

Doherty, Jane H.

From: marietta.bernot [REDACTED] (B) (6)
Sent: Monday, April 19, 2010 9:37 AM
To: Doherty, Jane H.; Rochette, Peggy
Cc: steve.rizk [REDACTED] (B) (6)
Subject: EU Color Warning Label - Current Investigative Activity

Hello Jane and Peggy, In anticipation of Ambassador Kirk's meeting with Commissioner DeGuchte I want to advise you of 3 initiatives underway that would justify a delay in implementation of Article 24 - the requirement that foods containing certain synthetic colors carry warning labels. The 3 initiatives are:

- 1. The University of Massachusetts Food Policy group and the Commonwealth of Massachusetts** have jointly sponsored a review on recommended best practices and gold standard methodology for diet and ADHD studies. A selected expert panel held a workshop summer 2009 and drafted a manuscript which uses colors and ADHD to demonstrate some of the pitfalls around study designs. The manuscript was submitted to the Journal of Pediatrics late last summer; received comments from reviewers; and has now been resubmitted to the Journal (as of early March) for review. The University and the experts expect to hear from the Journal in the 2-3 months.
- 2. International Life Sciences Institute North America.** The Life Sciences Research Office has conducted a literature review on colors and ADHD/hyperactivity. A copy of the literature review has been provided to the U.S. Food and Drug Administration. A panel of experts in the fields of ADHD, Pediatrics, Psychiatry/Psychology, Biostatistics, etc. is being assembled to evaluate the quality of the studies and strength of the science in this area and answer the question "Do artificial colors alone or in combination cause or exaggerate ADHD or its' symptoms?". The goal is to complete this work and have it published in a peer reviewed journal.
- 3. The U.S. Food and Drug Administration (FDA)** has completed its own literature review on colors and ADHD. FDA has reportedly identified an external expert panel to review these studies and provide their opinion on the strength of the science. We are told that FDA is aiming to complete this review by the end of 2010. This review is expected to be an Evidence Based Review. An Evidence-Based Review (EBR) system is an objective systematic science-based evaluation of the strength of the evidence to support or refute a statement. It evaluates the strength of the scientific evidence to support a proposed relationship between a substance (e.g., color) and an outcome (e.g., ADHD). An EBR panel would first define and agree upon the question being asked. Then, the evaluation process involves a series of steps to assess scientific studies and other data, eliminate those from which no conclusions about the substance/outcome can be drawn, rate the remaining studies for methodological quality and evaluate the strength of the totality of the scientific evidence by considering a number of factors (e.g., study types, methodological quality, quantity of evidence for and against the claim, relevance to the population, replication of the study results and overall consistency of the evidence).

Please let us know if there is additional information we can provide on the above activities or any other related subject.
Regards.

Marietta E. Bernot
Global Trade and Customs Advisor
Mars Incorporated

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(B)(6)

Doherty, Jane H.

7

From: marietta.bernot [REDACTED] (B)(6)
Sent: Monday, March 08, 2010 3:39 PM
To: Doherty, Jane H.
Subject: Re: EU color warning labels - EU Trade Commissioner's visit

Just thought it might be useful for Amb Kirk to. Flag as a fast emerging problem.

From: "Doherty, Jane H." [Jane_Doherty [REDACTED] (B)(2)]
Sent: 03/08/2010 03:04 PM EST
To: Marietta Bernot
Subject: RE: EU color warning labels - EU Trade Commissioner's visit

I'm not sure what's on the agenda. I can check, though I think we need to raise this at the technical level right now.

Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative
Executive Office of the President
Washington, DC

[REDACTED] (B)(2)

From: marietta.bernot [REDACTED] (B)(6)
Sent: Monday, March 08, 2010 1:31 PM
To: Doherty, Jane H.
Subject: EU color warning labels - EU Trade Commissioner's visit

Hi Jane. I see the EU Trade Commissioner is here this week and will see Amb. Kirk on Friday I believe. Any chance the color warning label might make it onto their agenda? Regards.

Marietta E. Bernot
Global Trade and Customs Advisor
Mars Incorporated
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Doherty, Jane H.

8

From: marietta.bernot [REDACTED] (B)(6)
Sent: Wednesday, June 09, 2010 2:48 PM
To: Doherty, Jane H.
Subject: Re: EU Color Warning label

I will immediately ask our science teams. Regards.

Marietta E. Bernot
Global Trade and Customs Advisor
Mars Incorporated
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<p>"Doherty, Jane H." <Jane.Doherty@[REDACTED]> (B)(2) 06/09/2010 02:40 PM</p>	<p>To: <marietta.bernot@[REDACTED]> (B)(6) cc: Subject: Re: EU Color Warning label</p>
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Thank you for that! You must be reading my calendar againI had a meeting with the EU this morning and am working very hard to get this delayed. I think it's a good sign that they asked to meet with me. We're trying to find how we could possibly get this deferred even if it is a regulation because we acknowledge the science is weak.

If we were to ask you to put together every study available on the six colors. Can you tell me how much time you would need?

Thank you,
Jane
Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative

From: marietta.bernot [REDACTED] (B)(6)
To: Doherty, Jane H.
Sent: Wed Jun 09 14:04:52 2010
Subject: EU Color Warning label

[REDACTED] (B)(4)

Marietta E. Bernot
Global Trade and Customs Advisor
Mars Incorporated

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(B)(6)

Doherty, Jane H.

9

From: marietta.bernot [REDACTED] (B)(6)
Sent: Wednesday, May 26, 2010 12:44 PM
To: Doherty, Jane H.
Subject: EU color warning label

Just to let you know that one of our industry advisors in the EU is meeting with Dall's Deputy Chief of Staff Dr. Nils Behrnt on Tuesday 15 June to give further background from the EU perspective on the color warning label requirement. Can you tell me whether the formal request for delay has been sent? Many thanks.

Marietta E. Bernot
Global Trade and Customs Advisor
Mars Incorporated
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Doherty, Jane H.

10

From: Sahagian, Margaret T.
Sent: Monday, June 07, 2010 12:32 PM
To: Doherty, Jane H.
Subject: RE: EU color warning label

I'm assuming we still need to get this downstairs----I know you're swamped but when you can make the changes I'll be sure to get it signed!

From: Doherty, Jane H.
Sent: Thursday, June 03, 2010 2:41 PM
To: Sahagian, Margaret T.
Subject: Re: EU color warning label

Darn, I can't do this on a BB.

I'll do it tonight and we'll get this done tomorrow. Ok?

Gracias!

Jane

Jane Doherty

Director, Sanitary and Phytosanitary Affairs

Office of the United States Trade Representative

From: Sahagian, Margaret T.
To: Doherty, Jane H.
Sent: Thu Jun 03 14:37:35 2010
Subject: RE: EU color warning label

The clean version you sent still had these comments/suggestions----please let me know which ones to use:

As [we/our staffs] have discussed previously, the United States remains concerned about the apparent lack of scientific basis for a warning statement requirement and the potential negative impact on trade that may result from such a requirement. Many of the specified color additives (Sunset Yellow, Allura Red, and Ponceau 4R, Tartrazine , Quinoline Yellow, and Carmoisine) are widely used by the global food industry, including in confectionary products and beverages.

While the United States supports a Member's right to impose measures to protect public health, a Member may only apply such measures to the extent necessary to protect public health and that are based on scientific evidence. Given the conclusions of the EFSA panel , we remain concerned that the warning statement requirement does not appear to have scientific basis and thus will require some manufacturers to adapt their manufacturing practices without cause.

From: Doherty, Jane H.
Sent: Wednesday, June 02, 2010 12:25 PM
To: Sahagian, Margaret T.
Subject: Fw: EU color warning label

Meg,

Could I ask you to prepare the clean document for ARK's signature and send it downstairs asap? Do you think we need to do a cover memo explaining why he needs to sign this asap? [REDACTED] (B)(5)

Thank you!

Jane

Jane Doherty

Director, Sanitary and Phytosanitary Affairs

Office of the United States Trade Representative

From: Strickler, J. Sloane

To: Doherty, Jane H.

Sent: Thu May 27 12:29:19 2010

Subject: RE: EU color warning label

Comments in redline and clean. It looks like a lot but I didn't change too much on the substance. Did some tightening up of some repetition and some tweaking here and there. Because of the context of the letter – asking for a delay on the article as a whole – you will be happy to know that I did not re-raise my objection to complaining about color additives not approved in the US. But that objection remains when we go back to complaining to them as burdens alone. Cheers.

From: Doherty, Jane H.

Sent: Thursday, May 27, 2010 11:09 AM

To: Strickler, J. Sloane

Subject: Re: EU color warning label

Gracias. I realize you're swamped.

Jane Doherty

Director, Sanitary and Phytosanitary Affairs

Office of the United States Trade Representative

From: Strickler, J. Sloane

To: Doherty, Jane H.

Sent: Thu May 27 11:08:00 2010

Subject: RE: EU color warning label

Looking at it now.

From: Doherty, Jane H.

Sent: Wednesday, May 26, 2010 5:26 PM

To: Strickler, J. Sloane

Subject: Fw: EU color warning label

Hey Sloane,

Have you cleared on the Kirk colors letter? I need to pass that on asap.

Thanks,

Jane

Jane Doherty

Director, Sanitary and Phytosanitary Affairs

Office of the United States Trade Representative

From: marietta.bernot [REDACTED] (B)(6)
To: Doherty, Jane H.
Sent: Wed May 26 12:43:35 2010
Subject: EU color warning label

Just to let you know that one of our industry advisors in the EU is meeting with Dall's Deputy Chief of Staff Dr. Nils Behrnt on Tuesday 15 June to give further background from the EU perspective on the color warning label requirement. Can you tell me whether the formal request for delay has been sent? Many thanks.

Marietta E. Bernot
Global Trade and Customs Advisor
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Doherty, Jane H.

//

From: marietta.bernot [REDACTED] (B)(6)
Sent: Friday, April 30, 2010 11:14 AM
To: Doherty, Jane H.
Cc: Rochette, Peggy
Subject: EU color warning label

Good morning Jane. Can you give us a read out on Amb. Kirk's discussion with the Commissioners on this issue? Also, I would like to know if the U.S. has formally asked the EU for a delay of implementation of the regulation?

Marietta E. Bernot
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(B)(6)

Doherty, Jane H.

12

From: marietta.bernot [REDACTED] (B)(6)
Sent: Tuesday, May 11, 2010 4:16 PM
To: Doherty, Jane H.
Subject: EU color warning label

Hi Jane. I think you mentioned to me that Amb. Kirk did not have the chance to talk with de Gucht about the color issue because the meeting was cut short. Can you tell me whether Amb. Kirk will send a letter to de Gucht saying that lack of time prevented him from raising this issue but that he has requested through Commissioner Dalli a delay in implementation in order to have a thorough review of the scientific material? Appreciate anything you can tell me as we are trying to work on the other end as well. Also, is "delay" an open ended request with period of time yet to be determined or more specific. Thanks and regards.

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(B)(6)

Doherty, Jane H.

13

From: marietta.bernot [REDACTED] (B)(6)
Sent: Tuesday, May 11, 2010 6:25 PM
To: Doherty, Jane H.
Subject: Re: EU color warning label

Thanks as always. I think a letter to deGucht would be good as it shares within the Commission the concern and dare we hope "responsibility." Regards.

Marietta E. Bernot
Global Trade and Customs Advisor
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<p>"Doherty, Jane H." <Jane_Doherty [REDACTED] (B)(2)> 05/11/2010 04:40 PM</p>	<p>To: <marietta.bernot [REDACTED] (B)(6)> cc: Subject: Re: EU color warning label</p>
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Marietta,

We are sending a letter to Dalli asking for an indefinite delay (until they have the scientific evidence), but that draft is currently in the internal clearance here at USTR. I had not prepared one for de Gucht, but am happy to ask senior management if we can prepare that letter as well. You know we will do whatever we can to help.

Warm regards,
Jane
Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative

From: marietta.bernot [REDACTED] (B)(6)
To: Doherty, Jane H.
Sent: Tue May 11 16:16:16 2010
Subject: EU color warning label

Hi Jane. I think you mentioned to me that Amb. Kirk did not have the chance to talk with de Gucht about the color issue because the meeting was cut short. Can you tell me whether Amb. Kirk will send a letter to de Gucht saying that lack of time prevented him from raising this issue but that he has requested through Commissioner Dalli a delay in implementation in order to have a thorough review of the scientific material? Appreciate anything you can tell me as we are trying to work on the other end as well. Also, is "delay" an open ended request with period of time yet to be

determined or more specific. Thanks and regards.

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(B)(6)

Doherty, Jane H.

14

From: marietta.bernot [REDACTED] (B)(6)
Sent: Thursday, September 24, 2009 4:33 PM
To: Doherty, Jane H.
Cc: Rochette, Peggy
Subject: EU color warning label issue - EFSA review of the Southhampton Study
Attachments: EFSA Review of Southhampton Study March 2008.doc; Do Foods or Additives Cause Behavior Disorders Pro.pdf

Thank you again for the meeting on Tuesday. We are so grateful for your time and attention. You had requested a copy of the EFSA review of the Southhampton Study which I attach. You had also asked whether other studies had been done and the outcomes. I attach an article from Pediatric Annals 2006 which reviews all the important studies on the links between colors and additives and hyperactivity in children. This article concludes:

The possible role of foods or additives in causing behavioral disorders in children particularly ADHD, has been a controversial subject both among health care providers and the public. However, a critical review of the literature provides very limited support for such a relationship. On encountering such cases, the healthcare professional should first establish an accurate diagnosis of the suspected "abnormal" behavior based on specific standard criteria. It is important to counsel the family regarding the standard of care practice and about the limited evidence of a role of foods and additives in causing behavior problems. If parents strongly suspect a specific dietary item, a trial of elimination may be warranted. If the child's behavior shows definite improvement, a challenge in a double-blind, placebo-controlled fashion under the supervision of an experienced physician would be necessary to verify the relationship.

