



FEB 04 1999

Food and Drug Administration
1401 Rockville Pike
Rockville MD 20852-1448

Dear Colleague:

On January 26, 1999, Pasteur-Merieux Connaught USA issued a voluntary recall of Tripedia™ DTaP vaccine lot number 0916490 which was distributed between February and June 1998. Routine stability testing determined that the potency of the diphtheria toxoid component, which had been acceptable at the time of release, had fallen below specifications. The potency of the tetanus and pertussis components of this lot continues to be acceptable. This recall applies only to Tripedia™ DTaP lot number 0916490 and not to other lots of Tripedia or other DTaP vaccines. The risk of diphtheria for most children who received Tripedia™ lot number 0916490 is extremely low because routine immunization has greatly diminished the incidence of diphtheria in the United States.

A primary series (three doses) of fully potent diphtheria toxoid-containing vaccine is required to reliably induce protective antibody levels against diphtheria, although five doses are recommended for pre-school aged children in the U.S. to provide optimal protection. While the risk of exposure to toxigenic strains of *C. diphtheriae* in the U.S. is low, diphtheria remains endemic in many countries. Additional doses of diphtheria toxoid-containing vaccine beyond those recommended in the childhood immunization schedule are associated with an increase in local reactions and therefore should be considered only for children vaccinated with Tripedia™ lot number 0916490 who will be at increased risk of exposure.

The U.S. Centers for Disease Control and Prevention (CDC), the American Academy of Pediatrics, and the American Academy of Family Physicians recommend the following for children who received one or more doses of Tripedia™ lot number 0916490:

Recommendations

1. **Remaining vaccine from Tripedia™ lot number 0916490 should not be administered.** Other lots of Tripedia™ can be used for vaccination of children.
2. **For children who are remaining in the United States until the scheduled 4th dose of DTaP at the age of 15-18 months, a supplemental dose of diphtheria toxoid-containing vaccine is not necessary regardless of the number of doses of Tripedia™ lot number 0916490 received.** Any remaining doses in the primary series should be administered using DTaP. It is recommended that the same DTaP product be used for all doses whenever possible.
3. **For children who are traveling outside of the United States and who received a scheduled 4th or 5th dose of DTaP with Tripedia™ lot number 0916490, a supplemental dose of diphtheria toxoid-containing vaccine is not necessary.**

4. For children who are traveling outside of the United States before the scheduled 4th dose of DTaP at the age of 15-18 months, the recommendation for a supplemental dose of diphtheria toxoid-containing vaccine depends on the risk of exposure to diphtheria and the number of doses of Tripedia™ lot number 0916490 (Table).

- a) **A supplemental dose of DT (diphtheria and tetanus toxoid vaccine) is recommended in the following setting:** Children who have completed a primary series with two or three doses of Tripedia lot number 0916490 and who have not yet received a 4th dose of DTaP at 15-18 months of age *and* who will be traveling to countries with a high risk of diphtheria. The CDC has determined these countries to include the Philippines, Indonesia, China, Thailand, Laos, Cambodia, Vietnam, Nepal, Bangladesh, India, Pakistan, Afghanistan, Iraq, Syria, Yemen, Mongolia, Algeria, Egypt, all countries in Sub-Saharan Africa, all countries of the former Soviet Union, Albania, Haiti, Dominican Republic, Ecuador, and Brazil. When a supplemental dose of DT vaccine is recommended:
- i) Minimum intervals between diphtheria toxoid-containing vaccines should be observed. The minimum interval is 4 weeks between a dose of DT and a dose of any other diphtheria toxoid-containing vaccine. There are no data on the use of DT at shorter intervals. The minimum interval is 6 months between the 3rd dose of DTaP (including doses of Tripedia™ lot number 0916490) and the 4th dose of DTaP, regardless of a supplemental dose of DT.
 - ii) Infants less than 12 months of age should receive a dose of DT before travel, followed by a 4th dose of DTaP at 15-18 months of age.
 - iii) Children 12 months of age or older who received the third dose of DTaP less than 6 months previously should receive a dose of DT before travel, followed by the 4th dose of DTaP at 15-18 months of age.
 - iv) Children 12 months of age or older who received the third dose of DTaP 6 or more months previously should receive the 4th dose of DTaP before travel, instead of a supplemental dose of DT.
- b) **A supplemental dose of DT is not necessary in the following settings:**
- i) Children who received only one dose of Tripedia™ lot number 0916490 as part of their primary series, regardless of the risk of diphtheria in the country of destination. These children should complete any remaining doses in the primary series with DTaP and should receive the 4th dose of DTaP at 15-18 months of age.
 - ii) Children who have received only two doses in the primary series, both of which were Tripedia™ lot number 0916490. These children should complete the primary series with DTaP and should receive the 4th dose of DTaP at 15-18 months of age. If these children will be traveling to a country with high risk of diphtheria following their 3rd dose of DTaP, a supplemental dose of DT should be given if time permits.

