

# Recommendations for the Prevention and Control of Influenza in California Long-Term Care Facilities, 2008-2009

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## Recommendations for the Prevention and Control of Influenza in California Long-Term Care Facilities, 2008-2009

This report updates the 2007-2008 recommendations regarding the prevention and control of influenza outbreaks in California long-term care facilities (LTCFs). These recommendations were developed by the California Department of Public Health (CDPH), Division of Communicable Disease Control, Infectious Diseases and Immunization Branches, using information from the Centers for Disease Control and Prevention (CDC), in consultation with the Licensing and Certification Program, and are revised annually. This information is intended to be advisory only and was developed to assist facility infection control committees in the development of a rational approach to the control of influenza in LTCFs.

The resources used to guide these recommendations are:

Prevention and Control of Influenza, Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2008:

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr57e717a1.htm>

Infection Control Measures for Preventing and Controlling Influenza Transmission in Long-Term Care Facilities:

<http://www.cdc.gov/flu/professionals/infectioncontrol/longtermcare.htm>

Using Antiviral Medications to Control Influenza Outbreaks in Institutions:

<http://www.cdc.gov/flu/professionals/infectioncontrol/institutions.htm>

All the CDC recommendations for infection control for influenza in healthcare facilities are available at: <http://www.cdc.gov/flu/professionals/infectioncontrol/index.htm>

Information on methods of reimbursement for influenza and pneumococcal vaccine are available from in "Prevention and Control of Vaccine-Preventable Diseases in Long-Term Care Facilities" at: [http://www.cdc.gov/vaccines/pubs/downloads/bk\\_long-term-care.pdf](http://www.cdc.gov/vaccines/pubs/downloads/bk_long-term-care.pdf)

Other infection control recommendations for long-term care facilities are available from CDHP at <http://www.cdph.ca.gov/programs/idb/Pages/default.aspx> and from CDC at [http://www.cdc.gov/ncidod/dhqp/gl\\_longterm\\_care.html](http://www.cdc.gov/ncidod/dhqp/gl_longterm_care.html)

Additional information on influenza, including influenza vaccine, is available from CDC at:

<http://www.cdc.gov/flu/> and from CDPH at:

[http://www.cdph.ca.gov/healthinfo/discond/Pages/Influenza\(Flu\).aspx](http://www.cdph.ca.gov/healthinfo/discond/Pages/Influenza(Flu).aspx) and

<http://www.cdph.ca.gov/programs/immunize/Pages/default.aspx>

<http://www.cdph.ca.gov/programs/vrdl/Pages/default.aspx>

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## I. CDPH Recommendations for LTCFs

- Vaccinate all LTCF residents and staff against influenza each autumn as soon as vaccine becomes available, and if possible by October, before influenza disease is present in the community. A federal rule requires that LTCFs serving Medicare and Medicaid (MediCal) patients must provide immunizations against influenza and pneumococcal disease to all residents if they want to continue in these programs.
- LTCFs should ensure that standing orders are in place for residents  $\geq 50$  years of age to receive pneumococcal vaccination at admission and annual influenza vaccination of as permitted by California law and required by Federal mandate.
- Residents admitted during influenza season should receive influenza vaccine when they are admitted if they have not been previously vaccinated that season.
- New staff hired during influenza season who have not yet been vaccinated should receive influenza vaccine at the time of hire.
- LTCFs are encouraged to ask staff who refuse influenza vaccination to sign a declination form as a means to increase staff vaccination rates. A sample declination form is provided in [Appendix 1](#).
- Consider requesting that staff who state they have been vaccinated elsewhere submit proof of vaccination to the facility.
- **Immediately report all outbreaks of respiratory illness to the local health department and the Licensing and Certification district office.** Health department personnel can provide information about influenza activity in the area and about diagnostic specimen collection and coordination.
- During influenza outbreaks, consider the use of antiviral medications (oseltamivir or zanamivir) and implement the other outbreak prevention and control measures described in this guidance.

## II. Influenza and Influenza-Like Illness

Influenza is a respiratory illness caused by influenza type A or type B viruses. Typical symptoms of influenza include the acute onset of fever, respiratory symptoms (such as cough, sore throat, and other “cold-like” symptoms), muscle aches and headache. Persons with acute onset of fever and cough, often with nasal congestion, are most likely to have influenza. However, elderly LTCF residents, particularly those with underlying illness, may not have typical symptoms, such as a fever. Some have underlying conditions or are receiving medications with antipyretic (anti-fever) effects that modify the manifestations of influenza. Many also have chronic cough and other respiratory symptoms due to chronic lung disease. Some cannot reliably report symptoms such as sore throat or muscle aches. Therefore, the presentation of influenza in LTCF residents is not consistent or predictable. Influenza should be considered (particularly during influenza season) in residents with any combination of the following:

- Fever  $\geq 37.8^{\circ}\text{C}$  (may be absent or low in elderly LTCF residents)
- New onset cough and/or sore throat
- Nasal congestion
- Malaise (feeling ill)
- Chills
- Muscle aches, joint aches, or headache
- Change in respiratory status (increased cough, sputum production, breathing rate); change in mental status or appetite

Other respiratory viruses and some bacteria can cause similar illnesses, particularly in elderly LTCF residents. These are referred to as “influenza-like illnesses.” The difference between influenza and other acute respiratory infections cannot be determined on the basis of symptoms alone and laboratory testing is necessary (see Section VI).

Most young, healthy people who are infected with influenza recover completely within 1-2 weeks. However, serious illness and death in otherwise healthy healthcare workers, while rare, can also occur. Severe pneumonia due to *Staphylococcus aureus* and methicillin *Staphylococcus aureus* (MRSA) following influenza in previously healthy persons is of increasing concern. Most importantly, influenza can cause serious illness and death in LTCF residents because of their age and chronic health problems. LTCF residents may also be at high risk of exposure to influenza, since the virus spreads easily in environments where people live close to each other and once influenza enters a LTCF, it can spread rapidly. Influenza occurs annually, typically in the winter between October and April and peak activity in a community usually lasts from 6 to 8 weeks, often spanning the New Year period.

