Safety and Benefits of Food Colors

A U.S. Perspective

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Sensient Colors LLC
IACM Mission Statement

“The mission of the International Association of Color Manufacturers is to advance the interests of manufacturers, producers, and users in the color industry by demonstrating the safety of colors and promoting the industry’s economic growth.”
IACM Objectives

• To protect and expand the worldwide use of colors.

• To serve as a trusted resource to interact with regulatory bodies and global organizations.

• To enhance confidence in the safe use of color.

• To provide members with a central source of scientific and regulatory expertise.

• To advocate global harmonization of standards and regulations.
CURRENT MEMBERS
Agenda

• Uses and Benefits of Colors
• Regulation of Colors in the United States
• Safety of Colors in the United States
• CODEX Colors
• Hyperactivity Concerns
• Labeling of Colors in Food
• Summary
USES AND BENEFITS OF COLORS
Why Use Colors?

• We eat with our eyes. Color provides a way to judge ripeness, perceive flavor and assess the quality of food.

• Food has been colored since antiquity

• Egyptians colored their food with saffron

• Mayans colored their food with annatto

• Romans whitened their bread with alum
Why Use Colors?

• Aesthetic Value
• Identification
• Flavor Perception
Global Harmonization

- IACM participates as non-governmental observer (NGO) at Codex Alimentarius
  - Active participant in Committee on Food Additives (CCFA)
- IACM encourages adoption of Codex standards when countries are developing new food regulations
  - Some colors approved for use in US not currently in General Standard for Food Additives (GSFA) due to slow, deliberate Codex process, not due to safety concerns
- IACM encourages countries to consider colors approved for use in US, EU OR Codex as basis for regulations
  - Each country takes its own approach to color additive approval and reauthorization
  - Populations have different needs and requirements for colors due to cultural variations
What Is Permitted Worldwide?
Color Additive Features

• Dyes
  – Soluble in water
  – Offer stability
  – Color proportional to concentration
  – Function by dissolution
• Oleoresins
  – Lipid-soluble version of some exempt pigments
  – Broadens application potential
• Aluminum lakes
  – Insoluble, function by dispersion
  – Improved light and heat stability
  – Used when color bleeding is not desirable (frostings)
  – Formed by chemically reacting dyes with precipitants and substrata of alumina
  – Lakes of FD&C colors and carmine are allowed for food uses in US
REGULATION OF COLORS
IN THE UNITED STATES
US Regulatory History

• 1958 Food, Drug and Cosmetic Act, with the Color Additive Amendment of 1960.
• The Delaney Clause—cannot cause cancer in man or animal at any level
• Based on toxicological testing, FDA determines safe exposure levels for the food and the color additive
• As absolute safety of any substance can never be proven, FDA must determine if the additive is safe based on the best scientific knowledge available
What is a color additive in the US?

The FDA defines a color additive as “any dye, pigment or other substance made or obtained from a vegetable, animal, mineral or other source capable of coloring a food, drug or cosmetic or any part of the human body.”

Example… but where a food substance such as beet juice is deliberately used as a color, as in pink lemonade, it is a color additive.

• A color additive is unsafe if not used in accord with a regulation/exemption
• No generally recognized as safe (GRAS) exemption
Colors permitted in the US

US Certified Colors or Synthetic Colors

Compounds of known structure, produced by chemical synthesis and conforming to the high purity specifications established by the FDA.

Certified colors

FD&C Red #40        FD&C Yellow #6
FD&C Yellow #5      FD&C Blue #1
FD&C Green #3       FD&C Blue #2
FD&C Red #3
FD&C Red No. 40

Example of a Certified Color

FD&C Red No. 40

• Synthetic dye
• Produces a red orange shade
• Degrades under retort
• Not stable with Vitamin C
21 CFR Section 74.340
FD&C Red No. 40 Chemical Specifications

FD&C Red No. 40 shall conform to the following specifications and shall be free from impurities other than those named to the extent that such other impurities may be avoided by good manufacturing practice:

