DEPARTMENT OF THE AIR FORCE
HEADQUARTERS UNITED STATES AIR FORCE
WASHINGTON DC

DEC 15 2010

MEMORANDUM FOR ALMAJCOM/SG

FROM: HQ USAF/SG3
1500 Wilson Boulevard, Suite 1600
Arlington, VA 22209

SUBJECT: Pneumococcal Conjugate Vaccine (PCV) – Change from 7-Valent to 13-Valent Formulation

As of 30 September 2010, the manufacturer of the pediatric vaccine PCV no longer is releasing the 7-valent form of the vaccine (PCV 7, Prevnar®) and is only selling the 13-valent form (PCV 13, Prevnar 13®).

The Advisory Committee on Immunization Practices (ACIP) recommends that clinics administering PCV change from the 7-valent to the 13-valent vaccine. Many MTFs have recently purchased PCV 7 before the vaccine was no longer being shipped. The current manufacturer of both PCV 7 and PCV 13 is Pfizer Pharmaceuticals (previously Wyeth), who has agreed to accept existing unopened vials of PCV 7 (Prevnar®) for a credit to the purchasing body (Prime Vendor or MTF if purchased directly). Information regarding return shipping is included in attachment 2. PCV 13 (Prevnar 13®) can be ordered exactly as PCV 7 was ordered by the MTF. Once PCV13 is available in your facility, remaining opened vials of PCV 7 (Prevnar®) vaccine should be disposed of according to the MTF's methods of destroying expired or otherwise unusable vaccine.

The attached MMWR summarizes the ACIP recommendations for use of PCV13 among children and provides guidance for the transition from PCV7 to the PCV13 immunization. Also attached is a talking paper highlighting a few areas from the MMWR to help clarify the MMWR. Before administering PCV13, vaccination providers should consult the package insert for precautions, warnings, and contraindications. It is advised that each MTF review the attached guidance and develop a local plan for the implementation of the new recommendations for the PCV13.

My POC for this memorandum is Lt Col Philip Gould, AFMSA/SG3PM, (703) 588-6470, DSN 425-6470, or philip.gould@pentagon.af.mil. The POC for logistics questions is Ms. Jan Mitchell, AFMSA/SGALC, (301) 619-4170, DSN 343-4170, or jan.mitchell@detrick.af.mil.

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Attachments:
1. Licensure of a 13-Valent Pneumococcal Conjugate Vaccine (PCV13) and Recommendations for Use Among Children --- Advisory Committee on Immunization Practices (ACIP), 2010. MMWR, 59(9): 258-261, 12 Mar 2010.
2. Talking Paper on Details Regarding Prevnar® Returns.
3. Talking Paper on Highlights From the ACIP Recommendations on the Use of PCV 13

Licensure of a 13-Valent Pneumococcal Conjugate Vaccine (PCV13) and Recommendations for Use Among Children — Advisory Committee on Immunization Practices (ACIP), 2010

On February 24, 2010, a 13-valent pneumococcal conjugate vaccine (PCV13 [Prevnar 13, Wyeth Pharmaceuticals Inc., a subsidiary of Pfizer Inc.]) was licensed by the Food and Drug Administration (FDA) for prevention of invasive pneumococcal disease (IPD) caused by the 13 pneumococcal serotypes covered by the vaccine and for prevention of otitis media caused by serotypes in the 7-valent pneumococcal conjugate vaccine formulation (PCV7 [Prevnar, Wyeth]). PCV13 is approved for use among children aged 6 weeks–71 months and succeeds PCV7, which was licensed by FDA in 2000. The Pneumococcal Vaccines Work Group of the Advisory Committee on Immunization Practices (ACIP) reviewed available data on the immunogenicity, safety, and cost-effectiveness of PCV13, and on estimates of the vaccine-preventable pneumococcal disease burden. The working group then presented policy options for consideration of the full ACIP. This report summarizes recommendations approved by ACIP on February 24, 2010, for 1) routine vaccination of all children aged 2–59 months with PCV13, 2) vaccination with PCV13 of children aged 60–71 months with underlying medical conditions that increase their risk for pneumococcal disease or complications, and 3) PCV13 vaccination of children who previously received 1 or more doses of PCV7 (*1*). CDC guidance for vaccination providers regarding transition from PCV7 to the PCV13 immunization program also is included.

