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AUG -3 1999

Dr. Bernard A. Schwetz, D.V.M, Ph.D  
Acting Principal Deputy Commissioner  
Dockets Management Branch  
Food and Drug Administration  
Room 1061  
5630 Fishers Lane  
Rockville, MD 20852

Dear Dr. Schwetz,

The undersigned submits this petition to request the Commissioner of Food and Drugs to revoke 21 CFR 74 subpart A section 74.705 and 21 CFR 74 subpart B section 74.1705. These sections provide for the listing of the color additive yellow #5 for use in food and drugs. It is the purpose of this petition to bring about the delisting of this additive in food and drugs. In this petition I will demonstrate that yellow #5 does not meet the Food and Drug Administrations criteria for safety, and therefore should be eliminated.

#### **Statement of Grounds**

The Congressional Research Service prepared a report for congress called "Food Additive Regulations: A Chronology." In this report analyst Donna U. Vogt explains that the legislative history of the "Food Additives Amendments of 1958" interpreted what Congress meant by safety. It said that a "reasonable certainty of no harm would be the standard. "An additive may be consumed by all citizens of all ages and all health conditions for a lifetime."(Vogt, 1995 p. 2). The "reasonable certainty of no harm" standard comes from the legislative history of the Food Additives Amendment of 1958, Public Law 85-929. In the report

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of the House Committee on Interstate and Foreign Commerce, which favorably reported on the bill, the committee stated:

The concept of safety used in this legislation involves the question of whether a substance is hazardous to the health of man or animal. Safety requires proof of a reasonable certainty that no harm will result from the proposed use of an additive. In determining the "safety" of an additive, scientists must take into consideration the cumulative effect of such additive on the diet of man or animals over their respective life spans together with any chemically or pharmacologically related substances in such diet. (Vogt, p3)

In addition, FDA has incorporated this concept of safety into its color additive regulations.

Under 21 CFR 70.3(i), a color additive is "safe" if "there is convincing evidence that establishes with reasonable certainty that no harm will result from the intended use of the color additive."

Therefore, the general safety clause prohibits approval of a color additive if doubts about the safety of the additive for a particular use are not resolved to an acceptable level in the minds of competent scientists." (Vogt, p3)

In this petition I will demonstrate that the FDA's standards of safety are not met by Yellow #5.

#### My Experience with Yellow #5

On December 18, 1999 my 20-month-old son had a cold, so as a treat I gave him a cup of commercially prepared eggnog. Rapidly he was overtaken by an asthma attack so severe he nearly died. Our local hospital, unable to handle the emergency, called in a team of doctors from Children's Hospital in Boston. They treated Ryan with a drug typically reserved for adults with COPD. Later we discovered the cause of this reaction was the artificial coloring in the eggnog.

### History of Problems with Yellow #5

FD&C Yellow # 5, also known as tartrazine, is the second most widely used dye in the United States (Center for Science in the Public Interest, 4) Yellow # 5 has a long history of health effects. In 1975 the number of reported cases of tartrazine reactions became large enough to make this a major public health concern. Studies have shown that Yellow No. 5 is a factor in asthma, Attention Deficit Hyperactivity Disorder, learning problems, and hives. In 1979 the FDA estimated that 50,000 to 100,000 individuals were sensitive to tartrazine. (Dipalma, 1347) The FDA did not consider this to be enough of a health concern to consider eliminating this dye from the American diet. In 1980 the Food and Drug Administration has required all products containing Yellow #5 to list the color on their labels.