• Sum of volatile matter (at 135 deg. C.) and chlorides and sulfates (calculated as sodium salts), not more than 14.0 percent.
• Water-insoluble matter, not more than 0.2 percent.
• Higher sulfonated subsidiary colors (as sodium salts), not more than 1.0 percent.
• Lower sulfonated subsidiary colors (as sodium salts), not more than 1.0 percent.
• Disodium salt of 6-hydroxy-5-[(2-methoxy-5-methyl-4-sulfophenyl) azo] -8-(2-methoxy-5-methyl-4-sulfophenoxy)-2-naphthalenesulfonic acid, not more than 1.0 percent.
• Sodium salt of 6-hydroxy-2-naphthalenesulfonic acid (Schaeffer's salt), not more than 0.3 percent.
• 4-Amino-5-methoxy-o- toluenesulfonic acid, not more than 0.2 percent.
• Disodium salt of 6,6'-oxybis (2-naphthalene-sulfonic acid), not more than 1.0 percent.
• Lead (as Pb), not more than 10 parts per million.
• Arsenic (as As), not more than 3 parts per million.
• Total color, not less than 85.0 percent.
Colors permitted in the US

US Colors Exempt from Certification or “Natural Colors”
Colors typically referred to as ‘Natural Colors’ by the food industry. They are obtained from vegetable, animal, and mineral sources, or are synthetic duplicates of naturally existing colorants.

Exempt colors
Turmeric oleoresin, Riboflavin, Carmine/Cochineal, Chlorophyll, Sodium Copper Chlorophyll, Caramel, Beta carotene, Beta-apo-8’ Caroteneal, Annatto, Paprika Oleoresin, Tomato Lycopene, Canthanxanthin, Beet Juice, Vegetable Juice, Fruit Juice, Saffron, Titanium Dioxide, Iron Oxides, Spirulina Blue, Grape Skin Extract.
Annatto

Example of an Exempt from Certification Color

- Annatto tree (*Bixa orellana*) seeds have extractable color
- Extracted with approved solvents
- Imparts butter yellow to orange shade—used in cheese, cheese rinds, and butter
21 CFR Section 73.30

Annatto Extract Identity & Specifications

(a) Identity. (1) The color additive annatto extract is an extract prepared from annatto seed, *Bixa orellana* L., using any one or an appropriate combination of the food-grade extractants listed in paragraph (a)(1) (i) and (ii) of this section:

(i) Alkaline aqueous solution, alkaline propylene glycol, ethyl alcohol or alkaline solutions thereof, edible vegetable oils or fats, mono- and diglycerides from the glycerolysis of edible vegetable oils or fats. The alkaline alcohol or aqueous extracts may be treated with food-grade acids to precipitate annatto pigments, which are separated from the liquid and dried, with or without intermediate recrystallization, using the solvents listed under paragraph (a)(1)(ii) of this section. Food-grade alkalis or carbonates may be added to adjust alkalinity.

(ii) Acetone, ethylene dichloride, hexane, isopropyl alcohol, methyl alcohol, methylene chloride, trichloroethylene.

(2) Color additive mixtures for food use made with annatto extract may contain only diluents that are suitable and that are listed in this subpart as safe in color additive mixtures for coloring foods.

(b) Specifications. Annatto extract, including pigments precipitated therefrom, shall conform to the following specifications:

(1) Arsenic (as As), not more than 3 parts per million; lead as Pb, not more than 10 parts per million.

(2) When solvents listed under paragraph (a)(1)(ii) of this section are used, annatto extract shall contain no more solvent residue than is permitted of the corresponding solvents in spice oleoresins under applicable food additive regulations in parts 170 through 189 of this chapter.
REGULATION OF COLORS
IN THE UNITED STATES
Color Additives Require Pre-Market Approval

• All color additives, except for some hair dyes, are subject to FDA pre-market approval before they may be used in:
  – Food
  – Drugs
  – Cosmetics
  – Medical devices that come in contact with the bodies of people or animals for a significant period of time
Color Additive Petition Process

- Petitioner submits information/raw data to Office of Food Additives Safety (OFAS)
- Filing decision – is the petition adequate?
- Filing notice in Federal Register
- Communication with petitioner during review
- Scientific evaluation of the petition
- Petition update meetings (internal)
- Scientific memos
- Final rule published in Federal Register
  - preamble provides rationale for decision
  - use is generic
  - effective 30 days after rule publishes unless objections received
  - must withstand legal/scientific challenge
Color Additive Petition Review

• What is the substance and what is the projected exposure?
  – Identity and composition
  – Method of manufacture
  – Specifications and purity
  – Use level and exposure
  – Technological justification

• Is it safe for its intended use?
  – Toxicology studies
  – FDA Redbook requirements

• Is other case-specific information needed?
Color Additive Petition
Identity and Specifications