I also have the case study that Alison Bodor mentioned that evaluates the history of additives issues in the EU and also gives extensive background on the Southhampton study. Rather than load you up with this document, just know that I have it and will send over if you would like to have it. Regards.

Marietta E. Bernot
Global Trade and Customs Advisor
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Opinions

Assessment of the results of the study by McCann *et al.* (2007) on the effect of some colours and sodium benzoate on children's behaviour [1] - Scientific Opinion of the Panel on Food Additives, Flavourings, Processing Aids and Food Contact Materials (AFC)

Question number: EFSA-Q-2007-171

Adopted: 7 March 2008

[Summary](#)  (0.1Mb)

[Opinion](#)  (0.4Mb)

Summary

Following a request from the European Commission, the Panel on Food Additives, Flavourings, Processing Aids and Food Contact Materials (AFC) was asked to assess the results of a recent study on the effect of mixtures of additives on children's behaviour and provide an opinion on the findings, taking into account, if possible, other available scientific literature in the related area.

A recent study by McCann *et al.* (2007) has concluded that exposure to two mixtures of 4 synthetic colours plus a sodium benzoate preservative in the diet result in increased hyperactivity in 3-year old and 8- to 9-year old children in the general population. In an earlier study by the same research team there was some evidence for adverse behavioural effects of a mixture of 4 synthetic colours and sodium benzoate in 3-year old children on the Isle of Wight (Bateman *et al.*, 2004).

In this recent study the effects of two combinations of Tartrazine (E102), Quinoline Yellow (E104), Sunset Yellow FCF (E110), Ponceau 4R (E124), Allura Red AC (E129), Carmoisine (E122) and sodium benzoate (E211) on children's behaviour were studied. Five of the six food colours belong to the class of synthetic azo dyes and one, Quinoline Yellow (E104), is a quinophthalone. Sodium benzoate is used as a preservative. The study involved one hundred and fifty three 3-year old and one hundred and forty four 8- to 9-year old children, selected to represent a broad range of behaviour in the general population including children with normal to high level behavioural activity. Children who were medicated for ADHD were not included. A global hyperactivity aggregate (GHA) score was the main outcome of the study, and this parameter was based on aggregated z-scores of observed behaviours and ratings by teachers, class room observers and parents, plus, for 8- to 9- year old children, a computerised test of attention.

Mix A containing Tartrazine (E102), Ponceau 4R (E124), Sunset Yellow FCF (E110), Carmoisine (E122) and sodium benzoate significantly increased GHA scores for all 3-year old children compared to the placebo control GHA scores (effect size 0.20 [CI 0.01 to 0.39], $p < 0.05$).

Mix B containing Sunset Yellow FCF (E110), Carmoisine (E122), Quinoline Yellow (E104), Allura Red AC (E129) and sodium benzoate had no effect on GHA scores in 3-year old children as compared to the placebo control GHA scores (effect size 0.17 [CI -0.03 to 0.36]).

This result persisted when analysis was restricted to 3-year old children who consumed more than 85% of juice and had no missing data (complete case group); in this analysis the effect of Mix A in the 3-year old children was still significantly increased compared to placebo control (effect size 0.32 [CI 0.05 to 0.60], $p < 0.05$) but for Mix B no significant effect on GHA scores was observed (effect size 0.21 [CI -0.06 to 0.48]). For the 8- to 9- year old children a significant effect of Mix A (effect size 0.12 [CI 0.02 to 0.23], $p < 0.05$) or Mix B (effect size 0.17 [CI 0.07 to 0.28], $p < 0.01$) was seen when analysis was restricted to those children

consuming at least 85% of drinks with no missing data (complete case group). When all 8- to 9- year old children that completed the study were taken into account, Mix A had no effect on the GHA scores compared to the placebo control (effect size 0.08 [CI -0.02 to 0.17]) and Mix B had a significant effect on GHA scores (effect size 0.12 [CI 0.03 to 0.22] $p < 0.05$).

The authors concluded that exposure to synthetic colours or a sodium benzoate preservative (or both) in the diet result in increased hyperactivity in 3-year old and 8- to 9-year old children in the general population. Based on surveys conducted from 2002 to 2005, the target colours are more frequently used in sweets but also occur commonly in soft drinks and benzoate is frequently present in soft drinks. Children consuming brightly coloured sweets may be exposed to levels comparable to those considered in the protocol of the McCann *et al.* study for one or more of the food colours studied. Comparable levels may also be reached in those children who consume brightly coloured soft drinks. The level of exposure to sodium benzoate is also likely to occur.

The Panel considers that the steps taken for score normalisation and aggregation are mathematical transformations that might affect the assumptions of normality and independence of the data which are essential for the whole statistical analysis. Therefore, the authors' primary analysis was repeated using a more justifiable and conventional statistical model, and this was supplemented by a set of additional analyses with the aim of aiding the interpretation of the results.

The Panel considers the re-analysis undertaken by EFSA, in which all single variables (minus the individual baseline value for that variable) were considered without normalisation, so that each subject served as its own reference, as the most adequate. This re-analysis was undertaken both at the level of the individual parameters as well as on the aggregated scores.

Based on the results obtained it was concluded that the analysis with the recalculated GHA score led to broadly similar conclusions to that in the original paper by McCann *et al.*, except for the following:

- (1) The Mix A versus placebo comparison was not statistically significant for the 3-year olds when all subjects were included (entire sample), while the significance for the $\geq 85\%$ consumption and complete case groups was increased slightly;
- (2) For the 8- to 9- year age group, the Mix A versus placebo comparison was no longer statistically significant in any of the three consumption groups.

In addition the data were analysed on the basis of a modified GHA score in which the parental scores were not included. The results from this analysis no longer revealed any statistically significant effects of Mix A or Mix B versus placebo, except for Mix B versus placebo in 8- to 9-year old completers.

A further analysis was carried out on the whole data set, comprising analysis of the single variables of parental scores, teacher scores and observer scores, and, in the case of 8- to 9-year old children, computer-based scores. There is a suggestion from these analyses that the statistically significant effects seen in the 3-year olds (Mix A versus placebo) and in the 8-to 9- year olds (Mix B versus placebo) are largely driven in the data by the parental scores and, in the older males in both comparisons, by the computer score.

The Panel notes that some, but not all, earlier studies have also reported effects of food colours on child behaviour, the majority of these studies being conducted on children described as hyperactive or with a clinical diagnosis of ADHD.

The Panel concludes that the McCann *et al.* study provides limited evidence that the two different mixtures of synthetic colours and sodium benzoate tested had a small and statistically significant effect on activity and attention in some children selected from the general population, although the effects were not observed for all children in all age groups and were not consistent for the two mixtures. The findings may thus be relevant for specific individuals within the population, showing sensitivity to food additives in general or to food colours in particular.

However, it is not possible to assess the overall prevalence of such sensitivity in the general population and reliable data on sensitivity to individual additives are not available.

The clinical significance of the observed effects also remains unclear, since it is not known whether these small alterations in attention and activity would interfere with schoolwork and other intellectual functioning. The clinical significance could possibly be clarified by assessments that used scales for functional impairment and diagnostic interviews, especially if a high proportion of children with high symptom scores were to be included in such a study.

There are thus a number of uncertainties that are apparent from this new research, some of which are echoed in earlier research. These include:

- the limited consistency of the results with respect to age and gender of the children, the effects of the two mixtures of additives tested and the type of observer (parent, teacher or independent observer);
- the unknown clinical relevance of the novel metric, i.e. the GHA score;
- the unknown relevance of the small effect size (as was also seen in the meta analysis of earlier studies by Schab and Trinh, (2004));
- the fact that the study has not been designed to identify the effects of individual additives;
- a lack of information on dose-response;
- the lack of a biologically plausible mechanism for induction of behavioural effects from consumption of food additives.

The Panel concludes that the McCann *et al.* study provides limited evidence that the two different mixtures of synthetic colours and sodium benzoate tested had a small and statistically significant effect on activity and attention in children selected from the general population excluding children medicated for ADHD, although the effects were not statistically significant for the two mixtures in both age groups.

Since mixtures and not individual additives were tested in the study by McCann *et al.*, it is not possible to ascribe the observed effects to any of the individual compounds.

The clinical significance of the observed effects also remains unclear.

In the context of the overall weight of evidence and in view of the considerable uncertainties, such as the lack of consistency and relative weakness of the effect and the absence of information on the clinical significance of the behavioural changes observed, the Panel concludes that the findings of the study cannot be used as a basis for altering the ADI of the respective food colours or sodium benzoate.

[1] For citation purposes: Scientific Opinion of the Panel on Food Additives, Flavourings, Processing Aids and Food Contact Materials (AFC) on a request from the Commission on the results of the study by McCann *et al.* (2007) on the effect of some colours and sodium benzoate on children's behaviour. The EFSA Journal (2008) 660, 1-5
Two members of the Panel did not participate in the discussion on the subject referred to above because of possible conflict with declared interests.

[Statistical report](#)  (1.8Mb)

Published: 14 March 2008

- [Home](#)
- [AFC - Former Panel on additives, flavourings, processing aids and materials in contact with food](#)
- [Opinions](#)



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Do Foods or Additives Cause Behavior Disorders?

Narrito V. Cruz, MD; and Sami L. Bahna, MD, DrPH

Attention-deficit/hyperactivity disorder (ADHD) is the most commonly diagnosed behavioral disorder in childhood, with a prevalence of 4% to 12% of elementary school population, affecting three boys to every girl.¹ Children with ADHD often have poor scholastic performance, impaired family and peer relationships, and other co-existing developmental and psychiatric disorders. With the shortage of mental healthcare providers, pediatricians and other primary care physicians provide the majority of care for such children. In a recent study of pediatric practices in North Carolina, 15% of children were found to have behavioral disorders, with ADHD the most frequent

diagnosis.² Another recent survey reported that about half of pediatricians conduct three or more new evaluations for ADHD per month.³

ADHD has gained much popularity among parents and schoolteachers and periodically is highly publicized by the media. In fact, many children are labeled "hyperactive" based merely on the personal impression of a parent or a teacher. The diagnosis should be based on specific standardized criteria published in the *Diagnostic and Statistical Manual of Mental Disorders (DSM)* by the American Psychiatric Association (Sidebar, see page 748).⁴

Multiple etiologies have been proposed for childhood behavioral problems, including ADHD. It is generally accepted that ADHD is a complex, multifactorial disorder. Underlying factors include any or combination of genetics, perinatal events, environmental causes, neurobiological mediators, and psychosocial influences. An association between food additives and behavior disorders in children was suggested many years ago and continued to gain momentum, par-

Dr. Cruz is senior fellow and Dr. Bahna is professor and chief, Section of Allergy and Immunology, Louisiana State University Health Sciences Center, Shreveport, LA.

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ticularly in the 1970s, after a publication by Benjamin Feingold.⁵ The introduction of this hypothesis generated conflicting reactions from health care professionals and the public. The purpose of this article is to provide a balanced review of the literature, both in support and against the possibility of such a relationship (Table, see pages 750-751).

HYPERACTIVITY AND DIET

Feingold⁶ postulated that some children have a genetic predisposition to hyperactivity, triggered by certain food components. He proposed that such children improve on a diet free of artificial flavors and colors and natural salicylates, which he used in his pediatric practice. He reported dramatic improvement in about 50% of children with hyperactivity who followed his proposed diet. Even though Feingold's hypothesis was based on anecdotal evidence, his proposed diet received wide publicity. Supported by certain groups of parents of hyperactive children, "Feingold Associations" were formed throughout the United States. A positive corollary was the generation of interest by several investigators to study the relationship between diet and childhood behavior.

REPORTS THAT MAY SUPPORT THE RELATIONSHIP

A few studies reported that food dyes, preservatives or other additives could adversely influence behavior in children. In such studies, the children's behavior was assessed primarily by parents, school teachers, or other professionals.

In a double-blind study, Conners et al.⁷ studied 15 hyperactive boys (ages 6 to 12) who met *DSM-II* criteria and were given either the Feingold diet or a control diet for 4 weeks. The teachers reported significant reduction in hyperkinetic

symptoms on the Feingold diet. Such an apparent improvement was neither observed by the parents nor reproduced when the order of giving the two diets was reversed. The authors concluded that further studies were required before definite recommendations were made.

