

# Fluconazole in NICU Not Linked to Resistance

BY DIANA MAHONEY  
New England Bureau

TORONTO — Fluconazole prophylaxis for invasive candidiasis in extremely low-birth-weight infants is not associated with the emergence of fluconazole-resistant *Candida* species, Dr. C. Mary Healy said at the annual meeting of the Infectious Diseases Society of America.

In infants weighing less than 1,000 g at birth, 42 days of fluconazole prophylaxis

(FP) has been shown to reduce *Candida* colonization and invasive candidiasis, “but the possibility that [this regimen] could lead to a resistant *Candida* species is an on-going concern,” said Dr. Healy of Baylor College of Medicine in Houston. “The worry is that FP will cause overgrowth and infection by inherently less susceptible species, particularly *C. glabrata*.”

To evaluate the impact of FP on the incidence of invasive candidiasis (IC), as well as IC-related mortality and fluconazole

susceptibility of *Candida* isolates, Dr. Healy and her colleagues reviewed data from the neonatal intensive care unit (NICU) at the Women’s Hospital of Texas in Houston for infants treated both before and after the implementation of an FP strategy in 2002. For the purposes of this investigation, IC was defined as the presence of a *Candida* species isolated from blood or cerebrospinal fluid in NICU infants.

Since April 2002, as per hospital protocol, extremely low-birth-weight infants

younger than 5 days in the NICU of the Women’s Hospital of Texas have been eligible to receive intravenous FP at a dose of 3 mg/kg for 6 weeks on a dosing schedule that varies by age: every third day for the first 3 weeks, every second day for the subsequent 2 weeks, and daily for the final 2 weeks, said Dr. Healy.

Using pharmacy and electronic records, Dr. Healy and her colleagues reviewed the demographic, clinical, and laboratory data for all of the NICU infants of any birth weight during the first 4 years of FP implementation and compared it with that of infants who were in the NICU in 2000-2001, before the use of FP.

Between April 2002 and March 2006, 362 extremely low-birth-weight infants in the hospital’s NICU received FP, along with 47 infants with a body weight greater than 1,000 g who were started on the preventive therapy at the discretion of the neonatologist. The median body weight of the 409 infants was 775 g, the median gestation was 26 weeks, and the median dose they received was 13 mg/kg over 29 days.

Twenty-nine percent of those infants receiving FP completed the 6-week protocol. Fifty-nine percent discontinued the therapy because IV access was no longer needed, 7% died from non IC-related causes, 2% transferred to other hospitals, 2% had breakthrough infections, and 1% had transient elevation of liver transaminases, which resolved when FP was discontinued, Dr. Healy reported.

Comparing infants who developed IC during the pre- and post-FP time periods showed 19 cases in 2000-2001 and 22 cases in 2002-2006. “Infants [who developed IC] during the FP period were of significantly greater gestational age and had significantly higher birth weight than those who developed it before FP,” said Dr. Healy. “There was also a strong trend toward them being older, although this did not reach significance.” There was no difference in prenatal or perinatal complications, nor were there differences in complications of prematurity.

Among the risk factors for infection in both groups, “there was a strong trend toward more antibiotic use, longer duration of infant vascular catheters, and longer duration of TPN [total parenteral nutrition] in the FP period, but the only risk factor that reaches statistical significance was the use of H<sub>2</sub> blockers,” said Dr. Healy.

With respect to potential resistance, “our findings are reassuring,” said Dr. Healy. “The IC species distribution remained stable both before and after FP implementation. In the IC cases prior to FP, *C. albicans* was identified in 14 infants, *C. parapsilosis* in 3, *C. tropicalis* in 1, and *C. glabrata* in 1. After FP, the species distribution was *C. albicans* in 13 infants, *C. parapsilosis* in 6, *C. tropicalis* in 1, and *C. glabrata* in 2. “It’s particularly reassuring that *C. glabrata* is no more common now than it was before FP,” she said.

Similarly, the minimum inhibitory concentrations (MICs) for fluconazole were consistent.

Dr. Healy reported having no conflicts of interest related to this presentation. ■

## Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine Menactra®

FOR INTRAMUSCULAR INJECTION

Brief Summary: Please consult package insert for full prescribing information.

