

POLICY & PRACTICE

HHS Names Autism Panel

The Health and Human Services department has named a new committee, authorized under the Combating Autism Act of 2006, to facilitate the exchange of information on autism activities among federal agencies as well as coordinate autism-related programs and initiatives, according to a statement from HHS. Dr. Thomas R. Insel, director of the National Institutes of Mental Health, will chair the panel; its first task will be to develop a strategic plan for autism research to guide public and private investments.

BadgerCare Overhaul Approved

The Centers for Medicare and Medicaid Services has given Wisconsin the go-ahead to restructure its BadgerCare State Children's Health Insurance Program (SCHIP) to cover approximately 7,600 more children. BadgerCare now will enroll children in families making up to \$51,625, or 250% of the federal poverty level for a family of four. Wisconsin sought to expand coverage to children in families making up to 300% of the federal poverty level but was forced to modify its request in order to stay within SCHIP guidelines designed to keep par-

ents from voluntarily switching their children from private insurance. CMS said that Wisconsin's program change addresses this problem by requiring a period without insurance prior to a family signing up for BadgerCare. Wisconsin also has agreed to move adults from BadgerCare and into its Medicaid program.

Parents Don't See Child's Obesity

More than 40% of parents with obese children aged 6-11 years describe their child as being "about the right weight," according to a study from the University of Michigan Health System, Ann Arbor. In fact, only 13% of parents with obese children in that

age bracket rated their child as being very overweight, compared with 31% of parents with obese children aged 12-17 years. The study, which included 2,060 adults, is part of the C.S. Mott Children's Hospital National Poll on Children's Health, which is funded by the university. Pediatricians can play an important role in helping parents to recognize obesity and take steps to modify a child's diet and activity levels, the study authors noted, adding that 84% of parents said they believe it is very important for doctors to address obesity with obese adolescents during routine checkups. "Parents' willingness to discuss obesity at their children's medical appointments indicates that many parents view doctors as a welcome source of information about obesity interventions for children," said Dr. Matthew Davis, who directs the National Poll on Children's Health.

WIC Program Adds Healthy Foods

In the first overhaul of the federal food vouchers program for women and children in nearly 3 decades, the U.S. Department of Agriculture has approved new rules that provide beneficiaries with fruits, vegetables, and whole grains. The new rules for the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) also provide less support for milk, eggs, and juice, and are designed to encourage breast-feeding by giving more fruits and vegetables to women who exclusively are nursing their children. More than 8 million low-income women and children receive WIC benefits, which amount to about \$39 a month.

Panel: More Smoking Prevention

Smoking rates have leveled off after nearly a decade of declines, and the nation's progress in reducing smoking is at risk unless states significantly increase funding for programs to prevent kids from smoking and to help smokers quit, warns a report from the Campaign for Tobacco-Free Kids. The annual report from the group, made up of a coalition of public health organizations, found that states have increased funding for tobacco prevention and cessation programs by 20% to \$717 million, the highest level in 6 years. However, it also found that most states fail to fund these programs at minimum levels recommended by the Centers for Disease Control and Prevention. The CDC recently reported that about 21% of adults smoked in 2006, the same as in 2004 and 2005. This follows a steady yearly decline from 1997 to 2004. High school smoking rates have similarly stalled, and 23% of high school students still smoke, according to the CDC.

FDA Sets User Fees for DTC Ads

The Food and Drug Administration is charging pharmaceutical companies about \$40,000 to review each of their direct-to-consumer television advertisements, according to a notice issued by the agency in December. Last September, Congress authorized FDA to create a user-fee program for the advisory review of DTC prescription-drug television advertisements. The program is voluntary; the \$41,390 fee established for fiscal year 2008 is based on the number of ads slated for review and is expected to generate \$6.25 million in total revenues.

—Jane Anderson

RotaTeq®
[Rotavirus Vaccine, Live, Oral, Pentavalent]

BRIEF SUMMARY OF PRESCRIBING INFORMATION

CONTRAINDICATIONS

A demonstrated history of hypersensitivity to any component of the vaccine. Infants who develop symptoms suggestive of hypersensitivity after receiving a dose of RotaTeq should not receive further doses of RotaTeq.

PRECAUTIONS

General: Prior to administration of RotaTeq, the health care provider should determine the current health status and previous vaccination history of the infant, including whether there has been a reaction to a previous dose of RotaTeq or other rotavirus vaccine. Febrile illness may be reason for delaying use of RotaTeq except when, in the opinion of the physician, withholding the vaccine entails a greater risk. Low-grade fever (<100.5°F [38.1°C]) itself and mild upper respiratory infection do not preclude vaccination with RotaTeq. The level of protection provided by only one or two doses of RotaTeq was not studied in clinical trials. As with any vaccine, vaccination with RotaTeq may not result in complete protection in all recipients. Regarding post-exposure prophylaxis, no clinical data are available for RotaTeq when administered after exposure to rotavirus.

