



Safety and Benefits of Food Colors

A U.S. Perspective

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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.

CHR HANSEN

Improving food & health

Emerald Performance Materials
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WE CREATE
Great Taste

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 #5

FD&C Green #3

FD&C Red #3

FD&C Yellow #6

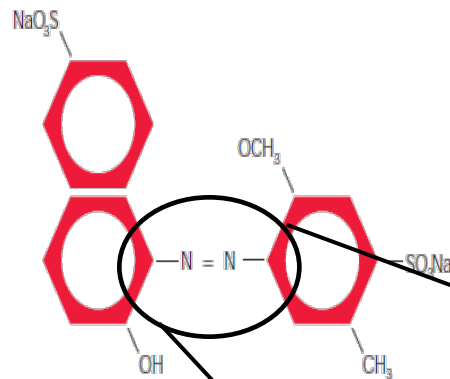
FD&C Blue #1

FD&C Blue #2



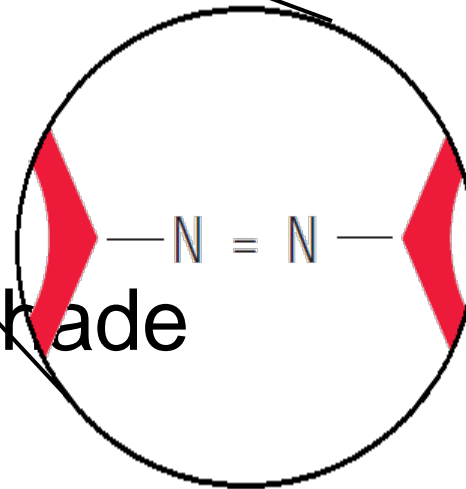
FD&C Red No. 40

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.

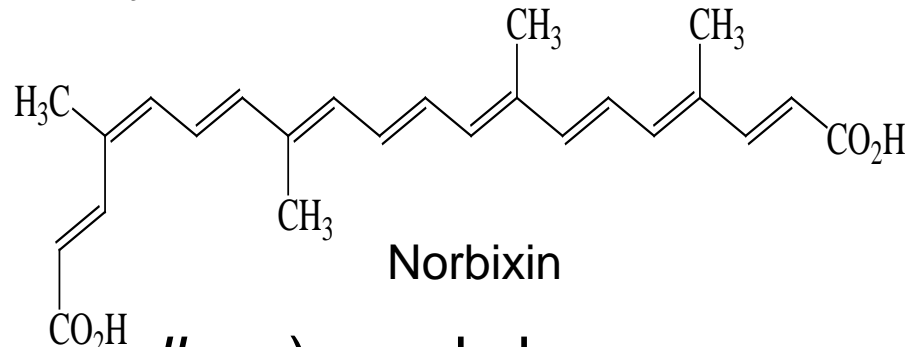
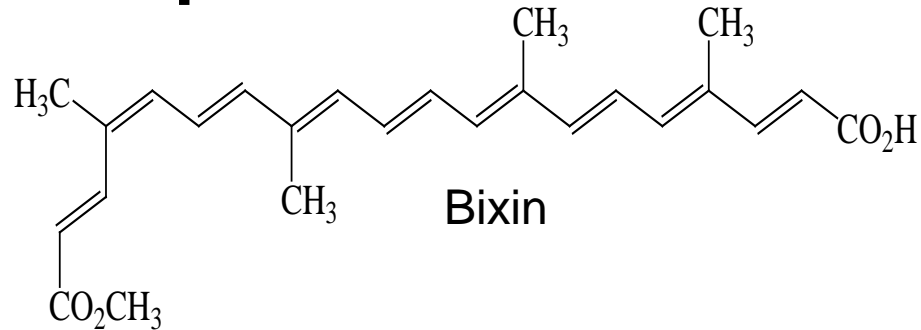
Exempt colors

Turmeric oleoresin, Riboflavin, Carmine/Cochineal, Chlorophyll, Sodium Copper Chlorophyll, Caramel, Beta carotene, Beta-apo-8’ Caroteneal, Annatto, Paprika Oleoresin, Tomato Lycopene, Canthaxanthin, 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

FAO/WHO, JECFA & Codex Alimentarius

- The work of JECFA feeds into Codex Alimentarius
- The GSFA is the Codex **G**eneral **S**tandard for **F**ood **A**dditives
 - 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.

