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the business community, as too costly.

In the days before Clinton signed the bill into law, both parties were competing for political brownie points for its enactment, with the Republicans arguing that it was the result of a Republican-led Congress and the Democrats saying it could never have happened without the momentum begun by Clinton's much more ambitious — and ultimately doomed — health reform proposal.

Although the legislation is not as sweeping as that proposed by Clinton, portability and protection for preexisting conditions were "two popular and fundamental parts of the Clinton package," said Representative Henry A. Waxman (Democrat, California).

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FDA approves first acellular pertussis vaccines for infants

This summer the US Food and Drug Administration (FDA) licensed Connaught Laboratories' acellular pertussis vaccine (trade name, Tripedia) for use as a primary product in infants and young children. The first acellular vaccine approved for infant use, such products are likely to move into wider use among children, and there is growing momentum to extend pertussis vaccination coverage to adolescents and, possibly, to adults, as understanding of the disease grows.

Although acellular pertussis vaccines came into use in 1992 as boosters for children in the United States, primary vaccination has until now entailed use of the traditional product — inactivated whole cells of the bacterial pathogen *Bordetella pertussis*. Usually administered in combination with diphtheria and tetanus toxoids, this older vaccine has been associated with several deleterious side effects, generating a noisy and prolonged debate over its potential dangers.

Health officials in several countries, including the United Kingdom, Sweden and Japan, recommended switching over to use of acellular vaccines years ago. However, US public health officials were hamstrung while clinical safety and efficacy trials were being conducted and appropriate licensing applications filed with FDA before being approved. As recently as June, FDA officials were voicing frustration because long-awaited product licensing applications were still waiting in the wings.

Although certain claims about the older vaccine's safety record are not conclusive, fears about it linger, particularly among a group of vocal parents who maintain that the pertussis vaccine has caused permanent brain damage to their children. Several years ago, however, the authors of an Institute of Medicine report concluded that the evidence for such long-term damage is, at best, equivocal. Nonetheless, they and other experts also said the traditional pertussis vaccine did appear to be associated with other, less serious, side effects, including soreness at the site of injection, transient fevers, and fretfulness.

Frustration at the FDA over approval delays has given way to enthusiasm for the new products. "This new acellular pertussis vaccine, the first of several in the pipeline, represents an important advance," says FDA Commissioner David Kessler. In approving Connaught's acellular vaccine, FDA officials relied principally on two large-scale clinical trials conducted in Europe, one in Sweden and the other in Germany. In these studies, various formulations of the vaccine gave protective efficacies ranging from 69 to 80 percent. Other clinical studies, sponsored in part by the National Institute for Allergy and Infectious Diseases (NIAID), indicate efficacy rates of about 85 percent while also providing evidence of mild and infrequent side effects. In general, these efficacy rates are somewhat lower than those for the whole-cell vaccine, but the gain in safety seems to make this small sacrifice in efficacy worth accepting, many researchers in this field agree.

Pertussis, or whooping cough, can be especially serious for infants — causing paroxysmal coughing that can be deadly. According to data from the Centers for Disease Control and Prevention (CDC), nearly 9,500 cases of whooping cough were reported during 1994 and 1995 in the United States, where vaccination is nearly universal. Officials at the World Health Organization (WHO) report that nearly 50 million cases and about 350,000 deaths occur worldwide each year among unvaccinated individuals.

Grim as this picture is, it may be a seriously flawed underestimate of the real problem according to many experts in the field, who say that the prevalence of milder forms of pertussis could be much higher than is generally appreciated. If that is the case, public health officials may well revise current vaccination policies, adding teenagers and even adults to the list of those receiving booster doses of acellular pertussis vaccines.

In an effort to address such questions, officials at NIAID say they are now planning a study of pertussis infections in adult populations. Although data are scarce, some public health officials suspect that milder cases of *B. pertussis* infections among adolescents and adults help to maintain and spread the disease to more vulnerable populations, particularly to infants who are just beginning their vaccination regimens. If so, wider use of the newer acellular vaccines might curtail those cases among infants as well as extended bouts of coughing from misdiagnosed "colds" among those older populations.

Meanwhile, a debate about the appropriate makeup of acellular pertussis vaccines is under way, and evaluation of those products will be complicated further by the more expansive definition of pertussis that many experts now favor (that is, the recognition and diagnosis of "milder" cases). In any case, several recombinant acellular pertussis vaccines have been formulated using one or more components derived from *B. pertussis*, including pertussis toxin, filamentous hemagglutinin, an outer membrane protein from the bacterium called pertactin, and a few other antigens, to elicit better protective immune responses. John Robbins of NIAID argues that only one of those components, pertussis toxin, is needed for a vaccine to be effective. However, most vaccine developers favor multi-component products. With so many possibilities and combinations to try, as well as different population groups, an important challenge will involve finding a simpler, more efficient means for choosing, evaluating and eventually bringing into wide use the next generation of acellular pertussis vaccines.

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