Intussusception: Following administration of a previously licensed live rhesus rotavirus-based vaccine, an increased risk of intussusception was observed. In REST[†] (n=69,625), the data did not show an increased risk of intussusception for RotaTeq when compared to placebo. In post-marketing experience, cases of intussusception have been reported in temporal association with RotaTeq. See ADVERSE REACTIONS, Intussusception and Post-marketing Reports.

Immunocompromised Populations: No safety or efficacy data are available for the administration of RotaTeq to infants who are potentially immunocompromised including: Infants with blood dyscrasias, leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic system; Infants on immunosuppressive therapy (including high-dose systemic corticosteroids). RotaTeq may be administered to infants who are being treated with topical corticosteroids or inhaled steroids; Infants with primary and acquired immunodeficiency states, including HIV/AIDS or other clinical manifestations of infection with human immunodeficiency viruses; cellular immune deficiencies; and hypogammaglobulinemic and dysgammaglobulinemic states. There are insufficient data from the clinical trials to support administration of RotaTeq to infants with indeterminate HIV status who are born to mothers with HIV/AIDS; Infants who have received a blood transfusion or blood products, including immunoglobulins within 42 days. No safety or efficacy data are available for administration of RotaTeq to infants with a history of gastrointestinal disorders including infants with active acute gastrointestinal illness, infants with chronic diarrhea and failure to thrive, and infants with a history of congenital abdominal disorders, abdominal surgery, and intussusception. Therefore, caution is advised when considering administration of RotaTeq to these infants.

Shedding and Transmission: Shedding was evaluated among a subset of subjects in REST 4 to 6 days after each dose and among all subjects who submitted a stool antigen rotavirus positive sample at any time. RotaTeq was shed in the stools of 32 of 360 [8.9%, 95% CI (6.2%, 12.3%)] vaccine recipients tested after dose 1; 0 of 249 [0.0%, 95% CI (0.0%, 1.5%)] vaccine recipients tested after dose 2; and in 1 of 385 [0.3%, 95% CI (<0.1%, 1.4%)] vaccine recipients after dose 3. In phase 3 studies, shedding was observed as early as 1 day and as late as 15 days after a dose. Transmission was not evaluated. Caution is advised when considering whether to administer RotaTeq to individuals with immunodeficient close contacts such as: Individuals with malignancies or who are otherwise immunocompromised; or Individuals receiving immunosuppressive therapy. There is a theoretical risk that the live virus vaccine can be transmitted to non-vaccinated contacts. The potential risk of transmission of vaccine virus should be weighed against the risk of acquiring and transmitting natural rotavirus.

Information for Parents/Guardians: Parents or guardians should be given a copy of the required vaccine information and be given the "Patient Information" appended to the Prescribing Information. Parents and/or guardians should be encouraged to read the patient information that describes the benefits and risks associated with the vaccine and ask any questions they may have during the visit. See PRECAUTIONS and Patient Information.

Drug Interactions: Immunosuppressive therapies including irradiation, antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than physiologic doses), may reduce the immune response to vaccines. For administration of RotaTeq with other vaccines, see DOSAGE AND ADMINISTRATION, Use with Other Vaccines in the Prescribing Information.

Carcinogenesis, Mutagenesis, Impairment of Fertility: RotaTeq has not been evaluated for its carcinogenic or mutagenic potential or its potential to impair fertility.

Pediatric Use: Safety and efficacy have not been established in infants less than 6 weeks of age or greater than 32 weeks of age. Data are available from clinical studies to support the use of RotaTeq in pre-term infants according to their age in weeks since birth. (See ADVERSE REACTIONS, Safety in Pre-Term Infants.) Data are available from clinical studies to support the use of RotaTeq in infants with controlled gastroesophageal reflux disease.

ADVERSE REACTIONS

71,725 infants were evaluated in 3 placebo-controlled clinical trials including 36,165 infants in the group that received RotaTeq and 35,560 infants in the group that received placebo. Parents/guardians were contacted on days 7, 14, and 42 after each dose regarding intussusception and any other serious adverse events. The racial distribution was as follows: White (69% in both groups); Hispanic-American (14% in both groups); Black (8% in both groups); Multiracial (5% in both groups); Asian (2% in both groups); Native American (RotaTeq 2%, placebo 1%), and Other (<1% in both groups). The gender distribution was 51% male and 49% female in both vaccination groups. Because clinical trials are conducted under conditions that may not be typical of those observed in clinical practice, the adverse reaction rates presented below may not be reflective of those observed in clinical practice.