These recommendations are being issued in anticipation of possible influenza outbreaks in California LTCFs this season. During the influenza season, information on influenza activity in California can be accessed at: <http://www.cdph.ca.gov/programs/vrdl/Pages/default.aspx>

### III. Influenza Transmission

Influenza is thought to be primarily spread from person-to-person by large droplets of respiratory secretions from an infected person. This occurs when infected persons cough, sneeze, or talk, expelling droplets, which are then directly deposited onto the surfaces of the upper respiratory tracts (nose, throat) of susceptible persons who are within approximately 3 feet of the infected person.

Transmission also may occur by direct or indirect (person-object-person) contact when a susceptible person picks up the virus on their hands and then touches their nose. Influenza virus can survive for 24-48 hours on nonporous surfaces and 8-12 hours on porous surfaces such as paper or cloth. Airborne transmission, inhalation of small droplets (droplet nuclei) expelled into the air when an infected person is coughing or during aerosol-generating procedures, may also occur. The degree to which airborne transmission contributes to influenza transmission is uncertain and has not been adequately studied.

The most important sources of influenza virus are infected persons. Infected persons are most infectious during the first 3 days of illness; however, they can shed the virus beginning the day before, and up to 7 or more days after the onset of symptoms. Children and severely immunodeficient persons may shed virus for longer periods. In addition, infected but asymptomatic persons can shed the virus and be infectious.

### IV. Influenza Vaccine

People 65 years of age and older account for more than 90% of influenza deaths. Vaccination is the most effective measure for reducing the illness and deaths from influenza. Since the primary source of infection in residents is staff and the efficacy of vaccination is often reduced in elderly residents, facilities should make a concerted effort to ensure the annual vaccination of staff. Studies have shown that staff vaccination reduces deaths from respiratory infections in residents. Vaccination can also lower staff absenteeism.

California law now requires that acute care hospitals offer influenza vaccine to staff at no charge and to require those declining vaccination to sign a declination form.

There are two types of influenza vaccine: trivalent inactivated influenza vaccine (TIV) and live, attenuated influenza vaccine (LAIV).

#### **Trivalent Inactivated Influenza Vaccine (TIV)**

TIV must be injected and contains inactivated (killed) influenza virus; it cannot cause influenza. TIV is the type of vaccine typically used in LTCFs because live vaccines are not recommended for LTCF residents. When the vaccine and circulating virus strains are similar, TIV is expected to prevent influenza in 70%-90% of healthy vaccinated adults <65 years of age.

Although TIV effectiveness in preventing illness in elderly LTCF residents is estimated at 20%-40%, it can be up to 80% effective in preventing influenza-related death.

The following persons should not receive TIV:

- persons known to have anaphylactic hypersensitivity to eggs or to other components of the influenza vaccine without first consulting a physician;
- persons with moderate-to-severe acute febrile illness usually should not be vaccinated until their symptoms have abated (minor illnesses with or without fever do not contraindicate use of influenza vaccine, particularly among children with mild upper-respiratory tract infection or allergic rhinitis);
- persons who are not at high risk for severe influenza complications and who are known to have experienced Guillain-Barré syndrome within 6 weeks after a previous influenza vaccination.

### **Live Attenuated Influenza Vaccine (LAIV)**

FluMist®, the nasal-spray LAIV, is an option for healthy individuals, ages 2-49 years of age, and may be used as a substitute for standard inactivated injectable influenza vaccine for staff in LTCFs. LAIV is given intranasally.

LAIV is **not** recommended for LTCF residents. Staff who care for patients with severely weakened immune systems (i.e., patients who have recently had a bone marrow transplant and require a protected environment) can receive LAIV, but should refrain from contact with severely immunosuppressed patients for 7 days after vaccine receipt.

The following persons should not receive LAIV:

- persons aged <2 years or those aged  $\geq 50$  years of age;
- history of recurrent wheeze in those <5 years of age;
- persons with asthma, reactive airways disease, or other chronic disorders of the pulmonary or cardiovascular systems; persons with other underlying medical conditions, including metabolic diseases such as diabetes, renal dysfunction, and hemoglobinopathies; or persons with known or suspected immunodeficiency diseases or who are receiving immunosuppressive therapies;
- children or adolescents receiving aspirin or other salicylates (because of the association of Reye syndrome with wild-type influenza infection);
- persons with a history of Guillain-Barré syndrome;
- pregnant women; or
- persons with a history of hypersensitivity, including anaphylaxis, to any of the components of LAIV or to eggs.

LAIV should not be administered until 48 hours after cessation of influenza antiviral therapy, and influenza antiviral medications should not be administered for 2 weeks after receipt of LAIV. LAIV should not be given within 4 weeks of another live vaccine.

### **Vaccine Storage**

Both types of vaccine should be stored in the refrigerator at 35°-46°F at all times and should not be exposed to freezing temperature.

### **Thimerosal**

Multidose vials of TIV contain the mercury-containing preservative, thimerosal. California law specifies that thimerosal containing influenza vaccines given to pregnant women or children younger than 3 years of age in California may not exceed 1.0 microgram of mercury per 0.5 milliliters of vaccine. Therefore, women who are “knowingly pregnant” or children <3 years of age may only receive influenza vaccines that contain <1.0 mcg of mercury per 0.5 ml of vaccine. **All single dose influenza vaccines approved for use in the U.S. for the 2008-2009 influenza season meet this requirement.**

Non-influenza vaccines given to pregnant women or children <3 years of age may not contain more than 0.5 mcg of mercury per 0.5 ml of vaccine per California law. For more information on the thimerosal law see:

<http://www.cdph.ca.gov/programs/immunize/Pages/CaliforniaThimerosalLaw.aspx>

### **Recommendations for TIV and LAIV during the 2008-2009 influenza season**

Both TIV and LAIV prepared for the 2008-09 season will include A/Brisbane/59/2007 (H1N1)-like, A/Brisbane/10/2007 (H3N2)-like, and B/Florida/4/2006-like antigens. These viruses will be used because they are representative of influenza viruses that are forecasted to be circulating in the U.S. during the 2008-2009 influenza season and have favorable growth properties in eggs.

