County of San Diego

PHYSICIANS' BULLETIN

Health and Human Services Agency ◆ P.O. Box 85222, San Diego, CA ◆ 92186-5222 ◆ www.co.san-diego.ca.us/cnty/cntydepts/health

October 2005 *"Focusing on Families as Our Customers"* No. 454

Influenza Immunization Recommendations for 2005-2006

Note: Medicare B reimburses for influenza vaccines.

Influenza is a viral respiratory illness which is mainly spread through sneezing and coughing. Each year in the United States about 36,000 people die due to influenza and its complications. Administration of influenza vaccine is the primary method for preventing flu and its severe complications. Both the trivalent inactivated influenza vaccine (TIV) and the live, attenuated influenza vaccine (LAIV) can be used to reduce the risk of influenza.

Extensive information on influenza disease and vaccine is available on the Web at www.cdc.gov/flu and in print in the Centers for Disease Control and Prevention (CDC) *MMWR Recommendations and Reports, Vol. 54, RR-8,* Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP), as well as subsequent MMWR publications on these subjects. The information in this Physicians' Bulletin is summarized from these sources.

Target Groups for Vaccination 2005-2006

Recommendations from the CDC for priority groups to receive influenza vaccine were published on Sept. 2, 2005. These are the recommendations that private and public health care providers are asked to follow. The conditions considered as priorities for the TIV in early October are:

- persons aged ≥65 years with and without chronic health conditions
- residents of long-term care facilities
- persons aged 2–64 years with **chronic health conditions**
  - heart disease
  - lung disease including asthma
  - kidney disease
  - metabolic diseases including diabetes
  - blood disorders including anemia
  - a weakened immune system caused, for example, by cancer or cancer treatment, HIV/AIDS, or steroid therapy
  - *(new this year)* persons with conditions that can compromise their respiratory function or handling of respiratory secretions or that increase their risk of aspiration--examples would be cognitive dysfunction, spinal cord injuries or other neuromuscular disorders
- children ages 6 months through 18 years old who are receiving long-term aspirin therapy and therefore might be at risk for developing Reye's syndrome if they develop influenza.
- children aged 6–23 months
- pregnant women
- household contacts and out-of-home caregivers of children aged<6 months
- health care workers (HCW) **who provide direct patient care**
  - physicians, nurses, and other personnel in hospital, long term care, and outpatient care settings
  - medical emergency response workers (paramedics and emergency medical technicians)

Importance of Vaccinating HCWs

HCWs should be vaccinated against influenza annually. Persons who are clinically or subclinically infected with influenza disease can transmit influenza virus to persons at high risk for complications from influenza. Studies indicate that hospital-based influenza outbreaks frequently occur where unvaccinated HCWs are employed. Beginning in October each year, health care facilities should offer influenza vaccinations to all workers, including night and weekend staff. Particular emphasis should be placed on providing vaccinations to persons who care for members of groups at high risk. Efforts should be made to educate HCWs regarding the benefits of vaccination and the potential health consequences of influenza illness for themselves, their family members, and their patients. All HCWs should be provided convenient access to influenza vaccine at the worksite, free of charge, as part of employee health programs.

Remaining Target Groups for Vaccination

October 24 and later is the time when those in the remaining priority groups are advised to get their flu vaccine. Those groups include:

- those who are household contacts of children and adults who are at increased risk for complications from influenza
- all persons aged 50 through 64 years
- anyone who wishes to reduce his or her chance of catching influenza

It is not necessary to use the prioritization recommendations for the intra-nasal spray vaccine, LAIV (FluMist™). Use of LAIV, when available, is encouraged for eligible persons (see below)

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and this may increase the availability of the inactivated influenza vaccine (TIV) for those in the priority groups.

LAIV may be administered at any time to:

- nonpregnant healthy persons aged 5-49 years, which includes most HCW, other persons in close contact with groups at high risk for influenza-related complications, and others desiring protection from influenza.