In further testing the Feingold hypothesis, 36 school-age boys (ages 6 to 12) and 10 of preschool age (ages 3 to 5) were randomly assigned in a double-blind, crossover study to either the Feingold diet or a control diet for 3 to 4 weeks.⁸ The participants were selected on the basis of a physician's diagnosis of hyperkinetic behavior or according to a Conners Parent-Teacher Score of 15 or greater, indicative of moderate to severe behavioral disruption. Only four of the 36 school-age children showed improvement on the Feingold diet by both parent and teacher behavior ratings. No chang-



Diagnostic Criteria for Attention-deficit/Hyperactivity Disorder*

- Six or more of the following symptoms of inattention and/or hyperactivity-impulsivity persisting at least 6 months and inconsistent with the developmental level of the child:

Inattentive

- Often fails to give close attention to details, makes careless mistakes
- Often has trouble sustaining attention in tasks/activities
- Often does not seem to listen
- Often does not follow through on instructions
- Often has trouble organizing tasks
- Often avoids/dislikes tasks requiring sustained mental effort
- Often loses important things
- Often easily distracted by extraneous stimuli
- Often forgetful in routine activities

Hyperactive-impulsive

- Often squirms and fidgets
- Often can't stay seated
- Often runs/climbs excessively
- Often has difficulty remaining quiet during play or leisure activities
- Often blurts out answers before questions are finished
- Often "on the go," acts as if "driven by a motor"
- Often talks excessively
- Often has difficulty awaiting turn in play/activity
- Often interrupts/intrudes on others

- Onset of symptoms that cause impairment present before age 7.
- Presence of symptoms in two or more settings (eg, home, school, work).
- Evidence for significant impairment in social, academic, or occupational functioning.
- Symptoms that do not occur exclusively during a course of pervasive developmental disorder, schizophrenia, or other psychotic disorder and are not better accounted for by another mental disorder (eg, mood, anxiety, dissociative, or personality disorder).

*Adapted from the Diagnostic and Statistical Manual of Mental Disorders, fourth edition.⁴

es were noted by neuropsychological testing or in observer ratings. In the 10 preschool boys, however, all 10 mothers and four of the seven fathers reported improvement in behavior in response to the Feingold diet.

In another study of 13 hyperkinetic children ages 3 to 10, parent ratings were recorded within 3 hours after the children ate cookies containing artificial colors or cookies without colorings.⁹ The parents

reported that the children's behavior was worse following eating cookies with the colorings compared with the placebo.

A study from Australia investigated the possible role of tartrazine in 34 children (ages 2 to 14) referred for hyperactivity (23 strongly suspected reactors and 11 uncertain reactors) and 20 controls.¹⁰ The children were maintained on a dye-free diet and then each morning for 21 days were given a placebo or tar-

trazine in a capsule or added to orange juice. After a 3-day placebo administration, tartrazine was given in one of six doses (1, 2, 5, 10, 20, or 50 mg), with at least 2 days between doses. Each child was his or her own control regarding change in behavior. The investigators identified consistent behavioral changes in 24 of the 54 participants: 82.6% of the suspected reactors, compared with 27.3% of the uncertain reactors and 10% of controls. The changes observed in younger children (ages 2 to 6) were constant crying, irritability, restlessness, and disruptiveness. The changes in the older children (ages 7 to 14) were irritability, aimless activity, whining, and unhappiness. Interestingly, all 24 reactors were atopic, with a history of asthma, eczema, or allergic rhinitis. Therefore, the change in behavior cannot be directly attributed to the change in diet.

Some investigators used a mixture of multiple food colorings for challenge rather than single agents. Swanson and Kinsbourne¹¹ investigated 40 children; 20 were considered as hyperactive, with an average score of 16.2 on the Conners Rating Scale (CRS) and a favorable response to stimulant medications, and the other 20 had a lower average CRS score of 12.3 and were considered not hyperactive. After 3 days of a diet free of dyes and other additives, oral challenges with either a blend of nine food dyes (total 100 or 150 mg) or placebo were administered to 10 children of each group on days 4 and 5. The findings suggested that food dyes (in this large dose) decrease attention span in hyperactive children. However, CRS showed no difference between the dye and placebo intake periods. The performance of the nonhyperactive group was not affected by the food dye challenge.

Pollock and Warner¹² evaluated 39 children (ages 2 to 15) whose behavior was reported by parents to improve on an additive-free diet. The children were challenged with a capsule containing a

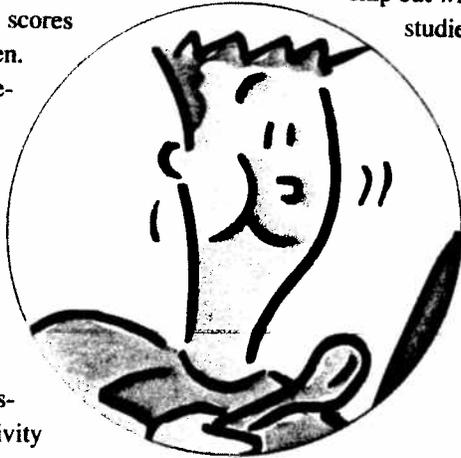
12.5 mg dye mixture (tartrazine, sunset yellow, carmoisine, and amaranth) given daily for a week on two occasions, separated by 3-week daily intake of placebo capsules. In the 19 children who completed the trial, the intake of food dyes was associated with an adverse effect on daily CRS scores in 17 (89.5%) children.

A recent double-blind, placebo-controlled crossover challenge was conducted on 277 children (ages 3.2 to 4.1) in England.¹³ The children were divided into four groups based on assessment of hyperactivity and presence or absence of

atopy, then randomly assigned to fruit juice with 20 mg of artificial colorings (sunset yellow, tartrazine, ponceau, and carmoisine) plus 45 mg of sodium benzoate or to placebo fruit juice for 1 week each. Behavior was assessed weekly by research psychologists using validated tests, as well as daily by the parents using the Weiss-Werry-Peters Activity Scale.¹⁴ There was significant reduction in hyperactivity during the initial elimination of dyes and benzoates. In addition, the parents reported greater increases in hyperactivity during the active challenge than the placebo. These effects were not related to the initial presence or absence of hyperactivity or atopy. The investigators concluded that there seems to be a general adverse effect noticed by parents of artificial food dyes and benzoate on the behavior of preschool children.

A widespread belief is that sweeteners (natural or artificial) cause hyperactivity in some children. Our literature search revealed very few studies that might support this belief. In a retrospective study, dietary records of 28 hyperactive children (ages 4 to 7) were reviewed and compared with the child's behavior as observed by

an independent professional.¹⁵ It was noted that the amount of sugar consumed correlated significantly with increased aggressive-destructive and restless behaviors. The literature contains a few additional anecdotes about such a relationship but without any systematic studies.^{16,17}



A few studies reported that food dyes, preservatives, or other additives could adversely influence behavior in children. In such studies, the children's behavior was assessed primarily by parents, school teachers, or other professionals.

Bradstock et al.¹⁸ analyzed 231 consumer complaints of adverse effects of aspartame, 69% of which were neurobehavioral in nature. However, the authors found no definite symptom complex that suggests a health hazard to aspartame.

DATA THAT REFUTE THE RELATIONSHIP

Several double-blind, placebo-controlled studies do not support the relationship between food additives and behavior disorders. In 1978, Harley et al.¹⁹ studied nine hyperactive boys who were the most responsive to the Feingold diet in a previous study.⁸ The food of the entire family was limited to the Feingold diet for 11 weeks. Following a 4-week baseline period, the children were subjected to multiple double-blind, placebo-controlled crossover challenges with cookies or candy bars that contain a mixture of artificial food colors or placebo. No adverse effects on behavior were observed according to parent or teacher ratings, classroom observation, or psychological testing. One child exhibited extreme behavior disruption but was

discovered to be receiving the placebo cookie during that period.

Levy et al.²⁰ conducted a double-blind, placebo-controlled, crossover study on 22 hyperactive children, ages 4 to 8, using a tartrazine challenge (5 mg in biscuits). They found no significant differences in the children's behavior

by Conners parent-teacher ratings or by standard neuropsychological testing.

In 1980, Weiss et al.²¹ reported a study on 22 children, ages 2.5 to 7, with behavior problems and histories of marked improvement on the Feingold diet. The children were challenged in a double-blind, placebo-controlled fashion with 35.6 mg/day of a mixture of seven artificial food dyes in a soft drink on 8 separate days. There was no overall effect of the challenge in 21 of the 22 children, based on parental observation. One 34-month-old child seemed to react consistently to food coloring but not to the placebo.

In another series, 11 hyperactive children (ages 4 to 13) with histories of remarkable response to the Feingold diet underwent double-blind, placebo-controlled crossover challenge with cookies containing food coloring mixture (13 mg/cookie) or placebo cookies for 1 week each.²² The children received one cookie the first day with an additional cookie each day to a maximum of six cookies on days 6 and 7. No change in behavior was noted by parents, teachers, or psychiatrists.

TABLE

Summary of Studies on the Relationship Between Food Additives and Behavior

Author	Year	Design	Subjects
Conners et al.	1976	Double-blind, crossover challenge	15 hyperkinetic boys (ages 6 to 12)
Goyette et al.	1978	Double-blind, crossover challenge	13 hyperkinetic children (ages 3 to 10)
Harley et al.	1978	Double-blind, crossover challenge	36 school-age boys (ages 6 to 12) and 10 preschool boys (ages 3 to 5)
Harley et al.	1978	Multiple DBPC, crossover challenge	Nine hyperactive boys who were most responsive to Feingold diet from a previous study
Levy et al.	1978	DBPC, crossover challenge	22 hyperactive children (ages 4 to 8)
Weiss et al.	1980	DBPC, repeated crossover challenge	22 children (ages 2.5 to 7) with behavior problems and a history of response to elimination diet
Swanson and Kinsbourne	1980	DBPC challenge	40; 20 considered hyperactive (mean CRS=16.2), 20 nonhyperactive (average CRS=12.3)
Mattes and Gittelman	1981	DBPC, crossover challenge	11 hyperactive children (ages 4 to 12) with improvement on Feingold diet per history
Gross	1984	DBPC, crossover challenge	50 hyperactive children (ages 5 to 17) whose mothers were convinced that sugar caused the child's symptoms
Wolraich et al.	1985	DBPC, crossover challenge	Two separate groups of 16 hyperactive boys (ages 7 to 12)
David	1987	DBPC challenge	24 children (ages 1.6 to 12.4) with history of adverse behavior reaction to tartrazine or benzoic acid
Pollock and Warner	1990	DBPC challenge	39 children (ages 2 to 15); 19 completed trial
Wender and Solanto	1991	DBPC, crossover challenge	17 children with ADHD (ages 5 to 7) and nine age-matched normal control subjects
Rowe and Rowe	1994	DBPC, crossover challenge	54 children (ages 2 to 14); 23 suspected reactors, 11 uncertain reactors, 20 controls
Wolraich et al.	1994	DBPC, three-way crossover challenge	23 children (ages 6 to 10) described to respond adversely to sugar; 25 normal children (ages 3 to 5)
Shaywitz et al.	1994	DBPC, crossover challenge	15 children (ages 5 to 13) with ADD
Bateman et al.	2004	DBPC, crossover challenge	277 children (ages 3.2 to 4.1); divided into four groups based on presence or absence of hyperactivity and atopy

DBPC = double-blind, placebo-controlled; CRS = Conners Rating Scale; ADHD = attention deficit hyperactivity disorder; ADD = attention deficit disorder

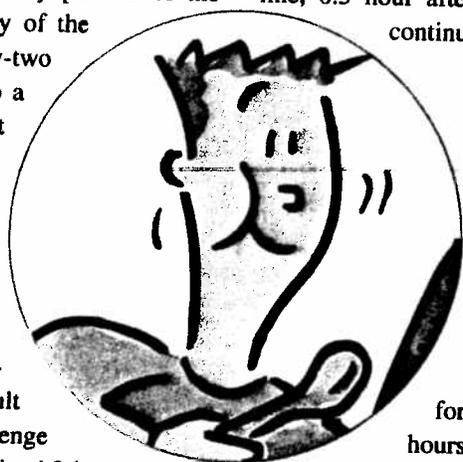
Diets/Challenges	Evaluation	Apparent Relationships
Feingold diet or control diet	Parent and teacher behavior rating	Feingold diet more effective than control diet on teacher ratings. Improved parent and teacher ratings on Feingold diet compared to baseline.
Challenge (artificial colors) and placebo cookies	Parent ratings	Significant effect of challenge cookies 3 hours after challenge.
Feingold diet or control diet	Parent and teacher behavior rating, neuropsychological data, classroom and laboratory observation	Four of 36 school-age boys improved on Feingold diet in parent and teacher ratings. Mothers of all 10 preschool boys reported improvement on Feingold diet.
Cookies or candy bars with artificial colors or placebo	Parent and teacher ratings, classroom observations, neuropsychological tests	No adverse effects on all parameters.
Tartrazine in biscuits or placebo	Parent and teacher ratings, objective tests of attention, perceptual-motor tests and subtests from Wechsler Intelligence Scale for Children	No differences between challenge and placebo periods in parent and teacher ratings or in standard tests.
Soft drink with mixture of seven artificial food dyes or placebo	Parent rating scale	No overall effect in 21/22 subjects on parent ratings.
Capsule containing nine food dyes or placebo	Paired-associate learning test, CRS	Increase in errors on the learning tests in the hyperactive children. No difference in CRS between food dye and placebo.
Cookies with food coloring mixture vs placebo	Parent and teacher ratings, psychiatric evaluation/rating, psychological tests	No evidence of food coloring effect on all evaluation parameters.
Lemonade containing sucrose or placebo (saccharin) with equal sweetness	Parent behavior rating	No consistent response to sucrose.
Challenge drink with sucrose or placebo (aspartame) Group 1: challenge given 1 hour after lunch. Group 2: challenge given in the morning after overnight fast.	Behavioral measures (playroom observation and examiner ratings), cognitive measures (learning and memory tasks)	Neither group showed a difference between sucrose and aspartame effect on behavior.
Tartrazine in orange juice/blackcurrant drink or placebo. Challenge with benzoate on a separate day.	Parent and nursing staff observation. No specific scoring system employed.	No changes in behavior as reported by the parents and the nursing staff.
Capsule containing a mixture of four food dyes or placebo	Parent ratings	17/19 with higher behavioral scores on food color challenge.
Orange drink either with sucrose, saccharin or aspartame on 3 separate days	Playroom observation, cognitive performance tasks	No significant effect of sugar, saccharin, or aspartame on aggressive behavior of either group. Increase inattention on cognitive tasks in the ADHD group following sucrose.
Capsule containing different doses of tartrazine given randomly over 3 weeks	Parent ratings on Behavior Rating Inventory devised by the authors	24/54 with consistent variations in behavior to tartrazine challenge.
Diets: high in sucrose, with no artificial sweeteners; low in sucrose and with aspartame; low in sucrose with saccharin	Behavioral and cognitive measures	No significant differences among the three diets in any variables for the school-aged children. No consistent pattern of difference observed in the preschool group.
Capsules containing aspartame or placebo (microcrystalline cellulose)	Parent and teacher ratings, cognitive tests	Aspartame at 10 times usual consumption has no effect on behavior and cognitive status.
Fruit juice with artificial colors plus sodium benzoate or placebo fruit juice	Parent ratings using Weiss-Werry-Peters Activity Scale, objective testing by research psychologists	Increase in hyperactivity during active challenge compared to placebo on parent ratings. No difference on objective testing.