### The Problem with Declaring Ingredients as Opposed to a Ban

Unfortunately sensitivity to Yellow # 5 is not a true allergy but ones that some call pseudoallergic, so there is no skin or blood test that can reliably test for this sensitivity. Unlike a true allergy sensitivity to Yellow #5 cannot be treated by shots or medications. Some people who are unaware they are sensitive to yellow #5 spend years treating their idiopathic urticaria, sometimes with steroids, drugs that have serious side effects. The only way to deal with sensitivity to tartrazine is to avoid it. Unfortunately avoiding Yellow #5 in foods is difficult and for some nearly impossible. Avoiding Yellow #5 in restaurants is also a very difficult proposition. The FDA has frequently needed to recall items that have undeclared Yellow #5 as an ingredient. This is a waste of the resources of the FDA and a nightmare for those with the sensitivity. While the FDA maintains that this is not a serious health risk, there are individuals that have gone into anaphylactic shock from Yellow #5. According to the Freedom of Information request I filed with the FDA there have been three dozen reports of adverse

reactions to yellow #5 from 1995-1999, and these are just the reports from people that were able to tie their reaction to Yellow #5, not the many others who may have reported adverse reactions to a food but were unaware of what ingredient caused the reaction.

#### Health Effects of Yellow #5

Medical studies have shown that Yellow #5 is a factor in asthma, attention deficit hyperactivity disorder (ADHD), learning problems and hives. Unfortunately there is no test for sensitivity to yellow #5 so it is difficult to diagnose. The only way to diagnose a patient with sensitivity to yellow #5 is through the oral provocation test, which is difficult and requires complete compliance from the patient. The only remedy available to people with sensitivity to yellow #5 is to avoid it altogether, which is very difficult.

#### Asthma

Asthma is the most common chronic disease in childhood, afflicting 5 million American children. The prevalence of asthma in the United States is rising each year for unknown reasons. In the past decade the death rate for asthma in the United States has doubled to more than 5,000 deaths annually. (Pelton, 1998, p. 34) Beginning in 1958 scientists linked artificial colorings in the diet and asthma in children (Stevenson). Many studies since then have attempted to disprove this link, with even the FDA's website suggesting that there is no link, but studies continue to show a link. Many of the studies that indicate there is no link used very small amounts of dye in the study generally 1 mg, when the average consumption by typically American children is much higher. (Rowe, 692) Children are especially sensitive to colorings in foods because they generally consume more dye as a percentage of body weight than adults do. Sensitivity to tartrazine manifests itself as increased bronchial sensitivity in sensitive asthmatics. After ingesting tartrazine some asthmatics react with changes in forced expiratory flow, these are severe

reactions. "Recently, it has been shown that when sensitive individuals are exposed to certain allergens or food substances enhanced bronchial reactivity may occur without detectable alteration in baseline lung function. The significance of this is clear. When bronchial sensitivity is heightened other trigger factors may more easily provoke an asthma attack". (Hariparsad, 81-82) This aspect of the tartrazine sensitivity makes it difficult for patients to notice a causal link between the food dye and the asthma attack. It is unknown how many asthmatics are sensitive to tartrazine, but some studies indicate it is approximately 20% (Dipalma, 1347, Harisparsad, 81) Asthmatics who are sensitive to aspirin are even more likely to be sensitive to tartrazine. (Dipalma, 1347). Because children do not consume aspirin because it's links with Reye's syndrome it is often not known if a child is an aspirin sensitive asthmatic.

#### Attention Deficit Hyperactivity Disorder

Attention Deficit Hyperactivity Disorder is another diagnosis affecting American children and growing at an alarming rate. The prevalence of ADHD is unknown but many experts place it at 3 to 5%, but some surveys find percentages as high as 17%. (Center for Science in the Public Interest, 1) ADHD takes a significant toll on children and their families. The child typically has problems in school and with peers and can put a strain on the other relationships within the family. Researchers agree that ADHD has genetic roots, but it cannot be diagnosed with any diagnostic test. (Center for Science in the Public Interest, 1)

In the 1970's Dr. Benjamin Feingold found that 30 to 50% of hyperactive children benefited from a diet free of dyes and other chemical additives.