Prevnar 13 Licensure

Vaccine formulation. PCV13 contains polysaccharides of the capsular antigens of *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F, individually conjugated to a nontoxic diphtheria CRM_{197} (CRM, cross-reactive material) carrier protein. A 0.5-mL PCV13 dose contains approximately 2 μg of polysaccharide from each of 12 serotypes and approximately 4 μg of polysaccharide from serotype 6B; the total concentration of CRM_{197} is approximately 34 μg. The vaccine contains 0.125 mg of aluminum as aluminum phosphate adjuvant and no thimerosal preservative. PCV13 is administered intramuscularly and is available in single-dose, prefilled syringes that do not contain latex (*2*).

Immunogenicity profile. The immunogenicity of PCV13 was evaluated in a randomized, double-blind, active-controlled trial in which 663 U.S. infants received at least 1 dose of PCV13 or PCV7 (*3*). To compare PCV13 antibody responses with those for PCV7, criteria for noninferior immunogenicity after 3 and 4 doses of PCV13 (pneumococcal immunoglobulin G [IgG] antibody concentrations measured by enzyme immunoassay) were defined for the seven serotypes common to PCV7 and PCV13 (4, 6B, 9V, 14, 18C, 19F, and 23F) and for the six additional serotypes in PCV13 (serotypes 1, 3, 5, 6A, 7F, and 19A). Functional antibody responses were measured by opsonophagocytosis assay (OPA) in a subset of the study population. Evaluation of these immunologic parameters indicated that PCV13 induced levels of antibodies that were comparable to those induced by PCV7 and shown to be protective against IPD (*3*).

Among infants receiving the 3-dose primary series, responses to three PCV13 serotypes (the shared serotypes 6B and 9V, and new serotype 3) did not meet the prespecified, primary endpoint criterion (percentage of subjects achieving an IgG seroresponse of ≥0.35 μg/mL 1 month after the third dose); however, detectable OPA antibodies to each of these three serotypes indicated the presence of functional antibodies (*3*). The percentages of subjects with an OPA titer ≥1:8 were similar for the seven common serotypes among PCV13 recipients (range: 90%–100%) and PCV7 recipients (range: 93%–100%); the proportion of PCV13 recipients with an OPA titer ≥1:8 was >90% for all of the 13 serotypes (*3*).

After the fourth dose, the IgG geometric mean concentrations (GMCs) were comparable for 12 of the 13 serotypes; the noninferiority criterion was not met for serotype 3. However, measurable OPA titers were present for all serotypes after the fourth dose; the percentage of PCV13 recipients with an OPA titer ≥1:8 ranged from 97% to 100% for the 13 serotypes and was 98% for serotype 3 (*3*).

A schedule of 3 doses of PCV7 followed by 1 dose of PCV13 resulted in somewhat lower IgG GMCs for the six additional serotypes compared with a 4-dose PCV13 series. However, the OPA responses after the fourth dose were comparable for the two groups, and the clinical relevance of these lower antibody responses is not known. The single dose of PCV13 among children aged ≥12 months who had received 3 doses of PCV7 elicited IgG immune responses to the six additional serotypes that were comparable to those after a 3-dose infant PCV13 series (*3*).

Safety profile. The safety of PCV13 was assessed in 13 clinical trials in which 4,729 healthy infants and toddlers were administered at least 1 dose of PCV13 and 2,760 children received at least 1 dose of PCV7, concomitantly with other routine pediatric vaccines. The most commonly reported (more than 20% of subjects) solicited adverse reactions that occurred within 7 days after each dose of PCV13 were injection-site reactions, fever, decreased appetite, irritability, and increased or decreased sleep (*2*). The incidence and severity of solicited local reactions at the injection site (pain/tenderness, erythema, and induration/swelling) and solicited systemic reactions (irritability, drowsiness/increased sleep, decreased appetite, fever, and restless sleep/decreased sleep) were similar in the PCV13 and PCV7 groups. These data suggest that the safety profiles of PCV13 and PCV7 are comparable (*2*); CDC will conduct postlicensure monitoring for adverse events, and the manufacturer will conduct a Phase IV study.