David²³ studied 24 children (ages 1.6 to 12.4) whose parents reported that tartrazine caused severe, immediate behavioral change, with six having a similar reaction to benzoic acid. The children underwent a double-blind, placebo-controlled challenge in the hospital with tartrazine or benzoic acid in pure orange juice or a blackcurrant drink. The first challenge dose was 50 mg, followed by 250 mg 2 hours later. No change in behavior was noted by parents or the nursing staff to any of the challenges. Twenty-two patients returned to a normal diet without any food related problems. The parents of one patient, who was only taking three foods at the time of investigation, refused to accept the negative result of their child's challenge test. One family declined follow-up and also insisted on continuing with the diet.

A meta-analysis by Kavale and Forness of 23 published studies indicated that diet modification had negligible effects on hyperactivity.²⁴ They concluded that the existing research at that time had not validated the Feingold hypothesis and that diet modification be questioned as an efficacious treatment for hyperactivity.

The claimed association of sugar and hyperkinesis has been refuted by several studies. Fifty hyperkinetic children (ages 5 to 17) described by their mothers as having behavioral reactions to natural sugar were challenged blindly to lemonade containing sugar (sucrose) or saccharin as a placebo sweetener.²⁵ None showed consistent response to sugar and the parents could not differentiate between the two challenges. Subsequently, 49 of the participants were given pharmacotherapy for hyperkinesis, with good response.

Wolraich et al.²⁶ studied 32 hyperactive boys in a double-blind, placebo-controlled crossover challenge in a clinical research center. While on a sucrose-free diet, the children were challenged with a drink containing either sucrose or placebo (aspartame). In 16 of the group, the challenge drink was given 1 hour after lunch and in the other 16 in the morning after an overnight fast. Behavioral and cognitive evaluation were done at baseline, 0.5 hour after the challenge and continued every 0.5 hour



for approximately 2.5 hours. Neither group showed a difference between sucrose and aspartame effects on behavior. The conclusion remained the same when the analysis was limited to 20 children whose parents claimed that sugar adversely affected their behavior.

Wender and Solanto²⁷ evaluated the response of 17 children with ADHD and nine age-matched normal controls to the ingestion of orange drink of the same taste using either 35 gm of sucrose, 175 mg of saccharin, or 175 mg of aspartame on three separate days. Stimulant medications were discontinued for at least 2 days prior to testing. Cognitive attention and aggressive behavior were assessed for 4 hours: hourly in the playroom for behavior, and every 2 hours on performance task. No significant effect of sugar, saccharin or aspartame on the aggressive behavior of either group was observed.

Another study examined the effects of a diet high in sucrose or aspartame on the behavior of two groups: 23 children (ages 6 to 10) who were described by

their parents as adversely affected by sugar and 25 children (ages 3 to 5) without such a history.²⁸ The children and their families followed three different diets for 3 weeks each in a blinded, three-way crossover fashion. One diet was high in sucrose with no artificial sweeteners; a second diet was low in sucrose and contained aspartame; and the third was low in sucrose and contained saccharin as a placebo. The children were assessed by a standard set of behavioral and cognitive variables, 39 for school-age children and

A meta-analysis by Kavale and Forness of 23 published studies indicated that diet modification had negligible effects on hyperactivity.

31 for preschool children. The alleged sugar-sensitive school children showed no significant differences regarding the three diets. In the preschool group, four of the 31 behavioral variables differed significantly among the three diets, but there was no consistent pattern.

Aspartame has been implicated to cause behavioral changes in anecdotal reports.¹⁸ Shaywitz et al.²⁹ studied 15 children (ages 5 to 13) with attention-deficit disorder who were challenged in a double-blind, placebo-controlled crossover design to aspartame (at greater than 10 times the usual intake) or placebo (microcrystalline cellulose) for 2-week periods. Parents and teachers assessed the children's behavior. The children were also admitted for 2 days in a study center for cognitive tests, complete blood count, and several biochemical tests. No significant differences were noted in behavior and cognitive evaluation or in any biochemical test.

PARENT BELIEFS

Despite the very limited scientific ev-

idence to support a relationship between food additives and behavioral changes, many parents continue to believe the relationship exists. With the increasing acceptance of natural and homeopathic therapies, some parents may seek dietary management instead of pharmacologic agents. Foods devoid of food additives appeal to parents who may be averse to commercial food processing. Media sources, especially the wide use of the Internet, unfortunately tend to perpetuate information that may appeal to the public without scientific evidence.

It also may be easier for the parents to accept the idea that their child's behavioral problem is due to a dietary factor rather than to psychosocial issues that are often difficult to evaluate and tackle. The perceived favorable effect of certain elimination diets might be attributed to the fact that it gives the family a sense of solving the problem and provides the child with substantial attention.

CASE REPORTS

We evaluated one 8.5-year-old girl with a history of allergic rhinitis who, according to the mother, had behavioral disorder since age 6. The family repeatedly noticed that, within minutes to less than an hour after eating chocolate, the child becomes "aggressive, nasty, talks back, refuses to follow directions, bully both physically and verbally." Skin prick testing, primarily for allergic rhinitis, was done to aeroallergens, as well as to cocoa, at the mother's request. The child showed positive tests to several aeroallergens, but not to cocoa. To further assure the mother, cocoa-specific IgE antibody was obtained and was also negative. Two double-blind, placebo-controlled challenges to cocoa caused no abnormal behavior during observation for 3 hours in the clinic or later at home. After the child was assured of the absence of chocolate "allergy," she was openly challenged with three types of chocolate, without any adverse effects. The result was rein-

forced to the mother and the child, who subsequently continued to eat chocolate without any problems.

We also evaluated an 11-year-old boy with behavior problems for several years that the mother believed to be food-related. He was diagnosed with ADHD at age 9, but his mother refused giving him specific medications. The child had cochlear implants and attends a special program in school for the hearing-impaired. The mother reported that, within 30 minutes to an hour of ingesting red dye or artificial sweeteners in soft drinks, he becomes "hyperactive, defiant, angry, wild, beats the dog and on three occasions pulled a steak knife at his mother and older sister." The school was not offering him foods or drinks with red dye or artificial sweeteners, yet the teachers reported that he "ignores requests, refuses directions, pushing, hitting, tripping, cries or gets angry when being corrected." Double-blind, placebo-controlled challenges³⁰ were done with red dye #3 (erythrosine), red dye #40 (allura red), yellow dye #5 (tartrazine), aspartame, saccharin, and placebo (glucose). During each of these visits, no misbehavior was noted during a 3-hour observation in the clinic, or later at home.

ROLE OF HEALTHCARE PROFESSIONALS

When parents seek professional help regarding a child's behavioral disorder for possible relationship to foods, additives or sugar, it would be prudent first to establish the diagnosis of ADHD based on specific criteria (Sidebar). Also, relevant practice guidelines have been published by the American Academy of Pediatrics.³¹ Therefore, such parents should be counseled with empathy about the limited evidence of such a relationship. The family often expects "allergy testing" to reveal the specific agent. However, routine allergy skin testing or blood tests are primarily for immunoglobulin E-mediated reactions, and there

is no evidence for such mechanism in behavioral disorder.

Out of heightened concern by the National Institutes of Health about the widespread belief of diet as a cause of childhood hyperactivity, a Consensus Development Conference was held.³² A scientific panel listened to presentations by researchers, clinicians, and parents. The panel concluded that there is "a limited positive association between 'the defined diet' and a decrease in hyperactivity. Some hyperactive children demonstrated less evidence of hyperactivity on defined diets, or modifications thereof, than on an appropriate control diet. Such decreases involved only a small proportion of patients; furthermore, the decreases in hyperactivity were not observed consistently." The panel recommended that elimination diets generally should not be instituted in the management of childhood hyperactivity, but that a trial of dietary intervention or continuation of such a diet in children whose parents observe benefits may be reasonable. Nevertheless, consideration of all other traditional therapies should be initiated before any diet is considered.

With continued good relationships among the physician, parents, and patient, the family is likely to be more open to scientific approaches to evaluation and therapy. Although we strive for evidence-based practice, in certain instances, the practitioner may yield to a harmless management claimed by parents as beneficial. It may be reasonable to agree on the avoidance of a specific food or additive that the family strongly believes to be causing behavioral problem in the child, even if it is a placebo effect.

SUMMARY

The possible role of foods or additives in causing behavioral disorders in children, particularly ADHD, has been a controversial subject both among health care providers and the public. However, a critical review of the literature provides very

limited support for such a relationship. On encountering such cases, the healthcare professional should first establish an accurate diagnosis of the suspected "abnormal" behavior based on specific standard criteria. It is important to counsel the family regarding the standard of care practice and about the limited evidence of a role of foods and additives in causing behavior problems. If parents strongly suspect a specific dietary item, a trial of elimination may be warranted. If the child's behavior shows definite improvement, a challenge in a double-blind, placebo-controlled fashion under the supervision of an experienced physician would be necessary to verify the relationship.

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Doherty, Jane H.

15

From: Sahagian, Margaret T.
Sent: Monday, June 07, 2010 3:53 PM
To: Doherty, Jane H.
Subject: FW: EU color warning label
Attachments: ARK to Dalli on colors jss CLEAN.doc; ARK to Dalli on colors jss.doc

Dear John,

It was my pleasure to meet with you during your recent visit to Washington. Once again, our discussions focused on the need to ensure that our respective food safety measures are based on scientific evidence. It is with that intention in mind that I write to ask you to delay implementation of Article 24 of the European Union's Regulation (EC) No 1333/2008 on food additives, which requires warning statements on food products that contain one or more of six specified color additives, until sufficient scientific evidence is available to support implementation of the measure.

As [we/our staffs] have discussed previously, the United States remains concerned about the apparent lack of scientific basis for a warning statement requirement and the potential negative impact on trade that may result from such a requirement. Many of the specified color additives (Sunset Yellow, Allura Red, and Ponceau 4R, Tartrazine, Quinoline Yellow, and Carmoisine) are widely used by the global food industry, including in confectionary products and beverages.

In 2007, the University of Southampton released a much criticized study regarding the potential link between the use of these color additives in children's food and hyperactivity. In November 2009, the European Food Safety Authority (EFSA) released scientific opinions on its re-evaluation of the color additives used in the Southampton Study. EFSA's scientific panel on food additives concluded that currently available data – including the Southampton Study – did not substantiate a link between the individual colors and possible behavioral effects.

While the United States supports a Member's right to impose measures to protect public health, a Member may only apply such measures to the extent necessary to protect public health and that are based on scientific evidence. Given the conclusions of the EFSA panel, we remain concerned that the warning statement requirement does not appear to have scientific basis and thus will require some manufacturers to adapt their manufacturing practices without cause.

The potential trade effects of such a requirement are significant. Depending on the number of colors included in the product, the proposed regulation will impose costs on manufacturers that may range from a few million to \$34 million per manufacturer. In addition, a number of U.S. firms are reporting that some retailers in the EU will not allow candy with warning labels to be sold in their outlets, further burdening trade.

Given our mutual interest and obligation to apply only science-based sanitary and phytosanitary measures, I would propose that our regulatory authorities meet to exchange relevant scientific data to resolve this serious trade concern in the spirit of ongoing cooperation as soon as possible. While that work continues, I respectfully request that the Directorate-General for Health and Consumers (SANCO) delay the July 2010 implementation date until scientific evidence exists to support the measure.

Best regards,

Ron Kirk

From: Doherty, Jane H.
Sent: Wednesday, June 02, 2010 12:25 PM
To: Sahagian, Margaret T.
Subject: Fw: EU color warning label

Meg,

Could I ask you to prepare the clean document for ARK's signature and send it downstairs asap? Do you think we need to do a cover memo explaining why he needs to sign this asap? Mars is pressuring me to get this out.