Serious Adverse Events: Serious adverse events occurred in 2.4% of recipients of RotaTeq when compared to 2.6% of placebo recipients within the 42-day period of a dose in the phase 3 clinical studies of RotaTeq. The most frequently reported serious adverse events for RotaTeq compared to placebo were: bronchiolitis (0.6% RotaTeq vs. 0.7% Placebo), gastroenteritis (0.2% RotaTeq vs. 0.3% Placebo), pneumonia (0.2% RotaTeq vs. 0.2% Placebo), fever (0.1% RotaTeq vs. 0.1% Placebo), and urinary tract infection (0.1% RotaTeq vs. 0.1% Placebo).

Deaths: Across the clinical studies, 52 deaths were reported. There were 25 deaths in the RotaTeq recipients compared to 27 deaths in the placebo recipients. The most commonly reported cause of death was sudden infant death syndrome, which was observed in 8 recipients of RotaTeq and 9 placebo recipients.

Intussusception: In REST, 34,837 vaccine recipients and 34,788 placebo recipients were monitored by active surveillance to identify potential cases of intussusception at 7, 14, and 42 days after each dose, and every 6 weeks thereafter for 1 year after the first dose. For the primary safety outcome, cases of intussusception occurring within 42 days of any dose, there were 6 cases among RotaTeq recipients and 5 cases among placebo recipients (see Table 1). The data did not suggest an increased risk of intussusception relative to placebo.

	RotaTeq (n=34,837)	Placebo (n=34,788)
Confirmed intussusception cases within 42 days of any dose	6	5
Relative risk (95% CI) [†]		1.6 (0.4, 6.4)
Confirmed intussusception cases within 365 days of dose 1	13	15
Relative risk (95% CI)		0.9 (0.4, 1.9)

[†]Relative risk and 95% confidence interval based upon group sequential design stopping criteria employed in REST.

Among vaccine recipients, there were no confirmed cases of intussusception within the 42-day period after the first dose, which was the period of highest risk for the rhesus rotavirus-based product (see Table 2).

Day Range	Dose 1		Dose 2		Dose 3		Any Dose	
	RotaTeq	Placebo	RotaTeq	Placebo	RotaTeq	Placebo	RotaTeq	Placebo
1-7	0	0	1	0	0	0	1	0
1-14	0	0	1	0	0	1	1	1
1-21	0	0	3	0	0	1	3	1
1-42	0	1	4	1	2	3	6	5

All of the children who developed intussusception recovered without sequelae with the exception of a 9-month-old male who developed intussusception 98 days after dose 3 and died of post-operative sepsis. There was a single case of intussusception among 2,470 recipients of RotaTeq in a 7-month-old male in the phase 1 and 2 studies (716 placebo recipients).

Hematochezia: Hematochezia reported as an adverse experience occurred in 0.6% (39/6,130) of vaccine and 0.6% (34/5,560) of placebo recipients within 42 days of any dose. Hematochezia reported as a serious adverse experience occurred in <0.1% (4/36,150) of vaccine and <0.1% (7/35,536) of placebo recipients within 42 days of any dose.

Seizures: All seizures reported in the phase 3 trials of RotaTeq (by vaccination group and interval after dose) for RotaTeq compared to placebo, respectively, were: days 1-7 (10 vs. 5), days 1-14 (15 vs. 8), and days 1-42 (33 vs. 24). Seizures reported as serious adverse experiences occurred in <0.1% (27/36,150) of vaccine and <0.1% (18/35,536) of placebo recipients (not significant). Ten febrile seizures were reported as serious adverse experiences, 5 were observed in vaccine recipients and 5 in placebo recipients.

Kawasaki Disease: In the phase 3 clinical trials, infants were followed for up to 42 days of vaccine dose. Kawasaki disease was reported in 5 of 36,150 vaccine recipients and in 1 of 35,536 placebo recipients with unadjusted relative risk 4.9 (95% CI 0.6, 239.1).

Most Common Adverse Events

Solicited Adverse Events: Detailed safety information was collected from 11,711 infants (6,138 recipients of RotaTeq) which included a subset of subjects in REST and all subjects from Studies 007 and 009 (Detailed Safety Cohort). A Vaccination Report Card was used by parents/guardians to record the child's temperature and any episodes of diarrhea and vomiting on a daily basis during the first week following each vaccination. Table 3 summarizes the frequencies of these adverse events and irritability.