Healthy, nonpregnant persons aged 2-49 years can receive either vaccine. Some TIV formulations are FDA-licensed for use in persons as young as age 6 months and there is no maximum age for TIV vaccination. TIV is licensed for use in persons with high-risk conditions. LAIV is FDA-licensed for use only for persons aged 2-49 years. In addition, FDA has indicated that the safety of LAIV has not been established in persons with underlying medical conditions that confer a higher risk for influenza complications.

### **2008-2009 Influenza Vaccine Availability**

It is expected that sufficient supplies of influenza vaccine will be available for the 2008-2009 influenza season. Manufacturers began to ship influenza vaccine in September and almost all of the vaccine is expected to be shipped and distributed in October and November.

Up to date information and recommendations can be obtained at:

<http://www.cdph.ca.gov/programs/immunize/Pages/default.aspx> and <http://www.cdc.gov/flu/>.

The toll-free CDPH Influenza Vaccine Information Line is 866-470-3788.

**Approved U.S. influenza vaccines, 2008-2009**

The following list of approved influenza vaccines, is from “Prevention and Control of Influenza, Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2008” at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr57e717a1.htm>

**TABLE 2. Approved influenza vaccines for different age groups — United States, 2008–09 season**

Vaccine	Trade name	Manufacturer	Presentation	Mercury content (mcg Hg/0.5 mL dose)	Age group	No. of doses	Route
TIV*	Fluzone	sanofi pasteur	0.25 mL pre-filled syringe	0	6–35 mos	1 or 2†	Intramuscular‡
			0.5 mL pre-filled syringe	0	≥36 mos	1 or 2†	Intramuscular‡
			0.5 mL vial	0	≥36 mos	1 or 2†	Intramuscular‡
			5.0 mL multi-dose vial	25	≥6 mos	1 or 2†	Intramuscular‡
TIV*	Fluvirin	Novartis Vaccine	5.0 mL multi-dose vial	24.5	≥4 yrs	1 or 2†	Intramuscular‡
			0.5 mL pre-filled syringe	<1.0	≥4 yrs	1 or 2†	Intramuscular‡
TIV*	Fluarix	GlaxoSmithKline	0.5 mL pre-filled syringe	<1.0	≥18 yrs	1	Intramuscular‡
TIV*	FluLaval	GlaxoSmithKline	5.0 mL multi-dose vial	25	≥18 years	1	Intramuscular‡
TIV*	Afluria	CSL Biotherapies	0.5 mL pre-filled syringe	0	≥18 years	1	Intramuscular‡
			5.0 mL multi-dose vial	25	≥18 years	1	
LAIV¶	FluMist**	MedImmune	0.2 mL sprayer	0	2–49 yrs	1 or 2††	Intranasal

\* Trivalent inactivated vaccine (TIV). A 0.5-mL dose contains 15 mcg each of A/Brisbane/59/2007 (H1N1)-like, A/Brisbane/10/2007 (H3N2)-like, and B/Florida/4/2006-like antigens.

† Two doses administered at least 1 month apart are recommended for children aged 6 months–8 years who are receiving TIV for the first time and those who only received 1 dose in their first year of vaccination should receive 2 doses in the following year.

‡ 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.

¶ Live attenuated influenza vaccine (LAIV). A 0.2-mL dose contains 10<sup>6.5–7.5</sup> fluorescent focal units of live attenuated influenza virus reassortants of each of the three strains for the 2008–09 influenza season: A/Brisbane/59/2007(H1N1), A/Brisbane/10/2007(H3N2), and B/Florida/4/2006.

\*\* FluMist is shipped refrigerated and stored in the refrigerator at 2°C to 8°C after arrival in the vaccination clinic. The dose is 0.2 mL divided equally between each nostril. Health-care providers should consult the medical record, when available, to identify children aged 2–4 years with asthma or recurrent wheezing that might indicate asthma. In addition, to identify children who might be at greater risk for asthma and possibly at increased risk for wheezing after receiving LAIV, parents or caregivers of children aged 2–4 years should be asked: “In the past 12 months, has a health-care provider ever told you that your child had wheezing or asthma?” Children whose parents or caregivers answer “yes” to this question and children who have asthma or who had a wheezing episode noted in the medical record during the preceding 12 months, should not receive FluMist.

†† Two doses administered at least 4 weeks apart are recommended for children aged 2–8 years who are receiving LAIV for the first time, and those who only received 1 dose in their first year of vaccination should receive 2 doses in the following year.

**V. Laboratory Diagnosis of Influenza**

A person with influenza may not appear or feel different than when infected with many other respiratory pathogens. However, during outbreaks where influenza has been confirmed through laboratory tests, it can be presumed that other persons with similar symptoms also have influenza. Therefore, **when a cluster of cases of acute respiratory illness with symptoms suggestive of influenza (see Section I above) occurs, it is of critical importance to try to establish the diagnosis through laboratory testing.**

Several commercial rapid diagnostic tests are available that can detect influenza viruses within 30 minutes. Some of these rapid tests detect only influenza A viruses, whereas other rapid tests detect both influenza Type A and B viruses but do not distinguish between the two types. These tests can be performed on nasopharyngeal-swab or nasal-wash specimens. This information can then be used to determine if influenza antiviral drug therapy should be implemented to prevent the outbreak from spreading. Precise identification of the strain of virus can be made by growing the virus from nasopharyngeal secretions of acutely ill persons. Viral culture and molecular tests are available at the CDPH Viral and Rickettsial Disease Laboratory and some local health departments for the investigation of outbreaks.