Thank you!
Jane
Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative

From: Strickler, J. Sloane
To: Doherty, Jane H.
Sent: Thu May 27 12:29:19 2010
Subject: RE: EU color warning label

Comments in redline and clean. It looks like a lot but I didn't change too much on the substance. Did some tightening up of some repetition and some tweaking here and there. Because of the context of the letter – asking for a delay on the article as a whole – you will be happy to know that I did not re-raise my objection to complaining about color additives not approved in the US. But that objection remains when we go back to complaining to them as burdens alone. Cheers.

From: Doherty, Jane H.
Sent: Thursday, May 27, 2010 11:09 AM
To: Strickler, J. Sloane
Subject: Re: EU color warning label

Gracias. I realize you're swamped.
Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative

From: Strickler, J. Sloane
To: Doherty, Jane H.
Sent: Thu May 27 11:08:00 2010
Subject: RE: EU color warning label

Looking at it now.

From: Doherty, Jane H.
Sent: Wednesday, May 26, 2010 5:26 PM
To: Strickler, J. Sloane
Subject: Fw: EU color warning label

Hey Sloane,

Have you cleared on the Kirk colors letter? I need to pass that on asap.

Thanks,
Jane
Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative

From: marietta.bernot [REDACTED] (B)(6)
To: Doherty, Jane H.
Sent: Wed May 26 12:43:35 2010
Subject: EU color warning label

Just to let you know that one of our industry advisors in the EU is meeting with Dalli's Deputy Chief of Staff Dr. Nils Behrndt on Tuesday 15 June to give further background from the EU perspective on the color warning label requirement. Can you tell me whether the formal request for delay has been sent? Many thanks.

Marietta E. Bernot
Global Trade and Customs Advisor
Mars Incorporated
Direct line: [REDACTED] (B)(6)
Main: [REDACTED]
Mobile: [REDACTED]

Doherty, Jane H.

16

From: Sahagian, Margaret T.
Sent: Monday, June 07, 2010 4:58 PM
To: Doherty, Jane H.
Subject: RE: EU color warning label

What's John's last name and where is he from and do you have an address I can attach to the letter?

From: Doherty, Jane H.
Sent: Monday, June 07, 2010 4:07 PM
To: Sahagian, Margaret T.
Subject: Re: EU color warning label

Thanks Meg for sending this downstairs!

Jane

Dear John, It was my pleasure to meet with you during your recent visit to Washington. Once again, our discussions focused on the need to ensure that our respective food safety measures are based on scientific evidence. It is with that intention in mind that I write to ask you to delay implementation of Article 24 of the European Union's Regulation (EC) No 1333/2008 on food additives, which requires warning statements on food products that contain one or more of six specified color additives, until sufficient scientific evidence is available to support implementation of the measure. As we have discussed previously, the United States remains concerned about the apparent lack of scientific basis for a warning statement requirement and the potential negative impact on trade that may result from such a requirement. Many of the specified color additives are widely used by the global food industry, including in confectionary products and beverages. In 2007, the University of Southampton released a much criticized study regarding the potential link between the use of these color additives in children's food and hyperactivity. In November 2009, the European Food Safety Authority (EFSA) released scientific opinions on its re-evaluation of the color additives used in the Southampton Study. EFSA's scientific panel on food additives concluded that currently available data – including the Southampton Study – did not substantiate a link between the individual colors and possible behavioral effects. While the United States supports a Member's right to impose measures to protect public health, a Member may only apply such measures to the extent necessary to protect public health and that are based on scientific evidence. Given the conclusions of the EFSA panel, we remain concerned that the warning statement requirement does not appear to have scientific basis and thus will require some manufacturers to adapt their manufacturing practices without cause. The potential trade effects of such a requirement are significant. Depending on the number of colors included in the product, the proposed regulation will impose costs on manufacturers that may range from a few million to \$34 million per manufacturer. In addition, a number of U.S. firms are reporting that some retailers in the EU will not allow candy with warning labels to be sold in their outlets, further burdening trade. Given our mutual interest and obligation to apply only science-based sanitary and phytosanitary measures, I would propose that our regulatory authorities meet to exchange relevant scientific data to resolve this serious trade concern in the spirit of ongoing cooperation as soon as possible. While that work continues, I respectfully request that the Directorate-General for Health and Consumers (SANCO) delay the July 2010 implementation date until scientific evidence exists to support the measure. Best regards, Ron Kirk

Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative

From: Sahagian, Margaret T.
To: Doherty, Jane H.
Sent: Mon Jun 07 15:52:32 2010
Subject: FW: EU color warning label

Dear John,

It was my pleasure to meet with you during your recent visit to Washington. Once again, our discussions focused on the need to ensure that our respective food safety measures are based on scientific evidence. It is with that intention in mind that I write to ask you to delay implementation of Article 24 of the European Union's Regulation (EC) No 1333/2008 on food additives, which requires warning statements on food products that contain one or more of six specified color additives, until sufficient scientific evidence is available to support implementation of the measure.

As [we/our staffs] have discussed previously, the United States remains concerned about the apparent lack of scientific basis for a warning statement requirement and the potential negative impact on trade that may result from such a requirement. Many of the specified color additives (Sunset Yellow, Allura Red, and Ponceau 4R, Tartrazine , Quinoline Yellow, and Carmoisine) are widely used by the global food industry, including in confectionary products and beverages.

In 2007, the University of Southampton released a much criticized study regarding the potential link between the use of these color additives in children's food and hyperactivity. In November 2009, the European Food Safety Authority (EFSA) released scientific opinions on its re-evaluation of the color additives used in the Southampton Study. EFSA's scientific panel on food additives concluded that currently available data – including the Southampton Study – did not substantiate a link between the individual colors and possible behavioral effects.

While the United States supports a Member's right to impose measures to protect public health, a Member may only apply such measures to the extent necessary to protect public health and that are based on scientific evidence. Given the conclusions of the EFSA panel , we remain concerned that the warning statement requirement does not appear to have scientific basis and thus will require some manufacturers to adapt their manufacturing practices without cause.

The potential trade effects of such a requirement are significant. Depending on the number of colors included in the product, the proposed regulation will impose costs on manufacturers that may range from a few million to \$34 million per manufacturer. In addition, a number of U.S. firms are reporting that some retailers in the EU will not allow candy with warning labels to be sold in their outlets, further burdening trade. Given our mutual interest and obligation to apply only science-based sanitary and phytosanitary measures, I would propose that our regulatory authorities meet to exchange relevant scientific data to resolve this serious trade concern in the spirit of ongoing cooperation as soon as possible. While that work continues, I respectfully request that the Directorate-General for Health and Consumers (SANCO) delay the July 2010 implementation date until scientific evidence exists to support the measure.

Best regards,

Ron Kirk

From: Doherty, Jane H.
Sent: Wednesday, June 02, 2010 12:25 PM
To: Sahagian, Margaret T.
Subject: Fw: EU color warning label

Meg,

Could I ask you to prepare the clean document for ARK's signature and send it downstairs asap? Do you think we need to do a cover memo explaining why he needs to sign this asap? [REDACTED]

Thank you!
Jane
Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative

From: Strickler, J. Sloane
To: Doherty, Jane H.
Sent: Thu May 27 12:29:19 2010
Subject: RE: EU color warning label

Comments in redline and clean. It looks like a lot but I didn't change too much on the substance. Did some tightening up of some repetition and some tweaking here and there. Because of the context of the letter – asking for a delay on the article as a whole – you will be happy to know that I did not re-raise my objection to complaining about color additives not approved in the US. But that objection remains when we go back to complaining to them as burdens alone. Cheers.

From: Doherty, Jane H.
Sent: Thursday, May 27, 2010 11:09 AM
To: Strickler, J. Sloane
Subject: Re: EU color warning label

Gracias. I realize you're swamped.
Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative

From: Strickler, J. Sloane
To: Doherty, Jane H.
Sent: Thu May 27 11:08:00 2010
Subject: RE: EU color warning label

Looking at it now.

From: Doherty, Jane H.
Sent: Wednesday, May 26, 2010 5:26 PM
To: Strickler, J. Sloane
Subject: Fw: EU color warning label

Hey Sloane,

Have you cleared on the Kirk colors letter? I need to pass that on asap.

Thanks,
Jane
Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative

From: marietta.bernot [REDACTED]
To: Doherty, Jane H.

(B)(6)

Sent: Wed May 26 12:43:35 2010
Subject: EU color warning label

Just to let you know that one of our industry advisors in the EU is meeting with Dalli's Deputy Chief of Staff Dr. Nils Behrmdt on Tuesday 15 June to give further background from the EU perspective on the color warning label requirement. Can you tell me whether the formal request for delay has been sent? Many thanks.

Marietta E. Bernot
Global Trade and Customs Advisor
Mars Incorporated

Direct: line: [REDACTED]

Main: [REDACTED]

Mobile: [REDACTED]

(B)(6)

Doherty, Jane H.

17

From: marietta.bernot [REDACTED] (B)(6)
Sent: Monday, April 12, 2010 12:28 PM
To: Doherty, Jane H.
Cc: Rochette, Peggy
Subject: EU color warning label - WTO SPS Committee
Attachments: CAOBISCO report on WTO SPS Committee meeting.doc

I echo Peggy's thought that it would be very helpful to have a copy of the transcript from the SPS Committee meeting which we could use to gain the support of other countries. The EU admission that this regulation was media driven and not science based is very compelling. In the meantime, I attach a report sent out by the EU confectionery industry association, CAOBISCO, regarding the meeting. Best regards.

Marietta E. Bernot
Global Trade and Customs Advisor
Mars Incorporated
Direct: line: [REDACTED]
Main: [REDACTED] (B)(6)
Mobile: [REDACTED]

CAOBISCO

Association des industries de la Chocolaterie, Biscuiterie et Confiserie de l'UE
Tel : +32/2/539.18.00 Fax : +32/2/539.15.75

* Association of the Chocolate, Biscuits and Confectionery Industries of the EU
E-mail : caobisco@caobisco.be Website : www.caobisco.com

Ref : 711-2010-364

Date : 12.04.2010

Pour/For : RSC
De la part de/From : Pénélope Alexandre

Dear members,

FYI, US has raised the EU warning labeling requirement concerning the Southampton colors at the WTO SPS Committee meeting in March and also has urged the EU to delay the implementation of the labeling requirement. Here is an excerpt of the US report on the SPS related trade barriers.

2010 REPORT ON SANITARY AND PHYTOSANITARY MEASURES (USTR)
<http://www.ustr.gov/sites/default/files/SPS%20Report%20Final%282%29.pdf>

Food Safety
Food Additives

On July 2, 2009, the EU notified the WTO of adoption of its final regulations on food additives. The final regulations contain a provision, not present in the draft regulations, that mandates the inclusion of warning statements regarding hyperactivity on products containing six synthetic colors (Sunset Yellow, Quinoline Yellow, Carmoisine, Allura Red, Tartrazine, and Ponceau 4R). Manufacturers will now have to include on products containing any of these six colors a statement that that the color "may have an adverse effect on activity and attention in children."

The certified equivalents of three of the six colors (Sunset Yellow, Allura Red, and Tartrazine) are approved for use in food by FDA and are widely used by the global food industry. (FDA also has approved the use of Quinoline Yellow's certified equivalent for use in drugs, cosmetics, and medical devices.) The inclusion of such a statement on a warning label is neither required in the United States nor suggested in the applicable international standards (either adopted or currently proposed).

The EU's list of colors and the subject of hyperactivity was addressed in a much criticized research piece known as the Southampton Study. This study concluded that these six color additives presented a risk of hyperactivity. In November 2009, EFSA released scientific opinions on the color additives evaluated in the Southampton Study. EFSA's opinions contradicted the results of the Southampton Study, concluding that the currently available data did not substantiate a link between the individual color additives and possible behavioral effects.

The United States disagrees that these color additives, if FDA certified, have negative health impacts for children when these colors are included in food products in amounts prescribed under U.S. law, and therefore does not believe a warning label is necessary. The United States continues to urge the EU to delay implementation of this measure to minimize negative effects on trade, while technical discussions are underway. The United States recently raised this issue on the floor during the March 2010 SPS Committee meeting.

Doherty, Jane H.

18

From: Strickler, J. Sloane
Sent: Thursday, May 27, 2010 12:29 PM
To: Doherty, Jane H.
Subject: RE: EU color warning label
Attachments: ARK to Dalli on colors jss CLEAN.doc; ARK to Dalli on colors jss.doc

Comments in redline and clean. It looks like a lot but I didn't change too much on the substance. Did some tightening up of some repetition and some tweaking here and there. Because of the context of the letter – asking for a delay on the article as a whole – you will be happy to know that I did not re-raise my objection to complaining about color additives not approved in the US. But that objection remains when we go back to complaining to them as burdens alone. Cheers.

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To: Strickler, J. Sloane
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Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative

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To: Doherty, Jane H.
Sent: Thu May 27 11:08:00 2010
Subject: RE: EU color warning label

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Subject: Fw: EU color warning label

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Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative

From: marietta.bernot
To: Doherty, Jane H.

(B)(6)

Sent: Wed May 26 12:43:35 2010
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Marietta E. Bernot
Global Trade and Customs Advisor
Mars Incorporated
Direct line: [REDACTED]
Main: [REDACTED]
Mobile: [REDACTED]

(B)(6)

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Best regards,

Ron Kirk

Comment [JSS1]: Has RK discussed this particular issue with the EU before?