• Chemical Identity
  – Analytical chemistry and spectra
  – For plant sources, description of plant source
  – Physical, chemical and biological properties

• Specifications and Methods (for enforcing specs)
  – Multi-batch analyses
  – Identification of secondary coloring matters
  – Identification of non-coloring matters, impurities

• Manufacturing Process
  – Conditions; methods
  – Solvents; reagents
  – Variation/purity

• Stability
Color Additive Petitions

Exposure

• Petitions must include exposure estimate
  – Proposed concentrations that will be used in food
  – Consumer intake of foods that will contain the potential color additive

• FDA experts will produce an Estimated Daily Intake (EDI) for the color additive, and determine safety based on results of toxicity testing and no-observed effect levels

• This process is similar to the WHO/FAO Joint Expert Committee on Food Additives (JECFA) process to establish acceptable daily intakes (ADIs)
REGULATION OF COLORS IN
THE FAO/WHO, JECFA &
CODEX ALIMENTARIUS
The work of JECFA feeds into Codex Alimentarius

The GSFA is the Codex General Standard for Food Additives

- Defines the food categories
- Sets the conditions for use of additives
- Additives have INS numbers
- Color is a food additive, which adds or restores colour in a food

The GSFA online database is:
http://www.codexalimentarius.net/gsfaonline/index.html
Current Status of Colors in the GSFA

- There are currently 46 colors with draft and/or adopted provisions in the GSFA
  - 8 colors have a JECFA ADI of “not specified” and are listed in Table 3 of the GSFA
    - Examples include Beet red, 3 Lycopenes and Titanium dioxide
  - 38 colors have a numerical ADI and are only listed in Tables 1 and 2 of the GSFA
    - Examples include Erythrosine, Sunset yellow FCF and Tartrazine
Current Status of Colors in the GSFA

- Total of 1,895 draft and adopted provisions for colors in the GSFA
  - Represent ~ 1/3 of all provisions in the GSFA
- 990 adopted provisions
  - 973 for colors with numerical ADIs
  - 17 for Table 3 colors (i.e., ADI not specified)
- 905 draft provisions
  - 760 for colors with numerical ADIs
  - 145 for Table 3 colors
Current Status of Colors in the GSFA - Example

**FOOD CATEGORY DETAILS**

**Chewing gum (05.3)**

**Description:**
Product made from natural or synthetic gum base containing flavours, sweeteners (nutritive or non-nutritive), aroma compounds, and other additives.\(^1\) Includes bubble gum and breath-freshener gum products.

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<th>Limit</th>
<th>Category</th>
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<td>Allura red AC</td>
<td>300 mg/kg</td>
<td>05.3</td>
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<tr>
<td>559</td>
<td>Aluminium silicate</td>
<td>100 mg/kg</td>
<td>05.3</td>
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<td>951</td>
<td>Aspartame</td>
<td>10,000 mg/kg</td>
<td>05.3</td>
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<td><strong>BENZOATES</strong></td>
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<tr>
<td>901</td>
<td>Beeswax</td>
<td>GMP</td>
<td>05.3</td>
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<tr>
<td>133</td>
<td>Brilliant blue FCF</td>
<td>300 mg/kg</td>
<td>05.3</td>
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</tbody>
</table>

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\(^1\) Includes bubble gum and breath-freshener gum products.
HYPERACTIVITY CONCERNS
Color Additives and Hyperactivity Concerns

Historical Perspective

• Some past research has suggested a link between intake of food colors and hyperactive behavior in children.
• New research released in 2007 by the University of Southampton.

Food additives and hyperactive behaviour in 3-year-old and 8/9-year-old children in the community: a randomised, double-blinded, placebo-controlled trial

Donna McCann, Angelina Barrett, Alison Cooper, Debbie Crumpler, Lindy Dalen, Kate Grimshaw, Elizabeth Kitchin, Kris Lok, Lucy Porteous, Emily Prince, Edmund Sonuga-Barke, John O'Warner, Jim Stevenson

Lancet 2007; 370: 1560-67
Southampton Study
Authors’ Conclusions

• Mixtures of certain artificial colors together with a sodium benzoate preservative in the diet increased hyperactivity in 3 and 8/9 year old children in the general population.

• The average effect varied depending upon the mix and the age group.