## **VI. Infection Prevention and Control Precautions for Seasonal Influenza and Other Respiratory Infections**

The implementation of infection prevention measures for influenza-like respiratory infections, including seasonal influenza, can prevent their spread in LTCFs. Although vaccinating all facility personnel and residents is the primary influenza control measure, outbreaks of influenza and other viruses that mimic influenza can be prevented if the following recommendations are implemented as soon as possible to prevent person-to-person transmission.

### **A. Education and Monitoring**

- Provide education about the facility's respiratory hygiene/cough etiquette program (below) and how to report signs and symptoms of influenza and influenza-like respiratory infections to residents, facility personnel, visitors and volunteers at least annually and when influenza-like respiratory infections are identified in the facility.
- Develop an influenza or influenza-like illness outbreak management plan that includes vaccination for seasonal influenza and the use of the influenza vaccine declination form (see [Appendix 1](#)).
- Monitor residents and facility personnel for symptoms of respiratory infection, especially during the influenza season (October to April).
- If influenza or influenza-like respiratory illnesses are suspected, promptly contact the local health department and request assistance with laboratory testing.

### **B. Respiratory Hygiene/Cough Etiquette**

Respiratory hygiene/cough etiquette procedures should be implemented at the first point of contact with a potentially infected person to prevent the transmission of respiratory tract infections in healthcare settings. Additional information is available at:

<http://www.cdc.gov/flu/professionals/infectioncontrol/resphygiene.htm>

Respiratory hygiene/cough etiquette programs include:

- Posting visual alerts instructing residents, staff, visitors and volunteers to report symptoms of respiratory infection to a designated person.
- Providing tissues or masks to residents who are coughing or sneezing so that they can cover their nose and mouth.
- Encouraging coughing persons to remain at least 3 feet away from others, if possible.
- Ensuring that supplies for hand washing are available where sinks are located; and/or providing dispensers of alcohol-based hand rubs.
- Excluding staff, visitors, and volunteers with symptoms of respiratory infection.

### **C. Visitor Precautions**

- During influenza season, post signs notifying visitors that adults with respiratory symptoms should not visit for 5 days and children with symptoms should not visit for 10 days following the onset of illness.
- During an outbreak, consider restricting all children from visiting.

- Provide written information about influenza-like infections and seasonal influenza to visitors and why the infection control precautions are necessary.
- Provide visitors with written instructions (respiratory hygiene/cough etiquette) about the precautions implemented by the facility.
- Encourage visitors to get vaccinated for influenza.
- If visitation is necessary (e.g., visitation of a dying resident) instruct symptomatic visitors to: (1) wear a surgical or procedure mask over their mouth and nose while in the resident's room; (2) cough and sneeze into a tissue and discard contaminated tissues a waste receptacle; and (3) sanitize their hands before entering the resident's room, before and after resident contact and upon leaving the resident's room.
- Ensure that hand hygiene, tissues and masks are available.

## **VII. Outbreak Control Procedures for Influenza and Influenza-like Respiratory Infections**

### **A. Definitions**

- Cluster: Three or more cases of acute respiratory illness occurring within 48-72 hours in residents who are in close proximity to each other (e.g., in the same area of the facility).
- Outbreak: A sudden increase in acute respiratory illness cases over the normal background rate or when any resident tests positive for influenza. One case of confirmed influenza by any testing method in a LTCF resident is an outbreak.

### **B. Confirm Diagnosis by Laboratory Testing**

- The first three to four residents and/or staff suspected of influenza or influenza-like illness (acute respiratory illness with or without fever) should have specimens obtained for laboratory testing to confirm the diagnosis of influenza.
- Contact the local health department for appropriate diagnostic laboratory test recommendations. If rapid antigen tests and/or viral cultures are recommended, determine the appropriate laboratory to process the specimens.

### **C. Infection Control Precautions for Residents with Influenza-Like Illness**

- As soon as a resident develops an influenza-like acute respiratory illness (see Section II), confine the symptomatic resident and exposed roommate(s) to their room, restrict them from group activities, and serve meals in their room for 5 days after the onset of symptoms.
- If other residents become symptomatic, cancel group activities and serve all meals in residents' rooms.
- If residents are ill on specific nursing units, do not move residents or staff to other units, or admit new residents to the units with symptomatic residents.
- Avoid rotating staff between nursing units until no new cases have been identified for at one week.
- Limit admission of new and returning residents, if possible.

- If admissions are necessary, ensure that new or returning residents do not have acute respiratory illness and are not being transferred from a facility experiencing an influenza outbreak. Admit asymptomatic new or returning residents to unaffected nursing units.
- Wear a surgical or procedure mask when within 3 feet of ill residents or when entering the resident's room.
- Place a surgical or procedure mask over the ill resident's nose and mouth, if tolerated, when transport or movement of the resident is necessary outside of their room.
- Instruct ill residents to use tissues to cover their nose and mouth when coughing and sneezing. Provide a bag or other waste receptacle conveniently located for disposal of contaminated tissues.
- Wash or sanitize the hands of ill residents with an alcohol-based hand hygiene product frequently throughout the day, before they leave their room and after hand contact with respiratory secretions or contaminated tissues.

#### **D. Healthcare Worker Infection Control Precautions**

- Wear gloves when contact with the ill resident or contaminated environmental surfaces or objects in close vicinity to the resident is anticipated. Keep a supply of gloves in the resident's room.
- Wear gowns when providing direct care to an ill resident.
- Change gloves and gowns after each encounter with an ill resident and perform hand hygiene.
- Wear a surgical or procedure mask upon entering the ill resident's room or when working within 3 feet of a coughing or sneezing resident. Remove the mask upon leaving the resident's room and dispose in a waste receptacle.
- Wash or sanitize hands before and after touching the ill resident, after touching environmental surfaces and items potentially contaminated with respiratory secretions, whether or not gloves are worn. If hands are not visibly soiled, use an alcohol-based hand rub for routine decontamination of hands. Alternatively, wash hands with soap (either plain or antimicrobial) and water.
- Exclude staff with influenza-like illness from patient care for 5 days after the onset of symptoms and advise them not work in other facilities (i.e., a second job) during the same time period. During a facility outbreak, even well facility personnel should not work at another facility until the local health department has determined that the outbreak is controlled.
- Implement enhanced environmental cleaning of commonly touched surfaces such as door handles, hallway banisters, toilet or bath rails, bedrails, overbed tables, and nursing station counters.