Influenza Vaccine and Thimerosal

Thimerosal, a mercury-containing compound, has been used as a preservative in vaccines for many years. Although no scientific evidence indicates that thimerosal in vaccines leads to serious adverse events in vaccine recipients, in 1999 the U.S.Public Health Service and other organizations recommended that efforts be made to eliminate or reduce the thimerosal content in vaccines to decrease total mercury exposure, chiefly among infants.

LAIV does not contain thimerosal. Thimerosal preservative-containing inactivated influenza vaccines, distributed in multi-dose containers in the United States, contain 25 mcg of mercury/ 0.5-mL dose. Inactivated influenza virus vaccines distributed in the United States will also be available in 2005 in a *thimerosal-free* formulation in both 0.25 mL and 0.5-mL single-dose syringes and a preservative-free formulation (which contains trace amounts of thimerosal) in 0.25-mL–dose syringes.

The risks for severe illness from influenza infection are elevated among both young children and pregnant women, and both groups benefit from vaccination by preventing illness and death from influenza. In contrast, no scientifically conclusive evidence exists of harm from exposure to thimerosal preservative-containing vaccine, whereas evidence is accumulating of lack of any harm resulting from exposure to such vaccines. Therefore, the benefits of influenza vaccination outweigh the theoretical risk, if any, for thimerosal exposure through vaccination.

Side Effects and Adverse Reactions

When educating patients regarding potential side effects, clinicians should emphasize that 1) TIV contains noninfectious killed viruses and cannot cause influenza; and 2) coincidental respiratory disease unrelated to influenza vaccination can occur after vaccination. The Vaccine Information Statements (VISs), *Inactivated Influenza Vaccine, What You Need to Know,* 2005-2006, and *Live, Attenuated Intranasal Vaccine, What You Need to Know*, 2005-2006 (see *Influenza and Immunization Resources*) can be an effective tool to educate about the risks and benefits of the vaccine and side effects. VISs are to be given to patients to read before administering flu vaccine.

Health care professionals should promptly report all clinically significant adverse events after influenza vaccination to VAERS (see Influenza and Immunization Resources), even if they are not certain that the vaccine caused the event. Immediate, presumably allergic reactions (such as hives, angioedema, allergic asthma, and systemic anaphylaxis) rarely occur after influenza vaccination. These reactions probably result from hypersensitivity to certain vaccine components; the majority of reactions probably are caused by residual egg protein. Although current influenza vaccines, the LAIV as well as the inactivated, contain only a limited quantity of egg protein, this protein can induce immediate hypersensitivity reactions among persons who have severe egg allergy. Persons who have had hives or swelling of the lips or tongue, or who have experienced acute respiratory distress or collapse after eating eggs should consult a physician for appropriate evaluation to help determine if the vaccine should be administered. Persons who have documented immunoglobulinE (IgE)-mediated hypersensitivity to eggs, including those who have had occupational asthma or other allergic responses to egg protein, might also be at increased risk for allergic reactions to influenza vaccine, and consultation with a physician should be considered. See *MMWR Recommendations and Reports, Vol. 54, RR-8,* p. 15 referencing protocols to safely administer influenza vaccine to persons with egg allergies.

Live, Attenuated Influenza Vaccine Recommendations

The LAIV licensed for use in the United States is produced by MedImmune, Inc. (Gaithersburg, Maryland; http://www.medimmune.com) and marketed under the name FluMist®.

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Table 1: Inactivated Influenza Vaccine* Dose By Age Group, 2005-2006

Age group	Dose	Number of doses	Route§
6-35 mos.	0.25 mL	1 or 2¶	Intramuscular
3-8 yrs.	0.50 mL	1 or 2¶	Intramuscular
≥9 yrs.	0.50 mL	1	Intramuscular