### INDICATIONS AND USAGE

Menactra vaccine is indicated for active immunization of adolescents and adults 11–55 years of age for the prevention of invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y and W-135.

Menactra vaccine is not indicated for the prevention of meningitis caused by other microorganisms or for the prevention of invasive meningococcal disease caused by *N. meningitidis* serogroup B.

Menactra vaccine is not indicated for treatment of meningococcal infections.

Menactra vaccine is not indicated for immunization against diphtheria.

The Advisory Committee on Immunization Practices (ACIP) has published recommendations for the prevention and control of meningococcal disease in the US (refer to [www.cdc.gov](http://www.cdc.gov)).<sup>1</sup>

As with any vaccine, Menactra vaccine may not protect 100% of individuals.

### CONTRAINDICATIONS

Known hypersensitivity to any component of Menactra vaccine including diphtheria toxoid, or a life-threatening reaction after previous administration of a vaccine containing similar components,<sup>2</sup> are contraindications to vaccine administration.

Known history of Guillain-Barré Syndrome (see WARNINGS section) is a contraindication to vaccine administration.

Known hypersensitivity to dry natural rubber latex (see WARNINGS section) is a contraindication to vaccine administration.

### WARNINGS

Guillain-Barré Syndrome (GBS) has been reported in temporal relationship following administration of Menactra vaccine (see ADVERSE REACTIONS, POST-MARKETING REPORTS section). Persons previously diagnosed with GBS should not receive Menactra vaccine.

The stopper of the vial contains dry natural rubber latex, which may cause allergic reactions in latex-sensitive individuals.

Because of the risk of hemorrhage, Menactra vaccine should not be given to persons with any bleeding disorder, such as hemophilia or thrombocytopenia, or to persons on anticoagulant therapy unless the potential benefit clearly outweighs the risk of administration. If the decision is made to administer Menactra vaccine in such persons, it should be given with caution, with steps taken to avoid the risk of bleeding or hematoma formation following injection.

The ACIP has published guidelines for vaccination of persons with recent or acute illness (refer to [www.cdc.gov](http://www.cdc.gov)).<sup>3</sup>

### PRECAUTIONS

Before administration, all appropriate precautions should be taken to prevent adverse reactions. This includes a review of the patient’s previous immunization history, the presence of any contraindications to immunization, the current health status, and history concerning possible sensitivity to the vaccine, similar vaccine, or to latex.

AS A PRECAUTIONARY MEASURE, EPINEPHRINE INJECTION (1:1000) AND OTHER APPROPRIATE AGENTS AND EQUIPMENT MUST BE IMMEDIATELY AVAILABLE IN CASE OF ANAPHYLACTIC OR SERIOUS ALLERGIC REACTIONS.

As part of the patient’s immunization record, the date, lot number and manufacturer of the vaccine administered should be recorded. Special care should be taken to avoid injecting the vaccine subcutaneously since clinical studies have not been conducted to establish safety and efficacy of the vaccine using this route of administration.

A separate, sterile syringe and needle or a sterile disposable unit should be used for each patient to prevent transmission of blood borne infectious agents from person to person. Needles should not be recapped and should be disposed of according to biohazardous waste guidelines.

The immune response to Menactra vaccine administered to immunosuppressed persons has not been studied.

### INFORMATION FOR PATIENTS

Prior to administration of Menactra vaccine, the health-care professional should inform the patient, parent, guardian, or other responsible adult of the potential benefits and risks to the patient, and provide vaccine information statements (see ADVERSE REACTIONS and WARNINGS sections). Patients, parents or guardians should be instructed to report any suspected adverse reactions to their health-care professional. Females of childbearing potential should be informed that Sanofi Pasteur Inc. maintains a pregnancy registry to monitor fetal outcomes of pregnant women exposed to Menactra vaccine. If they are pregnant or become aware they were pregnant at the time of Menactra vaccine immunization, they should contact their health-care professional or Sanofi Pasteur Inc. at 1-800-822-2463 (see PRECAUTIONS section).

### DRUG INTERACTION

For information regarding concomitant administration of Menactra vaccine with other vaccines, refer to ADVERSE REACTIONS and DOSAGE AND ADMINISTRATION sections.

Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses) may reduce the immune response to vaccines.

### CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY

Menactra vaccine has not been evaluated in animals for its carcinogenic or mutagenic potentials or for impairment of fertility.

### PREGNANCY CATEGORY C

Animal reproduction studies were performed in mice using 0.2 mL of Menactra vaccine (900 times the human dose, adjusted by body weight). There were no effects on fertility, maternal health, embryo/fetal survival, or post-natal development. Skeletal examinations revealed one fetus (1 of 234 examined) in the vaccine group with a cleft palate. None were observed in the concurrent control group (0 of 174 examined). There are no data that suggest that this isolated finding is vaccine related, and no other skeletal and organ malformations were observed in this study. There are no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human response, Menactra vaccine should be used during pregnancy only if clearly needed. Health-care providers are encouraged to register pregnant women who receive Menactra vaccine in Sanofi Pasteur Inc.’s vaccination pregnancy registry by calling 1-800-822-2463.

### NURSING MOTHERS

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Menactra vaccine is administered to a nursing woman.

### PEDIATRIC USE

SAFETY AND EFFECTIVENESS OF MENACTRA VACCINE IN CHILDREN BELOW THE AGE OF 11 YEARS HAVE NOT BEEN ESTABLISHED.

### GERIATRIC USE

SAFETY AND EFFECTIVENESS OF MENACTRA VACCINE IN ADULTS OLDER THAN 55 YEARS HAVE NOT BEEN ESTABLISHED.

### ADVERSE REACTIONS

The safety of Menactra vaccine was evaluated in 6 clinical studies that enrolled 7642 participants aged 11–55 years who received Menactra vaccine and 3041 participants who received Menomune-AC/Y/W-135 vaccine. There were no substantive differences in demographic characteristics between the vaccine groups. Among Menactra vaccine recipients of all ages, 21.3%, 53.2% and 25.5% were in the 11–14, 15–25 and 26–55-year age groups, respectively. Among Menomune-AC/Y/W-135 vaccine recipients of all ages, 16.1%, 51.9% and 32.0% were in the 11–14, 15–25 and 26–55-year age groups, respectively.

The two primary safety studies were randomized, active-controlled trials that enrolled participants 11–18 years of age (Menactra vaccine, N=2270; Menomune-AC/Y/W-135 vaccine, N=972) and 18–55 years of age (Menactra vaccine, N=1384; Menomune-AC/Y/W-135 vaccine, N=1170), respectively. As the route of administration differed for the two vaccines (Menactra vaccine given intramuscularly, Menomune-AC/Y/W-135 given subcutaneously), study personnel collecting the safety data differed from personnel administering the vaccine. Solicited local and systemic reactions were monitored daily for 7 days post-vaccination using a diary card. Participants were monitored for 28 days for unsolicited adverse events and for 6 months post-vaccination for visits to an emergency room, unexpected visits to an office physician, and serious adverse events. Unsolicited adverse event information was obtained either by telephone interview or at an interim clinic visit. Information regarding adverse events that occurred in the 6-month post-vaccination time period was obtained via a scripted telephone interview. At least 94% of participants from the two studies completed the 6-month follow-up evaluation.

In the two concomitant vaccination studies with Menactra and either Typhim Vi or Td vaccines, local and systemic adverse events were monitored for 7 days post vaccination using a diary card. Serious adverse events occurring within 1 month after each vaccination were reported and recorded.

### SERIOUS ADVERSE EVENTS IN ALL SAFETY STUDIES

Serious adverse events reported within a 6-month time period following vaccination occurred at the same rate (1.3%) in the Menactra vaccine and Menomune-AC/Y/W-135 vaccine groups. The events reported were consistent with events expected in healthy adolescent and adult populations.

### SOLICITED ADVERSE EVENTS IN THE PRIMARY SAFETY STUDIES

The most commonly reported solicited adverse reactions in adolescents, ages 11–18 years (TABLE 1), and adults, ages 18–55 years (TABLE 2), were local pain, headache and fatigue. Except for redness in adults, local reactions were more frequently reported after Menactra vaccination than after Menomune-AC/Y/W-135 vaccination. The majority of local and systemic reactions following Menactra or Menomune-AC/Y/W-135 vaccination were reported as mild to intensity. No important differences in rates of malaise, diarrhea, anorexia, vomiting, or rash were observed between the vaccine groups.

