Influenza Virus Vaccine,

Trivalent, Types A and B
(Purified Subvirion)

FLUSHIELD®

2002-2003 Formula

DO NOT INJECT INTRAVENOUSLY

℞ **only**

DESCRIPTION

FluShield® (Influenza Virus Vaccine, Trivalent, Types A and B [Purified Subvirion]) is a sterile injectable for administration intramuscularly.

FluShield is prepared from the allantoic fluids of chick embryos inoculated with a specific type of influenza virus. During processing, not more than 500 µg of gentamicin is added to each embryonated chicken egg. The harvested virus is concentrated, purified, then inactivated with formaldehyde.

The viral antigens contained in FluShield, Trivalent (Purified Subvirion) are concentrated and refined by a column-chromatographic procedure. At the same time, addition of tri(n)butylphosphate and Polysorbate 80, USP, to the column-eluting fluids effects inactivation and disruption of a significant proportion of the virus to smaller subunit particles. The recovered subvirion (split-virus) suspension is freed of substantial portions of the disrupting agents by resin treatment and of other undesirable materials by dialysis through membranes of controlled pore size.

The viral antigen content has been standardized by immunodiffusion tests, according to current U.S. Public Health Service (PHS) requirements. Each dose (0.5 mL) contains the proportions and not less than the microgram amounts of hemagglutinin antigens (µg HA) representative of the specific components recommended for the 2002-2003 season: 15 µg HA of A/New Caledonia/20/99 (H1N1), 15 µg HA of A/Panama/2007/99 (H3N2) (A/Moscow/10/99 [H3N2]-like), and 15 µg HA B/Hong Kong/330/2001.

The vaccine contains 1:10,000 thimerosal (mercury derivative; 25 µg mercury per 0.5 mL dose) as a preservative (see **PRECAUTIONS - Pregnancy**). Gentamicin sulfate is used during manufacturing, but is not detectable in the final product by assay procedures (see **WARNINGS**). The product appears as a slightly opalescent solution.

CLINICAL PHARMACOLOGY

The administration of inactivated influenza virus vaccine each year before the influenza season is the single most important influenza-control measure.[1]

The injection of antigens prepared from inactivated influenza virus stimulates the production of specific antibodies. Any protection afforded is only against those strains of virus from which the vaccine is prepared or closely related strains. With the passage of time, the prevalent strains may undergo major antigenic changes, or more predictably, there may be continuous and progressive antigenic variation within a given virus subtype over time (antigenic drift), so that infection or immunization with one strain may not induce immunity to distantly related strains. For this reason, the PHS annually reviews the antigenic characteristics of circulating strains in order to select those to be included in the contemporary vaccine.

Influenza A and B are the two types of influenza viruses that cause epidemic human disease. Influenza A viruses are further classified into subtypes on the basis of two surface antigens: hemagglutinin (H) and neuraminidase (N). A person's immunity to the surface antigens, especially hemagglutinin, reduces the likelihood of infection and the severity of disease if infection occurs. Influenza virus vaccine prevents illness in approximately 70% to 90% of healthy persons younger than 65 years when the antigenic match between vaccine and circulating viruses is close.[1]

Based upon epidemiological studies of circulating influenza virus strains, the Public Health Service has recommended that the 2002-2003 trivalent vaccine include A/Moscow/10/99 (H3N2)-like, A/New Caledonia/20/99 (H1N1)-like, and B/Hong Kong/330/2001-like antigens. A/Panama/2007/99 is antigenically equivalent to A/Moscow/10/99.

INDICATIONS AND USAGE

FluShield® is indicated for active immunization against the specific influenza virus strains contained in the 2002-2003 formulation. FluShield is recommended for any person aged ≥6 months who, because of age or underlying medical condition, is at increased risk for complications of influenza. In addition, healthcare workers and other individuals (including household members) in close contact with persons at high risk should be vaccinated to decrease the risk for transmitting influenza to persons at high risk. Influenza vaccine also can be administered to any person aged ≥6 months to reduce the chance of becoming infected with influenza.[1] FluShield should only be administered if it is prescribed by a healthcare professional whose license includes the prescribing of biologicals.

