

August 22, 2011

## **“In Defense of 20 Parts Per Million”**

**A Letter from Alessio Fasano, M.D., and**

**The University of Maryland Center for Celiac Research**

In its efforts to establish a safer food environment, the U.S. Food and Drug Administration (FDA) has reopened the period for public comments on its 2007 proposal on defining gluten-free food and establishing a safe level of parts per million of gluten. The 2007 proposal included a proposed rule that defines gluten-free as less than 20 parts per million (ppm) of gluten.

In its recent research, the FDA has taken into consideration two methods for determining a safe gluten threshold for people suffering from celiac disease: an approach based on the sensibility of assays to detect gluten levels and an approach using evidence-based research from clinical trials and analytical studies. The matter of setting these safety standards is a complex one that involves social, economic and cultural factors as well as health and medical implications. We attempt to address some of these factors below in our discussion of the FDA’s report.

### **Testing Toxicity of a Substance**

In the typical method of establishing the toxicity of a substance (usually a drug), human clinical trials are preceded by animal studies. Since there are no reliable animal models for celiac disease, this cannot be the case for the assessment of a safe gluten threshold. However, we already have a vast “body of evidence” to support the safety of the gluten-free diet in current commercial gluten-free products.

For more than 30 years, millions of people worldwide have been following a gluten-free diet based on a safety level of 20 ppm or more (up to 100 ppm). The vast majority of those consumers have suffered no ill consequences.

### **Safety-Based Assessments Not the Best Measure**

Keeping in mind that a vast number of people have safely followed a gluten-free diet and the fact that the threshold was not extrapolated from animal studies, the safety assessment approach proposed by the FDA (Note: Abate the safety threshold by a factor of 10 or 100 to take into account the extrapolation of safety data from animal models to humans) does not apply in this case.

To take it further, let me share a little bit of scientific history. When we first began to measure the ppm level of gluten in products, the assay measurement used was only sensitive to a 100 ppm threshold. As assay measurements became more sensitive, the level of “safe” as defined as gluten-free was lowered.

Currently, the assay measurement is sensitive to a threshold of 5 ppm. However, just because we can measure gluten to the level of 5 ppm (an incredibly miniscule amount), does not mean that we should determine safety levels based on the sensitivity of the assay. This is not the best use of our scientific methods.

## **Need for Evidence-Based Science**

At the University of Maryland Center for Celiac Research, we support the use of evidence-based research to establish a safety level for ppms of gluten. Limits must be established through double-blind, randomized trials such as the one conducted by our center in 2007. The three-month trial showed that a daily intake of 10 mg of gluten (that, translated in ppms, would be equivalent to the daily ingestion of more than a pound of gluten free products containing 20 ppm of gluten!) for three months by adults with celiac disease caused no intestinal damage. However, the threshold of 50 mg was harmful to the majority of patients. (Visit <http://bit.ly/qG12X3> for safe daily levels of gluten consumption.)

The best use of science to measure safe levels of any substance is by collecting evidence through double-blind, randomized trials. When it comes to measuring safe levels of gluten, unfortunately there are few such studies. And, as far as I know, there are no evidence-based published studies that demonstrate toxicity with exposure to 20 ppm and safety with 5 ppm exposure.

## **Margin of Error of ELISA to Measure Gluten in Foodstuff**

(ELISA stands for Enzyme-linked Immunoassay)

Setting a safe gluten-free threshold below 20 ppm could result in a drastic reduction in the amount and availability of gluten-free products in the U.S. market. Since the assay variability (margin of error of the ELISA) measurement of gluten in safety-based assessments can range from 10 to 20 percent, extremely low thresholds (like 5 ppm) do not give manufacturers enough flexibility to produce good-tasting and safe products. For instance, a batch of brownies tested today could measure 3 ppm. Keeping in mind the 10 to 20 percent margin of error inherent in assay measurement, that same batch tested tomorrow could measure 7 ppm. If the safety threshold was set at 5 ppm, a manufacturer could test the product as safe at 3 ppm, and it could be measured as unsafe at 7 ppm in a different test.

Under these restrictive limits, manufacturers would either discontinue gluten-free products or be forced to create much more expensive and much less palatable products, resulting in a drastic loss of selection and quality.

If a very low threshold (such as 5 ppm) is chosen, even minimal cross contamination from various sources in the surrounding environment can come into play. In after-the fact contamination, products can pick up extra contamination from the factory to shipping to market, thus raising the level above the restrictively low threshold.

## **Effects on Gluten-Free Global Village**

A final, but very important implication in setting the safety threshold of ppm for gluten is the nature of our gluten-free “global village.” If U.S. manufacturers are forced to abide by an unnecessarily restrictive safety threshold, they will not be able to compete successfully in the gluten-free global marketplace. Conversely, overseas manufacturers with products that have a higher ppm level than the U.S. safety threshold will not be able to sell their products in the U.S.

Consequently, U.S. consumers of gluten-free products will find themselves in a conundrum while traveling overseas: they either bring their own gluten-free items or limit their diet while traveling outside the U.S. These developments would certainly worsen the quality of life for people with celiac disease and gluten sensitivity and deliver the opposite outcome that this law is intended to obtain for these patients.

We believe that establishing a restrictively low threshold of parts per million of gluten will complicate the lives of people with celiac disease and do nothing to improve their levels of safety and comfort. We urge the FDA to establish 20 ppm as the level that defines “gluten-free” in the U.S. marketplace.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Alessio Fasano". The signature is fluid and cursive, with the first name "Alessio" and the last name "Fasano" clearly distinguishable.

Alessio Fasano, M.D.

Director

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