* A 0.5-mL dose contains 15 µg each of A/California/7/2004(H3N2)-like, A/New Caledonia/20/99 (H1N1)-like, and B/Shanghai/361/2002-like antigens. For the A/California/7/2004(H3N2)-like antigen, manufacturers may use the antigenically equivalent A/New York/55/2004 virus, and for the B/Shanghai/361/2002-like antigen, manufacturers may use the antigenically equivalent B/Jilin/20/2003 virus or B/Jiangsu/10/2003 virus. Manufacturers include Sanofi Pasteur, Inc. (formerly Aventis Pasteur, Inc.) (Fluzone® split virus); GlaxoSmithKline, Inc. (Fluarix™), and Chiron (Fluvirin™ purified surface-antigen vaccine). Fluarix is licensed only for those 18 years of age and older. Fluzone is approved by the Food and Drug Administration for use among persons aged ≥6 months. Fluvirin is approved for use only among persons aged ≥4 years. For further product information, call Sanofi Pasteur at 800-822-2463, GlaxoSmithKline at 888-825-5249, or Chiron at 800-244-7668.

§ For adults and older children, the recommended site of vaccination is the deltoid muscle. The preferred site for infants and young children is the anterolateral aspect of the thigh.

¶ Two doses administered at least 1 month apart are recommended for children aged <9 years who are receiving influenza vaccine for the first time.

NOTE: MedImmune (877-358-6478) is the manufacturer of FluMist™, the intranasal LAIV. The dosage is one spray to each nostril. Children five through eight years of age who are receiving only LAIV or TIV/LAIV for the first time are recommended to have a second dose 6-10 weeks after the first dose.

It is a live, trivalent, intranasally administered vaccine that is attenuated, producing mild or no signs or symptoms related to influenza virus infection. LAIV is approved for healthy persons age 5 years through 49 years who are not pregnant. The vaccine is supplied in individual sprayers for nasal administration, and must be stored at 5ºF (–15ºC) or colder preferably in a manual-defrost freezer or in the freezer compartment of a refrigerator/ freezer with separate freezer and refrigerator doors. If necessary the vaccine can be thawed in a refrigerator and stored at 35-46ºF (2-8ºC) for up to 60 hours before use.

Details on storage, dosage, administration, side effects of LAIV are detailed at www.flumist.com, in the *MMWR Volume 54, RR-8,* as well as in the package insert. LAIV is intended for intranasal administration only and should not be administered by the intramuscular, intradermal, or intravenous route. Side effects can include runny nose and headache.

Low-level introduction of vaccine viruses into the environment is likely unavoidable when administering LAIV. The risk of acquiring vaccine viruses from the environment is unknown, but likely to be limited. Severely immunosuppressed persons (e.g., patients with hematopoetic stem cell transplants) should not administer LAIV. However, other persons at high risk for influenza complications may administer LAIV. People who have received LAIV may provide care or may visit anyone, except the severely immunosuppressed.

Optimal Timing of Influenza Vaccine Activities

The optimal time to vaccinate is usually during October–November. As noted above, for the beginning of this 2005-2006 season, ACIP recommends that vaccine providers focus their vaccination efforts in early October on those priority groups noted in the earlier section (see *Target Groups for Vaccination 2005-2006*). Vaccination of children aged <9 years who are receiving vaccine for the first time should also begin in October or earlier because those persons need a booster dose of the inactivated flu vaccine 1 month after the initial dose, or 6 weeks after if using the LAIV. Beginning Oct. 24, the prioritization recommendations are relaxed and other priority groups, as well as anyone who wishes to reduce their chances of getting the flu, are advised to get flu vaccine.

In facilities housing older persons (e.g., nursing homes), vaccination before October typically should be avoided because antibody levels in such persons can begin to decline within a limited time after vaccination.

Vaccination in December and Later

After November, many persons who should or want to receive influenza vaccine remain unvaccinated. In addition, substantial amounts of vaccine have remained unused during three of the past four influenza seasons. To improve vaccine coverage, influenza vaccine should continue to be offered in December and throughout the influenza season as long as vaccine supplies are available, even after influenza activity has been documented in the community. In the U.S., seasonal influenza activity may be noted as early as October or November, but influenza activity has not reached peak levels in the majority of recent seasons until late December (as experienced in the 2003-2004 season) through early March.