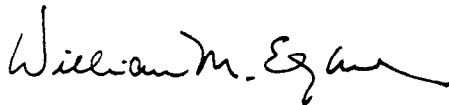
- iii) Children who received two or more doses of Tripedia™ lot number 0916490 as part of the primary series and have not yet received a 4th dose of DTaP and who are traveling to a country with a low risk of diphtheria.
4. To maintain optimal protection against diphtheria, all children should receive diphtheria toxoid-containing vaccine in a timely manner at the ages recommended in the childhood immunization schedule.

General questions regarding this voluntary recall can be directed to the FDA, Center for Biologics Evaluation and Research, Office of Communication, Training and Manufacturers Assistance at 1-800-835-4709.

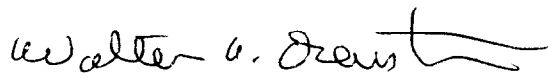
Questions regarding the need for supplemental doses of diphtheria toxoid-containing vaccines for children traveling outside the U.S. should be addressed to the Centers for Disease Control and Prevention's Immunization Hotline at 1-800-232-2522 for English and 1-800-232-0233 for Spanish.

Pasteur-Merieux Connaught USA has requested that any additional inventory of Tripedia™ lot number 0916490 be returned to them. Questions can be addressed to Pasteur-Merieux Connaught USA's Medical Affairs department at 1-800-325-7709.

Sincerely yours,



William M. Egan, Ph.D.
Acting Director
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research



Walter A. Orenstein, M.D.
Assistant Surgeon General
Director
National Immunization Program
Centers for Disease Control
and Prevention

Table. Recommendations for Children Who Travel to Areas of High Risk of Diphtheria and Who Received Tripedia™ Lot Number 0916490

Age (months)	Total doses of any diphtheria toxoid-containing vaccine (DTaP, DTwP, DT) received	Number doses administered as Tripedia™ lot number 0916490	Recommendation†
2 - 11	1-2	1-2	Complete primary series with DTaP‡
	3	1	4 th dose DTaP at 15-18 months of age
	3	2-3	Supplemental dose of DT, followed by 4 th dose DTaP at 15-18 months of age
12 or more	3	1	4 th dose DTaP at 15-18 months of age
	3	2 - 3	Supplemental dose of DT if less than 6 months has elapsed since 3 rd DTaP, followed by 4 th dose DTaP at 15-18 months of age <u>or</u> 4 th dose DTaP as early as 12 months of age if 6 months has elapsed since 3 rd DtaP
	4	1-3	5 th dose DTaP at 4 to 6 years of age
	5	1	Routine Td boosters

† The minimum interval is four weeks between a dose of DT and any other dose of diphtheria toxoid-containing vaccine. The minimum interval is six months between the third dose of DTaP (including doses of Tripedia™ lot number 0916490) and the fourth dose of DTaP.

‡ If time allows, those children who received 2 doses of Tripedia™ lot number 0916490 should also receive a supplemental dose of DT after the 3rd dose of DTaP and before travel.

DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine

DTwP = diphtheria and tetanus toxoids and whole-cell pertussis vaccine

DT = diphtheria and tetanus toxoids (for pediatric use)

Td = tetanus and diphtheria toxoids (for adolescent and adult use)