TABLE 1: PERCENTAGE OF PARTICIPANTS 11–18 YEARS OF AGE REPORTING SOLICITED REACTIONS

Reaction	Menactra vaccine			Menomune-AC/Y/W-135 vaccine		
	Any	Moderate	Severe	Any	Moderate	Severe
Redness†	10.9*	1.6*	0.6*	5.7	0.4	0.0
Swelling†	10.8*	1.9*	0.5*	3.6	0.3	0.0
Induration†	15.7*	2.5*	0.3	5.2	0.5	0.0
Pain†	59.2*	12.8*	0.3	28.7	2.6	0.0
Headache‡	35.6*	9.6*	1.1	29.3	6.5	0.4
Fatigue§	30.0*	7.5	1.1*	25.1	6.2	0.2
Malaise¶	21.9*	5.8*	1.1	16.8	3.4	0.4
Arthralgia§	17.4*	3.6*	0.4	10.2	2.1	0.1
Diarrhea¶	12.0	1.6	0.3	10.2	1.3	0.0
Anorexia†	10.7*	2.0	0.3	7.7	1.1	0.2
Chills†	7.0*	1.7*	0.2	3.5	0.4	0.1
Fever*	5.1*	0.6	0.0	3.0	0.3	0.1
Vomiting**	1.9	0.4	0.3	1.4	0.5	0.3
Rash††	1.6			1.4		
Seizure†††	0.0			0.0		

\* Denotes  $p < 0.05$  level of significance. The  $p$  values were calculated for each category and severity using Chi Square test; † Moderate: 1.0–2.0 inches; Severe:  $> 2.0$  inches; ‡ Moderate: interferes with normal activities; Severe: Disabling, unwilling to move arm; § Severe: Requiring bed rest; ¶ Severe:  $\geq 5$  episodes; † Severe: skipped  $\geq 3$  meals; † Severe:  $\geq 39.5^\circ\text{C}$ ; \*\* Severe:  $\geq 3$  episodes; †† These solicited adverse events were reported as present or absent only.

TABLE 2: PERCENTAGE OF PARTICIPANTS 18–55 YEARS OF AGE REPORTING SOLICITED REACTIONS

Reaction	Menactra vaccine			Menomune-AC/Y/W-135 vaccine		
	Any	Moderate	Severe	Any	Moderate	Severe
Redness†	14.4	2.9	1.1*	16.0	1.9	0.1
Swelling†	12.6*	2.3*	0.9*	7.6	0.7	0.0
Induration†	17.1*	3.4*	0.7*	11.0	1.0	0.0
Pain†	53.9*	11.3*	0.2	48.1	3.3	0.1
Headache‡	41.4	10.1	1.2	41.8	8.9	0.9
Fatigue§	34.7	8.3	0.9	32.3	6.6	0.4
Malaise¶	23.6	6.6*	1.1	22.3	4.7	0.9
Arthralgia§	19.8*	4.7*	0.3	16.0	2.6	0.1
Diarrhea¶	16.0	2.6	0.4	14.0	2.9	0.3
Anorexia†	11.8	2.3	0.4	9.9	1.6	0.4
Chills†	9.7*	2.1*	0.6*	5.6	1.0	0.0
Fever*	1.5*	0.3	0.0	0.5	0.1	0.0
Vomiting**	2.3	0.4	0.2	1.5	0.2	0.4
Rash††	1.4			0.8		
Seizure†††	0.0			0.0		

\* Denotes  $p < 0.05$  level of significance. The  $p$  values were calculated for each category and severity using Chi Square test; † Moderate: 1.0–2.0 inches; Severe:  $> 2.0$  inches; ‡ Moderate: interferes with normal activities; Severe: Disabling, unwilling to move arm; § Severe: Requiring bed rest; ¶ Severe:  $\geq 5$  episodes; † Severe: skipped  $\geq 3$  meals; † Severe:  $\geq 40.0^\circ\text{C}$ ; \*\* Severe:  $\geq 3$  episodes; †† These solicited adverse events were reported as present or absent only.