Recommendations for Using Antiviral Agents for Influenza

Antiviral drugs for influenza are an adjunct to influenza vaccine for controlling and preventing influenza. However, these agents are not a substitute for vaccination**.** Four licensed influenza antiviral agents are available in the United States: amantadine, rimantadine, zanamivir, and oseltamivir. The four drugs differ in pharmacokinetics, side effects, routes of administration, approved age groups, dosages, and costs. An overview of the indications, use, administration, and known primary side effects of these medications is presented in the MMWR. Information contained in that report might not represent FDA approval or approved labeling for the antiviral agents described. Package inserts should be consulted for additional information. Please see Table 2 on page 5 and the MMWR issue for further information.

Role of Laboratory Diagnosis

Appropriate treatment of patients with respiratory illness depends on accurate and timely diagnosis. Early diagnosis of influenza can reduce the inappropriate use of antibiotics and provide the option of using antiviral therapy. However, because certain bacterial infections can produce symptoms similar to influenza, bacterial infections should be considered and appropriately treated, if suspected. Influenza surveillance by state and local health departments and CDC can provide information regarding the presence of influenza viruses in the community.

Physicians and laboratories are encouraged to report positive influenza detections to the County of San Diego Public Health Laboratory by phone (619-692-8500) or fax (619-692-8558) and when possible, to submit specimens for viral culture and isolate subtyping. Surveillance data is available at **www.emansandiego.com**.

Influenza Vaccine Campaign Offers Opportunity to Provide Other Needed Adult Vaccines

Seniors and others at high risk of complications from influenza visit medical care providers each fall to receive influenza vaccine.

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The *Physicians' Bulletin* is published on an as-needed basis by the County of San Diego Health and Human Services Agency to provide updated information on health issues of concern to San Diego County's medical community.

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Medical care providers should use this opportunity to evaluate these adults for other needed vaccines as well.

Vaccines are listed below:

1. Pneumococcal polysaccharide vaccine (PPV-23),
2. Tetanus and diphtheria vaccine (Td),

And if medically and/or occupationally indicated:

3. Hepatitis A vaccine,
4. Hepatitis B vaccine,
5. Measles, mumps and rubella combination vaccine (MMR),
6. Varicella vaccine,
7. Meningococcal vaccine.

Physicians are urged to capitalize on office visits by those at risk for influenza to provide all needed vaccines. To receive a free chart on adult vaccine recommendations, call the Immunization Branch at (619) 692-8661.

Influenza and Immunization Resources

The CDC's 2005 report, *Prevention and Control of Influenza, Recommendations of the Advisory Committee on Immunization Practices (ACIP),* (Vol. 54, RR-8, July 29, 2005.) includes information on the disease, vaccine, target groups, strategies and the use of antiviral agents in preventing and/or treating influenza. **For a copy of this report, please go to the CDC website noted below or call the Immunization Program at (619) 692-8661.**

The following is a list of World Wide Web sites for accessing information and promotional materials on influenza, influenza vaccine and related topics:

http://www.cdc.gov/flu This is the CDC National Immunization Program's flu site, and contains information about vaccine supply, flu treatment and management, a weekly flu activity report, and other items. There will soon be a gallery of patient educational materials developed for the 2005-2006 flu season. The gallery will contain downloadable master copies suitable for an office photocopier, and other masters intended for reproduction by commercial printers.

In addition to the CDC's influenza reports mentioned above, this site contains pneumococcal vaccine educational materials and weekly influenza surveillance reports beginning in October. This site has a wide variety of links to other sites with fact sheets for providers and patients.

http://www.lumetra.com/physicianoffices/qualitymeasures/iz/index.asp: Lumetra, formerly CMRI, is the designated Quality Improvement Organization (QIO) in California for Medicare. Materials available about flu and pneumonia include information on Medicare billing, and materials on simple proven strategies to reduce flu and pneumonia illnesses. Order online or at 1-800-841-1602.