Elderly persons and persons with certain chronic diseases may develop lower postvaccination antibody titers than healthy young adults and thus may remain susceptible to influenza-related upper respiratory tract infections. Nevertheless, vaccination has been shown to be effective in helping to prevent lower respiratory tract involvement or other secondary complications, thereby reducing the risk of hospitalization and death.[1]

Guidelines for the use of influenza virus vaccine among different groups are given below.

Target Groups for Vaccination

Groups at increased risk for influenza-related complications:

1. Persons aged ≥65 years (see **PRECAUTIONS – Geriatric Use**).
2. Residents of nursing homes and other chronic-care facilities housing patients of any age with chronic medical conditions.
3. Adults and children with chronic disorders of the pulmonary or cardiovascular systems, including asthma.
4. Adults and children who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications or by human immunodeficiency virus [HIV]).
5. Children and teenagers (aged 6 months to 18 years) who are receiving long-term aspirin therapy and, therefore, might be at risk of developing Reye's syndrome after influenza infection.
6. Women who will be in the second or third trimester of pregnancy during the influenza season (see **PRECAUTIONS – Pregnancy,** and **Additional Groups for Vaccination** - *Pregnant Women).*[1]

Persons Aged 50-64 years:

Vaccination of this group is recommended because they have an increased prevalence of high risk conditions. Influenza vaccination of the entire age cohort has been recommended to raise the low vaccination rates among persons with high risk conditions within the cohort.[1]

Persons who can transmit influenza to persons at high risk:

Persons who are clinically or subclinically infected can transmit influenza virus to persons at high risk for complications from influenza. Decreasing transmission of influenza from caregivers to persons at high risk might reduce influenza-related deaths among persons at high risk. Evidence from two studies indicated that vaccination of healthcare workers is associated with decreased deaths among nursing home patients. Vaccination of healthcare workers and others in close contact with persons at high risk, including household members, is recommended.[1] The following groups should be vaccinated:

1. Physicians, nurses, and other personnel in both hospital and outpatient-care settings, including medical emergency response workers (eg, paramedics and emergency medical technicians).
2. Employees of nursing homes and chronic-care facilities who have contact with patients or residents.
3. Employees of assisted living and other residences for persons in groups at high risk.
4. Persons who provide home care to persons in groups at high risk.
5. Household members (including children) of persons in groups at high risk.[1]

In addition, because children aged 0-23 months are at an increased risk for influenza-related hospitalization, vaccination is encouraged for their household contacts and out-of home caretakers, particularly for contacts of children aged 0-5 months because influenza vaccines have not been approved by the U.S. Food and Drug Administration (FDA) for use among children aged <6 months (see **PRECAUTIONS - Pediatric Use**).[1]

Additional Groups for Vaccination

Pregnant Women:

Although animal reproductive studies have not been conducted, the prescribing healthcare professional should be aware of the recommendations of the Advisory Committee on Immunization Practices (ACIP), which are incorporated below. Influenza-associated excess mortality among pregnant women was documented during the pandemics of 1918-19 and 1957-58. Case reports and limited studies suggest that pregnancy may increase the risk for serious medical complications of influenza as a result of increases in heart rate, stroke volume and oxygen consumption, decreases in lung capacity, and changes in immunologic function. A study of the impact of influenza during 17 interpandemic influenza seasons demonstrated that the relative risk for hospitalization for selected cardiorespiratory conditions among Medicaid-enrolled pregnant women increased from 1.4 during weeks 14 to 20 of gestation to 4.7 during weeks 37 to 42 compared with women who were 1 to 6 months postpartum. Women in their third trimester of pregnancy were hospitalized at a rate comparable to that of nonpregnant women who have high risk medical conditions. Using data from this study, it was estimated that an average of 1 to 2 hospitalizations among pregnant women could be prevented for every 1,000 pregnant women immunized.[1]

Because of the increased risk for influenza-related complications, the ACIP recommends that women who will be beyond the first trimester of pregnancy (>14 weeks of gestation) during the influenza season should be vaccinated. Pregnant women who have medical conditions that increase their risk for complications from influenza should be vaccinated before the influenza season, regardless of the stage of pregnancy. A study of influenza immunization of more than 2,000 pregnant women demonstrated no adverse fetal effects associated with influenza virus vaccine; however, more data are needed to confirm the safety of vaccination during pregnancy (see **PRECAUTIONS - Pregnancy**).[1]