For many children food dyes and especially Yellow # 5 can be a significant threat to health and to quality of life. With manifestations ranging from asthma and urticaria to irritability

and sleep disturbance the range of affects of this chemical are varied. Children who tend to be most affected by food dyes are preschoolers, and children who have allergies, asthma or eczema. In 1994 Rowe and Rowe completed a double blind, placebo-controlled, repeated-measures study with 54 children (34 study and 20 control). Each child was tested with 6 dose levels of tartrazine 1,2,5,10,25 and 50 mg. The study identified 24 clear reactors at at least 5 of the 6 dosage levels. They discovered a dose-related response, with the effects of dosages over 10mg lasting more than 24 hours (Rowe, p. 697.) All of the children who reacted were atopic with a history of allergies, asthma, eczema or allergic rhinitis. (Rowe,696). They discovered that there were differences how children reacted:

There were, however, notable differences in the clinical features of the children aged 2 to 6 years, compared with those aged 7 to 14 years. The younger children had constant crying, tantrums, irritability, restlessness, and severe sleep disturbance and were described as "disruptive," "easily distracted and excited," "high as a kite" and "out of control." Their parents were exhausted through lack of sleep and the the constant demands of their children, who were unable to be comforted or controlled. The older children were described as "irritable," "aimlessly active," "Lacking self control," "Whiney and unhappy, " and "like a bear with a sore head;" sleep difficulties were less likely to disturb the entire family. (Rowe, 696).

In 1996 a study conducted by Neil Ward, PhD studied not only the behavioral response to tartrazine in hyperactive and control children but their serum zinc levels. He found that not only did the behavior of hyperactive children change but so did their zinc levels. Only hyperactive children showed a significant reduction in blood serum zinc levels and an increase in urinary zinc output following the consumption of tartrazine. The behavioral changes in the children were dramatic. Of the 23 children consuming a tartrazine beverage 18 had increased levels of activity, 16 were aggressive, 4 violent, 2 had poor speech, 12 developed poor coordination and 8 developed asthma or eczema. All of these responses occurred in the 120 minutes following the tartrazine challenge. (Ward, 333). Low zinc levels are associated with an increased susceptibility

to infection and impaired cell-mediated immunity. Hyperactive children suffer from more frequent coughs, ear and chest infections and skin problems. (Ward, 338)"The fact that an ever-increasing number of studies have confirmed a link between the ingestion of synthetic food colors and hyperactivity raises the question about the possible mechanisms between azo dyes and biochemical systems. One study reported that azo inhibit trypsin activity by 50% following the in vitro addition of tartrazine and sunset yellow. Similarly the enzyme activity of amylase was reduced 66% with tartrazine.."(Ward, 340) "Another important effect of azo dyes is their adverse effects on the integrity of the gastrointestinal tract. Tartrazine and Sunset yellow have been linked to changes on the gut flora in rodents. (Ward, 341). Other studies confirm the link between Yellow #5 and ADHD. Boris and Mandel studied atopic children and in the double-blind phase of the study discovered that 69% of the children deteriorated when they consumed restricted foods or dyes. They found those children with asthma, eczema, or hives might be particularly helped by dietary changes. (Center for Science in the Public Interest, 8-9). Other studies (Weiss, 1980, Harley et al) found that younger children may be likelier than older children to experience greater sensitivity to dyes, perhaps because they ingest more dye proportional to their smaller body weight. (Center for science in the Public Interest, 9-10). Despite evidence that food dyes can impact the behavior of children there is no limit to their use, on the contrary products marketed to children, and widely consumed by them are full of artificial colorings.

### Learning Problems

In addition to ADHD a study done by Dr. James M. Swanson and Published in the prestigious journal Science demonstrated that tartrazine significantly impaired children's performance on learning tests on hyperactive children. "A four factor analysis of variance

revealed that the challenge with the food dye blend significantly impaired performance of the learning task. The interaction of two factors-that is challenge and time of testing was significant, suggesting a rapid onset of the effect of the food dyes." (Swanson, 1486) In a time when high stakes testing of school children is on the forefront of the national agenda this is a serious concern.