Comment [JSS2]: Please check spelling. It is "tartrazine" in the SPS Report, although it may be that the SPS Report is wrong.

Comment [JSS3]: Can we point to any other science? Has fda ever done its own evaluation?



Doherty, Jane H.

19

From: marietta.bernot [REDACTED]
 Sent: Friday, November 20, 2009 2:38 PM (B)(6)
 To: Doherty, Jane H.; PRochette [REDACTED]
 Cc: Drozen, Mel; Mathews [REDACTED]
 steve.rizk [REDACTED]
 Subject: RE: EU color warning labels - EFSA statement
 Attachments: K&H Evaluation of EFSA Reports.docx

Dear Jane and Peggy, accompanying is a memo prepared by toxicologist Dr. Bob Mathews at law firm Keller and Heckman. He studied the EFSA reviews for each color and evaluated them from a toxicological perspective as well as conformance with accepted scientific protocols.

Dr. Mathews focused on the 3 colors where EFSA recommended changes in the allowable intake levels and also Carmoisine which in the end EFSA did not recommend a change in intake levels. The remaining two, FD&C Red 40 (Allura Red) and FD&C Yellow No. 5, are not discussed in the memo because no change was recommended by EFSA. Dr. Mathews memo is detailed. He concluded:

The wide ranging reports of the EFSA panels (the parent EFSA Panel and the Working Groups) responsible for the re-evaluation of the four food colors provide no rationale for the review nor information that significant new findings were available that raised questions regarding the safety of the colors. New information cited was either of doubtful value or raised questions that could be answered relatively easily. Of greatest concern with regard to the scientific credibility of the reports is that the panels made decisions to override previous conclusions using secondary information sources, rather than reviewing the original data and study reports that were used by previous groups of experts. [emphasis added] Inconsistencies of the conclusions in the reports with the evaluations made by other expert panels raise the question of whether the reviews were performed using accepted standards of safety assessments.

USTR is welcome to share this memo with FDA and other U.S. agencies as appropriate; and GMA with its own scientific staff if desired.

By separate memo I will also deliver to you an evaluation of the conformity with European Union law of the EU imposition of color warning labels. While it is not up to USTR to ensure European law is upheld, the divergence is very troubling to both the U.S. and EU food industry. The trans Atlantic food industry is being held to a standard of performance, i.e. rule of law, that the Parliament and the Commission apparently consider optional.

Thank you again for all your efforts.

Marietta E. Bernot
 Global Trade and Customs Advisor
 Mars Incorporated

Direct line: [REDACTED]
 Main: [REDACTED] (B)(6)
 Mobile: [REDACTED]

"Doherty, Jane H." <Jane_Doherty@...> (B)(2)

11/12/2009 09:52 AM

To: <marietta.bernot@...> (B)(6)

cc: "Rochette, Peggy" <...>

Subject: RE: EU color warning labels - EFSA statement

Marietta,

Thank you. This must be hot off the press because I just received the same thing from SANCO. Thank you so much for your offer to review these carefully. We can't thank you enough.

Pending your results and FDA's review, I will ask SANCO for a meeting to discuss our concerns in detail.

Peggy - I've got a call into Michael now on the status of the labels, but he's on travel. I'll probably hear from him next week.

Best wishes,
Jane

Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative
Executive Office of the President
Washington, DC

... (B)(2)

From: marietta.bernot@... (B)(6)
Sent: Thursday, November 12, 2009 9:47 AM
To: PRochette@... Doherty, Jane H. (B)(6)
Subject: EU color warning labels - EFSA statement

Below is EFSA's statement. Please note highlighted paragraph. I will have an informational memo for you evaluating the EFSA studies later this morning. Regards.

EFSA updates safety advice on six food colours

After reviewing all the available evidence, the European Food Safety Authority's scientific panel on additives, the ANS Panel, has lowered the Acceptable Daily Intakes (ADIs) for the artificial food colours Quinoline Yellow (E104), Sunset Yellow FCF (E110) and Ponceau 4R (E124).[1] As a result, the Panel concluded that exposure to these colours could exceed the new ADIs for both adults and children.

The Panel found that the currently available data did not require a change to the existing ADIs for the three other colours evaluated - Tartrazine (E102), Azorubine/Carmoisine (E122) and Allura Red AC (E129). According to the Panel, only some children who consume large amounts of food and drink containing Azorubine/Carmoisine or Allura Red AC could exceed the ADIs for these colours.

John Larsen, the Chair of the ANS Panel, said: "Many food colours have been in use for decades since their initial approval and so after such a long period of use we are now looking at the overall data available, including any new evidence on their safety, to help protect European consumers. We are doing this work systematically for all food additives, and have started with these colours for which some concerns have been raised."

The six colours re-evaluated by the Panel can be used in a range of foodstuffs including soft drinks, bakery products and desserts. The Panel concluded that one of the colours, Tartrazine, may bring about intolerance reactions – such as irritations to the skin – in a small part of the population. For the remaining five colours (Quinoline Yellow, Sunset Yellow FCF, Ponceau 4R, Azorubine/Carmoisine and Allura Red AC), no firm conclusion could be drawn on a possible link with intolerance reactions from the limited scientific evidence available.

EFSA is currently assessing the safety of all individual food additives which are approved for use in the EU, starting with food colours. The European Commission asked EFSA to consider these six colours as a priority after a study was published by Southampton University (McCann et al) in 2007 – the so-called "Southampton study" – linking certain mixtures of these colours and the preservative sodium benzoate with hyperactivity in children.

John Larsen added: "We have now reduced the ADIs for three of the six colours we assessed, but for different reasons in each case as different data were available on each individual compound. The data which are currently available – including the Southampton study itself – did not substantiate a causal link between the individual colours and possible behavioural effects."

EFSA's scientific advice will help to inform any follow-up action to be taken by the European Commission and the EU Member States.

- Scientific Opinion on the re-evaluation of Allura Red AC (E 129) as a food additive
- Scientific Opinion on the re-evaluation of Ponceau 4R (E 124) as a food additive
- Scientific Opinion on the re-evaluation of Quinoline Yellow (E 104) as a food additive
- Scientific Opinion on the re-evaluation of Sunset Yellow FCF (E 110) as a food additive
- Scientific Opinion on the re-evaluation Tartrazine (E 102)
- Scientific Opinion on the re-evaluation of Azorubine/Carmoisine (E 122) as a food additive
- Topics A-Z: Food additives
- FAQ: Food Colours

Marietta E. Bernot
Global Trade and Customs Advisor
Mars Incorporated

Direct: line: [REDACTED]

Main: [REDACTED] (B)(6)

Mobile: [REDACTED]

MEMORANDUM

TO:

FROM: Robert A. Mathews, Ph.D., D.A.B.T.
Toxicologist

DATE: November 11, 2009

RE: Re-evaluation of Certain Food Colorants by EFSA

This memorandum provides comments on four reports published by the European Food Safety Authority (EFSA) that evaluate the safety of colorants used widely in food.¹ The review of the colors was initiated in 2006² and provide a summary of general information, estimates of exposures from food ingestion, and a review of toxicological data previously used for safety evaluations by several other groups. A limited amount of new information on specific colors was available to the Working Groups (A & B) that reviewed the information and prepared the reports under the authority of the EFSA Panel on Food Additives and Nutrient Substances added to Food. As more fully explained below, the reports re-evaluate the safety of the colorants based on a very limited amount of new data and, in addition, rely heavily if not completely, on reviews by other groups rather on a direct evaluation of data. Thus, the re-evaluations appear scientifically questionable and inconsistent with current standards of risk assessment.

The reports provide reassessments of the safety of four widely used food colors:

- Azorubine/Carmoisine,
- Ponceau 4R,
- Quinoline Yellow, and
- Sunset Yellow FCF.

Sunset Yellow is also known as FD&C Yellow No. 6, which is cleared for use in food in the United States. Quinoline Yellow is also known as D&C Yellow No. 10 and is approved in the U.S. for use in certain cosmetics and medical devices. Each of the

¹ EFSA Journal, Volume 7(11), pages [unknown at this time].

² Food Colors: Call for data to support re-evaluation. http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178620787676.htm.

four colors had been reviewed multiple times by the WHO/FAO Joint Expert Committee on Food Additives (JECFA) and the Scientific Committee for Food (SCF) of the European Commission. In addition, the two yellow colors have been reviewed by FDA and the full group by a panel convened by several Nordic countries (See footnote 3, below). SCF has been replaced by the EFSA Panel on Food Additives and Nutrient Substances added to Food (the EFSA Panel).

General Comments on the Reports

The EFSA Panel dismisses or ignores the previous reviews of the same colors by expert groups that reviewed the original data (FDA, JECFA, DFG, and SCF).

The reports are presented as scientific analyses of information related to the safety and exposure to the four specific colors through food. However, the conclusions to revise the acceptable daily intakes (ADIs) for the individual colorants were not always based on the use of standard safety factors or methods used in current practices of risk assessment.

The reports cite no specific motivating factor(s) for the re-evaluation of the four colorants. Conventionally, re-evaluations of former risk assessments by expert groups require some explicit basis, such as a significant new toxicological reports, for justifying the re-analysis. In no case were such studies identified.

In no case were significant new toxicological findings reported. New studies that were reported were sometimes inconsistent and do not raise the level of concern justifying the recommendation made to adopt a revised ADI, for example, for Sunset Yellow. The recommendations to lower the ADI for Ponceau 4R and Quinoline Yellow were made in contradistinction to evaluations made by the U.S. Food and Drug Administration, the German DFG (German Research Foundation), and the panel convened by the Nordic countries.

In the re-evaluation of Ponceau 4R, the Working Group revised the ADI downward based on a no observed adverse effect level (NOAEL) derived from a study for which the original report and data were not available. In the specific case of Quinoline Yellow the EFSA report (page 22) cites two other formal reviews by governmental agencies (FDA and DFG) that had adopted higher NOAELs after reviewing the original data. Thus, the Working Group's inferred conclusion in this case is inconsistent with several other expert groups.

The reports do not always make clear the extent to which original toxicological reports or data were available and reviewed. Throughout the reports, the panel repeats that its evaluation was based on "previous evaluations," additional literature "when available," and information submitted after a "public call" for data. In some specific cases the Working Groups indicate that original reports that apparently were reviewed by JECFA and SCF were not available to the Working Groups.

The reports site other secondary reviews for the bases of conclusions. For example, the report of EFSA's cosmetic panel (SCCNFP) for Quinoline Yellow

(referred to as Acid Yellow 3 by SCCNFP), which also apparently made inferred conclusions based on secondary reviews. Other secondary reviews cited were the private organization now known as BIBRA (previously the British Industrial Biological Research Association) a report prepared by the Nordic Working Group on Food Toxicology and Risk Assessment (NNT).³ The recommendation by the experts writing the TemaNord report for Quinoline Yellow was:

A re-evaluation is not warranted, however, the apparent discrepancy between the NOAEL's and the safety factors used by SCF and JECFA should be clarified. [See below for a more complete explanation.]

In all four cases, the Working Groups indicated, with regard to the report from scientists at Southampton, U.K. (the Southampton study), evaluating a possible effect of a color mixture on the behavior of children that:

The Panel concurred with the conclusion from a previous EFSA opinion on the McCann et al. study that the findings of the study cannot be used as a basis for altering the ADI.⁴

Comments on Specific Reports

1. Azorubine/Carmoisine

The ADI adopted by JECFA and SCF of 0-4 mg/kg bw/day was not changed.

The Panel was provided with only two new studies, the Southampton epidemiological study mentioned above and a short term in vitro genotoxicity screen that was concluded to be nonstandard, and thus inapplicable to the evaluation. The Panel concurred with the conclusion from a previous EFSA opinion on the McCann *et al.* (Southampton) study that the findings of the study cannot be used as a basis for altering the ADI. The Panel concluded that the present database does not justify revision of the ADI of 4 mg/kg bw/day. The Panel also concluded that at the maximum reported levels of use, refined intake estimates are below the ADI, although in 1 to 10 year old children the high percentile of exposure (95th) can be slightly higher than the ADI at the upper end of the range.

2. Ponceau 4R:

The current ADI adopted by JECFA in 1983 and by SCF in 1984 was reduced from 4 mg/kg bw/day to 0.7 mg/kg bw/day. The reduction was based on the adoption of a NOAEL in an unpublished study that was not available to the Working Group, but was submitted to BIBRA by WHO. There is evidently an ambiguity in the conclusion

³ TemaNord (2000). Food additives in Europe 2000 - Status of safety assessments of food additives presently permitted in the EU.

⁴ McCann, D., et al. (2007). Food additives and hyperactive behaviour in 3-year-old and 8/9-year-old children in the community a randomized, double-blinded, placebo-controlled trial. *The Lancet*, Vol. 370(9598), pages 1560-1567.

of the JECFA report on Ponceau 4R. The JECFA report Food Additive Series 18 (1983)⁵ provides one conclusion with regard to a NOAEL in the discussion of the data, while the "Evaluation" section provides a different dose from which the ADI was derived. The origin of this inconsistency needs to be identified; for example, is it simply a typographical error.

There is no explanation in the EFSA report that the Working Group attempted to clarify this inconsistency. The Working Group cites secondary a BIBRA report in support of its conclusion that the JECFA and SCF evaluations should be overturned.

