Safety and Benefits of Food Colors

A U.S. Perspective

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Sensient Colors
IACM MISSION

“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

IACM Safety and Benefit of Food Colors
Agenda

• Use and Benefits of Colors
• Regulation of Colors in the United States
• Safety of Colors in the US
• Labeling of colors in foods in the US
Use and Benefits of Colors
Why use colorants?

• Aesthetic Value
• Identification
• Flavor Perception
Why use colorants?

• Aesthetic Value
• Identification
• Flavor Perception

• Offset color loss due to light, air, extremes of temperature, moisture, and storage conditions
Regulation of Colors in the United States
Colors Used Throughout Recorded History

• Foods colored with spices and minerals
  – Paprika, turmeric, saffron, iron oxides
  – Wine colored in 300 B.C.

• Cosmetics from vegetable and mineral sources
  – White lead
  – Kohl (contains lead or antimony)
  – Copper ore for eye shadow
  – Vegetable extracts for the skin
US Legal Framework

• 1906 Pure Food and Drug Act
  – Defined "misbranding" and "adulteration" for the first time and prescribed penalties for each
  – Regulated food and drugs moving in interstate commerce
• 1938 Food, Drug, and Cosmetics Act
  – Established safety standard – harmless and suitable
  – Established certification/FD&C certified
• 1960 Color Additive Amendments
  – Defined color additive
  – Identified new safety standard – reasonable certainty of no harm
  – Require pre-market approval
  – Authorized exempt from certification

Colors listed in US Code of Federal Regulations, Part 21, Section 73 & 74
FDA Definition of Color Additive (FD&C Act Section 201(t))

- A material which is a dye, pigment, or other substance … and when added or applied to a food, drug, or cosmetic, or to the human body or any part thereof, is capable (alone or through reaction with other substance) of imparting color thereto;
  - Excludes substances determined by the Secretary to be used solely for a purpose other than coloring.

- A color additive is unsafe if not used in accord with a regulation/exemption.

- No generally recognized as safe (GRAS) exemption.
Types of FDA Regulated Colorants

• Certified Colors
  – Known structure
  – Chemical synthesis
  – High purity specifications established by the FDA
  – Are known as FD&C colors

• Colors Exempt from Certification
  – Colors typically referred to as ‘natural colors’ by the food industry
  – Vegetable, animal, and mineral sources
  – Synthetic duplicates of naturally existing colorants
Certified Colors

- Each batch of certified colors is tested by the FDA to confirm that it is safe for addition to consumer products
- Synthetically produced, known structure
- Impart intense, uniform color
- Less expensive
- Blend more easily
- Stable
- Generally do not impart undesirable flavors to food.

IACM Safety and Benefit of Food Colors
Certified Colors (21 CFR 74)

<table>
<thead>
<tr>
<th>Certified color</th>
<th>Uncertified name</th>
</tr>
</thead>
<tbody>
<tr>
<td>FD&amp;C Red No. 40</td>
<td>Allura Red AC</td>
</tr>
<tr>
<td>FD&amp;C Blue No. 1</td>
<td>Brilliant Blue FCF</td>
</tr>
<tr>
<td>FD&amp;C Blue No. 2</td>
<td>Indigotine</td>
</tr>
<tr>
<td>FD&amp;C Yellow No. 5</td>
<td>Tartrazine</td>
</tr>
<tr>
<td>FD&amp;C Yellow No. 6</td>
<td>Sunset Yellow FCF</td>
</tr>
<tr>
<td>FD&amp;C Green No. 3</td>
<td>Fast Green FCF</td>
</tr>
<tr>
<td>Citrus Red No. 2</td>
<td></td>
</tr>
<tr>
<td>Orange B</td>
<td></td>
</tr>
<tr>
<td>Aluminum Lakes (21 CFR 82.51)</td>
<td></td>
</tr>
</tbody>
</table>
Certified Colorants

• **Dyes:** Colorants that function by *dissolution*

• **Lakes (Pigments)**
  • Insoluble colorants that function by *dispersion*
  • Formed by chemically reacting dyes with precipitants and substrata of alumina.
    – Color by dispersion, not by solution
    – Used when you don’t want bleeding (frostings)
    – Improved light and heat stability vs. dyes
  • Lakes of FD&C colors and carmine are allowed for food uses

*Each batch of FD&C Dyes and Lakes are sent in and certified by the FDA*
FD&C Red No. 40
Example of a Certified Color

