

# Updated Recommendations for Use of Tetanus Toxoid, Reduced Diphtheria Toxoid, and Acellular Pertussis (Tdap) Vaccine in Adults Aged 65 Years and Older — Advisory Committee on Immunization Practices (ACIP), 2012

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Since 2005, the Advisory Committee on Immunization Practices (ACIP) has recommended a tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine booster dose for all adolescents aged 11 through 18 years (preferred at 11 through 12 years) and for those adults aged 19 through 64 years who have not yet received a dose (1,2). In October 2010, despite the lack of an approved Tdap vaccine for adults aged 65 years and older, ACIP recommended that unvaccinated adults aged 65 years and older be vaccinated with Tdap if in close contact with an infant, and that other adults aged 65 years and older may receive Tdap (3). In July 2011, the Food and Drug Administration (FDA) approved expanding the age indication for Boostrix (GlaxoSmithKline Biologicals, Rixensart, Belgium) to aged 65 years and older (4). In February 2012, ACIP recommended Tdap for all adults aged 65 years and older. This recommendation supersedes previous Tdap recommendations regarding adults aged 65 years and older.

The Pertussis Vaccines Work Group of ACIP reviewed the epidemiology of pertussis in adults aged 65 years and older and two cost-effectiveness models to assess the epidemiologic and economic impact of pertussis vaccination in this population. The Work Group also considered safety and immunogenicity data from clinical trials and observational studies on the use of Tdap in adults aged 65 years and older (3).

The two Tdap vaccines available in the United States, Boostrix and Adacel (Sanofi Pasteur, Toronto, Canada), differ in composition and approved age for use (Table). Only Boostrix is approved for adults aged 65 years and older; however, ACIP discussed the use of Adacel in this age group. On February 22, 2012, ACIP approved use of Tdap for all adults aged 65 years and older. This report summarizes data considered and conclusions made by ACIP and provides guidance for implementing the recommendation.

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## **Epidemiology of Pertussis in Older Adults**

Because pertussis is underdiagnosed and underreported substantially in all age groups, the actual burden of disease in adults aged 65 years and older is unknown (5). During 2000–2010, an annual average of 318 pertussis cases (range: 71–719 cases) in adults aged 65 years and older were reported each year through the National Notifiable Diseases Surveillance System (CDC, unpublished data, 2011). Challenges to diagnosing and reporting pertussis in all adults include 1) underrecognition of pertussis as a cause for cough illness, 2) atypical presentation of symptoms in adults, and 3) a low index of suspicion among providers (6,7). Few studies are focused on the burden of pertussis in adults aged 65 years and older. Among reported prospective studies, the calculated pertussis incidence ranged from 66 to 500 cases per 100,000 persons per year (8–11). Reported

pertussis incidence ranges from one to five cases per 100,000 in adults of similar age ranges (CDC, unpublished data, 2011); this 70-fold to 100-fold difference suggests that actual pertussis incidence in older adults is much higher than reported (CDC, unpublished data, 2011). ACIP supported the conclusion that the actual burden of pertussis in adults aged 65 years and older likely is at least 100 times greater than that reported.

### **Cost Effectiveness Analysis**

ACIP reviewed two unpublished cost-effectiveness models, developed independently by GlaxoSmithKline and CDC (12,13). Both models were developed to assess the epidemiologic and economic impact of Tdap vaccination in adults aged 65 years and older and demonstrated that a dose of Tdap for older adults resulted in a moderate decrease in the number of cases and outcomes (e.g., outpatient visits, hospitalizations, and deaths), which might represent a cost-effective intervention. Model results were most sensitive to incidence of pertussis; however, sensitivity analyses showed that even with a range of underreporting of incidence, Tdap vaccination might be cost-effective in this population. Reassured by the concordance between the two cost-effectiveness models, ACIP's interpretations were that the cost per case averted and cost per quality-adjusted life-year saved were modest, and pertussis incidence estimates accounting for underreporting were reasonable based on limited data and expert opinion.

