The New York Times

Scrutiny for Laxatives as a Childhood Remedy

By Catherine Saint Louis

Jan. 5, 2015

The Food and Drug Administration has raised new questions about the safety of an adult laxative routinely given to constipated children, sometimes daily for years.

The agency has asked a team of scientists in Philadelphia to look more closely at the active ingredient in Miralax and similar generic products, called polyethylene glycol 3350, or PEG 3350. While outlining the scope of the research, the agency also disclosed that its scientists had discovered trace amounts of two potential toxins in batches of Miralax tested six years ago.

The news is likely to surprise parents and some doctors.

“Every pediatric GI physician, I would guarantee you, has told a family this is a safe product,” said Dr. Kent C. Williams, a gastroenterologist at Nationwide Children’s Hospital in Columbus, Ohio. Now, he worries, “it may not be true.”

Doctors have long recommended these laxatives for their convenience and on the grounds that very little PEG 3350 is absorbed in the intestines. But the F.D.A. says there is little data on its absorption in children, especially the very young and chronically constipated. The agency never approved long-term daily use of the laxatives, even in adults.

Moreover, for years the F.D.A. has received occasional reports of tremors, tics and obsessive-compulsive behavior in children given laxatives containing PEG 3350. It is not known whether the laxatives are the cause.

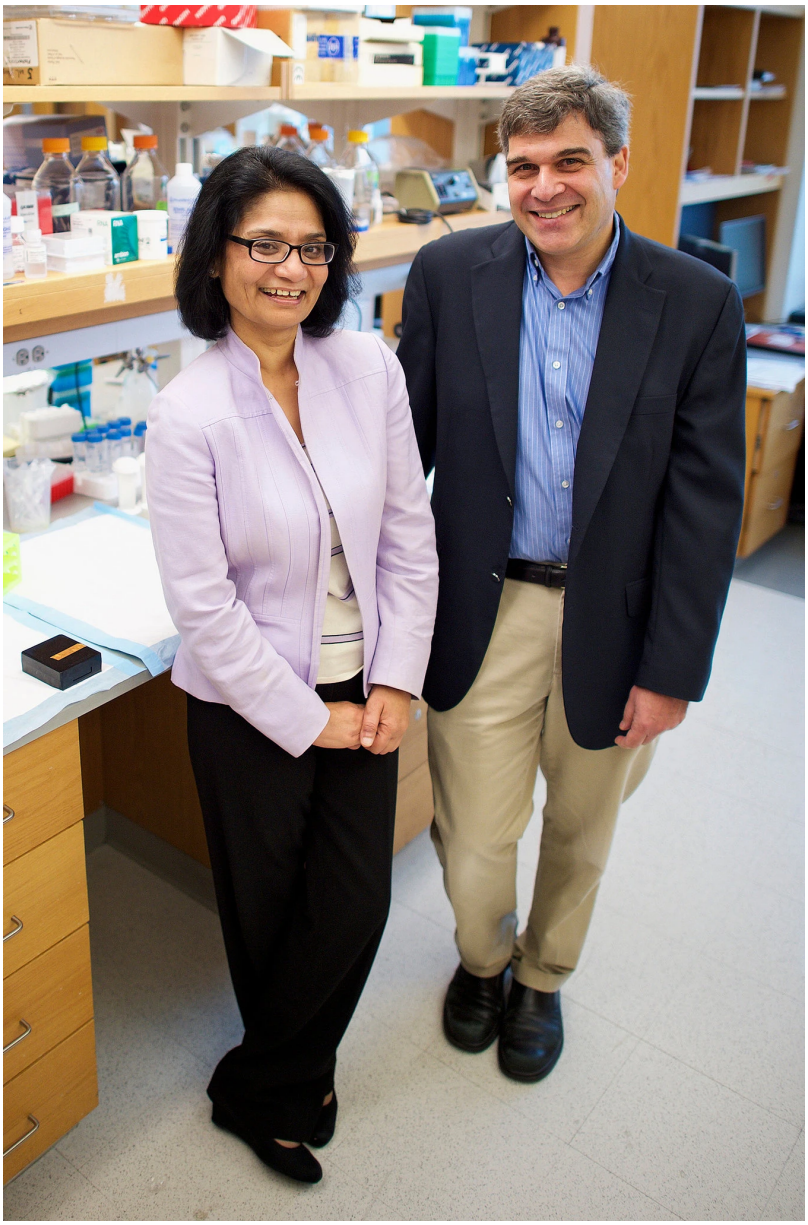
In September, the agency awarded nearly $325,000 to The Children’s Hospital of Philadelphia to study whether PEG 3350 might be absorbed by the very young and whether use of the laxatives is linked to development of psychiatric problems.