www.sdchip.org: This site is maintained by Community Health Improvement Partners (CHIP)**,** a collaboration of health care organizations, providers and community groups working in San Diego County to increase awareness of and responsiveness to community health needs. When vaccine becomes available, this web site will feature a list of more than 300 public and private locations in San Diego County where flu shots will be offered. Also, the site has downloadable flu and pneumococcal information in English and 7 other languages, and links to other immunization-related web sites. Flu shot clinic information is also available through CHIP's toll-free number at 1-877-FLU-0202 (1-877-358-0202).

www.immunization-sd.org: The San Diego County Immunization Initiative website contains immunization information specifically for local health care providers, including general immunization recommendations for children and adults, vaccine safety issues, the San Diego Immunization Registry, flu information, as well as the flu shot clinic schedule (when available) at the County Public Health Centers. There are also links to other websites, such as the CDC's influenza information site.

www.immunize.org: The Immunization Action Coalition has a wealth of print materials that can be downloaded and reproduced. Included are childhood and adult materials and official Vaccine Information Statements including, *"Influenza Vaccine, What You Need To Know"* in many languages. VISs are to be given to patients to read before flu vaccine is administered. The California DHS web site has the influenza VIS in English and Spanish with a consent portion attached (**www.dhs.ca.gov/ps/dcdc/izgroup/flu.htm**).

www.cms.hhs.gov/preventiveservices/2.asp: This is the Centers for Medicare and Medicaid Services (CMS) site about the influenza/pneumococcal campaign. (CMS is the new name of the Health Care Financing Administration or HCFA.) It also contains information on Medicare, Medicaid and other programs, including how they relate to influenza vaccine.

www.nfid.org: This is the web site of the National Foundation for Infectious Diseases (NFID), which offers information on various infectious diseases and has an "influenza web presentation." Timely and helpful resources with strategies on increasing influenza immunization rates in infants and children and in HCWs are available on this site. Another part of NFID's site is devoted to the National Coalition for Adult Immunization. It offers adult immunization standards, schedules, recommendations, fact sheets and more. Also, NFID will be promoting the National Adult Immunization Awareness Week from September 25-October 1, 2005.

www2.sdcounty.ca.gov/hhsa/ServiceDetails.asp?ServiceID=826: This is the County of San Diego Health and Human Services Agency website, which has location and contact information for clinics which provide low-cost childhood and adult immunizations. *(Please note that influenza immunization clinic information will probably not be available at this site until early October, when the specifics of the flu shot clinics are finalized.)*

http://vaers.hhs.gov: This is the website for The Vaccine Adverse Event Reporting System (VAERS). Health care providers and manufacturers are required by law to report suspect reactions to vaccines listed in the Vaccine Injury Table and are encouraged to report even if the vaccines are not listed. VAERS forms are available at 1-800-822-7967 or online at this site.

2005-2006 Influenza Vaccine Manufacturers/Distributors

Aventis-Pasteur, Inc. (*Fluzone*®) 1-800-VACCINE (1-800-822-2463)

Chiron (***Fluvirin***™) 1-800-244-7668

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GlaxoSmithKline (*Fluarix*™) 1-888-825-5249

MedImmune (*FluMist*® LAIV) 1-877-633-4411

Sources

1. Advisory Committee on Immunization Practices, National Immunization Program, Centers for Disease Control and Prevention. *Recommended Childhood and Adolescent Immunization Schedule, United States, July-December 2004.*
2. Advisory Committee on Immunization Practices, National Immunization Program, Centers for Disease Control and Prevention. *Prevention and Control of Influenza, Recommendations of the Advisory Committee on Immunization Practices.* MMWR 2005;Vol. 54:RR-8.
3. Centers for Disease Control and Prevention. *Inactivated Influenza Vaccine, What You Need To Know.*
4. National Foundation for Infectious Diseases. *Influenza Immunization Among Health Care Workers, Call To Action* and *Increasing Influenza Immunization Rates in Infants and Children: Putting Recommendations Into Practice.* Both are available at: www.nfid.org.