### ADVERSE EVENTS IN CONCOMITANT VACCINE STUDIES

Local and Systemic reactions when given with Td vaccine  
The two vaccine groups reported similar frequencies of local pain, induration, redness and swelling at the Menactra injection site, as well as, at the Td injection site. Pain was the most frequent local reaction reported at both the Menactra and Td injection sites. More participants experienced pain after Td vaccination than after Menactra vaccination (76% versus 47%). The majority (70%–77%) of local solicited reactions for both groups at either injection site were reported as mild and resolved within 3 days post-vaccination. In both groups, the most common systemic reaction was headache (Menactra + Typhim Vi vaccine, 41%; Typhim Vi vaccine + Placebo, 42%; Menactra vaccine alone, 33%) and fatigue (Menactra + Typhim Vi vaccine, 38%; Typhim Vi vaccine + Placebo, 35%; Menactra vaccine alone, 27%). No important differences in rates of malaise, diarrhea, anorexia, vomiting, or rash were observed between the groups. Fever  $\geq 40.0^\circ\text{C}$  occurred at  $\leq 0.5\%$  in all groups. No seizures occurred in either group.

Local and Systemic reactions when given with Typhim Vi Vaccine  
The two vaccine groups reported similar frequencies of local pain, induration, redness and swelling at the Menactra injection site, as well as, at the Typhim Vi injection site. Pain was the most frequent local reaction reported at both the Menactra and Typhim Vi injection sites. More participants experienced pain after Typhim Vi vaccination than after Menactra vaccination (76% versus 47%). The majority (70%–77%) of local solicited reactions for both groups at either injection site were reported as mild and resolved within 3 days post-vaccination. In both groups, the most common systemic reaction was headache (Menactra + Typhim Vi vaccine, 41%; Typhim Vi vaccine + Placebo, 42%; Menactra vaccine alone, 33%) and fatigue (Menactra + Typhim Vi vaccine, 38%; Typhim Vi vaccine + Placebo, 35%; Menactra vaccine alone, 27%). No important differences in rates of malaise, diarrhea, anorexia, vomiting, or rash were observed between the groups. Fever  $\geq 40.0^\circ\text{C}$  and seizures were not reported in either group.

### POST-MARKETING REPORTS

The following adverse events have been reported during post-approval use of Menactra vaccine. Because these events were reported voluntarily from a population of uncertain size, it is not always possible to reliably calculate their frequency or to establish a causal relationship to Menactra vaccine exposure.

Nervous system disorders - Guillain-Barré Syndrome, transverse myelitis

### DOSAGE AND ADMINISTRATION

Menactra vaccine should be administered as a single 0.5 mL injection by the intramuscular route, preferably in the deltoid region. Before injection, the skin at the injection site should be cleaned and prepared with a suitable germicide. After insertion of the needle, aspirate to ensure that the needle has not entered a blood vessel.

Do not administer this product intravenously, subcutaneously, or intradermally.

The need for, or timing of, a booster dose of Menactra vaccine has not yet been determined.

Parenteral drug products should be inspected visually for container integrity, particulate matter and discoloration prior to administration, whenever solution and container permit.

### CONCOMITANT ADMINISTRATION WITH OTHER VACCINES

Safety and immunogenicity data are available on concomitant administration of Menactra vaccine with Typhim Vi, and Td vaccines (see ADVERSE REACTIONS section). Concomitant administration of Menactra vaccine with Td did not result in reduced tetanus, diphtheria or meningococcal antibody responses compared with Menactra vaccine administered 28 days after Td.<sup>4</sup> However, for meningococcal serogroups C, Y and W-135, bactericidal antibody titers (GMTs) and the proportion of participants with a 4-fold or greater rise in Serum Bactericidal Assay (SBA) using baby rabbit complement (SBA-BR) titer were higher when Menactra vaccine was given concomitantly with Td than when Menactra vaccine was given one month following Td. The clinical relevance of these findings has not been fully evaluated.<sup>4</sup>

Concomitant administration of Menactra vaccine with Typhim Vi vaccine did not result in reduced antibody responses to any of the vaccine antigens.<sup>4</sup>

The safety and immunogenicity of concomitant administration of Menactra vaccine with vaccines other than Typhim Vi or Td vaccines have not been determined.