Supportive data for safety outcomes were provided by a catch-up study among 354 children aged 7–71 months who received at least 1 dose of PCV13. In addition, an open label study was conducted among 284 healthy U.S. children aged 15–59 months who had previously received 3 or 4 doses of PCV7 (*2*). Among these children, the frequency and severity of solicited local reactions and systemic adverse reactions after 1 dose of PCV13 were comparable to those among children receiving their fourth dose of PCV13 (*2*).

Indications and Guidance for Use

ACIP recommends PCV13 for all children aged 2–59 months. ACIP also recommends PCV13 for children aged 60–71 months with underlying medical conditions that increase their risk for pneumococcal disease or complications (Table 1).

No previous PCV7/PCV13 vaccination. The ACIP recommendation for routine vaccination with PCV13 and the immunization schedules for infants and toddlers through age 59 months who have not received any previous PCV7 or PCV13 doses are the same as those previously published for PCV7 (*4,5*). PCV13 is recommended as a 4-dose series at ages 2, 4, 6, and 12–15 months. Infants receiving their first dose at age ≤6 months should receive 3 doses of PCV13 at intervals of approximately 8 weeks (the minimum interval is 4 weeks). The fourth dose is recommended at age 12–15 months, and at least 8 weeks after the third dose (Table 2).

Children aged 7–59 months who have not been vaccinated with PCV7 or PCV13 previously should receive 1 to 3 doses of PCV13, depending on their age at the time when vaccination begins and whether underlying medical conditions are present (Table 2). Children aged 24–71 months with chronic medical conditions that increase their risk for pneumococcal disease should receive 2 doses of PCV13. Interruption of the vaccination schedule does not require reinstitution of the entire series or the addition of extra doses.

Incomplete PCV7/ PCV13 vaccination. Infants and children who have received 1 or more doses of PCV7 should complete the immunization series with PCV13 (Table 3). Children aged 12–23 months who have received 3 doses of PCV7 before age 12 months are recommended to receive 1 dose of PCV13, given at least 8 weeks after the last dose of PCV7. No additional PCV13 doses are recommended for children aged 12–23 months who received 2 or 3 doses of PCV7 before age 12 months and at least 1 dose of PCV13 at age ≥12 months.

Similar to the previous ACIP recommendation for use of PCV7 (*6*), 1 dose of PCV13 is recommended for all healthy children aged 24–59 months with any incomplete PCV schedule (PCV7 or PCV13). For children aged 24–71 months with underlying medical conditions who have received any incomplete schedule of <3 doses of PCV (PCV7 or PCV13) before age 24 months, 2 doses of PCV13 are recommended. For children with underlying medical conditions who have received 3 doses of PCV (PCV7 or PCV13) a single dose of PCV13 is recommended through age 71 months. The minimum interval between doses is 8 weeks.

TABLE 1. Underlying medical conditions that are indications for pneumococcal vaccination among children, by risk group — Advisory Committee on Immunization Practices (ACIP), United States, 2010

Risk group	Condition
Immunocompetent children	Chronic heart disease* Chronic lung disease† Diabetes mellitus Cerebrospinal fluid leaks Cochlear implant
Children with functional or anatomic asplenia	Sickle cell disease and other hemoglobinopathies Congenital or acquired asplenia, or splenic dysfunction
Children with immunocompromising conditions	HIV infection Chronic renal failure and nephrotic syndrome Diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease; or solid organ transplantation Congenital immunodeficiency§

* Particularly cyanotic congenital heart disease and cardiac failure.
† Including asthma if treated with prolonged high-dose oral corticosteroids.
§ Includes B- (humoral) or T-lymphocyte deficiency; complement deficiencies, particularly C1, C2, C3, and C4 deficiency; and phagocytic disorders (excluding chronic granulomatous disease).