Persons infected with HIV:

Limited information exists regarding the frequency and severity of influenza illness among HIV-infected persons, but reports suggest that symptoms might be prolonged and the risk of complications increased for some HIV-infected persons. Influenza virus vaccine has produced substantial antibody titers against influenza virus in vaccinated HIV-infected persons who have minimal AIDS-related symptoms and high CD4+ T-lymphocyte cell counts. In patients who have advanced HIV disease and low CD4+ T-lymphocyte cell counts, however, influenza virus vaccine may not induce protective antibody titers; a second dose of vaccine does not improve the immune response for these persons.

Studies have examined the effect of influenza vaccination on replication of HIV type 1 (HIV-1). Although some studies have demonstrated a transient (ie, 2- to 4-week) increase in replication of HIV-1 in the plasma or peripheral blood mononuclear cells of HIV-infected persons after vaccine administration, other studies using similar laboratory techniques have not indicated any substantial increase in replication. Deterioration of CD4+ T-lymphocyte cell counts and progression of HIV disease have not been demonstrated among HIV-infected persons who received vaccine compared with unvaccinated controls. Limited information is available concerning the effect of antiretroviral therapy on increases in HIV RNA levels after either natural influenza infection or influenza vaccination. Because influenza can result in serious illness and complications and because influenza vaccination may result in protective antibody titers, the ACIP recommendations state that vaccination will benefit many HIV-infected patients, including HIV-infected pregnant women (see **PRECAUTIONS – Pregnancy**).[1]

Travelers:

The risk of exposure to influenza during travel varies, depending on season and destination. Influenza can occur throughout the year in the tropics; the season of greatest influenza activity in temperate regions of the Southern Hemisphere is April through September. In temperature climate zones of the Northern and Southern hemispheres, travelers also can be exposed to influenza during the summer, especially when traveling as part of organized tourist groups that include persons from areas of the world where influenza viruses are circulating. Persons at high risk for complications of influenza who were not vaccinated with influenza vaccine during the preceding fall or winter should consider receiving the vaccine before travel if they 1) travel to the tropics, or 2) travel with large organized tourist groups at any time of year, or 3) travel to the Southern Hemisphere from April through September. Persons at high risk who received the previous season's vaccine prior to travel should be revaccinated in the fall or winter with the current vaccine.[1]

General population:

Physicians should administer influenza virus vaccine to any person who wishes to reduce the likelihood of becoming ill with influenza caused by the strains incorporated into this year's vaccine. Persons who provide essential community services should be considered for vaccination to minimize disruption of essential activities during influenza outbreaks. Students or other persons in institutional settings (eg, those who reside in dormitories) should be encouraged to receive vaccine to minimize the disruption of routine activities during epidemics.[1]

Immunization Programs

Persons planning substantial organized vaccination campaigns should consider scheduling these events after mid-October. Campaigns conducted before November should focus efforts on vaccination of persons at high risk, health-care workers, and household contacts of persons at high-risk to the extent feasible.[1]

If this product is to be used in an immunization program sponsored by an organization WHERE A TRADITIONAL PHYSICIAN/PATIENT RELATIONSHIP DOES NOT EXIST, each participant (or legal guardian) should be made aware of the possible risks and adverse events that have been associated with the use of influenza virus vaccines, including the possible risk of a form of paralysis sometimes known as Guillain-Barré syndrome (GBS). Information about possible side effects and adverse events is presented below, and informed consent, preferably written, should be obtained from the intended recipient (or legal guardian) before vaccine administration. FluShield® (Influenza Virus Vaccine, Trivalent, Types A and B [Purified Subvirion]) is a prescription product and shall only be administered upon prescription by a healthcare professional who is licensed to prescribe biologicals. The prescribing healthcare professional should be familiar with the text of this insert, including the **CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS** sections.

