# MedWatch Upgrade Urged by FDA's Pediatric Advisory Panel

BY DEEANNA FRANKLIN
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ROCKVILLE, MD. — Panelists on the Food and Drug Administration's Pediatric Advisory Committee strongly urged the FDA to overhaul MedWatch, its voluntary safety information and adverse event reporting program, to make the system less onerous.

Currently, the program entails the submission of a five-page report, and the submission often triggers a follow-up interview via telephone.

"Consider the possibility of streamlining the adverse event reporting system so that people don't mind doing it," advised Thomas Newman, M.D., of the University of California, San Francisco.

"Create a system that is more specific and less open to interpretation, so that way the data would be stronger and potentially cleaner," recommended another panel member.

Panelists suggested making the system more user friendly, in addition to having narrative descriptions that are more consistent across categories.

For example, one provider may use a description of "loose stool" while another would use the term "diarrhea."

"I feel like I'm not serving the general public or the government of the United States, with the current information that I'm receiving. I am not capable of being assured in any way about safety with the [current] passive surveillance system. We have to get better information," said Mary Glode, M.D., an infectious diseases specialist with the University of Colorado, Denver.

FDA representatives acknowledged that underreporting of adverse events and establishing causality are ongoing challenges under the current MedWatch system.

"There's a lot of missing information. We try to make the most out of this limited information. It's a good system to pick up some rare, serious events," said an FDA representative.

The panelists also heard data compiled as part of the 1-year postexclusivity adverse event review program mandated by the Best Pharmaceuticals for Children Act.

Information was presented on the following medications:

**Benazepril** (Lotensin, Lotensin HCT, Lotrel).
► **Approved:** June 25, 1991, manufactured by Novartis.
► **Indication**: This antihypertensive (ACE inhibitor) is used to treat hypertension in patients over 6 years of age.
► **Pediatric Adverse Events Reported:** Three adverse events (AEs) in 1-year period reviewed, and five total since its approval; all were serious, none were fatal. No patterns discernible in the AEs for benazepril monotherapy. No AEs reported for benazepril's combination products.
► **FDA Recommendation:** Return to routine monitoring. The agency recommended routine monitoring of AEs, focusing on serious AEs in all populations, as opposed to giving special attention to all pediatric AEs reported as mandated by the 1-year exclusivity period.
► **Panel Recommendation:** The panel did not concur, and regarded the data presented as too inadequate for a return to routine monitoring. They recommended the FDA "look closely at all case reports for benazepril for yet another year and then report back to the committee," said panel chair, P. Joan Chesney, M.D., an infectious diseases specialist and director of academic programs at St. Jude Children's Research Hospital, Memphis.

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**Esmolol** (Brevibloc).
► **Approved**: December 31, 1986, manufactured by Baxter Laboratories.
► **Indication**: No pediatric indication. In adults, this -1-selective (cardioselective) adrenergic receptor blocking agent is used to treat supraventricular tachycardia, intraoperative and postoperative tachycardia and/or hypertension.
► **Pediatric Adverse Events Reported**: During the 1-year postexclusivity period there was one pediatric AE reported. Since its approval there were 13 pediatric AEs reported (9 serious, 3 deaths). No discernible patterns in AEs.
► **FDA Recommendation**: Return to routine monitoring.
► **Panel Recommendation**: The panel did not concur, and regarded the data presented as insufficient. Recommended another year-long exclusivity period.

**Orlistat** (Xenical).
► **Approved**: April 23, 1999, manufactured by Roche.
► **Indication**: A lipase inhibitor for obesity management in conjunction with weight loss in patients aged 12 years and older with a body mass index greater than 30, or 27 with risk factors (hypertension, diabetes, dyslipidemia). Less than 1% (about 4,000) annual prescriptions for the drug were for pediatric patients.
► **Pediatric Adverse Events Reported**: Twenty-two pediatric AEs were reported (21 serious, no deaths). There was one serious AE reported during the 1-year postexclusivity period.
► **FDA Recommendation**: Return to routine monitoring.
► **Panel Recommendation**: The panel concurred.

