Folic acid fortification to prevent birth defects hits FDA roadblock

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Preventing certain devastating birth defects has become as easy as pie crust - and bread, cereal, pasta, and other grain products.

Seventeen years after the government required the addition of folic acid to enriched cereal grains, fortification spares 1,300 babies a year from being born with brains or spinal cords that are not fully formed, a new analysis by the U.S. Centers for Disease Control and Prevention shows. Averting those "neural tube" defects saves $508 million annually - not to mention untold heartache.

"Hands down, folic acid fortification is one of the most successful birth-defect prevention" measures in American history, said CDC epidemiologist and lead author Jennifer Williams.

But it could be even more successful.

Public health experts have long recognized that Hispanic women in this country have higher rates of folate insufficiency and neural tube defects than whites or African Americans. One reason is the U.S. does not allow fortification of corn masa flour, used to make tortillas, tamales, and other staples of the Hispanic diet.

The Food and Drug Administration was formally asked to permit enrichment of the flour nearly three years ago. The six petitioners, led by the March of Dimes, include Gruma of Mexico, the world's largest maker of tortillas, and the National Council of La Raza, a leading

Hispanic advocacy organization. They noted that corn masa fortification is already standard in Latin American countries such as Costa Rica, Mexico, and El Salvador.

To the petitioners' surprise, the FDA took the position that adding folic acid to corn masa flour might be risky, even though fortification has amassed a voluminous international safety record. The agency has demanded costly, time-consuming food laboratory studies.

Is the FDA being overzealous?

A spokeswoman said the FDA "does not discuss the substance of pending food-additive petitions."

The petitioners, acknowledging frustration, tried to be diplomatic.

Regulators' "job is to protect the food supply. They take it seriously," said March of Dimes medical director Edward R.B. McCabe.

Less tactful was the Center for Science in the Public Interest, a food-safety watchdog group that pushed for the fortification in the 1990s.

"No one is asking for something new," said Bonnie Liebman, the center's director of nutrition. "They're just trying to extend the benefit of preventing neural tube defects to Hispanic children. There really is no excuse for the FDA to delay."

Folate, a B vitamin abundant in green leafy vegetables, nuts, and beans, is vital to cell growth and division - which happens at a staggering pace in fetuses.

The link between insufficient folate and neural tube defects, suspected as early as 1965, was confirmed in the early 1990s. Studies demonstrated

that up to 70 percent of the defects could be prevented if women got about 400 micrograms of folate daily - two or three times more than most women get from their diets - shortly before and early in pregnancy.

Timing matters because the neural tube, the hollow structure that develops into the brain and spinal cord, is supposed to close just 28 days after conception - before many women even realize they're pregnant. If it doesn't close, part of the brain and skull will be missing, a fatal condition called anencephaly, or part of the spinal cord will be open, a disabling disorder called spina bifida.

The importance of folate levels at conception helped to sway the contentious, six-year debate that led to mandatory fortification in 1998; the consensus was that just urging women to pop vitamin pills when they got pregnant would not be effective.

The final rule required manufacturers to add 140 micrograms of folic acid for every 100 grams of grain product.

Enhancing the food supply hasn't been a panacea. About a quarter of women still have low blood folate levels, and other factors play a role in neural tube defects. Still, the average annual number of those defects has fallen dramatically from about 4,200 before fortification to 2,900 now, the new CDC analysis shows.

Although Hispanic women have benefited from this success, their risk for the defect remains up to three times higher for than non-Hispanic women.

Studies show Mexican migrants are especially vulnerable, for reasons including language barriers, lack of health care, and illegal immigration status.

The Maternity Care Coalition, a Philadelphia nonprofit that helps needy women access prenatal and child care, could not find a Hispanic woman willing to be interviewed for this article.

"Many of our Latina clients are undocumented and are fearful of speaking with others," director of programs Karen Pollack said.

To see whether fortifying corn masa flour would help, CDC researchers recently used national nutrition survey data and mathematical models. They estimated it would spare as many as 120 Hispanic newborns a year from neural tube defects.

In the 1990s, safety questions dominated the fortification debate.

There were concerns that adding folic acid would promote cancer, heart attacks, miscarriages, B12 deficiency, genetic damage, and more.

"Before we fortify the food supply for 250 million Americans, we have to make sure we get it right," said then-FDA commissioner David Kessler.

The fears have since been dispelled.

"We have compiled massive amounts of research, and, to date, there just are not any adverse effects," said Sarah Tinker, a CDC birth-defects researcher.

So what makes the FDA think fortifying corn masa flour might be risky?

Corn masa is a dough (masa is Spanish for "dough") produced by cooking dried corn kernels in hot water with an alkaline solution, a process called nixtamalization. The alkalinity of the dough breaks down added vitamins.

But adding vitamins to masa is old technology, as the March of Dimes explained in a 2011 editorial advocating fortification. The modern technique is to dry the corn masa, grind it into flour, then fortify it, "resulting in consistent and significant levels of folic acid in the finished product."

Nonetheless, the FDA insisted the petitioners study the stability of folate in corn masa flour.

"They were asking for a sizable expenditure - the high six figures - for a study," McCabe said. "We've been able to negotiate a much more reasonable stability trial."

That trial, which finally began last month, is being led by Michael Dunn, a food-fortification researcher at Brigham Young University. His team will measure how much folic acid is lost during the six-month shelf life of the flour, and during cooking to make tortillas and chips.

"I don't think we'll see anything much different than with wheat flour," which loses 15 percent to 25 percent of its folic acid, Dunn said. "If we're in that range, I think the FDA will be fine. But you never know."

If the agency still has qualms, it could require a study to identify the breakdown products of the lost folic acid.

"We're hoping not to have to do that. That's quite involved," Dunn said. "Is this degrading into something toxic? I can't find anything in the [scientific] literature at all about potentially toxic compounds resulting from the breakdown."

Even if the FDA is satisfied with the stability study, it must write a new rule, publish it, collect public comment - a process that takes a long time, Dunn said.

He had urged the petitioners to use a faster route by which the FDA would simply issue a legal definition of corn masa flour that included folic acid.

"They said, 'No, the FDA doesn't want to go that route,' " Dunn said.