TABLE 2. Recommended routine vaccination schedule for 13-valent pneumococcal conjugate vaccine (PCV13) among infants and children who have not received previous doses of 7-valent vaccine (PCV7) or PCV13, by age at first dose — Advisory Committee on Immunization Practices (ACIP), United States, 2010

Age at first dose (mos)	Primary PCV13 series*	PCV13 booster dose†
2–6	3 doses	1 dose at age 12–15 mos
7–11	2 doses	1 dose at age 12–15 mos
12–23	2 doses	—
24–59 (Healthy children)	1 dose	—
24–71 (Children with certain chronic diseases or immunocompromising conditions§)	2 doses	—

* Minimum interval between doses is 8 weeks except for children vaccinated at age <12 months for whom minimum interval between doses is 4 weeks. Minimum age for administration of first dose is 6 weeks.
† Given at least 8 weeks after the previous dose.
§ For complete list of conditions, see Table 1.

TABLE 3. Recommended transition schedule from 7-valent pneumococcal conjugate vaccine (PCV7) to 13-valent vaccine (PCV13) vaccination among infants and children, according to number of previous PCV7 doses received — Advisory Committee on Immunization Practices (ACIP), United States, 2010

Infant series			Booster dose	Supplemental PCV13 dose
2 mos	4 mos	6 mos	≥12 mos*	14–59 mos†
PCV7	PCV13	PCV13	PCV13	—
PCV7	PCV7	PCV13	PCV13	—
PCV7	PCV7	PCV7	PCV13	—
PCV7	PCV7	PCV7	PCV7	PCV13

* No additional PCV13 doses are indicated for children age 12–23 months who have received 2 or 3 doses of PCV before age 12 months and at least 1 dose of PCV13 at age ≥12 months.
† For children with underlying medical conditions (see Table 1), a single supplemental PCV13 dose is recommended through age 71 months

Complete PCV7 vaccination. A single supplemental dose of PCV13 is recommended for all children aged 14–59 months who have received 4 doses of PCV7 or another age-appropriate, complete PCV7 schedule (Table 3). For children who have underlying medical conditions, a single supplemental PCV13 dose is recommended through age 71 months. This includes children who have previously received the 23-valent pneumococcal polysaccharide vaccine (PPSV23). PCV13 should be given at least 8 weeks after the last dose of PCV7 or PPSV23.

In addition, a single dose of PCV13 may be administered to children aged 6–18 years who are at increased risk for IPD because of sickle cell disease, human immunodeficiency virus (HIV) infection or other immunocompromising condition, cochlear implant, or cerebrospinal fluid leaks, regardless of whether they have previously received PCV7 or PPSV23. Routine use of PCV13 is not recommended for healthy children aged ≥5 years.

Precautions and Contraindications

Before administering PCV13, vaccination providers should consult the package insert for precautions, warnings, and contraindications. Vaccination with PCV13 is contraindicated among persons known to have severe allergic reaction (e.g., anaphylaxis) to any component of PCV13 or PCV7 or to any diphtheria toxoid-containing vaccine (*2*).

Transition from PCV7 to PCV13

When PCV13 is available in the vaccination provider's office, unvaccinated children and children incompletely vaccinated with PCV7 should complete the immunization series with PCV13. If the only pneumococcal conjugate vaccine available in a provider's office is PCV7, that vaccine should be provided to children and infants who are due for vaccination; these children should complete their series with PCV13 at subsequent visits. Children for whom the supplemental PCV13 dose is recommended should receive it at their next medical visit, at least 8 weeks after the last dose of PCV7.

According to the manufacturer, supplies of PCV13 should be adequate to allow providers to vaccinate children according to the routine immunization schedule and provide a supplemental dose as recommended. For private vaccine supplies, providers should contact Pfizer's customer service department (telephone, 800-666-7248) with questions about purchasing quantities of PCV13 or returning PCV7 for credit. For public vaccine supplies, including Vaccines for Children Program vaccine, providers should contact their state/local immunization program to determine when PCV13 will become available for ordering in their jurisdiction and what to do with unused supplies of PCV7.

The PCV13 Vaccine Information Statement is available at http://www.cdc.gov/vaccines/pubs/vis/default.htm. Details about the routine pneumococcal conjugate vaccination schedule are available at http://www.cdc.gov/vaccines/recs/schedules/default.htm#child. Adverse events after receipt of any vaccine should be reported to the Vaccine Adverse Event Reporting System at http://vaers.hhs.gov.

