# FDA Advises Clinicians To Suspend Rotarix Use

BY HEIDI SPLETE

The Food and Drug Administration is advising clinicians to temporarily suspend use of the oral rotavirus vaccine Rotarix because of the unexpected finding of DNA from porcine circovirus type 1 in the product, FDA Commissioner Margaret A. Hamburg said in a teleconference

"There is no evidence at this time that this material from PCV1 in Rotarix poses any safety risk," she said.

"We are not taking the vaccine off the market, we are just asking clinicians to suspend using it in their practices during the 4- to 6-week period when we are collecting additional information," Dr. Hamburg added.

**The take-home message is to continue to vaccinate children on schedule with RotaTeq instead.**

PCV1 is a virus that is often found in meat and other foods, and it is not known to cause disease in humans or animals.

The virus was identified in Rotarix (manufactured by GlaxoSmithKline) as part of an academic research exercise, and the finding was unanticipated, Dr. Hamburg said.

The rotavirus vaccine is typically given orally to children aged 6 weeks and older to protect them against the diarrhea and vomiting associated with a rotavirus infection.

"PCV1 is a virus, not an animal product, and this has nothing to do with food safety," Dr. Hamburg emphasized.

The FDA conducted its own studies and confirmed that PCV1 has been present in Rotarix since its initial development, said Dr. Hamburg.

The FDA is reviewing the data and will convene an advisory committee in approximately 4-6 weeks to make recommendations about the use of Rotarix, she said in the teleconference.

Rotarix was studied extensively before and after its 2008 FDA approval and has an excellent safety record, Dr. Hamburg said.

But the FDA is obtaining additional information about the presence of PCV1 DNA in Rotarix, including whether DNA fragments or an intact virus is present. The agency is also studying how the virus came to be in the vaccine.

Meanwhile, the FDA recommends continuing vaccination of children in the United States using RotaTeq, a separate rotavirus vaccine manufactured by Merck & Co. that uses a different process from the one used by Rotarix. Studies of RotaTeq had not shown any evidence of PCV1, said Dr. Hamburg, adding that the take-home message for clinicians is to reassure parents and continue to vaccinate children on schedule with RotaTeq.

"We are definitely recommending that if you have given one dose of Rotarix, you follow that with two doses of RotaTeq in order to provide the full regimen to protect against rotavirus, and we are definitely encouraging ongoing rotavirus vaccination," she said.

Dr. Hamburg noted that the FDA recommendations apply to clinicians in the United States only, because of the relatively low burden of disease and the availability of an alternative product.

The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) reviewed the Rotarix findings and concluded that no action is necessary at this time, according to a statement issued by CHMP. ■

# *Vaccine Found to Decrease Admissions for Rotavirus*

BY MICHELE G. SULLIVAN

**VITALS**

**Major Finding:** Of 200 hospitalized children tested for rotavirus before approval of the vaccine, 27% tested positive. Of 161 and 180 hospitalized children tested in the subsequent 2 years after vaccine approval, 12% and 14% tested positive for rotavirus infections.

**Data Source:** A retrospective cohort study of 1,996 children admitted to a single hospital.

**Disclosures:** Dr. Hamwi said he had no relevant financial conflicts of interest. One of the coinvestigators, Dr. David DiJohn, disclosed that he is on the speakers bureau for both GlaxoSmithKline and Sanofi-Aventis.

PHILADELPHIA — The introduction of the rotavirus vaccine was associated with a significant decrease in the number of children admitted to a New York City hospital for rotavirus infections, as well as a decline in the severity of the rotavirus season.

The annual percentage of admitted patients who tested positive for the virus decreased from more than 12% before the vaccine was available to 3% afterward, Dr. Haytham Hamwi said at the annual meeting of the Eastern Society for Pediatric Research.

Dr. Hamwi of the Flushing (N.Y.) Hospital Medical Center discussed a retrospective study of rotavirus testing and admissions spanning three time periods: September 2004 through August 2005 (before the vaccine was available), and after the vaccine was available, September 2007 through August 2008 and September 2008 through August 2009. The hospital database and the New York City vaccine registry provided the data for the study.