- Is synthetic dye
- Produces a red orange shade
- Degrades under retort
- Not Stable with Vitamin C
(b) 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-0- 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.
Exempt Colors

- Derived from natural sources such as vegetables, minerals, or animals
- Synthetic extracts
- May not be stable in certain food
- May add unintended flavors to food
Exempt Colors (21 CFR 73)

- Annatto extract
- Astaxanthin
- Dehydrated beets (beet powder)
- Ultramarine blue
- Canthaxanthin
- Caramel
- beta-Apo-8'-carotenal
- beta-Carotene
- Cochineal extract; carmine
- Sodium copper chlorophyllin
- Toasted partially defatted cooked cottonseed flour
- Ferrous gluconate
- Ferrous lactate
- Grape color extract
- Grape skin extract (Enocianina)
- Haematococcus algae meal
- Synthetic iron oxide
- **Fruit juice**
- **Vegetable juice**
- Dried algae meal
- Tagetes (Aztec marigold) meal and extract
- Carrot oil
- Corn endosperm oil
- Paprika/oleoresin (extract)
- Phaffia yeast
- Riboflavin
- Saffron
- Titanium dioxide
- Turmeric/oleoresin
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
(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.
Safety 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 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 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 exactly is the substance and what is the projected exposure?
  – Identity and composition
  – Method of manufacture
  – Specifications
  – Use level and exposure

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

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

• Chemical Identity
• Manufacturing Process
  – Conditions
  – Solvents
  – Variation
• Identification of secondary coloring matters
  – Range
• Identification of non-coloring matters
  – Range
Color Additive Petition
Use/Technological Justification

• What food categories will the color additive be used in? (Dairy Products, Baked Goods, etc)
• What levels are required? (generally ppm, excluding caramel color and some unique applications)
• How will application levels vary within a food category? (10-100 ppm? 100-1000 ppm?)
• Why is the color additive useful?
• This information allows the FDA to consider potential exposure and gauge the need for use of the color additive within a food category
### Color Additive Petition
**FDA Recommended Tox Testing**

<table>
<thead>
<tr>
<th>Toxicity Tests</th>
<th>Concern Level Low (I)</th>
<th>Concern Level Intermediate (II)</th>
<th>Concern Level High (III)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic Toxicity Tests</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Short-term toxicity tests with rodents</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Subchronic toxicity studies with rodents</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Subchronic toxicity studies with non-rodents</td>
<td></td>
<td>X</td>
<td>X</td>
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<tr>
<td>One-year toxicity studies with non-rodents</td>
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<td></td>
<td>X</td>
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<tr>
<td>Chronic toxicity or Combined chronic toxicity/carcinogenicity studies with rodents</td>
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<td></td>
<td>X</td>
</tr>
<tr>
<td>Carcinogenicity studies with rodents</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Reproduction studies</td>
<td>X</td>
<td>X</td>
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<td>Developmental toxicity studies</td>
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<td>X</td>
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<tr>
<td>Metabolism and Pharmacokinetic studies</td>
<td>X</td>
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</tr>
<tr>
<td>Human studies</td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

*Concern based on exposure and structure*
Color Additive Petition
Exposure

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

• For main color additive, FDA will generally
  consider chronic intake

• Ultimately, FDA experts will produce an
  Estimated Daily Intake (EDI) for the color
  additive, and gauge results of toxicity testing and
  no-observed effect levels against this EDI
Color Risk Assessment

• US requirements for color additive petitions have created substantial safety datasets for many colors
• This data has also been reviewed by WHO/FAO Joint Expert Committee on Food Additives (JECFA) to establish acceptable daily intakes (ADIs)
• Some additional data has been collected since FDA & JECFA reviews
  – Genotoxicity, allergenicity, other studies
# 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>
</tr>
</thead>
<tbody>
<tr>
<td>In use since</td>
<td>1929</td>
<td>1927</td>
</tr>
<tr>
<td>Genetox</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Acute/Subchronic</td>
<td>Rat</td>
<td>Rat</td>
</tr>
<tr>
<td>Chronic</td>
<td>Rats/Mice</td>
<td>Rats/Mice</td>
</tr>
<tr>
<td>Carcinogenicity</td>
<td>Rats/Mice</td>
<td>Rats/Mice</td>
</tr>
<tr>
<td>Reproductive/Teratogenic</td>
<td>Neg/Neg</td>
<td>Neg/Neg</td>
</tr>
<tr>
<td>Special studies</td>
<td>Diverse animals</td>
<td>Rats</td>
</tr>
<tr>
<td>Human studies</td>
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<td></td>
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<tr>
<td>ADMEK</td>
<td>0-12.5</td>
<td>0-25</td>
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</tbody>
</table>