### Hives

In 1979 the Food and Drug Administration agreed that Yellow #5 causes hives in a number of sensitive individuals. It estimated that this number was approximately 100,000. I would not be surprised to find the incidence of hives from yellow #5 sensitivity to be much greater than estimated. Many suffer from chronic idiopathic urticaria (chronic hives, cause unknown) for many years without knowing the cause of their problem. Unfortunately many people suffer from hives for years unaware that their problem is caused by the food they eat. Because tartrazine sensitivity is not a true allergy the only test for it is through the oral provocation test which can be time consuming and requires complete cooperation from the patient, and in the case of children, from their families. (Genton, p. 44) Elimination diets are very difficult with yellow #5 because it is in such a wide range of products from foods, to vitamins and prescription medications, to toothpaste. Treating chronic hives when the cause is unknown can be expensive and frustrating, with unintended side effects from the medication.

### Contamination with Known Carcinogen

Another reason that the approval of Yellow #5 should be revoked is the Delaney Clause. The Delaney Clause establishes a zero cancer risk for food additives. Tartrazine has not been shown to cause cancer. But one of the chemicals used in making tartrazine benzidine is a carcinogen. The CFR mandates that the level of benzidine in tartrazine be less than 1 part per



billion but studies in the journal *Food Additives Contamination* have shown that in many cases this level is more than 200 parts per billion. (Lancaster, 1999)

### **Action Requested**

The Food and Drug Administration should reconsider its approval of Yellow #5 for use in food and drug products. There is ample evidence to indicate that Yellow #5 is not a safe product for potentially millions of Americans, especially children. Two of the most pressing health concerns of the twenty-first century, Asthma and Attention Deficit Hyperactivity Disorder are strongly linked to ingestion of this chemical. The rates of both are increasing as the use of this color additive is increasing. Additionally hives is an incredibly uncomfortable condition that the Food and Drug Administration admits is caused by this dye. All of these conditions are very expensive, and many Medicaid dollars are spent treating these conditions. In 1990 6.2 billion dollars was spent on the treatment of asthma in the United States, and the prevalence of asthma grew 42% in the decade between 1982 and 1992. (Pelton, 34) The estimated educational cost of ADHD is 3.5 to 4.0 billion annually although there is no systematic way to calculate the cost of ADHD for the nation. (Hinshaw et al p.3) Using Medicaid managed care figures including drug costs the average reimbursement for total treatment costs of a child with ADHD was 1,795 as compared to 1,666 for a child with asthma. (Hinshaw, et al p 2)

Twenty years ago when the FDA decided to require the listing of yellow #5 on product packaging Americans ate very differently than they do today. Food additives were not as widespread, yellow #5 was initially contained in only a few hundred products. Now it is contained in thousands of products and is so pervasive on the supermarket shelves that it is nearly impossible to avoid. Americans eat more processed foods than they did in 1979. Children's products are especially likely to contain artificial colorings.

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**Food and Drug Administration**  
**Room 1061**  
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**Environmental Impact**

Under 21 CFR Subpart C section 25.32 (m) This petition is categorically excluded and, therefore, does not require the preparation of an EA or an EIS.

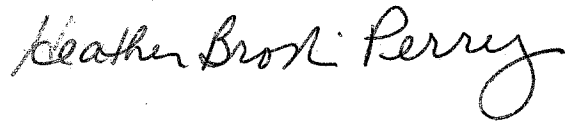
The Food and Drug Administration is charged with ensuring that the food that is consumed in this country is safe. You must consider whether or not Yellow #5 meets the rigorous criteria necessary for the FDA's continued approval.

**Certification**

I certify that to the best of my knowledge this petition includes all information relevant to this petition.

I thank you for your consideration.

Sincerely,



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