Plague Vaccine "Regulations": Ensuring Quality

We offer the following information for purposes of clarifying statements in the article about plague vaccine by Steve Sternberg "Bottleneck keeps existing vaccine off the market" (News & Comment, 7 Oct., p. 22). Greer Laboratories, Inc. of Lenoir, North Carolina, was licensed by the Center for Biologics Evaluation and Research (CBER) of the Food and Drug Administration on 5 October 1994 to manufacture plague vaccine.

Existing requirements specify that biological products must be safe, pure, and potent and be consistent with good manufacturing practices. In approving the Greer vaccine, CBER reviewed data demonstrating comparability with a previously approved plague vaccine manufactured by Miles, Inc., whose efficacy data were derived from the military's use during the Vietnam era; very few cases of plague occurred among U.S. soldiers immunized with this predecessor plague vaccine compared with unvaccinated Vietnamese civilians, who suffered many cases of plague. Because the incidence of plague is so low in the United States, obtaining further efficacy data through conventional clinical trials was not feasible. For this reason, the Food and Drug Administration asked Greer Laboratories to conduct a clinical trial in small numbers of volunteers to compare adverse reactions and antibody responses with the predecessor vaccine and the new vaccine.

Consistent production of biological products, particularly those that have replicating pathogens as their starting point, is difficult and demanding. This is true even for experienced manufacturers but particularly so for companies such as Greer that are new to vaccine production. Our focus therefore became ensuring that this vaccine, made in a new facility with new equipment and new staff, was comparable to the previous vaccine and was handled properly throughout a contained production process. We believe this focus was appropriate to ensure the manufacture of quality vaccine.

In review of biological products, we strive to use our best scientific judgment to responsibly apply requirements designed to protect the public health. In this situation, a committee of CBER experts worked with both Greer Laboratories and the Department of Defense to resolve the many scientific and regulatory issues involved in this application as quickly as possible.

Kathryn C. Zoon
Director,
Center for Biologics Evaluation and Research,
Food and Drug Administration,
Rockville, MD 20852–1448, USA

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Significance of $d_{x^2-y^2}$ Pairing in the Cuprates

In the News article "New clues to superconductivity" (12 Aug., p. 860), Daniel Clery notes that recent experiments suggesting that the high-temperature cuprate superconductors have a $d_{x^2-y^2}$ gap provided important clues regarding the pairing mechanism. However, P. W. Anderson (Letters, 23 Sept., p. 1789) states that "the symmetry of the gap is of little importance."

I believe the momentum dependence of the gap reflects the momentum dependence of the effective pairing interaction, just as the frequency dependence of the gap reflects the frequency dependence of the interaction. Studies of the frequency dependence of the gap in the traditional low-temperature superconductors provided detailed evidence that the exchange of phonons was responsible for pairing in these materials. In the case of the high-

temperature cuprate superconductors, the "$d_{x^2-y^2}$-wave" momentum dependence of the gap, $\Delta_0(\cos k_x - \cos k_y)$, is consistent with an effective pairing interaction that has a positive peak for momentum transfers near (π, π). This is what one would expect if the pairing mechanism is associated with the exchange of antiferromagnetic spin fluctuations (*1*). Indeed, this type of structure in the effective interaction has been found in Monte Carlo studies of the Hubbard model (*2*).

Clearly, further measurements of both the momentum and frequency dependence of the gap, along with additional theoretical work relating this structure to the pairing interaction, are needed. Nevertheless, the symmetry of the gap, reflected in its momentum dependence, provides an important clue to the mechanism responsible for pairing in the cuprates.

Douglas J. Scalapino
Department of Physics,
University of California,
Santa Barbara, CA 93106–9530, USA

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2. N. Bulut, D. J. Scalapino, S. R. White, *Phys. Rev. B* **50**, 9623 (1994).

Chernobyl Thesis

The ScienceScope item "MIT student's Chernobyl analysis flawed" (12 Aug., p. 859) states that my thesis (*1*) concluded that more than 185 million curies of radioactivity were released in the 1986 Chernobyl accident in Ukraine. The "185 million" refers only to seven isotopes of three biologically hazardous and volatile elements—tellurium, iodine, and cesium. The total release (which includes the many more radioactive isotopes produced in the core of a nuclear power reactor but does not include the noble-gas isotopes) was estimated to be on the order of 200 to 250 million curies, or four to five times more than the initial Soviet total release figure of 50 million curies (excepting noble gases). The Nuclear Regulatory Commission (NRC) correctly pointed out that I overestimated the amount of Cs-136 calculated to be in the core at the time of the accident. However, they do not mention that this miscalculation was traced to an error in a British computer code used for the initial core inventory calculations. Moreover, NRC nuclear engineer George Sege concluded that "Sich's results are [thus] reduced by about a factor of two" (*2*). Even if this is correct (although it is still disputed because subtle arguments in the thesis support the fact that this estimate was deliberately skewed toward a lower value), the 185 million curies (for only those *three* volatile elements) is reduced to 93 million curies (already almost twice the Soviet *total* estimate), and thus the *total* can be roughly estimated to be in the range of 120 to 150 million curies, or 2.5 to 3 times the Soviet *total* release figure.

My estimate of the radioactivity released is not central to the main arguments posed in my thesis. It merely confirms earlier Western concerns (and published reports) that more was released (*2*). The main conclusions of my thesis are (i) the accident management actions taken in the early days after the explosions destroyed the core were not as effective as the Soviets said they were in Vienna in August 1986—the Soviets did not succeed in smothering the "burning" core with more than 5000 metric tons of materials dropped from helicopters; and (ii) given this fact, along with new release data and results of radiochemical analyses of the core presented in my thesis, a scenario is hypothesized as to what may have happened to the core during the first 10 days after the accident. These aspects of my thesis have not been challenged.