IACM Safety and Benefit of Food Colors
### FD&C Blue No. 2

<table>
<thead>
<tr>
<th>Name of color</th>
<th>FD&amp;C Blue No. 2</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Indigotine</td>
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<td>In use since</td>
<td>1907</td>
</tr>
<tr>
<td>Genetox</td>
<td>Negative</td>
</tr>
<tr>
<td>Acute/Subchronic</td>
<td>Rat, Mouse/90-day</td>
</tr>
<tr>
<td>Chronic</td>
<td>Rats/Mice</td>
</tr>
<tr>
<td>Carcinogenicity</td>
<td>Rats/Mice</td>
</tr>
<tr>
<td>Reproductive/Teratogenic</td>
<td>Neg/Neg</td>
</tr>
<tr>
<td>Special studies</td>
<td></td>
</tr>
<tr>
<td>Human studies</td>
<td></td>
</tr>
<tr>
<td>ADMEK</td>
<td>Rats</td>
</tr>
<tr>
<td>JECFA ADI (mg/kg/d)</td>
<td>0-17</td>
</tr>
</tbody>
</table>

IACM Safety and Benefit of Food Colors
# FD&C Red No. 3

<table>
<thead>
<tr>
<th>Name of color</th>
<th>FD&amp;C Red No. 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Erythrosine</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>In use since</th>
<th>1907</th>
</tr>
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<tbody>
<tr>
<td>Genetox</td>
<td>Negative</td>
</tr>
<tr>
<td>Acute/Subchronic</td>
<td>Rat, Mouse</td>
</tr>
<tr>
<td>Chronic</td>
<td>Rats/Mice</td>
</tr>
<tr>
<td>Carcinogenicity</td>
<td>Rats/Mice</td>
</tr>
<tr>
<td>Reproductive/Teratogenic</td>
<td>Neg/Neg</td>
</tr>
<tr>
<td>Special studies</td>
<td>Thyroid/Mechanism of Action</td>
</tr>
<tr>
<td>Human studies</td>
<td>Thyroid</td>
</tr>
<tr>
<td>ADMEK</td>
<td>Rats</td>
</tr>
<tr>
<td>JECFA ADI (mg/kg/d)</td>
<td>0-0.1</td>
</tr>
</tbody>
</table>
## FD & C Red 40, Yellow 5 & Yellow 6

<table>
<thead>
<tr>
<th>Name of color</th>
<th>FD&amp;C Red No. 40 Allura Red AC</th>
<th>FD&amp;C Yellow No. 5 Tartrazine</th>
<th>FD&amp;C Yellow No. 6 Sunset Yellow FCF</th>
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<tr>
<td>In use since</td>
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<td>1916</td>
<td>1929</td>
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<td>Genetox</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Acute/Subchronic</td>
<td>Animals</td>
<td>Mice</td>
<td>R,M/90d</td>
</tr>
<tr>
<td>Chronic</td>
<td>Rats/Mice</td>
<td>Rats/Mice</td>
<td>Rats/Mice</td>
</tr>
<tr>
<td>Carcinogenicity</td>
<td>Rats/Mice</td>
<td>Rats/Mice</td>
<td>Rats/Mice</td>
</tr>
<tr>
<td>Reproductive/ Teratological</td>
<td>Neg/Neg</td>
<td>Neg/Neg</td>
<td>Neg/Neg</td>
</tr>
<tr>
<td>Special studies</td>
<td></td>
<td>Allergenicity</td>
<td>Allergenicity</td>
</tr>
<tr>
<td>Human studies</td>
<td></td>
<td>Allergenicity</td>
<td>Allergenicity</td>
</tr>
<tr>
<td>ADMEK</td>
<td>Dogs, rats</td>
<td>Humans, animals</td>
<td>Humans, animals</td>
</tr>
<tr>
<td>JECFA ADI (mg/kg/d)</td>
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<td>0-7.5</td>
<td>0-2.5</td>
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# Exempt Colors