References

1. CDC. ACIP provisional recommendations for use of 13-valent pneumococcal conjugate vaccine (PCV13) among infants and children. Available at http://www.cdc.gov/vaccines/recs/provisional/downloads/pcv13-mar-2010-508.pdf. Accessed March 9, 2010.
2. Food and Drug Administration. Vaccines: approved products. Prevnar 13 (pneumococcal 13-valent conjugate vaccine). Available at http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm201667.htm. Accessed March 5, 2010
3. Food and Drug Administration. Prevnar 13: clinical review of new product license application. Rockville, MD: Food and Drug Administration; 2010.
4. CDC. Preventing pneumococcal disease among infants and young children: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2000;49(No. RR-9).
5. CDC. Recommended immunization schedule for persons aged 0 through 18 years—United States, 2010. MMWR 2010;58(51&52).
6. CDC. Updated recommendation from the Advisory Committee on Immunization Practices (ACIP) for use of 7-valent pneumococcal conjugate vaccine (PCV7) in children aged 24–59 months who are not completely vaccinated. MMWR 2008;57:343–4.

TALKING PAPER

ON

PNEUMOCOCCAL CONJUGATE VACCINE PREVNAR® (PCV 7) VACCINE RETURNS

- Pfizer Pharmaceuticals is no longer releasing the 7-valent pneumococcal conjugate vaccine known as Prevnar®, as of 30 Sep 2010. In its place, the manufacturer is releasing the 13-valent form (Prevnar 13®).

- Pfizer is accepting returns of unopened, unexpired Prevnar® vaccine for credit to the purchasing body (to Prime Vendor , or to the MTF if purchased directly)

- Returns should include the following information:

  -- Full MTF Name
  -- Account number used in the purchase of Prevnar®
  -- DEA Number
  -- Number of Doses/Vials being returned
  -- Batch/Lot Numbers (if possible)
  -- Include "Pfizer DoD Accounts: Ms. Allison Becker (484) 865-1105" as an additional contact

- Returns of unopened, unexpired Prevnar® vaccine should be packaged appropriately and shipped to the following address:

  Stericycle, Inc
  Attn: Return Goods
  2670 Executive Dr, Suite A
  Indianapolis IN 46241
  Telephone: 866-608-3942

- Credits should take between 4 – 6 weeks. If credit has not been applied by this point, contact Ms Allison Becker at (484) 865-1105.

- Replacement Prevnar 13® should be ordered to replace quantities returned through the same mechanism as the original Prevnar® was ordered.

- Opened vials of Prevnar® vaccine should be destroyed according to MTF protocols for destroying unused vaccine that has expired or is otherwise unusable.

Jan Mitchell/AFMOA SGALC/343-4170/1 Dec 10

TALKING PAPER

ON

HIGHLIGHTS FROM THE ACIP RECOMMENDATIONS ON THE USE OF

PNEUMOCOCCAL CONJUGATE VACCINE, 13 VALENT (PCV 13)

- PCV13 is recommended as a 4-dose series at ages 2, 4, 6 and 12-15 months as shown in table 2 in the MMWR article[i].
- ACIP has provided a transition schedule for those children who have initiated the vaccination series with PCV7, see table 3.
- ACIP recommends PCV13 for all children aged 24-59 months to complete any incomplete PCV schedule (PCV7 or PCV13).
- ALL children aged 24-71 months with certain chronic diseases (see Table 1) should receive PCV13, the number of doses (1 or 2) will be determined on primary series.
- A single supplemental dose of PCV13 is recommended for ALL children ages 14-59 months who have received 4 doses of PCV7, or another age-appropriate, complete PCV7 schedule.
- A single dose of PCV13 may be administered to children aged 6-18 years of age who are at risk of invasive pneumococcal disease (sickle cell, HIV or other immunocompromising condition, cochlear implant, or cerebrospinal fluid leaks, regardless of previously received PCV7 or PPSV23.
- Routine use of PCV13 is not recommended for healthy children aged ≥5 years.

[i] Licensure of a 13-Valent Pneumococcal Conjugate Vaccine (PCV13) and Recommendations for Use Among Children --- Advisory Committee on Immunization Practices (ACIP), 2010. MMWR, 59(9): 258-261, 12 Mar 2010.

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