#### **E. Collect, Analyze, and Report Data**

- Initiate the use of the daily active surveillance log (see [Appendix 2](#)) and collect data on all newly symptomatic residents and staff until at least one week after the last influenza case occurs.
- Monitor facility personnel absenteeism due to influenza-like respiratory illness.

- Report all resident(s) and facility personnel with symptoms of influenza-like illness to the infection prevention and control practitioner (ICP). New cases should be reported and recorded daily using the case log (see [Appendix 2](#)).
- Analyze reports of resident and facility personnel illness submitted by the nursing unit and other departments (environmental services) daily.
- Determine the infection attack rates for residents and facility personnel (# of infected residents/total number of vaccinated **and** total of non-vaccinated residents) and (# total number of infected facility personnel/total number of vaccinated **and** the total number of non-vaccinated facility personnel).
- Report data to the quality assurance/infection control committee and the Licensing and Certification district office with jurisdiction over the facility (see notification).
- Review the infection surveillance and outbreak management plan to determine necessary revisions.
- Make revisions for implementing the outbreak management plan and influenza vaccination during the next influenza year.

#### **F. Outbreak Notification**

- Notify the facility medical director immediately.
- Notify the local health department **and** Licensing and Certification district office with jurisdiction over your facility (<http://www.cdph.ca.gov/programs/Pages/LnC.aspx>)

#### **G. Vaccination**

- Vaccinate unvaccinated facility personnel and residents as soon as possible.

### **VIII. Antiviral Drugs for the Control of Influenza Outbreaks**

Use of antiviral drugs for treatment and chemoprophylaxis of influenza is a key component of influenza outbreak control in institutions. Although chemoprophylactic drugs are not a substitute for vaccination, they are critical adjuncts in preventing and controlling influenza. In community studies of healthy adults, both oseltamivir and zanamivir had similar efficacy in preventing febrile, laboratory-confirmed influenza illness (zanamivir, 84%; oseltamivir, 82%). Studies have demonstrated moderate to excellent efficacy for prevention of influenza among patients in institutional settings. For example, a 6-week study of oseltamivir chemoprophylaxis among long-term care facility residents demonstrated a 92% reduction in influenza illness.

When confirmed or suspected outbreaks of influenza occur in institutions that house persons at high risk, chemoprophylaxis with a neuraminidase inhibitor medication (see below) should be started as early as possible to reduce the spread of the virus.

Four currently licensed antiviral agents are available in the U.S.: amantadine, rimantadine, oseltamivir, and zanamivir. In the past, amantadine and rimantadine (together known as adamantanes) were commonly used for treatment and prophylaxis of influenza type A. However, recent evidence indicates that a high proportion of currently circulating influenza A viruses in California and in the U.S. have developed resistance to adamantanes.

**Therefore, neither amantadine nor rimantadine should be used for the treatment or prophylaxis of influenza A in the U.S.** More information on antiviral resistance is available at the end of this section.

The two remaining antiviral agents, oseltamivir (Tamiflu®) and zanamivir (Relenza®), together called neuraminidase inhibitors, are an important additional measure for the control of influenza outbreaks. CDC and CDPH recommend their use during outbreaks and they should be considered for use when an influenza outbreak occurs. During an outbreak, these antiviral drugs should be given to residents and offered to staff in accordance with current recommendations at: <http://www.cdc.gov/flu/professionals/treatment>

When oseltamivir or zanamivir are used for treatment or chemoprophylaxis, adverse reactions to these drugs should be monitored using the format of [Appendix 5](#). Side effects can include bronchospasm (zanamivir) as well as gastrointestinal disturbances (oseltamivir).

### **Antiviral Treatment**

Oseltamivir and zanamivir are effective against both type A and type B influenza. Both medications can reduce the duration of uncomplicated influenza A and B illnesses by about one day compared with a placebo. If used, it is recommended that antiviral treatment be started **within 2 days of illness onset**. Oseltamivir is currently approved for treatment of persons aged  $\geq 1$  year, and zanamivir is approved for treatment of persons aged  $\geq 7$  years.

### **Antiviral Treatment Recommendations**

For treatment, oseltamivir is administered twice a day orally for 5 days and zanamivir is administered as 2 oral inhalations twice a day for 5 days. Separate symptomatic residents on antiviral treatment from others, including those taking antiviral chemoprophylaxis, to the extent possible in the facility to decrease the possibility of transmitting antiviral-resistant influenza.

### **Antiviral Chemoprophylaxis**

Oseltamivir and zanamivir can also be used for chemoprophylaxis of influenza. Oseltamivir is licensed for chemoprophylaxis in persons aged  $\geq 1$  year, and zanamivir is licensed for use in persons  $\geq 5$  years. When considering the use of antiviral medications for chemoprophylaxis, cost, compliance, and potential side effects should be evaluated.

When outbreaks of influenza occur in a LTCF, and antiviral chemoprophylaxis is undertaken, drug administration should begin as early in the outbreak as possible to reduce influenza transmission. Contingency planning is needed to ensure immediate availability and rapid administration of the drugs. This might include obtaining prior approval from personal physicians for administration of antiviral drugs to residents in the event of an outbreak. Since it is difficult to know in advance how long antiviral drugs will need to be administered, some nursing homes have a policy that also allows facility staff or a consultant to decide when they should be discontinued.