<table>
<thead>
<tr>
<th>Name of color</th>
<th>Annatto (Bixin, Norbixin)</th>
<th>Grape Skin Extract (Anthocyanins)</th>
<th>Beet Red</th>
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</thead>
<tbody>
<tr>
<td>In use since</td>
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<td></td>
</tr>
<tr>
<td>Genetox</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Acute/Subchronic</td>
<td>Rat</td>
<td>Rat/90-day</td>
<td>Rat/14-day</td>
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<tr>
<td>Chronic</td>
<td>Rats/Mice</td>
<td></td>
<td>Rat</td>
</tr>
<tr>
<td>Oncogenicity</td>
<td>Rats/Mice</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reproductive/Teratological</td>
<td>Neg/Neg</td>
<td>Neg/Neg</td>
<td>Neg/Neg</td>
</tr>
<tr>
<td>Special studies</td>
<td>Allergenicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human studies</td>
<td>Allergenicity</td>
<td></td>
<td>ADMEK</td>
</tr>
<tr>
<td>ADMEK</td>
<td></td>
<td>Animals</td>
<td>Animals/ Humans</td>
</tr>
<tr>
<td>JECFA ADI (mg/kg/d)</td>
<td>0-0.065 (Bixin)</td>
<td>0-2.5</td>
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# Exempt Colors

<table>
<thead>
<tr>
<th>Name of color</th>
<th>Turmeric/Curcumin</th>
<th>Carmine/Cochineal/Carminic acid</th>
<th>Paprika Extract</th>
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<tbody>
<tr>
<td>In use since</td>
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<tr>
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<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Acute/Subchronic</td>
<td>Rats/Mice/90d</td>
<td>Mice/90d</td>
<td>Mice</td>
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<td>Chronic</td>
<td>Rats/Mice</td>
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<tr>
<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>
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<td>Human studies</td>
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<td>Allergenicity</td>
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</tr>
<tr>
<td>ADMEK</td>
<td>Rats</td>
<td></td>
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</tr>
<tr>
<td>JECFA ADI (mg/kg/d)</td>
<td>0-0.1</td>
<td>0-5</td>
<td>Not completed (2008)</td>
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</tbody>
</table>
Labeling of Colors in Food in the United States
Labeling of Colors

• In the US all color additives are considered artificial for labeling purposes.

• 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 U.S. as a “Natural Color”
Labeling of Colors
Certified

• 21 CFR 101.22(k)(1)
• Certified color additives must be declared
  – Either by names listed in 21 CFR Parts 74 and 82
  – Or, by abbreviated names (e.g., Red 40)
  – An alternative name may be declared in parentheses (e.g., common name, E.U. E numbers)
Labeling of Colors
Exempt

• 21 CFR.22(k)(2)
• Must be declared
  – Either as “artificial color,” artificial color added,” or “color added”
  – Or, as “colored with _____” or “_______” color”
  – Unless name specifically required by regulation
    • Carmine/cochineal is now labeled as an ingredient because of allergenicity concerns
    • Consumers have the clear knowledge needed to decide whether to buy a product containing carmine/cochineal
Global Harmonization

• IACM participates as NGO at Codex
  – Active participant in Committee on Food Additives (CCFA)
• Collaboration and cooperation in building regulatory
  coherence and international harmonization
  – Facilitates trade
  – Increases consumer confidence in global food supply
• Encourage adoption of Codex standards when countries
  are developing new food regulations
  – some colors approved for use in US not currently in GSFA due to
    slow, deliberate Codex process, not due to safety concerns
    -encourage countries to consider colors approved for use in US, EU
      OR Codex as basis for regulations

IACM advocates for global harmonization of standards and
regulations
Summary

• Strong and robust dataset supports the safety of colors
• Colors are useful additives that provide important and beneficial technical effects
• Colors are clearly labeled as ingredients in the US and this allows consumers to make informed choices
• Support global harmonization of color regulations and approval
Thank You
Azo Compounds

Yellow No. 5
- Bright yellow
- Good light/heat
- Cold precipitate

Yellow No. 6
- Bright orange
- Fair light/heat

Red No. 40
- Red orange
- Degrades under retort
- Not Stable with Vitamin C
Triphenylmethane (TPM) Compounds

• Blue No. 1
  – Blue green
  – Stable in most food processes
  – GI tract resistant
  – Keep usage below 50 mg/day

Green No. 3
  - Teal green
  - pH shade variation
  - Similar to Blue 1
Indigoid Compounds

Blue No. 2
- Denim blue
- Light stable
- Low water activity applications
- Unstable in aqueous solutions
Xanthene Compounds

Red No. 3

– Bright pink
– Light unstable
– Heat stable
– Insoluble at low pH
– Lake is not permitted in US
– Neon shades alone or in combination
– May produce off flavor from Iodine groups