3. Quinoline Yellow

The current ADI adopted by JECFA in 1984 and by SCF in 1984 was reduced from 10 mg/kg bw/day to 0.5 mg/kg bw/day. The reduction was based on the adoption of a NOAEL in an unpublished study that apparently was not reviewed by the Working Group, but was submitted to BIBRA by Biodynamics, Inc. and/or ILSI.

The Panel based its review on essentially the same information (but without reviewing the original data) available to JECFA, SCF, and other panels that have reviewed Quinoline Yellow. However, the Panel noted, that one study may not have been available to JECFA, but apparently did not confirm this conclusion. Using a NOAEL of 50 mg/kg bw/day provided by a chronic toxicity and carcinogenicity study with a reproductive toxicity phase carried out in rats and applying an uncertainty factor of 100 to this NOAEL, the Panel established an ADI of 0.5 mg/kg bw/day. The Panel observed that at the maximum levels of use of Quinoline Yellow, refined intake estimates are generally well over the ADI of 0.5 mg/kg bw/day, but did not comment on exposures relative to the current ADI. As noted above, the report (page 22) cites two other formal reviews by governmental agencies (FDA and DFG) that had adopted higher NOAELs (derived from the same study) after apparently reviewing the original data. Thus, the Working Group's inferred conclusion in this case is very puzzling and apparently scientifically questionable.

4. Sunset Yellow FCF

The current ADI adopted by JECFA in 1982 and by SCF in 1984 was reduced from 2.5 mg/kg bw/day to 1.0 mg/kg bw/day. The reduction was based on the publication of a study by an Indian group that reported adverse testicular effects in mice after a 90-day exposure.⁶

The Panel based its review on essentially the same information (but without reviewing the original data) available to JECFA, SCF, and other panels that have reviewed Sunset Yellow FCF. New studies included studies by Mathur *et al.* reporting significant effects on the testes in rats exposed for 90 days to 250 and 1500 mg Sunset Yellow FCF/kg bw/day. The Panel observed that the Sunset Yellow FCF administered

⁵ See: <http://www.inchem.org/documents/jecfa/jecmono/v18je12.htm>.

⁶ Mathur, N.R.A., et al. (2005). Effect of Sunset Yellow on testis in rats. *J. Ecophysiol. Occup. Health*, Vol. 5, pages 1-3.

in the Mathur, et al. study was obtained at the local market and that its specifications or purity were not defined. The Panel also noted that the 90 day rat study used by JECFA to derive the ADI also reported effects on testes weight, occurring without accompanying histological changes, although sperm morphology and sperm mobility were not analyzed.

The Mathur, et al. study appears to be incompatible with a multigenerational reproductive study (reviewed by other groups and cited by the Working Group) that found no adverse reproductive effects after exposure of male and female mice for 5 weeks.⁷ This latter study was published and is readily available. However, the Working Group did not mention the inconsistency between the two observations. The inconsistency is that if the testicular effects are real and as dramatic as portrayed, there should have been some effect on reproductive efficiency in the published reproductive study (Tanaka, 1996). Furthermore, the Indian group that reported the effects is based in a zoology department, so the credentials of the scientists involved should be examined.

The Panel concluded that these findings justified re-definition of the ADI. The Panel decided to reduce the ADI, by an extra uncertainty factor of 2.5, to 1 mg/kg bw/day (without explaining this unconventional approach) and to make the ADI temporary for 2 years. Within this period, clarification of the effects of Sunset Yellow FCF on the testis, sperm morphology and sperm mobility should be provided, based on a 28-day study performed according to the recently updated OECD test guideline 407. The Panel concluded that at the maximum reported levels of use of Sunset Yellow FCF, refined intake estimates are generally below the temporary ADI of 1 mg/kg bw/day, although in 1- to 10-year old children the mean and the high percentiles of exposure (95th/97.5th) can be higher than this ADI, at the upper end of the range.

Comments on Estimates of Exposure to Colors Made by the Panel

The EFSA Panel estimated exposures to colors by three methods, all of which exaggerated the actual exposures. The first method, the Budget Method, is well known to yield high estimates that assume everyone consumes the same amount of food based on the average body weight. As shown in all four reports, this method yields a greatly exaggerated exposure. The second method, referred to as Tier 2, incorporated maximum permitted levels of the colors in all foods, i.e., the method assumes that all foods contain the maximum levels permitted by law. The third method, Tier 3, incorporated the maximum levels of colors reported by industry to be used in specific foods. Obviously, some food products will contain the maximum permitted levels, or nearly so, resulting in essentially no difference in intake estimates between Tiers 2 & 3. Reporting these approaches as different methods is misleading. In fact, none of the three methods used estimated average intakes of colors, because in none of the models were average use levels incorporated. Results are reported as mean values and higher percentile intakes, but this presentation is inappropriate, because none of the methods

⁷ Tanaka, T., (1996). Reproductive and neurobehavioral effects of Sunset Yellow FCF administered to mice in the diet. *Toxicol. Ind. Health*, Vol. 12, pages 69-79.

attempt to incorporate mean use levels, although methods are readily available to incorporate this approach.⁸ In short, all methods used by the Panel to estimate intakes of colors from food exaggerate to an unknown degree the actual exposures.

A major problem with the presentation and discussion of the intake data is that estimates of intakes by children are compared to ADIs. The historical and continuing purpose of ADIs (and all other toxicological reference exposures) is to compare lifetime animal exposures to lifetime human exposures. JECFA states this principle explicitly in its Glossary of Terms.⁹ The most common safety factor used in all risk assessments, 100, is based on reducing the chronic lifetime average exposure of test animals to a chemical by two factors of 10 to estimate a safe human average lifetime exposure. This approach to safety evaluation has stood the test of over one-half century. All modifications of this approach incorporate additional factors derived for various shortcomings in the data; e.g., less than lifetime exposures, incomplete database, etc. Thus, all maximum permissible exposures to chemicals in food, whether they are called ADIs, reference doses (RfD), or tolerable daily intakes (TDIs) assume exposures will be averaged over a lifetime, consistent with the information from test animal exposures from which they were derived.

Conclusion

The wide ranging reports of the EFSA panels (the parent EFSA Panel and the Working Groups) responsible for the re-evaluation of the four food colors provide no rationale for the review nor information that significant new findings were available that raised questions regarding the safety of the colors. New information cited was either of doubtful value or raised questions that could be answered relatively easily. Of greatest concern with regard to the scientific credibility of the reports is that the panels made decisions to override previous conclusions using secondary information sources, rather than reviewing the original data and study reports that were used by previous groups of experts. Inconsistencies of the conclusions in the reports with the evaluations made by other expert panels raise the question of whether the reviews were performed using accepted standards of safety assessments.

⁸ See, for example: Gibney, M.J., and van der Voet, H., (2003). Introduction to the Monte Carlo project and the approach to the validation of probabilistic models of dietary exposure to selected food chemicals. *Food Addit. Contam.*, Vol. 20, Suppl. 1, pages S1-7.

⁹ JECFA Glossary of Terms: ADI (Acceptable Daily Intake): An estimate of the amount of a substance in food or drinking water, expressed on a body-weight basis, that can be ingested daily over a lifetime without appreciable risk (standard human = 60 kg). The ADI is listed in units of mg per kg of body weight. At <http://www.who.int/ipcs/food/jecfa/glossary.pdf>.

Doherty, Jane H.

20

From: marietta.bernot [REDACTED] (B)(6)
Sent: Thursday, April 22, 2010 2:56 PM
To: Doherty, Jane H.
Cc: marietta.bernot [REDACTED] Rochette, Peggy (B)(6)
Subject: RE: EU Color Warning Label with EU Law

Working on it.

Marietta E. Bernot
 Global Trade and Customs Advisor
 Mars Incorporated
 Direct: line: [REDACTED]
 Main: [REDACTED] (B)(6)
 Mobile: [REDACTED]

<p>"Doherty, Jane H." <Jane.Doherty@[REDACTED]> (B)(2) 04/22/2010 01:17 PM</p>	<p>To: <marietta.bernot@[REDACTED]>, "Rochette, Peggy" [REDACTED] (B)(6) cc: Subject: RE: EU Color Warning Label with EU Law</p>
--	--

We're preparing Ambassador Kirk for next week's meeting with Dalli and I've been asked if we could put a dollar figure on what the regulation will cost our industry. Would you have any ideas on an estimate that we could pass along?

I'm purchasing some products to pass along to make the point at the meeting, but I really hope Jim Murphy won't each them beforehand!

Thank you,
Jane

Jane Doherty
 Director, Sanitary and Phytosanitary Affairs
 Office of the United States Trade Representative
 Executive Office of the President
 Washington, DC

[REDACTED] (B)(2)

From: marietta.bernot [REDACTED]
Sent: Tuesday, November 24, 2009 3:03 PM (B)(6)
To: Doherty, Jane H.; PRochette [REDACTED]
Subject: Compliance of EU Color Warning Label with EU Law

As promised attached is a memo from law firm Keller and Heckman in Brussels concerning the compliance of the EU color warning label requirement with EU law. The entire memo is attached but below are the concluding paragraphs.

- Regulation 178/2002 clearly establishes that the risk assessment will be undertaken by EFSA which will take the role of an independent scientific point of reference in risk assessment. The role of EFSA within the Community is to give opinions on contentious scientific issues in order to enable the Community institutions and the Member States to take informed risk management decisions necessary to ensure food safety and to avoid the adoption of unjustified or unnecessary obstacles to the free movement of food within the Community. (Preamble recital 34 Regulation 178/2002)
- In this particular case, there was no plausible legal basis for the Community institutions to overlook the conclusions of EFSA's assessment: EFSA's opinion of 7 March 2008 identified the flaws in the Southampton study as it concluded that the study used mixtures and not individual additives making it difficult to ascribe the observed effects to any individual compound. It also concluded that there was an absence of information on the clinical significance of the observed effects.
- Further, as part of the Community re-evaluation of the safety of all approved food colors in the EU, the EFSA dealt as a priority with the six colors in the Southampton study (Sunset Yellow (E110), Quinoline Yellow (E104), Carmoisine (E122), Allura red (E129), Tartrazine (E102) and Ponceau 4R (E124)) and published its opinions on those colors on 12 November 2009.
- While the EFSA reduced the Acceptable Daily Intake (ADI) for three of them for alleged reasons about toxicological safety having nothing to do with the alleged effect on behavior, it did reiterate its previous conclusions that the data in the Southampton study did not substantiate a causal link between the individual colors and possible behavioral effects (the basis for the labeling warning)
- Such consistently repeated conclusions by EFSA provide sufficient basis to determine that the labeling requirement set-up by Article 24 of Regulation 1333/2008 is not based on sound scientific evidence therefore constituting an unjustified barrier to trade, and does not justify application of the precautionary principle.
- The United Kingdom's Food Standards Agency has recommended the voluntary removal of the food colors used in the Southampton study. Actions have already been voluntarily taken by major retailers in the UK. As a result, we are not only talking of an unjustified labeling requirement but of a de-facto product ban, without any scientific basis clearly contrary to the principle of legal certainty as a general principle of EU law.

Marietta E. Bernot
Global Trade and Customs Advisor
Mars Incorporated

Direct line: [REDACTED]

Main: [REDACTED]

Mobile: [REDACTED]

(B)(6)

Doherty, Jane H.

21

From: marietta.bernot [REDACTED] (B)(6)
Sent: Friday, April 09, 2010 11:57 AM
To: Peggy Rochette; Doherty, Jane H.
Cc: Joe Dages
Subject: Re: EU Color Warning labels

OK for me.

From: "Rochette, Peggy" [PRochette [REDACTED]] (B)(6)
Sent: 04/09/2010 11:36 AM AST
To: Marietta Bernot; "Doherty, Jane H." <Jane_Doherty [REDACTED]> (B)(2)
Cc: "Dages, Joe M." [REDACTED] (B)(6)
Subject: RE: EU Color Warning labels

Shall I set it up at 2:00? I CANT DO 12

Peggy S. Rochette
Sr. Director of International Affairs
Grocery Manufacturers Association (GMA)

1350 I Street NW
Washington, DC 20005

[REDACTED] (B)(6)
prochette [REDACTED]

This message is for the use of the intended recipient only. It may contain information that is privileged and confidential. If you are not the intended recipient any disclosure, copying, future distribution, or use of this communication is prohibited. If you have received this communication in error, please advise us by return e-mail and delete/destroy the document.

From: marietta.bernot [REDACTED] (B)(6)
Sent: Friday, April 09, 2010 11:08 AM
To: Doherty, Jane H.; Rochette, Peggy
Cc: Dages, Joe M.
Subject: RE: EU Color Warning labels

I can do a call at noon although will be getting ready to walk into another meeting. Peggy, can you set up the conference?
Regards.

Marietta E. Bernot
Global Trade and Customs Advisor
Mars Incorporated

Direct: line: [REDACTED]
Main: [REDACTED] (B)(6)
Mobile: [REDACTED]

"Doherty, Jane H." <Jane_Doherty (B)(2)>
04/09/2010 09:50 AM
To: "Rochette, Peggy" (B)(6)
cc: "Dages, Joe M." (B)(6), <marietta.bernot (B)(6)>
Subject: RE: EU Color Warning labels

I have a 10 and an 11 o'clock, but should be done by 11:45. Do you still have time for a call?