### **Antiviral Chemoprophylaxis Recommendations**

Immediately upon confirmation of influenza A or B, consider the use of the antiviral medications oseltamivir or zanamivir to prevent further spread of influenza in the facility.

CDC and CDPH recommend that when confirmed or suspected outbreaks of influenza occur in institutions that house persons at high risk, chemoprophylaxis should be started as early as possible to reduce the spread of the virus. For additional information see: <http://www.cdc.gov/flu/professionals/infectioncontrol/institutions.htm>.

- Having preapproved orders from physicians or plans to obtain orders for antiviral medications on short notice can substantially expedite administration of antiviral medications.
- Specimens should be collected from ill cases for viral culture to assess antiviral resistance and provide data on the outbreak viruses.
- Chemoprophylaxis should be administered to all eligible residents, regardless of whether they received influenza vaccinations during the previous fall, and should continue for a minimum of 2 weeks. If surveillance indicates that new cases continue to occur, chemoprophylaxis should be continued until approximately 7-10 days after illness onset in the last patient.
- Chemoprophylaxis also can be offered to unvaccinated staff members who provide care to persons at high risk.
- Chemoprophylaxis should be considered for all employees, regardless of their vaccination status, if indications exist that the outbreak is caused by a strain of influenza virus that is not well-matched by the vaccine. Such indications might include multiple documented breakthrough influenza-virus infections among vaccinated persons, studies indicating low vaccine effectiveness, or circulation in the surrounding community of suspected index case(s) of strains not contained in the vaccine.
- Chemoprophylaxis also can be considered for controlling influenza outbreaks in other closed or semiclosed settings (e.g., dormitories, correctional facilities, or other settings in which persons live in close proximity).
- To limit the potential transmission of drug-resistant virus during outbreaks in institutions, whether in chronic or acute-care settings or other closed settings, measures should be taken to reduce contact between persons taking antiviral drugs for treatment and other persons, including those taking chemoprophylaxis.
- Chemoprophylaxis can also be offered to unvaccinated staff members (or staff vaccinated less than 2 weeks prior to the outbreak).
- If the outbreak is suspected to be caused by a strain of influenza virus that is not well-matched to the vaccine, antivirals may be considered for chemoprophylaxis of all LTCF staff, regardless of their vaccination status.

### **Antiviral Dosage Information**

- For chemoprophylaxis, oseltamivir is administered once a day orally and zanamivir is administered as 2 oral inhalations once a day.
- The dosage for each resident should be determined individually taking into account the resident's age, weight, and renal function.

- The dosage of oseltamivir may need to be decreased for those with impaired renal function.
- Exercise caution when administering oseltamivir or zanamivir to persons with:
  - decreased renal function (adjust the dose based on creatinine clearance for oseltamivir);
  - concomitant use for drugs excreted in urine via glomerular filtration and tubular secretion via the anionic pathway; or
  - pregnancy.
- Zanamivir is not recommended for treatment for patients with underlying airway disease (e.g., asthma, chronic obstructive pulmonary disease). If physicians choose to prescribe zanamivir to patients with underlying chronic respiratory disease after considering potential risks and benefits, the medication should be used with caution under conditions of appropriate monitoring and supportive care, including short-acting bronchodilators.

The following table from “Prevention and Control of Influenza, Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2008” at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr57e717a1.htm> describes the recommended daily dosage of antiviral medications for treatment and chemoprophylaxis.

**TABLE 4. Recommended daily dosage of influenza antiviral medications for treatment and chemoprophylaxis — United States**

Antiviral agent	Age group (yrs)				
	1–6	7–9	10–12	13–64	≥65
Zanamivir* Treatment, influenza A and B	NA	10 mg (2 inhalations) twice daily			
Chemoprophylaxis, influenza A and B	NA	10 mg (2 inhalations) once 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
Chemoprophylaxis, influenza A and B	Dose varies by child's weight‡	Dose varies by child's weight‡	Dose varies by child's weight‡	75 mg/day	75 mg/day

**NOTE:** Zanamivir is manufactured by GlaxoSmithKline (Relenza® — inhaled powder). Zanamivir is approved for treatment of persons aged ≥7 years and approved for chemoprophylaxis of persons aged ≥5 years. Oseltamivir is manufactured by Roche Pharmaceuticals (Tamiflu® — tablet). Oseltamivir is approved for treatment or chemoprophylaxis of persons aged ≥1 year. No antiviral medications are approved for treatment or chemoprophylaxis of influenza among children aged <1 year. This information is based on data published by the Food and Drug Administration (FDA), which is available at <http://www.fda.gov>.

\* Zanamivir is administered through oral 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 recommended for those persons with underlying airway disease.

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

‡ The treatment dosing 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. For children who weigh >40 kg, the dose is 75 mg twice a day.

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

**Persons Aged ≥65 Years**

No reduction in dosage for oseltamivir or zanamivir is recommended on the basis of age alone.

**Persons with Impaired Renal Function**

Limited data are available regarding the safety and efficacy of zanamivir for patients with impaired renal function. Among patients with renal failure who were administered a single intravenous dose of zanamivir, decreases in renal clearance, increases in half-life, and increased systemic exposure to zanamivir were reported. However, a limited number of healthy volunteers who were administered high doses of intravenous zanamivir tolerated systemic levels of zanamivir that were substantially higher than those resulting from administration of zanamivir by oral inhalation at the recommended dose. On the basis of these considerations, the manufacturer recommends no dose adjustment for inhaled zanamivir for a 5-day course of treatment for patients with either mild-to-moderate or severe impairment in renal function.

Serum concentrations of oseltamivir carboxylate, the active metabolite of oseltamivir, increase with declining renal function. For patients with creatinine clearance of 10-30 mL per minute, a reduction of the treatment dosage of oseltamivir to 75 mg once daily and in the chemoprophylaxis dosage to 75 mg every other day is recommended. No treatment or chemoprophylaxis dosing recommendations are available for patients undergoing routine renal dialysis treatment.