Simultaneous Administration with Adult Vaccines

The target groups for influenza and 23-valent pneumococcal polysaccharide vaccination overlap considerably. For persons at high risk who have not previously been vaccinated with 23-valent pneumococcal polysaccharide vaccine, the ACIP states healthcare professionals should strongly consider administering 23-valent pneumococcal polysaccharide and influenza virus vaccine concurrently. These vaccines can be administered at the same time at different sites without increasing side effects. However, influenza virus vaccine is given annually, whereas 23-valent pneumococcal polysaccharide vaccine is not.[1]

Simultaneous Administration with Childhood Vaccines

According to the ACIP, no studies regarding the simultaneous administration of inactivated influenza vaccine and other childhood vaccines have been conducted; however, typically, inactivated vaccines do not interfere with the immune response to other inactivated or live vaccines and children at high risk for influenza-related complications, including those aged 6-23 months, can receive influenza vaccine at the same time they receive other routine vaccinations,[1] at differing administration sites.

As with any vaccine, FluShield may not protect 100% of individuals receiving the vaccine.

CONTRAINDICATIONS

FLUSHIELD® SHOULD NOT BE ADMINISTERED TO INDIVIDUALS WITH A HISTORY OF HYPERSENSITIVITY (ALLERGY) TO CHICKEN EGG OR TO ANY COMPONENT(S) OF INFLUENZA VIRUS VACCINE, INCLUDING THIMEROSAL, WITHOUT FIRST CONSULTING A PHYSICIAN (see **ADVERSE REACTIONS**). Before being vaccinated, persons known to be hypersensitive to egg protein or other components should be given a skin test or other allergy-evaluating test, using the influenza virus vaccine as the antigen. Persons with adverse reactions to such testing should not be vaccinated. Chemoprophylaxis may be indicated for prevention of influenza in such persons. However, persons with a history of anaphylactic hypersensitivity to vaccine components but who are also at highest risk for complications of influenza infections may benefit from vaccine after appropriate allergy evaluation and desensitization.[1]

Persons with a past history of GBS should not be given influenza virus vaccine (see **ADVERSE REACTIONS**).

Persons with acute febrile illnesses usually should not be vaccinated until their symptoms have abated. However, minor illnesses with or without fever should not contraindicate the use of influenza virus vaccine, particularly in children with a mild upper respiratory tract infection or allergic rhinitis.[1,2]

WARNINGS

Patients with impaired immune responsiveness, whether due to the use of immunosuppressive therapy (including irradiation, large amounts of corticosteroids, antimetabolites, alkylating agents, and cytotoxic agents), a genetic defect, HIV infection, leukemia, lymphoma, generalized malignancy, or other causes, may have a reduced antibody response to immunization. Short-term (less than 2 weeks) oral corticosteroid therapy or administration via topical (skin or eyes), or inhalational route, or intra-articular, bursal, or tendon injections is thought not to be immunosuppressive.[3] Because patients with immunodeficiencies may not have an adequate response to immunizing agents, they may remain susceptible despite having received an appropriate vaccine. If feasible, specific serum antibody titers or other immunologic responses may be determined after immunization to assess immunity.[2] Chemoprophylaxis may be indicated for high risk persons who are expected to have a poor antibody response to influenza virus vaccine.[1]

Healthcare professionals should prescribe and/or administer this product with caution to patients with a possible history of latex sensitivity since this packaging contains dry natural rubber.

Healthcare professionals should be aware that there is a potential risk for allergic reaction in patients with a history of aminoglycoside hypersensitivity since gentamicin is used in manufacturing (see **DESCRIPTION**).

PRECAUTIONS

General

Care should be taken by the healthcare professional for the effective use of this product.