“It’s a medicine that helps a fair number of children,” said Dr. Ritu Verma, a study co-investigator and the section chief of clinical gastroenterology at The Children’s Hospital of Philadelphia. “We want to be sure it’s not harming them.”

In a statement, Bayer, which acquired Miralax last year, reiterated that the product was intended to be used once daily by adults and said, “We are committed to ensuring the product meets all specifications for quality.”

The new study is a victory of sorts for the Empire State Consumer Project, an advocacy group in Rochester that petitioned the F.D.A. in 2012 to reopen an investigation into the safety of PEG 3350.

“Finally, they will measure changes in behavior,” said Carol Chittenden, a co-director of the group said of the new research. “We absolutely want that.”



Dr. Ritu Verma and Dr. Robert O. Heuckeroth of The Children's Hospital of Philadelphia will help lead a study into how children metabolize an ingredient in adult laxatives.
Mark Makela for The New York Times

Buried in the agency's brief to researchers, issued last year, was some disquieting news. The F.D.A. said that it had tested eight batches of Miralax and found tiny amounts of ethylene glycol (EG) and diethylene glycol (DEG), ingredients in antifreeze, in all of them. The agency said the toxins were impurities resulting from the manufacturing process.

Those tests were conducted in 2008, but the results were not disclosed. Jeff Ventura, an F.D.A. spokesman, said batches were tested because "many of the reported adverse events were classic symptoms of ethylene glycol ingestion."

Schering-Plough, the manufacturer of Miralax in 2008, was acquired a year later by Merck. Officials at Merck declined to comment on the impurities discovered by the F.D.A. The agency again tested PEG 3350 laxatives from five makers in 2013, Mr. Ventura said. None had detectable amounts of EG or DEG. "The amounts were so low," he added, and "complied with internationally recognized safety standards."

As it turns out, extremely small amounts of DEG and EG are permitted in finished drug products, and the F.D.A. considers the laxatives "safe to use in accordance with approved labeling" — that is, only by adults for not longer than seven days.

Yet no one knows if small amounts of EG or DEG found in the laxatives or present once metabolized might harm children, especially those given the laxatives chronically. No detectable amount of either chemical should be present in food or medication, said Jon Clark, the vice president for chemical medicines and external development at U.S. Pharmacopeia, a nonprofit that sets quality standards for medicines and other products.

Psychiatric illnesses like those reported in children taking the laxatives have also been observed in cases in which a child took substantial amounts of ethylene glycol. Some children taking Miralax chronically also have developed acidic blood, according to F.D.A. records, which can be a consequence of ingesting EG.

The new study in Philadelphia will address how PEG 3350 is metabolized by children and whether they have evidence of toxins in their blood. “Due to the frequent use of PEG 3350 products in children,” Mr. Ventura said, “we believe further study is warranted to understand the absorption of EG and DEG by pediatric patients who take these products.”

The researchers will enroll children who have already been taking a PEG 3350 laxative for at least a month. They will be divided into three groups: children who are healthy except for their constipation; those with bowel ailments, like Crohn’s disease or celiac disease; and those who have underlying issues with their nervous system, like cerebral palsy patients. The study also will include a comparison group not taking PEG 3350.

First, the research team must create an extremely sensitive blood test capable of detecting whether children have absorbed small amounts of diethylene glycol or ethylene glycol. If so, the researchers will be testing three possible explanations. Are the impurities created during the manufacturing process, or when the laxative is mixed with liquids then stored, or by metabolism of PEG 3350?

“We think we know what’s in the medicine itself, but in the body, once you take it, it could potentially do something,” said Dr. Robert O. Heuckeroth, a principal investigator and a pediatric gastroenterologist at The Children’s Hospital of Philadelphia.

Most children taking PEG 3350 do not report behavioral or psychiatric side effects, he emphasized. Still, Dr. Heuckeroth and his colleagues want to know which children may be more susceptible to these adverse effects. “We will do our best to get a clear answer about whether or not there are detectable components and metabolites in the blood of children taking the medicine,” he said.

“People are incredibly emotional about this topic,” he added.

Ms. Chittenden says she supports the new study, but not without reservations. “To knowingly put a product that might contain ethylene glycol, or degrade into it, into the body of a child is still worrisome,” she said.

A version of this article appears in print on Jan. 5, 2015, Section D, Page 3 of the New York edition with the headline: Scrutiny for a Childhood Remedy