**Persons with Liver Disease**

Use of zanamivir or oseltamivir has not been studied among persons with hepatic dysfunction.

**Persons with Seizure Disorders**

Seizure events have been reported during postmarketing use of zanamivir and oseltamivir, although no epidemiologic studies have reported any increased risk for seizures with either zanamivir or oseltamivir use.

**Persons with Immunosuppression**

A recent retrospective case-control study demonstrated that oseltamivir was safe and well tolerated when used during the control of an influenza outbreak among hematopoietic stem cell transplant recipients living in a residential facility.

**Route**

Oseltamivir is administered orally in capsule or oral suspension form. Zanamivir is available as a dry powder that is self-administered via oral inhalation by using a plastic device included in the package with the medication. Patients should be instructed about the correct use of this device.

**Zanamivir Pharmacokinetics**

In studies of healthy volunteers, approximately 7%-21% of the orally inhaled zanamivir dose reached the lungs, and 70%-87% was deposited in the oropharynx. Approximately 4%-17% of the total amount of orally inhaled zanamivir is absorbed systemically. Systemically absorbed zanamivir has a half-life of 2.5-5.1 hours and is excreted unchanged in the urine. Unabsorbed drug is excreted in the feces.

**Oseltamivir Pharmacokinetics**

Approximately 80% of orally administered oseltamivir is absorbed systemically. Absorbed oseltamivir is metabolized to oseltamivir carboxylate, the active neuraminidase inhibitor, primarily by hepatic esterases. Oseltamivir carboxylate has a half-life of 6-10 hours and is excreted in the urine by glomerular filtration and tubular secretion via the anionic pathway. Unmetabolized oseltamivir also is excreted in the urine by glomerular filtration and tubular secretion.

**Adverse Events**

When considering use of influenza antiviral medications (i.e., choice of antiviral drug, dosage, and duration of therapy), clinicians must consider the patient's age, weight, and renal function; presence of other medical conditions; indications for use (i.e., chemoprophylaxis or therapy); and the potential for interaction with other medications.

**Zanamivir Adverse Events**

Limited data are available about the safety or efficacy of zanamivir for persons with underlying respiratory disease or for persons with complications of acute influenza, and zanamivir is licensed only for use in persons without underlying respiratory or cardiac disease. In a study of zanamivir treatment of ILI among persons with asthma or chronic obstructive pulmonary disease in which study medication was administered after use of a B2-agonist, 13% of patients receiving zanamivir and 14% of patients who received placebo (inhaled powdered lactose vehicle) experienced a >20% decline in forced expiratory volume in 1 second (FEV1) after treatment. However, in a phase-I study of persons with mild or moderate asthma who did not have ILI, one of 13 patients experienced bronchospasm after administration of zanamivir. In addition, during postmarketing surveillance, cases of respiratory function deterioration after inhalation of zanamivir have been reported.

Because of the risk for serious adverse events and because efficacy has not been demonstrated among this population, zanamivir is not recommended for treatment for patients with underlying airway disease. Allergic reactions, including oropharyngeal or facial edema, also have been reported during postmarketing surveillance.

In clinical treatment studies of persons with uncomplicated influenza, the frequencies of adverse events were similar for persons receiving inhaled zanamivir and for those receiving placebo (i.e., inhaled lactose vehicle alone). The most common adverse events reported by both groups were diarrhea, nausea, sinusitis, nasal signs and symptoms, bronchitis, cough, headache, dizziness, and ear, nose, and throat infections. Each of these symptoms was reported by <5% of persons in the clinical treatment studies combined. Zanamivir does not impair the immunologic response to TIV.

**Oseltamivir Adverse Events**

Nausea and vomiting were reported more frequently among adults receiving oseltamivir for treatment (nausea without vomiting, approximately 10%; vomiting, approximately 9%) than among persons receiving placebo (nausea without vomiting, approximately 6%; vomiting, approximately 3%).

Among children treated with oseltamivir, 14% had vomiting, compared with 8.5% of placebo recipients. Overall, 1% discontinued the drug secondary to this side effect, and a limited number of adults who were enrolled in clinical treatment trials of oseltamivir discontinued treatment because of these symptoms. Similar types and rates of adverse events were reported in studies of oseltamivir chemoprophylaxis. Nausea and vomiting might be less severe if oseltamivir is taken with food. No published studies have assessed whether oseltamivir impairs the immunologic response to TIV. Transient neuropsychiatric events (self-injury or delirium) have been reported postmarketing among persons taking oseltamivir; the majority of reports were among adolescents and adults living in Japan. FDA advises that persons receiving oseltamivir be monitored closely for abnormal behavior.

### **Use During Pregnancy**

Oseltamivir and zanamivir are both "Pregnancy Category C" medications, indicating that no clinical studies have been conducted to assess the safety of these medications for pregnant women. Because of the unknown effects of influenza antiviral drugs on pregnant women and their fetuses, these two drugs should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus; the manufacturers' package inserts should be consulted. However, no adverse effects have been reported among women who received oseltamivir or zanamivir during pregnancy or among infants born to such women.

### **Drug Interactions**

Clinical data are limited regarding drug interactions with zanamivir. However, no known drug interactions have been reported, and no clinically critical drug interactions have been predicted on the basis of in vitro and animal study data. Limited clinical data are available regarding drug interactions with oseltamivir.

Because oseltamivir and oseltamivir carboxylate are excreted in the urine by glomerular filtration and tubular secretion via the anionic pathway, a potential exists for interaction with other agents excreted by this pathway. For example, coadministration of oseltamivir and probenecid resulted in reduced clearance of oseltamivir carboxylate by approximately 50% and a corresponding approximate twofold increase in the plasma levels of oseltamivir carboxylate.

No published data are available concerning the safety or efficacy of using combinations of any of these influenza antiviral drugs. Package inserts should be consulted for more detailed information about potential drug interactions.