• Although the results of the study suggest that some mixtures of certain artificial food colors and benzoate preservative may affect the level of hyperactive behavior in children, removal of these additives from the diet would not be a panacea for ADHD.
Southampton Study Limitations and Reviews

HYPERACTIVITY CONCERNS
No Proven Causality to Hyperactivity

- Reviewed by Stevenson et. al., 2010
- Study design was poor
- Observed effects lack clear statistical significance
- Slightly amended behavior was observed in all groups given the additives
- But this does not necessarily lead to the conclusion that the additive mixes caused an increase in hyperactivity

Reviews of Southampton Work

• U.S. Food & Drug Administration (FDA)
• European Food Safety Authority (EFSA)
• Norwegian Food Safety Authority
• German Federal Institute for Risk Assessment (BfR)
• Food Safety Australia/New Zealand (FSANZ)
• Others (e.g., UK Council on Toxicology)
FDA Food Advisory Committee Meeting

- Reviewed US FDA report discussing available scientific data and whether there is evidence for a link
- 2-Day meeting, March 30/31, 2011
- Food Advisory Committee, 14 members
- Public comments from consumer groups and other invited participants
FDA Food Advisory Committee Findings

- Were FDA evaluation criteria robust?
  - Yes, 13-1
  - Should criteria/review be modified? Yes 8-6

- Is there a causal relationship?
  - No, 11-3

- Should recommendation regarding additive free diet for children which show effects still be given?
  - Yes 13-1

- Should a warning labeling be required?
  - No, 8-6

- Are further studies needed?
  - Yes, 13-1
EFSA Opinion

EFSA’s AFC Panel were assisted by experts in behavior, child psychiatry, allergy and statistics

Conclusions:

– study provided limited evidence that the mixtures of additives tested had a small effect on the activity and attention of some children.
– inability to pinpoint which additives may have been responsible for the effects observed in the children given that mixtures and not individual additives were tested
– Effects observed were not consistent for the two age groups and for the two mixtures used in the study.

• Findings of the McCann et al study could not be used as a basis for altering the acceptable daily intakes
United States

LABELING OF COLORS IN FOOD
Labeling of Colors

• In the US all color additives are considered artificial for labeling purposes
  – Artificial Color
  – Color Added

• The addition of color to a product must be indicated on a label regardless of whether it is an exempt or certified (FD & C) color.

• Cannot label any color additive in the US as a “Natural Color”
Labeling of Color Additives

- Certified colors must be labeled by name listed in 21 CFR 74 and 82
  - For example “Yellow 5, Red 40 lake, blue 1”
  - The word “lake” must appear when appropriate
  - An alternative name may be declared in parentheses (e.g., common name, E numbers)

- Exempt colors can be labeled:
  - “Artificial color”
  - “Artificial color added”
  - “Color added”
  - “Colored with (name of color)”
  - “(Name of color) (color)”
  - Unless name specifically required by regulation-
    - Example- Carmine/Cochineal require labeling by name to allow consumers to make an informed choice.

- Exempt colors cannot use the term “natural”
- Do not need to declare “Titanium Dioxide” by name
European Union

LABELING OF COLORS IN FOOD
EU Regulations

Usage Directive:
• Regulation (EC) No 1333/2008 of 16 December 2008

Purity Directive:
• Regulation (EU) No 231/2012 of 9 March 2012

Colouring Foods
• Guidance notes on the classification of food extracts with colouring properties
Labeling Summary EC

Color additives must be declared by category name (colour) and E number of specific colour, name, or both name and number, e.g.,

- Colour: E102, E133, or
- Tartrazine (E102), Brilliant Blue FCF (E133)

If by name, the language of the country to which it is being exported must be used

If the color has another purpose, such as spice, it can be labeled as “Paprika spice” or “concentrated fruit juices”
Southampton Study- Labeling

Labeling shall include: 
» name or E number of the colour(s): may have an adverse effect on activity and attention in children «.

Food colors that require special labeling:

- Sunset yellow (E 110)*
- Quinoline yellow (E 104)*
- Carmoisine (E 122)*
- Allura red (E 129)*
- Tartrazine (E 102)*
- Ponceau 4R (E 124)*
Warning Labels

LABELING OF COLORS IN FOOD
Do ingredient labels need a warning for colors?

• IACM does not support a warning for colors on ingredient labels - **No proven causality to hyperactivity**
  
  – Data from the Southampton Study does not clearly indicate a causal association between the intake of color additives and hyperactive behavior.
  
  – As with all food ingredients, if consumers choose to not eat a specific ingredient, they can see it on the label and make an informed product choice.
Do ingredient labels need a warning for colors?