### **Tdap Products in the United States**

Safety and immunogenicity data of Tdap administered to adults aged 65 years and older were reviewed by ACIP in October 2010 and in February 2012 (3). Published and unpublished data from clinical trials of Boostrix (N = 1,104) and Adacel (N = 1,170) on the safety and immunogenicity of Tdap in adults aged 65 years and older who received vaccine were provided by GlaxoSmithKline and Sanofi Pasteur.

**Safety.** For both Tdap products, the frequency and severity of adverse events in persons aged 65 years and older were comparable to those among persons aged less than 65 years. No increase in local or generalized reactions in Tdap recipients was observed, compared with persons who received Td. No serious adverse events were considered related to vaccination (3). Postmarketing data from the Vaccine Adverse Event Reporting System (VAERS) suggest that the safety profile of Tdap vaccine in adults aged 65 years and older was comparable to that of Td vaccine (14).

**Boostrix immunogenicity.** For diphtheria and tetanus, immune responses to Boostrix were noninferior to the immune responses elicited by a comparator Td vaccine (15). Immune responses to pertussis antigens (i.e., pertussis toxin [PT], filamentous hemagglutinin [FHA], and pertactin [PRN]) were noninferior to those observed following a 3-dose primary DTaP series with Infanrix (GlaxoSmithKline), according to predefined criteria discussed with and agreed to by FDA before study initiation (16). Boostrix contains the same three pertussis antigens as Infanrix, but in reduced quantities. The geometric mean concentrations for antibodies to PT, FHA, and PRN after Boostrix administration increased 7.4-fold to 13.7-fold over baseline levels (15).

**Adacel immunogenicity.** Antibody responses to diphtheria and tetanus toxoids in Adacel were noninferior to a comparator Td vaccine. Because a limited quantity of sera remained from infant efficacy trials, immune responses to three of the four pertussis antigens (FHA, PRN, and fimbriae [FIM]) in Adacel were bridged to a 3-dose DTaP (Daptacel [Sanofi Pasteur]) series, and PT was bridged to a 4-dose series. Immune responses were observed to all Adacel pertussis antigens but some did not meet predefined noninferiority criteria as agreed upon by FDA and Sanofi Pasteur (16); however, a 4.4-fold to 15.1-fold increase in anti-pertussis antibodies, depending on the antigen, was observed. Multiple other countries, including Canada, Australia, and European Union members have approved Adacel for use in persons aged 65 years and older. ACIP concluded that Adacel likely would provide protection in adults aged 65 years and older.

### **Guidance for Use**

**Tdap use in adults.** ACIP recommends that all adults aged 19 years and older who have not yet received a dose of Tdap should receive a single dose. Tdap should be administered regardless of interval since last tetanus or diphtheria toxoid-containing vaccine. After receipt of Tdap, persons should continue to receive Td for routine booster immunization against tetanus and diphtheria, according to previously published guidelines (1,2).

Currently, Tdap is recommended only for a single dose across all age groups. ACIP will begin discussions on the need for additional doses of Tdap and timing of revaccination of persons who have received Tdap previously.

**Tdap products in adults aged 65 years and older.** Providers should not miss an opportunity to vaccinate persons aged 65 years and older with Tdap. Therefore, providers may administer the Tdap vaccine they have available. When feasible, Boostrix should be used for adults aged 65 years and older; however, ACIP concluded that either vaccine administered to a person 65 years or older is immunogenic and would provide protection. A dose of either vaccine may be considered valid.

**Tetanus prophylaxis in wound management for adults.** As part of standard wound management care to prevent tetanus, a tetanus toxoid–containing vaccine might be recommended for wound management in adults aged 19 years and older if 5 years or more have elapsed since last receiving Td. If a tetanus booster is indicated, Tdap is preferred over Td for wound management in adults aged 19 years and older who have not received Tdap previously.

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**TABLE. Composition and approved age for use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccines, by trade name — United States, 2012**

Trade name	Manufacturer	FDA-approved age for use* (yrs)	Pertussis antigens ( $\mu\text{g}$ )				Diphtheria toxoid (Lf)	Tetanus toxoid (Lf)
			PT	FHA	PRN	FIM		
Boostrix	GlaxoSmithKline Biologicals	10 and older	8	8	2.5	—	2.5	5
Adacel	Sanofi Pasteur	11 through 64	2.5	5	3	5†	2	5