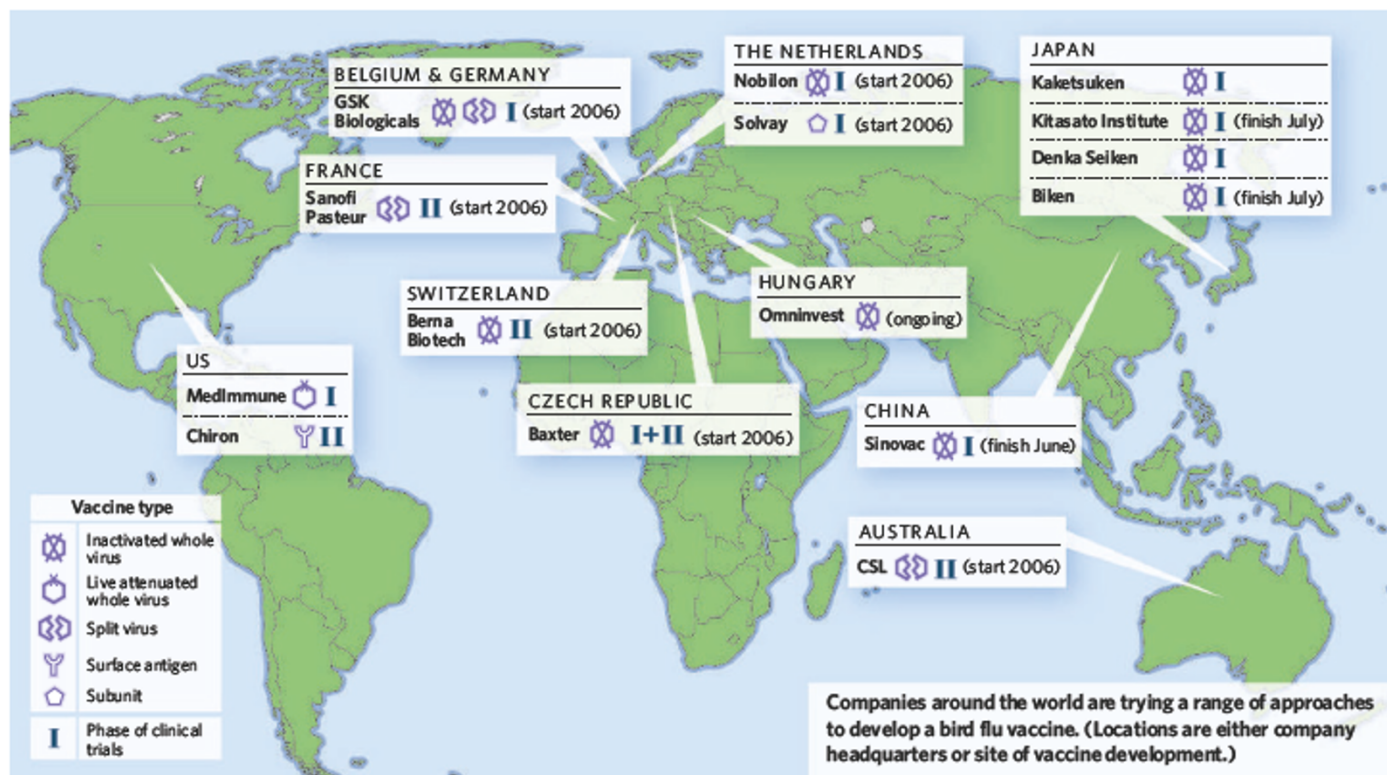




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Flu-vaccine makers toil to boost supply

The threat of a bird-flu pandemic is forcing vaccine developers to make tough choices about the types of vaccine to pursue. Many advanced trials are testing vaccines that use disrupted viruses, which have few side effects. But some experts now argue that, with such a wide gap between how much vaccine would be needed in a pandemic and how much the world's manufacturers could produce, attention should focus on vaccines that use the intact virus. Although thought to be riskier, they are far more effective at lower doses.

The likely shortfall in the available vaccine is highlighted this week by a study modelling the effectiveness of various interventions for mitigating a bird-flu pandemic. Using Britain and the United States as examples, Neil Ferguson at Imperial College London and his co-authors found that, to curb the spread of the disease, vaccinations would need to begin within one to two months of the pandemic starting (N. M. Ferguson *et al.* *Nature* doi:10.1038/nature04795; 2006). And a stockpile of vaccine for 20% of the population would greatly reduce the number of cases, even if it wasn't a perfect match for the pandemic strain.

"There is a significant gap between the desir-

able and actual access to the vaccine," says Klaus Stöhr, an adviser on flu-pandemic vaccine development at the World Health Organization. "There need to be fundamental changes in the way we produce and use influenza vaccines."

More than a dozen groups are developing pandemic vaccines, testing a range of strategies to boost potency and production capacity (see map). Some companies are testing more potent

"Companies should use the whole virus, because there would be more vaccine to go round."

vaccine 'adjuvants', which are used with a vaccine to boost the immune response. Others are developing cell-based systems to grow the virus, rather than the chicken eggs currently used, to increase vaccine yields.

But some experts argue that a quicker path to a greater vaccine supply is to switch to using whole (but inactivated) virus, rather than the 'split' virus conventionally used. The intact virus triggers a more powerful immune response, and such vaccines would potentially increase stocks, because a lower dose could be used.

"Companies should be using the whole virus, because there would be more to go round," says Graeme Laver, a virologist who has worked on flu for more than 40 years, primarily at the Australian National University in Canberra.

The risk is that such vaccines could trigger

toxic reactions — whole-virus flu vaccines used in the 1960s sometimes caused problems such as fever and pain, especially in children. So companies switched to split viruses, in which the viral coat is disrupted with a detergent.

But David Fedson, former medical director of Paris-based Sanofi-Aventis, believes the threat of bird flu makes whole-virus vaccines an attractive option again. "When death is the other option, a sore arm is not a bad price to pay," he says.

Several companies are in the early stages of developing whole-virus vaccines (see map). But many vaccine makers, including Sanofi Pasteur, the vaccine arm of Sanofi-Aventis, say they won't be switching to whole virus in the near future, mainly because their facilities are geared to making split-virus vaccines. "If a pandemic was declared this year, we would go with what we already have up our sleeve," says Rachel David, a spokeswoman for Melbourne-based CSL, which has a split-virus vaccine in clinical trials.

But Stöhr cautions against being too obsessed with the whole-versus-split virus issue. "There are many avenues for improving the vaccines," he points out. He says a global action plan is urgently needed to prioritize research efforts and rally more funding to develop flu-pandemic vaccines.

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