

Smallpox vaccination becomes a social, financial...

Through donation and dilution, the US government may soon have more than enough to vaccinate the nation's entire population. In addition, it will be purchasing new, second-generation vaccine with which to inoculate its citizens. But the country's senior scientists are asking for a public discussion about the risks and benefits of smallpox vaccination before mass immunization proceeds.

Research released online on 28 March in *The New England Journal of Medicine* (<http://nejm.org/earlyrelease/index.asp>) reports that stocks of smallpox vaccine made 20 years ago by Wyeth Laboratories retain full efficacy when diluted 5-fold, instantly boosting US government stockpiles of the vaccine to 77 million doses. On the same day, the Department of Health and Human Services (HHS) announced that vaccine company Aventis Pasteur had agreed to donate 85 million additional doses of smallpox vaccine that the company had apparently discovered in its freezers. If the Aventis stocks are as potent as those from Wyeth, the US government will have over half a billion doses of smallpox vaccine, more than enough to vaccinate its population of 250 million.

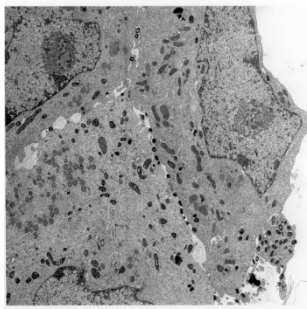
Nationwide vaccination would eliminate the threat of an attack with *Variola major*, the virus that causes smallpox. But experts urge caution. Sharon Frey, a researcher at St. Louis University, Missouri, who led the vaccine dilution study, says, "You can't just willy-nilly do a massive campaign," as the vaccine has "a tremendous risk of major life-threatening side effects," particularly for immunocompromised patients.

Routine smallpox vaccination used to kill approximately one patient per million, and a few hundred people per million developed serious side effects, often including permanent brain damage. Mass vaccination of the current US population would be expected to kill over 200 people and make thousands more seriously ill.

In an editorial accompanying Frey's paper on the *NEJM* website, Anthony Fauci, director of the National Institute of Allergy and Infectious Disease calls, asks for a more informed public debate on the issue of mass vaccination versus contained vaccination after a terrorist attack. And William Bicknell, the founder of Boston

University School of Public Health, considers the issue of voluntary vaccination.

Since 11 September, many governments have offered lucrative contracts for new 'second-generation' vaccines. These vaccines, which consist of live *Vaccinia virus* grown in cell culture rather than cattle, meet modern quality control standards. The US government has awarded two contracts for such a vaccine to British company, Acambis (*Nature Med.* 7, 1167; 2001), which beat pharmaceutical giants like



Cells infected with vaccinia virus

Aventis, GlaxoSmithKline and Merck for the deal. "I think that all of the companies saw it as an opportunity not only to get good PR, but actually to make some money out of it as well," says Gordon Cameron, Acambis's chief financial officer.

Acambis is producing 209 million doses of a second-generation vaccine for the US for \$771 million, revenue that will catapult the tiny company to profitability. Acambis is in discussions with European governments that have also expressed interest in its product and Cameron believes that the public will demand to be given new rather than old vaccine. "From a public perception standpoint, the public... would naturally want the material from the second generation rather than the first generation," he says. This seems to be confirmed by the fact that negotiations for the Aventis donation began in October, a

month before the US contracts was awarded to Acambis.

Aventis estimates the value of its donation at \$150 million, and spokesman Len Lavenda says, "we feel that we have an obligation as citizens of this nation to... help protect the safety and security of the country." But Aventis's actions are not rooted in altruism. Lavenda admits that before 11 September "we were in the process of developing protocols for disposing of [the stocks]," which would have required FDA approval because the vaccine is live and infectious. Instead, HHS expressed interest in acquiring the vaccine, and at the end of March, Aventis finished testing the stocks' viability. "We have asked the US government to reimburse us for some of the expenses we've incurred for testing and final packaging," says Lavenda. Thus, donating the vaccine not only brings good PR, but also will be considerably cheaper than disposing of it, particularly if the government reimburses Aventis for its expenses.

In addition, the value of \$150 million is almost impossible to contest, but Aventis will be able to deduct this amount in tax from their company finances, in essence meaning that they will be paid for their 'donation'. Moreover, if the liability for the well-known side effects of this vaccine is transferred to the US government—which may well happen, and would not have been the case if the vaccine had been sold—Aventis will have washed its hands of the problem at no cost. Thus, the smallpox vaccine seems to present a case where public interest lines up neatly with corporate interest.

Alan Dove, Philadelphia

...and political issue

The production of a second-generation smallpox vaccine has caused a political row in the UK. In mid-April, it was revealed that the British government had awarded a £32 million (\$46 million) contract to Oxford-based PowderJect, a vaccine company that donated £50,000 to the Labor Party last year. In placing the contract with PowderJect, the Labor government has bypassed Cambridge-based Acambis, which is to produce 155 million doses of smallpox vaccine over the next 12 months for the US government.

Some members of Parliament are now demanding an inquiry into the PowderJect deal. In addition to determining whether there was any impropriety in awarding the

contract to a company with financial links to the government, they want to know why the government has opted for a vaccine against a different strain of the virus than that selected by the US government, and why only enough doses are being made to vaccinate half of the adult population—16 million.

Government ministers insist that PowderJect is the only company that can produce doses of the vaccine quickly; however, Acambis's John Brown says, "I think it is unlikely anyone is going to be able to get a fully tested vaccine and make it available before us." PowderJect is reported to be purchasing supplies of its vaccine and the manufacturing technology from Danish biotechnology company Bavarian Nordic.

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