Table 2: Recommended Daily Dosage of Influenza Antiviral Medications for Treatment and Prophylaxis

Recommended daily dosage of influenza antiviral medications for treatment and prophylaxis — United States

	Age group (yrs)				
Antiviral agent	**1–6**	**7–9**	**10–12**	**13–64**	**≥65**
Amantadine*					
Treatment, influenza A	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	100 mg twice daily§	100 mg twice daily§	≤100 mg/day
Prophylaxis, influenza A	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	100 mg twice daily§	100 mg twice daily§	≤100 mg/day
Rimantadine¶					
Treatment,** influenza A	NA††	NA	NA	100 mg twice daily§ §§	100 mg/day
Prophylaxis, influenza A	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	100 mg twice daily§	100 mg twice daily§	100 mg/day¶¶
Zanamivir* ††† **					
Treatment, influenza A and B	NA	10 mg twice daily	10 mg twice daily	10 mg twice daily	10 mg twice daily
Oseltamivir					
Treatment,§§§ influenza A and B	Dose varies by child's weight¶¶¶	Dose varies by child's weight¶¶¶	Dose varies by child's weight¶¶¶	75 mg twice daily	75 mg twice daily
Prophylaxis, influenza A and B	NA	NA	NA	75 mg/day	75 mg/day

NOTE: Amantadine manufacturers include Endo Pharmaceuticals (Symmetrel® — tablet and syrup); Geneva Pharms Tech (Amantadine HCL — capsule); USL Pharma (Amantadine HCL — capsule and tablet); and Alpharma, Carolina Medical, Copley Pharmaceutical, HiTech Pharma, Mikart, Morton Grove, and Pharmaceutical Associates (Amantadine HCL — syrup), and Sandoz. Rimantadine is manufactured by Forest Laboratories (Flumadine® — tablet and syrup); Corepharma, Impax Labs (Rimantadine HCL — tablet), and Amide Pharmaceuticals (Rimantadine HCL — tablet). Zanamivir is manufactured by GlaxoSmithKline (Relenza® — inhaled powder). Oseltamivir is manufactured by Roche Pharmaceuticals (Tamiflu® — tablet). This information is based on data published by the Food and Drug Administration (FDA), which is available at http://www.fda.gov.

* The drug package insert should be consulted for dosage recommendations for administering amantadine to persons with creatinine clearance ≤50 mL/min/1.73m^2.

† 5 mg/kg body weight of amantadine or rimantadine syrup = 1 tsp/2.2 lbs.

§ Children aged ≥10 years who weigh <40 kg should be administered amantadine or rimantadine at a dosage of 5 mg/kg body weight/day.

¶ A reduction in dosage to 100 mg/day of rimantadine is recommended for persons who have severe hepatic dysfunction or those with creatinine clearance ≤10 mL/min. Other persons with less severe hepatic or renal dysfunction taking 100 mg/day of rimantadine should be observed closely, and the dosage should be reduced or the drug discontinued, if necessary.

** Only approved by FDA for treatment among adults.

†† Not applicable.

§§ Rimantadine is approved by FDA for treatment among adults. However, certain specialists in the management of influenza consider rimantadine appropriate for treatment among children. Studies evaluating the efficacy of amantadine and rimantadine in children are limited, but they indicate that treatment with either drug diminishes the severity of influenza A infection when administered within 48 hours of illness onset (*243*).

¶¶ Older nursing-home residents should be administered only 100 mg/day of rimantadine. A reduction in dosage to 100 mg/day should be considered for all persons aged ≥65 years, if they experience possible side effects when taking 200 mg/day.

*** Zanamivir administered through inhalation by using a plastic device included in the medication package. Patients will benefit from instruction and demonstration of the correct use of the device.

††† Zanamivir is not approved for prophylaxis.

§§§ A reduction in the dose of oseltamivir is recommended for persons with creatinine clearance <30 mL/min.

¶¶¶ The dose recommendation for children who weigh ≤15 kg is 30 mg twice a day. For children who weigh >15–23 kg, the dose is 45 mg twice a day. For children who weigh >23–40 kg, the dose is 60 mg twice a day. And, for children who weigh >40 kg, the dose is 75 mg twice a day.

Source: CDC. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2005;Vol. 54, RR-8 (July 29, 2005):26.