- IACM feels strongly that governments should make regulatory decisions based on sound science.
- The EU warning label based on request of European Parliament (Legislature) rather than EFSA (Scientific body).
- For this reason, warning statements for the Southampton colors are not used in geographies that use science to set policy, such as the United States, Canada, Australia, New Zealand, China or Japan.
Do ingredient labels need a warning for colors?

• The US government has expressed its concerns regarding EU’s action to the World Trade Organization
• Consumers, including children, are not at risk from the presence of color additives in foods
• A warning label is completely unnecessary.
• This leads to consumer confusion by indicating cause for concern where none exists.
Summary

• Colors are useful additives that provide important and beneficial technical effects
• Strong and robust dataset supports the safety of colors
• Support global harmonization of color regulations and approval
• Southampton Study is intriguing but no proven causality for hyperactive behavior
• Colors are clearly labeled as ingredients in the US and this allows consumers to make informed choices
think in colors
Additional information
Websites

US:  www.fda.gov


EU Website:  
https://webgate.ec.europa.eu/sanco_foods/main/?event=display

GSFA (CODEX):  www.codexalminentarius.net/gsfaonline/index.html

Japan:  http://www.mhlw.go.jp/

Australia/New Zealand:  
http://www.foodstandards.govt.nz/thecode/foodstandardscode.cfm
SAFETY OF COLORS IN THE UNITED STATES

Safety Data Sets

SAFETY OF COLORS IN THE UNITED STATES

International Association of Color Manufacturers
# FD&C Blue No. 1 & Green No. 3

<table>
<thead>
<tr>
<th>Name of color</th>
<th>FD&amp;C Blue No. 1 Brilliant Blue FCF</th>
<th>FD&amp;C Green No. 3 Fast Green FCF</th>
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<tr>
<td>In use since</td>
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<td>Genetox</td>
<td>Negative</td>
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<td>Rat</td>
<td>Rat</td>
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<td>Special studies</td>
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## FD&C Blue No. 2

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Erythrosine |
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## Exempt Colors

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<td>Reproductive/Teratological</td>
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## Exempt Colors

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<td>Oncogenicity</td>
<td>Rats/Mice</td>
<td>Rats</td>
<td></td>
</tr>
<tr>
<td>Reproductive/Teratological</td>
<td>Neg/Neg</td>
<td>Neg/Neg</td>
<td></td>
</tr>
<tr>
<td>Special studies</td>
<td></td>
<td>Allergenicity</td>
<td></td>
</tr>
<tr>
<td>Human studies</td>
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<td>Allergenicity</td>
<td></td>
</tr>
<tr>
<td>ADMEK</td>
<td>Rats</td>
<td></td>
<td></td>
</tr>
<tr>
<td>JECFA ADI (mg/kg/d)</td>
<td>0-3</td>
<td>0-5</td>
<td>None allocated</td>
</tr>
</tbody>
</table>
Southampton Study Design Details
Southampton Study Design

• Randomized, double-blind, placebo-controlled, crossover trial

• Two age groups from the general population
  – 3-year-olds (153 children)
  – 8/9-year-olds (144 children)

• Week 1: Baseline (usual diet)

• Over subsequent 6 weeks series of placebo or additive mix drinks given daily in a randomised sequence

• Hyperactivity measured using parent and teacher ratings, observations of child in preschool setting or classroom and a computerized test of attention for 8/9-year-olds

• Combined to form a new method for assessing hyperactivity:
  – Global Hyperactivity Aggregate (GHA)
## Two Mixes Used

<table>
<thead>
<tr>
<th>FD&amp;C (E-Number)</th>
<th>Common Name</th>
<th>Mix A</th>
<th>Mix B</th>
</tr>
</thead>
<tbody>
<tr>
<td>FD&amp;C Yellow 5 (E102)</td>
<td>Tartrazine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E104</td>
<td>Quinoline yellow</td>
<td></td>
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<tr>
<td>FD&amp;C Yellow 6 (E110)</td>
<td>Sunset Yellow</td>
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<tr>
<td>E122</td>
<td>Carmoisine</td>
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<td>E124</td>
<td>Ponceau 4R</td>
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<tr>
<td>FD&amp;C Red 40 (E129)</td>
<td>Allura Red AC</td>
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<tr>
<td>E211 (Preservative)</td>
<td>Sodium benzoate</td>
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</tbody>
</table>

Children given either Mix A or Mix B during the ‘challenge’ periods