1. Prior to the administration of any dose of FluShield®, the patient, parent, or guardian should be asked about the personal history, family history, and recent health status of the vaccine recipient. The healthcare professional should ascertain previous immunization history, current health status, and occurrence of any symptoms and/or signs of an adverse event after previous immunization in order to determine the existence of any contraindication to immunization with FluShield and to allow an assessment of benefits and risks.
2. Influenza virus is remarkably capricious antigenically, and significant changes may occur from time to time. *It is known definitely that influenza virus vaccine, as now constituted, is not effective against all possible strains of influenza virus. Any protection afforded is only against those strains of virus from which the vaccine is prepared or against closely related strains.*
3. Influenza virus vaccine often contains one or more antigens used in previous years. However, immunity declines during the year following immunization. Therefore, revaccination on a yearly basis is necessary to provide optimal protection for the current season. REMAINING 2001-2002 VACCINE SHOULD NOT BE USED.
4. Before the injection of any biological, the healthcare professional should take all precautions known for the prevention of allergic or any other side reactions. This should include: a review of the patient's history regarding sensitivity; the ready availability of epinephrine injection (1:1000) and other appropriate agents used for control of immediate or delayed allergic reactions; and a knowledge of recent literature pertaining to use of the biological concerned, including the nature of side effects and adverse reactions that may follow its use.
5. A separate sterile syringe and needle or a sterile disposable unit should be used for each patient to prevent transmission of hepatitis or other infectious agents from one person to another. Reusable glass syringes and needles should be heat-sterilized. Needles should be disposed of properly and should not be recapped.
6. Special care should be taken to prevent injection into or near a blood vessel or nerve.
7. The needle should be of sufficient length to ensure intramuscular injection.[1]
8. Guidance should be provided to the patient, parent, or guardian on measures to be taken should suspected adverse events occur, such as antipyretic measures for elevated temperatures and the need to report any suspected adverse occurrence to the healthcare professional.

9. Healthcare professionals should administer FluShield® (Influenza Virus Vaccine, Trivalent, Types A and B [Purified Subvirion]) with caution to patients with a possible history of latex sensitivity, since this packaging contains dry natural rubber.

Drug Interactions

There have been conflicting reports of the effects of influenza virus vaccine on the elimination of some drugs metabolized by the hepatic cytochrome P-450 system. Increases in prothrombin time in patients receiving warfarin, elevated serum theophylline concentrations, and alterations in steady-state concentrations of phenytoin and other anticonvulsants have been reported.[4] Most studies have failed to show any adverse clinical effects of altered drug levels or increased reactogenicity from influenza virus vaccine in patients receiving these drugs.[4,5] A pharmacokinetic study found that influenza immunization does not significantly change the activity of one cytochrome P-450 enzyme, CYP3A4; however most drugs are substrates for more than one CYP enzyme.[6] Nonetheless, monitoring for possible enhanced drug effect or toxicity should be considered for those persons taking medications metabolized by the cytochrome P-450 system, including warfarin and theophylline, or anticonvulsants when they receive influenza virus vaccination.

Individuals receiving therapy with immunosuppressive agents (large amounts of corticosteroids, antimetabolites, alkylating agents, cytotoxic agents) may not respond optimally to active immunization procedures (see **WARNINGS**).

As with other intramuscular injections, this product should be given with caution to a person on anticoagulant therapy.

Carcinogenesis, Mutagenesis, Impairment of Fertility

FluShield has not been evaluated for its carcinogenic or mutagenic potential or for impairment of fertility.

Pregnancy

Pregnancy Category C:

Animal reproduction studies have not been conducted with influenza virus vaccine. It is also not known whether influenza virus vaccine can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Influenza virus vaccine should be given to a pregnant woman only if clearly needed. The benefits of preventing influenza-related complications versus the theoretical risk of fetal harm should be considered, and discussed with the patient before administering influenza virus vaccine to a pregnant woman. The ACIP states that, if used during pregnancy, administration of influenza virus vaccine after 14 weeks of gestation may be preferable to avoid coincidental association of the vaccine with spontaneous abortion[1] (see **INDICATIONS AND USAGE, Additional Groups for Vaccination**). The ACIP further states that the majority of influenza vaccine distributed in the United States contains thimerosal, a mercury-containing compound, as a preservative, but influenza vaccine with reduced thimerosal content might be available in limited quantities. Thimerosal has been used in U.S. vaccines since the 1930s. No data or evidence exists of any harm caused by the level of mercury exposure that might occur from influenza vaccination. Because pregnant women are at an increased risk for influenza-related complications and because a substantial safety margin has been incorporated into the health guidance values for organic mercury exposure, the benefit of influenza vaccine with reduced or standard thimerosal content outweighs the potential risk, if any, for thimerosal.[1]

Nursing mothers

Influenza virus vaccine does not affect the safety of breastfeeding for mothers or infants. Breastfeeding does not adversely affect immune response and is not a contraindication for vaccination.[1]

