NASPGHAN
North American Society for Pediatric Gastroenterology, Hepatology and Nutrition

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

March 20, 2012

Ms. Margaret Hamburg, M.D.
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: Gluten in Drug Products [FDA-2011-N-0842]

Dear Commissioner Hamburg:

The North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) and the American Academy of Pediatrics (AAP) appreciate the opportunity to respond to the Food and Drug Administration's (FDA) Dec. 21, 2011 *Federal Register* notice requesting information and comments on the subject of gluten in drug products.

NASPGHAN is an organization comprised of 1,500 members who have specialized training and expertise in caring for children with disorders of the digestive system, liver and nutrition. The mission of NASPGHAN is to advance understanding of normal development, physiology and pathophysiology of diseases of the gastrointestinal tract and liver in children, improve quality of care by fostering the dissemination of this knowledge through scientific meetings, professional and public education, and policy development, and serve as an effective voice for members and the profession.

The AAP is a non-profit professional medical organization of 60,000 primary care pediatricians, pediatric medical subspecialists, and pediatric surgical specialists dedicated to the health, safety, and well being of infants, children, adolescents, and young adults.

NASPGHAN has played an active role in raising awareness of celiac disease in the United States through the publication of the first evidence-based guidelines for the diagnosis and management of celiac disease in children, as well as through a national campaign organized by the NASPGHAN Foundation to educate health care workers on the subject.

In preparing a response to the FDA's request for comment on the use of gluten in drug products, NASPGHAN and AAP took into consideration the following facts:

1. Celiac disease is one of the most common chronic conditions affecting the general population and occurs in as many as 1 percent of individuals. In effect, this means there are 2-3 million affected people in the United States, many of whom are undiagnosed. The prevalence of celiac disease in children is thought to be between 3 and 13 per 1000 children.

2. Celiac disease is a lifelong condition, which, if left untreated, has potential for multiple long-term adverse health effects, including an increased mortality rate. Children with celiac disease may experience abdominal pain, diarrhea with failure to thrive, constipation, abdominal distension and vomiting. Non-gastrointestinal symptoms may include dermatitis herpetiformis, osteoporosis, short stature, and delayed puberty.

3. Currently, the only acceptable treatment for celiac disease is lifelong avoidance of all products containing wheat, barley and rye, which are collectively known as gluten.

4. Adhering to a gluten-free diet imposes a considerable burden on the individual and can adversely impact his/her quality of life. Because gluten is not always easily identified in commercial products, people with celiac disease have to be constantly vigilant and may have to go to extraordinary lengths to confirm a product does not contain gluten prior to ingestion.

5. The concept of a "minimal allowable amount of gluten" that will not cause harm to an individual with celiac disease, even when ingested on a regular basis, is appealing. However, the marked variability in response to even small amounts of gluten ingestion that occurs in people with celiac disease probably precludes identification of a minimum safe level for all individuals, particularly children.

6. For those with celiac disease, the knowledge that ingestion of gluten imposes potential for adverse health consequences is a source of significant anxiety. As a result, many with celiac disease choose to avoid ingesting any product they are unable to confirm is gluten free rather than run the risk of having an adverse reaction. It is conceivable those who need to take medications will adopt this approach and, if so, this can have additional adverse health consequences.

In consideration of these facts, NASPGHAN and AAP believe there is an urgent need to help people, especially children, with celiac disease avoid the risks of inadvertent ingestion of gluten. This can be facilitated by provision of clear reassurance that a product is gluten free.

While it is not known precisely how often gluten is incorporated in the production of prescription and nonprescription drugs used in the United States, even if this involves only a relatively small percentage of all drugs, it adversely impacts people with celiac disease. Furthermore, because NASPGHAN and AAP are not aware of any potential therapeutic benefits to the use of gluten in a drug, and there are satisfactory non-gluten alternatives that can be used in the manufacturing process, we believe that gluten should not be used in oral drug formulations whenever possible.

Newly approved oral drugs should not include gluten, as we know of no reason why this would ever be necessary. In addition, the removal of gluten from existing products as an inactive ingredient or incipient would also benefit children with celiac disease. However, this may lead to changes in the bioavailability of a drug, potentially altering how the drug works in children and necessitating new pediatric drug studies. The pharmacologic effect of reformulating existing drugs to remove gluten needs further study.

The knowledge that any drug available in the United States is guaranteed to be gluten free would significantly improve the lives of those with celiac disease and is an important goal. In instances where a manufacturer of a drug maintains a particular drug cannot be manufactured free of gluten, we believe the burden of evidence should be on the manufacturer as to why gluten is necessary and appropriate labeling should be required. The FDA should require that all oral drug

products that use gluten prominently disclose that information on the labeling in a uniform manner.

For all these reasons, we strongly endorse the concept that prescription and over-the-counter drugs manufactured for use in the United States discontinue the use of gluten in the manufacturing process whenever possible.

Should you have any questions or require additional information, please contact Camille Bonta, NASPGHAN representative, at cbonta@summithealthconsulting.com or (202) 320-3658; or James Baumberger, AAP Department of Federal Affairs, at jbaumberger@aap.org or (202) 347-8600.

Sincerely,

Kathleen B. Schwarz, M.D.

Kathleen Schwarz, MD
President
North American Society for Pediatric Gastroenterology, Hepatology and Nutrition

Robert W. Block, MD, FAAP
President
American Academy of Pediatrics

Ivor Hill, MD
Chair, NASPGHAN Celiac Guidelines Committee
Member, NASPGHAN Scientific Advisory Board on Celiac Disease