Jane

Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative
Executive Office of the President
Washington, DC

(B)(2)

From: Rochette, Peggy (B)(6)
Sent: Tuesday, April 06, 2010 2:04 PM
To: Doherty, Jane H.; marietta.bernot (B)(6)
Cc: Dages, Joe M. (B)(6)
Subject: RE: EU Color Warning labels

Friday morning?

Peggy S. Rochette
Sr. Director of International Affairs
Grocery Manufacturers Association (GMA)

1350 I Street NW
Washington, DC 20005

(B)(6)
prochette@...

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From: Doherty, Jane H. (B)(2)
Sent: Tuesday, April 06, 2010 1:58 PM
To: Rochette, Peggy; marietta.bernot (B)(6)
Cc: Dages, Joe M. (B)(6)
Subject: RE: EU Color Warning labels

I'm afraid I can't do a call before 6 p.m. I have a series of meetings here.

Sorry!

Jane

Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative
Executive Office of the President
Washington, DC

[REDACTED] (B)(2)

From: Rochette, Peggy [REDACTED] (B)(6)
Sent: Tuesday, April 06, 2010 1:57 PM
To: Doherty, Jane H.; marietta.bernot [REDACTED] (B)(6)
Cc: Dages, Joe M.
Subject: RE: EU Color Warning labels

I could do a Thursday call after 2:00 – Do you want me to set it up?

Peggy S. Rochette
Sr. Director of International Affairs
Grocery Manufacturers Association (GMA)

1350 I Street NW
Washington, DC 20005

[REDACTED] (B)(6)
prochette [REDACTED]

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From: Doherty, Jane H. [REDACTED] (B)(2)
Sent: Tuesday, April 06, 2010 12:16 PM
To: marietta.bernot [REDACTED]; Rochette, Peggy (B)(6)
Subject: RE: EU Color Warning labels

That works for me. I also need to ask Amb Kirk to tell us how his discussions went in Brussels.

Safe travels, Marietta.

Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative
Executive Office of the President
Washington, DC

[REDACTED] (B)(2)

From: marietta.bernot [REDACTED] (B)(6)
Sent: Tuesday, April 06, 2010 12:14 PM
To: Doherty, Jane H.; Rochette, Peggy
Subject: EU Color Warning labels

Hi Jane and Peggy. I wonder whether there is a chance for us to talk this week about the outcome of discussions at the

WTO SPS Committee last month on the EU color warning label. I am in Peru but home on Thursday and could do a Thursday afternoon call if that might be possible. Regards.

Marietta E. Bernot
Global Trade and Customs Advisor
Mars Incorporated

Direct: line: [REDACTED]

Main: [REDACTED]

Mobile: [REDACTED]

(B)(6)

Doherty, Jane H.

22

From: Wu, Chih-Yung [REDACTED] (B)(2)
Sent: Friday, October 02, 2009 3:05 PM
To: Doherty, Jane H.
Subject: RE: EU Color Warning Labels - Clarifications

Everyday is fine except Friday Oct 9th.

Would this be an evening or morning conference?

Chih-Yung Wu
International Trade Specialist
Processed Products & Technical Regulations Div.
USDA Foreign Agriculture Service/OSTA
1400 Independence Ave. S.W. [REDACTED]
Washington D.C. 20250-1027
Phone: [REDACTED] (B)(2)
Fax: [REDACTED]

FAS Website: www.fas.usda.gov
PPTRD page: http://www.fas.usda.gov/itp/OSTA_PPTRD/PPTRD.asp

From: Doherty, Jane H. [REDACTED] (B)(2)
Sent: Friday, October 02, 2009 2:59 PM
To: Wu, Chih-Yung; Bernot, Marietta
Cc: PRochette [REDACTED] steve.rizk [REDACTED] (B)(6)
Subject: RE: EU Color Warning Labels - Clarifications

Chih – thank you. Anything you learn from Post would be greatly appreciated. I'll press further with Brussels as well.

Our EC colleagues are suggesting a government – government videoconference on this issue and I'd like to get that set up asap. What is your availability for the next two weeks?

Regards,
Jane

Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative
Executive Office of the President
Washington, DC

[REDACTED] (B)(2)

From: Wu, Chih-Yung [REDACTED] (B)(2)
Sent: Friday, October 02, 2009 2:57 PM
To: Doherty, Jane H.; Bernot, Marietta

Cc: PRochette [redacted]; steve.rizk [redacted]
Subject: RE: EU Color Warning Labels - Clarifications

(B)(6)

Jane-

I heard the same as Marietta from my research. Basically, industry was given two "pick your own poison" for choices – either facing a complete ban or warning labels. I guess publically, you can call it an agreement per say, but it looks more like industry reluctantly compromising with the Commission and not given the opportunity to challenge this decision.

I'll check in with Post Brussels to see if they can dig up who and which industry was exactly involved in this 'agreement.'

Cheers,

Chih-Yung Wu
International Trade Specialist
Processed Products & Technical Regulations Div.
USDA Foreign Agriculture Service/OSTA
1400 Independence Ave. S.W. [redacted]
Washington D.C. 20250-1027
Phone: [redacted]
Fax: [redacted]

(B)(2)

FAS Website: www.fas.usda.gov
PPTRD page: http://www.fas.usda.gov/itp/OSTA_PPTRD/PPTRD.asp

From: Doherty, Jane H. [redacted] (B)(2)
Sent: Friday, October 02, 2009 2:28 PM
To: Bernot, Marietta; Wu, Chih-Yung
Cc: PRochette [redacted]; steve.rizk [redacted]
Subject: RE: EU Color Warning Labels - Clarifications (B)(6)

Marietta,

As always, thank you for your note. This is the first I've heard of the claim that "industry" agreed to the labels. I've had some initial discussions with my colleagues in Brussels and was told that the "retail industry, especially in the UK, is insisting on their removal from their food supplies independently of the official measures," but no one inferred that your industry was supportive or prepared to switch to natural colors.

I'll keep you posted as we continue to discuss this with the Commission.

Chih- have you heard about this?

Jane

Jane Doherty
Director, Sanitary and Phytosanitary Affairs

Office of the United States Trade Representative
Executive Office of the President
Washington, DC

[REDACTED] (B)(2)

From: marietta.bernot [REDACTED] (B)(6)
Sent: Friday, October 02, 2009 1:55 PM
To: Doherty, Jane H.; Chih-Yung.Wu [REDACTED] (B)(2)
Cc: PROchette [REDACTED] steve.rizk [REDACTED] (B)(6)
Subject: EU Color Warning Labels - Clarifications

During recent discussions we learned that the U.S. Mission in Brussels had been told by the Commission that industry had agreed to the color warning label rather than have the colors banned. Other U.S. officials reported that they were told industry did not really care as they would be going to natural colors. We realize this is second and third hand information but nevertheless feel some investigation and clarification is needed.

We have queried some of our EU business colleagues and they were skeptical that "industry" had agreed to the warning labels. Certainly they did not. They pointed out that the normal prior consultation process in advance of regulatory action in the EU was not carried out in this case and that, to their knowledge, industry never had the chance to engage with the Commission on this matter. As you have seen from the information brief on this issue, CIAA expressed great concern over the warning labels. However, this was after Parliament and the Commission had agreed to the warning labels. We are investigating further in an effort to find out who agreed to the warning labels ostensibly on behalf of industry.

With respect to banning the colors, that is a highly unlikely scenario as there would be basis on which to ban them. So, this is a very curious situation and we will do our best to bring some clarity.

I might add that companies indicating that they will use natural colors, especially given the media onslaught that was occurring in the UK at the time, is not the same thing as agreeing to color warning labels. Please be assured of our grave concern over the EU warning label scheme, its global consequences, and the precedent it will set for regulatory action on food additives in the future.

Regards.

Marietta E. Bernot
Global Trade and Customs Advisor
Mars Incorporated

Direct: line: [REDACTED]
Main: [REDACTED] (B)(6)
Mobile: [REDACTED]

Doherty, Jane H.

23

From: marietta.bernot [REDACTED] (B)(6)
Sent: Tuesday, November 03, 2009 3:22 PM
To: Doherty, Jane H.
Cc: marietta.bernot [REDACTED] PRochette [REDACTED] (B)(6)
Subject: RE: EU color warning labels - debrief on discussions with the EU

This all sounds very helpful. We are beginning to see the results come out of the EFSA review on some of the colors. Need to get clarification on this "new" Southampton study as none of our contacts in the EU were aware that another one was being done. Will keep you advised. Thanks as always.

Marietta E. Bernot
 Global Trade and Customs Advisor
 Mars Incorporated
 Direct line: [REDACTED]
 Main: [REDACTED]
 Mobile: [REDACTED] (B)(6)

<p>"Doherty, Jane H." <Jane.Doherty@[REDACTED]> (B)(6)</p> <p>11/03/2009 02:37 PM</p>	<p>To: <marietta.bernot@[REDACTED]> (B)(6)</p> <p>cc: <PRochette@[REDACTED]></p> <p>Subject: RE: EU color warning labels - debrief on discussions with the EU</p>
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Marietta,

Sure. The bilateral discussion with the EC was very helpful. They explained that a new EFSA review of a new Southampton study was underway and that they would be sharing data with the USG as soon as it is available. They also agreed that if the USG has questions after reviewing the data, we could conduct a technical discussion. They were very receptive to working with us and they wanted us to identify our concerns with the second review. They admitted that the labels were a political resolution.

Hope that helps.
Jane

PS: Did you know that Korea is only intending to ban Green #3 and that the ban is on hold indefinitely?

Jane Doherty
 Director, Sanitary and Phytosanitary Affairs
 Office of the United States Trade Representative
 Executive Office of the President
 Washington, DC

[Redacted]

(B)(2)

From: marietta.bernot [Redacted]

(B)(6)

Sent: Tuesday, November 03, 2009 2:29 PM

To: Doherty, Jane H.

Cc: PRochette [Redacted]

(B)(6)

Subject: EU color warning labels - debrief on discussions with the EU

Hi Jane. Is there anything you can share with Peggy and me on recent discussions with the EU. Regards.

Marietta E. Bernot
Global Trade and Customs Advisor
Mars Incorporated

Direct line: [Redacted]

Main: [Redacted]

Mobile: [Redacted]

(B)(6)

Doherty, Jane H.

24

From: McPherson, Nefeterius A.
Sent: Tuesday, April 13, 2010 3:10 PM
To: Doherty, Jane H.
Subject: Re: EU Color questions

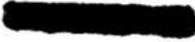
Sure

From: Doherty, Jane H.
To: McPherson, Nefeterius A.
Sent: Tue Apr 13 15:09:08 2010
Subject: RE: EU Color questions

Can I have a few hours and if we don't hear by 5 from FDA, then you can send this as is?

Thank you!

Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative
Executive Office of the President
Washington, DC

 (B)(2)

From: McPherson, Nefeterius A.
Sent: Tuesday, April 13, 2010 2:34 PM
To: Doherty, Jane H.
Subject: Re: EU Color questions

Thanks Jane. I haven't made it in yet. Is it okay for me to send these responses to the reporter or do we need to wait to hear from FDA?

From: Doherty, Jane H.
To: McPherson, Nefeterius A.
Sent: Tue Apr 13 14:32:23 2010
Subject: EU Color questions

Here are the responses cleared by Sloane.

Unfortunately, I never heard back from FDA.

Hope this helps,
Jane

Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative
Executive Office of the President
Washington, DC



(B)(2)

Doherty, Jane H.

From: Davies, Paul
Sent: Tuesday, May 18, 2010 5:43 PM
To: Doherty, Jane H.
Subject: RE: EU color labelling

25
(B)(6)
(B)(2)

[Redacted]

(B)(4)

From: Doherty, Jane H.
Sent: Tuesday, May 18, 2010 5:30 PM
To: Davies, Paul;
Subject: Re: EU color labelling

(B)(2)
(B)(6)

Dear Paul,

Thank you for your note. The letter is being reviewed internally here and should be out shortly. I'll try to send you a copy.

Regards,
Jane
Jane Doherty
Director, Sanitary and Phytosanitary Affairs
Office of the United States Trade Representative

From: Davies, Paul
To: jane_doherty
Sent: Tue May 18 17:25:35 2010
Subject: EU color labelling

(B)(6)
(B)(2)

Jane

[Redacted]

(B)(4)

[Redacted]

Paul Davies
Director
C & M International
1001 Pennsylvania Ave NW
WASHINGTON DC 20004

(B)(6)

Doherty, Jane H.

26

From: Davies, Paul [REDACTED]
Sent: Tuesday, June 15, 2010 4:16 PM
To: Doherty, Jane H.
Subject: RE: EU color labeling - Mars

(B)(6)

[REDACTED] (B)(4)

From: Doherty, Jane H. [REDACTED]
Sent: Tuesday, June 15, 2010 4:15 PM
To: Davies, Paul; [REDACTED]
Subject: RE: EU color labeling - Mars

(B)(2)

(B)(6)

Letter was sent ob Friday. Here's your copy. Sorry, I had to leave for TPP negotiations before I sent it.

From: Davies, Paul [REDACTED]
Sent: Tuesday, June 15, 2010 4:13 PM
To: jane_doherty [REDACTED]
Subject: EU color labeling - Mars

(B)(6)

(B)(2)

Jane

(B)(4)

[REDACTED]

Paul Davies
Director
C & M International
1001 Pennsylvania Ave NW
WASHINGTON DC 20004

[REDACTED] (B)(6)