Adverse experience	Dose 1		Dose 2		Dose 3	
	RotaTeq	Placebo	RotaTeq	Placebo	RotaTeq	Placebo
Elevated temperature*	n=5,616 17.1%	n=5,077 16.2%	n=5,215 20.0%	n=4,725 19.4%	n=4,865 18.2%	n=4,382 17.6%
Vomiting	n=6,130 6.7%	n=5,560 5.4%	n=5,703 5.0%	n=5,173 4.4%	n=5,496 3.6%	n=4,989 3.2%
Diarrhea	10.4%	9.1%	8.6%	6.4%	6.1%	5.4%
Irritability	7.1%	7.1%	6.0%	6.5%	4.3%	4.5%

*Temperature $\geq 100.5^{\circ}\text{F}$ [38.1°C] rectal equivalent obtained by adding 1 degree F to otic and oral temperatures and 2 degrees F to axillary temperatures

Other Adverse Events: Parents/guardians of the 11,711 infants were also asked to report the presence of other events on the Vaccination Report Card for 42 days after each dose. Fever was observed at similar rates in vaccine (N=6,138) and placebo (N=5,573) recipients (42.6% vs. 42.8%). Adverse events that occurred at a statistically higher incidence (ie, 2-sided p-value <0.05) within the 42 days of any dose among recipients of RotaTeq (N=6,138) as compared with placebo (N=5,573) recipients, respectively, include: diarrhea (24.1% [n=1,479] vs. 21.3% [n=1,186]), vomiting (15.2% [n=929] vs. 13.6% [n=758]), otitis media (14.5% [n=887] vs. 13.0% [n=724]), nasopharyngitis (6.9% [n=422] vs. 5.8% [n=325]), and bronchospasm (1.1% [n=66] vs. 0.7% [n=40]).

Safety in Pre-Term Infants: RotaTeq or placebo was administered to 2,070 pre-term infants (25 to 36 weeks gestational age, median 34 weeks) according to their age in weeks since birth in REST. All pre-term infants were followed for serious adverse experiences; a subset of 308 infants was monitored for all adverse experiences. There were 4 deaths throughout the study, 2 among vaccine recipients (1 SIDS and 1 motor vehicle accident) and 2 among placebo recipients (1 SIDS and 1 unknown cause). No cases of intussusception were reported. Serious adverse experiences occurred in 5.5% of vaccine and 5.8% of placebo recipients. The most common serious adverse experience was bronchiolitis, which occurred in 1.4% of vaccine and 2.0% of placebo recipients. Parents/guardians were asked to record the child's temperature and any episodes of vomiting and diarrhea daily for the first week following vaccination. The frequencies of these adverse experiences and irritability within the week after dose 1 are summarized in Table 4.

Adverse event	Dose 1		Dose 2		Dose 3	
	RotaTeq	Placebo	RotaTeq	Placebo	RotaTeq	Placebo
Elevated temperature*	N=127 18.1%	N=133 17.3%	N=124 25.0%	N=121 28.1%	N=115 14.8%	N=108 20.4%
Vomiting	N=154 5.8%	N=154 7.8%	N=137 2.9%	N=137 2.2%	N=135 4.4%	N=129 4.7%
Diarrhea	6.5%	5.8%	7.3%	7.3%	3.7%	3.9%
Irritability	3.9%	5.2%	2.9%	4.4%	8.1%	5.4%

*Temperature $\geq 100.5^{\circ}\text{F}$ [38.1°C] rectal equivalent obtained by adding 1 degree F to otic and oral temperatures and 2 degrees F to axillary temperatures

Post-marketing Reports: The following adverse events have been identified during post-approval use of RotaTeq from reports to the Vaccine Adverse Event Reporting System (VAERS). Reporting of adverse events following immunization to VAERS is voluntary, and the number of doses of vaccine administered is not known; therefore, it is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to vaccine exposure using VAERS data. In post-marketing experience, the following adverse events have been reported in infants who have received RotaTeq: *Gastrointestinal disorders*—Intussusception, Hematochezia. *Skin and subcutaneous tissue disorders*—Urticaria. *Infections and infestations*—Kawasaki disease.

Reporting Adverse Events: Parents or guardians should be instructed to report any adverse events to their health care provider. Health care providers should report all adverse events to the US Department of Health and Human Services' Vaccine Adverse Event Reporting System (VAERS). VAERS accepts all reports of suspected adverse events after the administration of any vaccine, including but not limited to the reporting of events required by the National Childhood Vaccine Injury Act of 1986. For information or a copy of the vaccine reporting form, call the VAERS toll-free number at 1-800-822-7967 or report on line to www.vaers.hhs.gov.

For more detailed information, please read the Prescribing Information.

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[†]Rotavirus Efficacy and Safety Trial