Geriatric Use

The effectiveness of influenza virus vaccine in preventing or attenuating illness varies, depending primarily on the age and immunocompetence of the vaccine recipient and the degree of similarity between the virus strains included in the vaccine and those that circulate during the influenza season. Studies have indicated that the effectiveness of influenza virus vaccine in preventing hospitalization for pneumonia and influenza among elderly persons living in settings other than nursing homes or similar chronic-care facilities ranges from 30% to 70%.[1]

Among elderly persons residing in nursing homes, influenza virus vaccine is most effective in preventing severe illness, secondary complications, and death. Studies of this population have indicated that the vaccine can be 50% to 60% effective in preventing hospitalization and pneumonia and 80% effective in preventing death, even though effectiveness in preventing influenza illness may often be in the range of 30% to 40% among the frail elderly. Vaccination of healthcare workers in nursing homes also has been effective in reducing the impact of influenza among residents.[1]

Pediatric Use

The safety and effectiveness of influenza virus vaccine in pediatric patients under 6 months of age have not been established. However, the ACIP recommends influenza vaccination in certain circumstances for persons 6 months of age or older who, because of age or underlying medical condition, are at increased risk for complications of influenza (see **INDICATIONS AND USAGE,** and **DOSAGE AND ADMINISTRATION**).[1]

The ACIP supports vaccination of healthy children aged ≥6 months whose parents wish to decrease their child's risk for influenza infection, in addition to vaccinating children with high risk medical conditions.[1]

Studies indicate that rates of hospitalization are higher among young children than older children when influenza viruses are in circulation. The increased rates of hospitalization are comparable with rates for other groups considered at high risk for influenza-related complications. Because children aged 6-23 months are at substantially increased risk for influenza-related hospitalizations, influenza vaccination of all children in this age group is encouraged when feasible. The current inactivated influenza vaccine is not approved by FDA for use among children <6 months, the pediatric group at greatest risk for influenza-related complications. Vaccinating their household contacts and out-of-home caretakers might decrease the probability of influenza among these children.[1]

Information for Patients

BECAUSE FLUSHIELD CONTAINS ONLY NONINFECTIOUS VIRUSES, IT CANNOT CAUSE INFLUENZA. When educating patients regarding potential side effects, clinicians should emphasize that, a) inactivated influenza vaccine contains non-infectious killed virus and cannot cause influenza; and b) coincidental respiratory disease unrelated to influenza vaccination can occur after vaccination.[1]

ADVERSE REACTIONS

The most frequent side effect of vaccination is soreness at the vaccination site for up to 2 days. These local reactions generally are mild and rarely interfere with the ability to conduct usual daily activities.[1] In addition the following injection site reactions have been reported: edema, pain or tenderness, erythema, inflammation, skin discoloration, induration, mass; and hypersensitivity reactions including pruritus and urticaria.

In addition, the following types of systemic events have occurred:

Fever, malaise, myalgia, and other systemic symptoms can occur following vaccination and most often affect persons who have had no exposure to the influenza virus antigens in the vaccine (eg, young children). These reactions usually begin 6 to 12 hours after vaccination and can persist for 1 or 2 days.[1]

Other systemic events that have been reported include: arthralgia, asthenia, chills, dizziness, headache, lymphadenopathy, pruritus, rash, nausea, vomiting, diarrhea, and pharyngitis. Recent placebo-controlled trials suggest that in elderly persons and healthy young adults, split-virus influenza vaccine is not associated with higher rates of systemic symptoms (eg, fever, malaise, myalgia, and headache) when compared with placebo injections.[1] Additional events that have been reported include angiopathy and vasculitis.[7-9]

A report of delayed anaphylaxis or delayed onset of severe asthma or hypersensitivity reaction in a known asthmatic after administration of FluShield® (Influenza Virus Vaccine, Trivalent, Types A and B [Purified Subvirion]) has been received; the reaction began approximately 6 hours following receipt of influenza virus vaccine and resulted in death within the next hour.