Dr. Hamwi and his colleagues included in their study all patients aged 0-6 years who were admitted to the hospital during those periods, except any child who had received the rotavirus vaccine within 3 weeks of a hospital admission.

"The vaccine can cause shedding of antigen in the stool, leading to a false-positive result," Dr. Hamwi said.

During the first study period (2004-2005), 442 patients aged 0-6 years were admitted to the hospital; 200 of those were tested for rotavirus.

Of these, 55 (27%) tested positive for the virus. Patients with rotavirus infections comprised 12% of all hospital admissions among 0-6 year olds.

During the second study period (2007-2008), 744 children aged 0-6 years were admitted to the hospital.

The surge in admissions occurred because several neighboring hospitals had closed, Dr. Hamwi said.

Of the admissions, 161 were tested for rotavirus and 20 (12%) tested positive. Rotavirus accounted for 2.6% of admissions for 0- to 6-year-old children during that time.

In the third study period (2008-2009), there were 810 admissions. Of these, 180 were tested for the virus and 26 (14%) tested positive. Children with rotavirus accounted for 3% of the admissions.

A vaccination history was available for 76 children who tested positive for the virus in the study.

Of these, 75 were unvaccinated against rotavirus and 1 had been incompletely vaccinated, Dr. Hamwi said. No rotavirus was found in unvaccinated children.

The investigators also examined the relationship between the vaccine and rotavirus seasonality.

In the prevaccine study periods, rotavirus appeared in November, peaked in February, and had a second peak in April.

In both postvaccination study periods, the disease appeared later and did not show the typical winter peak.

A smaller peak occurred in March and April of the second of the two study periods. ■

# Interferon-Gamma TB Tests Not Ready for Widespread Use

BY DAMIAN McNAMARA

MIAMI — Cost and other challenges need to be overcome before interferon-gamma release assays are adopted for widespread tuberculosis testing in children, according to Dr. John Bradley.

Although interferon-gamma release assays (IGRAs) are more accurate than standard tuberculin skin tests, they require 2-5 cc of blood, which can be a challenge in some children, Dr. Bradley said.

In addition, the accuracy of IGRAs is not well studied for children with latent TB infection, miliary TB or other disseminated infections, or active infections such as meningitis.

"There are insufficient data at present to recommend switching from tuberculin skin testing to an IGRA blood test for all kids," Dr. Bradley said at a pediatric update sponsored by Miami Children's Hospital. Also, "there are insufficient data to recommend a specific IGRA test," said Dr. Bradley, an editor of the 2010 Red Book who is also with the division of infectious diseases, Rady Children's Hospital, San Diego.

There is a role for IGRA tests in specific clinical situations, however, Dr. Bradley said. For example, if a pediatrician believes a parent is unlikely to return for the reading of a tuberculin skin test result, the IGRA may be indicated. In addition, the blood test is preferred for Bacillus Calmette-Guérin–immunized children with a positive tuberculin skin test result, as well as for a child with a positive skin test with no known exposures (these are presumed to be false-positive tuberculin skin tests, he said).

"Although the [IGRA] test is clearly an advance, it's not a perfect solution," Dr. Bradley said.

The two Food and Drug Administration–cleared IGRAs (QuantiFERON-TB Gold, Cellestis; T-SPOT.TB, Oxford Immunotec Ltd.) measure an in vitro lymphocyte response to *Mycobacterium tuberculosis* proteins.

"We believe the IGRA is a more sensitive test," Dr. Bradley said. However, "they cost a lot more, so we're not ready to recommend them for widespread use."

The tuberculin skin test remains the recommended TB assay in the 2010 Red Book, Dr. Bradley said, despite its having some limitations.

The immune competence of the child can impact the sensitivity, for example. In addition, tuberculin skin tests are difficult to place intradermally, and if they are not intradermal, you cannot interpret them, he said.

"Uncooperative, screaming children are challenges [also]. Two- and three-year-olds can be contortionists." ■

***Disclosures:*** *None was reported.*