### **Antiviral Resistance**

During the 2007-08 influenza season, influenza A (H1N1) viruses with a mutation that confers resistance to oseltamivir were identified in the U.S. and other countries. As of June 27, 2008, 111 (7.6%) of 1,464 influenza A viruses tested, and none of 305 influenza B viruses tested in the U.S. were found to be resistant to oseltamivir. Influenza A (H1N1) virus strains that are resistant to oseltamivir remain sensitive to zanamivir.

**Because the proportion of influenza viruses that are resistant to oseltamivir remains low, oseltamivir or zanamivir remain the medications recommended for treatment and chemoprophylaxis of influenza in the U.S. However, clinicians should be alert to changes in antiviral recommendations that might occur as additional antiviral resistance data becomes available during the 2008-09 influenza season. See: <http://www.cdc.gov/flu/professionals/antivirals/index.htm> for more information.**

Influenza caused by oseltamivir-resistant viruses appears to be indistinguishable from illness caused by oseltamivir-sensitive viruses. When local viral surveillance data indicates that oseltamivir-resistant viruses are widespread in the community, clinicians have several options. Consultation with CDPH to aid in decision-making is recommended as a first step.

Persons who are candidates for receiving chemoprophylaxis as part of an outbreak known to be caused by oseltamivir-resistant viruses or who are being treated for influenza illness in communities where oseltamivir-resistant viruses are known to be circulating widely can receive zanamivir. However, zanamivir is not licensed for chemoprophylaxis in children aged <5 years or for treatment in children aged <7 years. In addition, zanamivir is not recommended for use in persons with chronic cardiopulmonary conditions, and can be difficult to administer to critically ill patients because of the inhalation mechanism of delivery. In these circumstances, a combination of oseltamivir and either rimantadine or amantadine can be considered, because influenza A (H1N1) viruses characterized to date that were resistant to oseltamivir have usually been susceptible to adamantanes. However, **adamantanes should not be used for chemoprophylaxis or treatment of influenza A unless they are part of a regimen that also includes a neuraminidase inhibitor. Influenza B viruses are not sensitive to adamantane drugs.**

## IX. References and Other Sources of Information

See page 1 for references and resources used in the development of these recommendations.

1. Centers for Disease Control and Prevention. Prevention and Control of Influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2008. <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr57e717a1.htm>
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6. Centers for Disease Control and Prevention, Influenza Web Site Home Page. <http://www.cdc.gov/flu/>
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8. Infection Control Measures for Preventing and Controlling Influenza Transmission in Long-Term Care Facilities. <http://www.cdc.gov/flu/professionals/infectioncontrol/longtermcare.htm>
9. Centers for Disease Control and Prevention, Infection Control in Long-Term Care Settings. [http://www.cdc.gov/ncidod/dhqp/gl\\_longterm\\_care.html](http://www.cdc.gov/ncidod/dhqp/gl_longterm_care.html)
10. Immunization Branch of the California Department of Health Services Influenza Information: [http://www.cdph.ca.gov/healthinfo/discond/Pages/Influenza\(Flu\).aspx](http://www.cdph.ca.gov/healthinfo/discond/Pages/Influenza(Flu).aspx)
11. California Influenza Surveillance Project, Viral and Rickettsial Disease Laboratory Branch, California Department of Health Services. <http://www.cdph.ca.gov/programs/vrdl/Pages/default.aspx>

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*Appendix 1. Sample Influenza Vaccine Declination Form***Declination of Influenza Vaccination**

My employer \_\_\_\_\_, has offered that I receive influenza vaccination in order to protect myself and the patients I serve.

I acknowledge that I am aware of the following facts:

- Influenza vaccination is strongly recommended for me and all other healthcare workers to prevent influenza disease and its complications, including death.
- Due to my occupation, I may transmit influenza to my patients and other healthcare workers, as well as to my family and friends, even though I have no symptoms.
- If I become infected with influenza, even when my symptoms are mild, I can spread severe illness to others, particularly to those in this healthcare facility that are at high risk for influenza complications.
- I understand that the strains of virus that cause influenza infection change almost every year, which is why a different influenza vaccine is recommended each year.
- I have received education about the effectiveness of influenza vaccination as well as possible adverse events.
- I cannot get the influenza disease from the influenza vaccine.
- I understand that if I have not been vaccinated, by declining this vaccine, I continue to be at risk of acquiring influenza, which could endanger my health and the health of those with whom I have contact, including:
  - patients in this healthcare facility
  - my coworkers
  - my family
  - my community

I have been given the opportunity to be immunized with influenza vaccine at no charge to myself. However, I decline influenza vaccination at this time.

I understand that I may change my mind at any time and accept influenza vaccination, if vaccine is available.

I have read and fully understand the information on this declination form.

Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Name (print): \_\_\_\_\_







*Appendix 5. Sample Line List of Residents with Adverse Reactions to Antiviral Medication*

Facility name: \_\_\_\_\_

Infection control coordinator: \_\_\_\_\_

Phone number: \_\_\_\_\_

Dates: \_\_\_\_\_

Resident identification			Resident location			Respiratory illness		Antiviral drug/dosing					Adverse reaction						Actions taken				
Name	Age	Sex (M/F)	Building	Unit	Room #	AFRI (Y/N)	Date of illness onset	Oseltamivir (O)	Zanamivir (Z)	Date antiviral started	Dose (mg)	Frequency	Creatinine	Nervous/anxious	Confusion	Nausea	Anorexia	Agitation	Seizure	Other symptom	Antiviral discontinued (Y/N)	Date discontinued	Dose reduced (Y/N)

Severe adverse events associated with the administration of antiviral medications used to prevent or treat influenza (e.g., those resulting in hospitalization or death) should be reported to MedWatch, FDA's Safety Information and Adverse Event Reporting Program, at telephone 1-800-FDA-1088, by fax at 1-800-FDA-0178, or via the Internet by sending Report Form 3500 (available at <http://www.fda.gov/medwatch/safety/3500.pdf>).