Menactra vaccine must not be mixed with any vaccine in the same syringe. Therefore, separate injection sites and different syringes should be used in case of concomitant administration.

### STORAGE

Store between 2° to 8°C (35° to 46°F). DO NOT FREEZE. Product that has been exposed to freezing should not be used. Protect from light. Do not use after expiration date.

REFERENCES: 1. Recommendations of the Advisory Committee on Immunization Practices (ACIP). Prevention and Control of Meningococcal Disease and Meningococcal Disease and College Students. MMWR 2000;49(RR-7). 2. Ball R, et al. Safety Data on Meningococcal Polysaccharide Vaccine from the Vaccine Adverse Event Reporting System. CID 2001;32:1273-1280. 3. ACIP. General recommendations on immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP). MMWR 2002;51(RR02):1-36. 4. Data on file, Aventis Pasteur Inc. – 092503.

Concomitant administration of Menactra vaccine with Typhim Vi vaccine did not result in reduced antibody responses to any of the vaccine antigens.<sup>4</sup>

The safety and immunogenicity of concomitant administration of Menactra vaccine with vaccines other than Typhim Vi or Td vaccines have not been determined.

Menactra vaccine must not be mixed with any vaccine in the same syringe. Therefore, separate injection sites and different syringes should be used in case of concomitant administration.

### STORAGE

Store between 2° to 8°C (35° to 46°F). DO NOT FREEZE. Product that has been exposed to freezing should not be used. Protect from light. Do not use after expiration date.

REFERENCES: 1. Recommendations of the Advisory Committee on Immunization Practices (ACIP). Prevention and Control of Meningococcal Disease and Meningococcal Disease and College Students. MMWR 2000;49(RR-7). 2. Ball R, et al. Safety Data on Meningococcal Polysaccharide Vaccine from the Vaccine Adverse Event Reporting System. CID 2001;32:1273-1280. 3. ACIP. General recommendations on immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP). MMWR 2002;51(RR02):1-36. 4. Data on file, Aventis Pasteur Inc. – 092503.

Concomitant administration of Menactra vaccine with Typhim Vi vaccine did not result in reduced antibody responses to any of the vaccine antigens.<sup>4</sup>

The safety and immunogenicity of concomitant administration of Menactra vaccine with vaccines other than Typhim Vi or Td vaccines have not been determined.

Menactra vaccine must not be mixed with any vaccine in the same syringe. Therefore, separate injection sites and different syringes should be used in case of concomitant administration.

### STORAGE

Store between 2° to 8°C (35° to 46°F). DO NOT FREEZE. Product that has been exposed to freezing should not be used. Protect from light. Do not use after expiration date.

REFERENCES: 1. Recommendations of the Advisory Committee on Immunization Practices (ACIP). Prevention and Control of Meningococcal Disease and Meningococcal Disease and College Students. MMWR 2000;49(RR-7). 2. Ball R, et al. Safety Data on Meningococcal Polysaccharide Vaccine from the Vaccine Adverse Event Reporting System. CID 2001;32:1273-1280. 3. ACIP. General recommendations on immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP). MMWR 2002;51(RR02):1-36. 4. Data on file, Aventis Pasteur Inc. – 092503.

Concomitant administration of Menactra vaccine with Typhim Vi vaccine did not result in reduced antibody responses to any of the vaccine antigens.<sup>4</sup>

The safety and immunogenicity of concomitant administration of Menactra vaccine with vaccines other than Typhim Vi or Td vaccines have not been determined.

Menactra vaccine must not be mixed with any vaccine in the same syringe. Therefore, separate injection sites and different syringes should be used in case of concomitant administration.

### STORAGE

Store between 2° to 8°C (35° to 46°F). DO NOT FREEZE. Product that has been exposed to freezing should not be used. Protect from light. Do not use after expiration date.

REFERENCES: 1. Recommendations of the Advisory Committee on Immunization Practices (ACIP). Prevention and Control of Meningococcal Disease and Meningococcal Disease and College Students. MMWR 2000;