Immediate, presumably allergic, reactions such as hives, angioedema, allergic asthma, or systemic anaphylaxis occur rarely after influenza vaccination. These reactions probably result from hypersensitivity to some vaccine component — the majority of reactions are most likely related to residual egg protein. Although current influenza virus vaccines contain only a small quantity of egg protein, this protein can induce immediate hypersensitivity reactions among persons who have severe egg allergy. Persons who have developed hives, have had swelling of the lips or tongue, or experienced acute respiratory distress or collapse after eating eggs should consult a physician for appropriate evaluation to help determine if vaccine should be administered. Persons who have documented immunoglobulin E (IgE)-mediated hypersensitivity to eggs, including those who have had occupational asthma or other allergic responses due to exposure to egg protein, might also be at increased risk for reactions from influenza virus vaccine and similar consultation should be considered. Protocols have been published for safely administering influenza vaccine to persons with egg allergies.[1] Hypersensitivity reactions to any vaccine component can occur. Although exposure to vaccines containing thimerosal can lead to induction of hypersensitivity, most patients do not develop reactions to thimerosal when administered as a component of vaccines even when patch or intradermal tests for thimerosal indicate hypersensitivity. When reported, hypersensitivity to thimerosal has usually consisted of local, delayed-type hypersensitivity reactions.[1]

One study reports a decrease in pulmonary function in some asthmatics who received influenza vaccine[10] however, another recent large-scale study indicated that influenza vaccination was not associated with clinically significant asthma exacerbation or worsening of asthma symptoms in the two weeks after vaccination.[11,12,13]

There have been rare reports of GBS following receipt of influenza virus vaccine.[14] GBS is an uncommon illness characterized by ascending paralysis which is usually self-limited and reversible. Though most persons with GBS recover without residual weakness, approximately 5% of cases are fatal.

The 1976 swine influenza vaccine was associated with an increased frequency of GBS. Among persons who received the swine influenza vaccine in 1976, the rate of GBS that exceeded the background rate was <10 cases/1,000,000 persons vaccinated.[14] Evidence for a causal relationship of GBS with subsequent vaccines prepared from other influenza viruses is unclear. Obtaining strong epidemiologic evidence for a possible limited increase in risk is difficult for such a rare condition as GBS, which has an annual incidence of 10-20 cases/1,000,000 adults, and stretches the limits of epidemiologic investigation. More definitive data probably will require the use of other methodologies (eg, laboratory studies of the patho-physiology of GBS). During three of four influenza seasons studied during 1977-1991, the overall relative risk estimates for GBS after influenza vaccination were slightly elevated but were not statistically significant in any of these studies. However, in a study of the 1992-1993 and 1993-1994 seasons, the overall relative risk for GBS was 1.7 (95% confidence interval = 1.0-2.8; p = 0.04) during the 6 weeks after vaccination, representing approximately 1 additional case of GBS/1,000,000 persons vaccinated. The combined number of GBS cases peaked 2 weeks after vaccination. Thus, investigations to date indicate no substantial increase in GBS associated with influenza vaccines (other than the swine influenza vaccine in 1976) and that, if influenza vaccine does pose a risk, it is probably slightly more than one additional case per million persons vaccinated. Cases of GBS after influenza infection have been reported, but no epidemiologic studies have documented such an association. Substantial evidence exists that several infectious illnesses, most notably *Campylobacter jejuni,* as well as upper-respiratory tract infections typically are associated with GBS.[1]

Even if GBS were a true side effect of vaccination in the years after 1976, the estimated risk for GBS of approximately 1 additional case/1,000,000 persons vaccinated is substantially less than the risk for severe influenza, which could be prevented by vaccination among all age groups, especially persons aged ≥65 years and those who have medical indications for influenza vaccination. The potential benefits of influenza vaccination in preventing serious illness, hospitalization, and death greatly outweigh the possible risks for developing vaccine-associated GBS.[14] The average case-fatality ratio for GBS is 6% and increases with age. No evidence indicates that the case-fatality ratio for GBS differs between vaccinated persons and those not vaccinated.[1]

The incidence of GBS among the general population is low, but persons with a history of GBS have a substantially greater likelihood of subsequently developing GBS than persons without such a history. Thus, the likelihood of coincidentally developing GBS after influenza vaccination is expected to be greater among persons with a history of GBS than among persons with no history of this syndrome. Whether influenza vaccination specifically might increase the risk for recurrence of GBS is not known; therefore, avoiding vaccinating persons who are not at high risk for severe influenza complications and who are known to have developed GBS within 6 weeks after a previous influenza vaccination is prudent. As an alternative, physicians might consider the use of influenza antiviral chemoprophylaxis for these persons.[1]