**Glyburide-Metformin** (Glucovance).
► **Approved**: July 31, 2000, manufactured by Bristol-Myers Squibb Co.
► **Indication**: An antihyperglycemic for the adjunct treatment of type 2 diabetes mellitus along with diet and exercise, as well as a second-line treatment for type 2 diabetes if metformin or sulfonylurea fail. The glyburide stimulates release of insulin while the metformin improves glucose tolerance.
► **Pediatric Adverse Events Reported**: No AE reports in this population since Glucovance's approval. Both drugs have minimal use in pediatric patients.
► **FDA Recommendation**: Return to routine monitoring for the drug combo.
► **Panel Recommendation**: The panel concurred.

**Atovaquone-Proguanil** (Malarone Pediatric).
► **Approved**: July 14, 2000, manufactured by GlaxoSmithKline
► **Indication**: An antimalarial used in the treatment of *Plasmodium falciparum* malaria in patients over 5 kg and prophylaxis in patients over 1 kg.
► **Pediatric Adverse Events Reported**: Seven AEs were reported during the 1-year postexclusivity period (six serious, no deaths). There were 17 AEs reported since the drug's approval (15 serious, 3 deaths).
► **FDA Recommendation**: Return to routine monitoring.
► **Panel Recommendation**: The panel unanimously concurred.

**Nelfinavir Mesylate** (Viracept).
► **Approved**: March 14, 1997, manufactured by Pfizer Inc.
► **Indication**: A protease inhibitor indicated for the treatment of HIV infection in patients over 2 years of age. Accounted for about 16.4% of the 1.9 million prescriptions dispensed in this drug class from Sept. 2003 to Aug. 2004.
► **Pediatric Adverse Events Reported**: There were 377 AEs reported since the drug's approval (374 serious, 19 deaths). During the 1-year postexclusivity period, there were 30 AEs reported (30 serious, 2 deaths).
► **FDA Recommendation**: Return to routine monitoring.
► **Panel Recommendation**: The panel agreed. ■

# *Alternatives Could Improve Health Care Coverage*

BY JENNIFER SILVERMAN
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WASHINGTON — Rewarding states based on quality is one way to cover more uninsured Americans, Henry J. Aaron said at the annual meeting of the National Governors Association.

Following up on a trend that has already affected the physician community, Mr. Aaron proposed a "pay-for-performance" system, where states could receive federal grants based on their "actual measured progress of increasing the number and proportion of state residents covered by health insurance." The grants would be set to cover much or all of the costs of extending coverage.

"Any state that succeeded in boosting a fraction of its population [covered by] health insurance would receive federal support. The states that made no such progress would receive nothing," said Mr. Aaron, senior fellow for economic studies at the Brookings Institution.

The federal government should first define a standard for health insurance coverage, Mr. Aaron said, suggesting that the minimum be "similar to the actuarial value of the Federal Employees Health Benefits Program."

His plan also would include a "first do no harm" standard, prohibiting states from materially eroding coverage for the current Medicaid population. "Even now, Medicaid is substantially less costly than private insurance of the same scope. Still, state costs for long-term care [are] on track to rise relentlessly as baby boomers age." This means that states need continued financial protection from adverse trends—and not a cap on federal support.

"[States] also need flexibility to modernize Medicaid but within the limits that maintain the per capita protection of the most vulnerable populations in our nation," Mr. Aaron said.

Within these broad guidelines, states should be encouraged to pursue any approach that would increase the proportion of state residents with health insurance coverage, he continued. Depending on local conditions and political preferences, states could use refundable tax credits or vouchers to promote individual insurance.

States could also facilitate new insurance groups by allowing churches, unions, and the like to create association health plans; extend Medicaid or the State Children's Health Insurance Program; impose employer mandates; or try to create an intrastate single-payer plan. None of these would be mandatory, he said.

Another panelist, Stuart M. Butler, Ph.D., vice president, domestic and economic policy studies, the Heritage Foundation, Washington, suggested that Congress enact a policy "toolbox" that would make a range of ideas available to states. Under such an approach, states could propose an initiative for preserving coverage, selecting certain elements from the toolbox, and negotiating with the U.S. Health and Human Services department on appropriate waivers to pull such an option together, he explained.

In an attempt to maintain and extend the functional equivalent of Medicaid during these very tight budget times, states could utilize an enhanced federal refundable tax credit from the policy toolbox, using additional federal funds to create purchasing alliances or pools, he said. The key is to make sure that Medicaid populations are protected, "encouraging innovations through the states [and] rewarding pay-for-performance successes by the states, to reach these goals." ■