 Lancet. Supply and safety issues surrounding an H1N1 vaccine. *Lancet* 2009; **374**: 358.

Retraction—ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children



Following the judgment of the UK General Medical Council's Fitness to Practise Panel on Jan 28, 2010, it has become clear that several elements of the 1998 paper by Wakefield et al¹ are incorrect, contrary to the findings of an earlier investigation.² In particular, the claims in the original paper that children were "consecutively referred" and that investigations were "approved" by the local ethics committee have been

proven to be false. Therefore we fully retract this paper from the published record.

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- 1 Wakefield AJ, Murch SH, Anthony A, et al. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* 1998; **351**: 637-41.
- 2 Hodgson H. A statement by The Royal Free and University College Medical School and The Royal Free Hampstead NHS Trust. *Lancet* 2004; **363**: 824.

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