Other neurologic disorders not defined as GBS, including encephalopathies, facial paralysis, unspecified neuritis, encephalitis, peripheral nerve disease, paresthesia, hypoesthesia, brachial neuritis, optic neuritis, demyelinating disease, labyrinthitis, and meningitis have been temporally associated with influenza vaccination.[15] Rarely, transverse myelitis has been reported.[16]

ADVERSE EVENT REPORTING

The manufacturer and lot number of the vaccine administered should be recorded in the vaccine recipient's permanent medical record, along with the date of administration of the vaccine and the name, address, and title of the person administering the vaccine. Any adverse events following immunizations should be reported by the healthcare professional to the U.S. Department of Health and Human Services (DHHS).

The U.S. DHHS has established the Vaccine Adverse Event Reporting System (VAERS) to accept all reports of suspected adverse events after administration of any vaccine. The toll-free number for VAERS forms and information is 800-822-7967.

The FDA Web Site is http:www.fda.gov/cber/vaers/vaers.htm

DOSAGE AND ADMINISTRATION

FOR INTRAMUSCULAR INJECTION ONLY

AGE GROUP	DOSAGE SCHEDULE
9 years and older	0.5 mL (one dose)
3 to 8 years	0.5 mL (1 or 2 doses)*
6 to 35 months	0.25 mL (1 or 2 doses)*

*Two doses are recommended for children under 9 years who are receiving influenza virus vaccine for the first time. With the 2-dose regimen, allow 4 weeks or more between doses. Both doses are recommended for maximum protection.

For those under 13 years, only split-virus (subvirion) vaccine is recommended. Immunogenicity and reactogenicity of split- and whole-virus vaccines are similar in adults when used according to the recommended dosage.[1]

Although influenza virus vaccine often contains one or more antigens used in previous years, immunity declines during the year following vaccination. Therefore, a history of vaccination in any previous year with a vaccine containing one or more antigens included in the current vaccine does NOT preclude the need for revaccination for the 2002-2003 influenza season to help provide optimal protection. REMAINING 2001-2002 VACCINE SHOULD NOT BE USED.

ACIP recommends that vaccine providers focus their vaccination efforts in October and earlier on persons at high risk and health-care workers. Vaccination of children aged <9 years who are receiving vaccine for the first time should also begin in October because they need a booster dose 1 month after the initial dose. Vaccination of all other groups should begin in November, including household members of persons at high risk, healthy persons aged 50-64 years, and other persons who wish to decrease their risk for influenza infection. In the United States, seasonal influenza activity can begin to increase as early as November or December, but influenza activity has not reached peak levels in the majority of recent seasons until late December through early March. Therefore, although the timing of influenza activity can vary by region, vaccine administered after November is likely to be beneficial in the majority of influenza seasons. Adults develop peak antibody protection against influenza infection 2 weeks after vaccination.[1]

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. The product should not be used if particulate matter or discoloration is found. The product appears as a slightly opalescent solution.

DO NOT INJECT INTRAVENOUSLY. Injections of FluShield® (Influenza Virus Vaccine, Trivalent, Types A and B [Purified Subvirion]) are recommended to be given intramuscularly. The recommended site is the deltoid muscle for adults and older children.[1] The preferred site for infants and young children is the anterolateral aspect of the thigh musculature. Because of lack of adequate evaluation of other routes in high risk persons, the preferred route of vaccination is intramuscular whenever possible. Before injection, the skin over the site to be injected should be cleansed with a suitable germicide. After insertion of the needle, aspirate and wait to see if any blood appears in the syringe, which will help avoid inadvertent injection into a blood vessel. If blood appears, withdraw the needle and prepare for a new injection at another site.

HOW SUPPLIED

Influenza Virus Vaccine, Trivalent, Types A and B, (Purified Subvirion), FluShield®, is available as a 5 mL Vial:

NDC 0008-0987-01

Storage

Store at 2°C to 8°C (36°F to 46°F). Potency is destroyed by freezing; do not use FluShield that has been frozen.

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