129	Allura red AC	300 mg/kg		05.3
559	Aluminium silicate	100 mg/kg	 Note 174  Note 6	05.3
951	Aspartame	10,000 mg/kg	 Note 191  Note 161	05.3
	BENZOATES	1,500 mg/kg	 Note 13	05.3
901	Beeswax	GMP		05.3
133	Brilliant blue FCF	300 mg/kg		05.3



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**

- Stevenson J, Sonuga-Barke E, McCann D, Grimshaw K, Parker KM, Rose-Zerilli MJ, Holloway JW, Warner JO. (2010) Stevenson J, Sonuga-Barke E, McCann D, Grimshaw K, Parker KM, Rose-Zerilli MJ, Holloway JW, Warner JO. (2010) The role of histamine degradation gene polymorphisms in moderating the effects of food additives on children's ADHD symptoms, Am J Psychiatry 167(9)

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

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

Canada: <http://laws.justice.gc.ca/en/F-27/C.R.C.-c.870/index.html>

EU Website:

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

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

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

Australia/New Zealand:

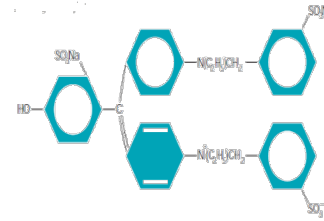
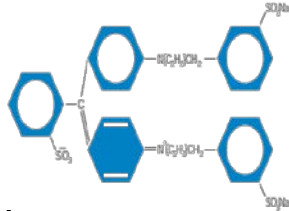
<http://www.foodstandards.govt.nz/the-code/foodstandardscode.cfm>



Safety Data Sets

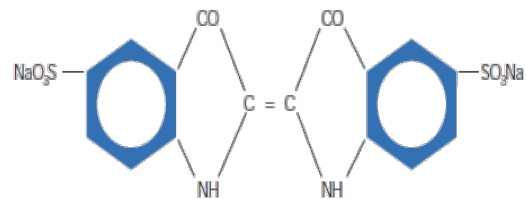
SAFETY OF COLORS IN THE UNITED STATES

FD&C Blue No. 1 & Green No. 3



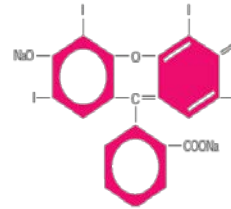
Name of color	FD&C Blue No. 1 Brilliant Blue FCF	FD&C Green No. 3 Fast Green FCF
In use since	1929	1927
Genetox	Negative	Negative
Acute/Subchronic	Rat	Rat
Chronic	Rats/Mice	Rats/Mice
Carcinogenicity	Rats/Mice	Rats/Mice
Reproductive/ Teratogenic	Neg/Neg	Neg/Neg
Special studies		
Human studies		
ADMEK	Diverse animals	Rats
JECFA ADI (mg/kg/d)	0-12.5	0-25

FD&C Blue No. 2



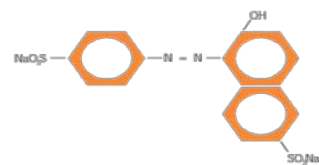
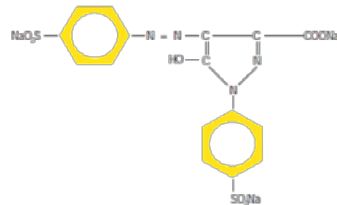
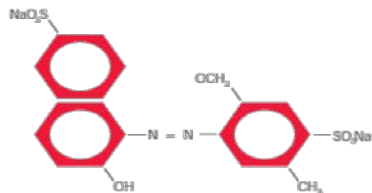
Name of color	FD&C Blue No. 2 Indigotine
In use since	1907
Genetox	Negative
Acute/Subchronic	Rat, Mouse/90-day
Chronic	Rats/Mice
Carcinogenicity	Rats/Mice
Reproductive/ Teratogenic	Neg/Neg
Special studies	
Human studies	
ADMEK	Rats
JECFA ADI (mg/kg/d)	0-5

FD&C Red No. 3



Name of color	FD&C Red No. 3 Erythrosine
In use since	1907
Genetox	Negative
Acute/Subchronic	Rat, Mouse
Chronic	Rats/Mice
Carcinogenicity	Rats/Mice
Reproductive/Teratogenic	Neg/Neg
Special studies	Thyroid/Mechanism of Action
Human studies	Thyroid
ADMEK	Rats
JECFA ADI (mg/kg/d)	0-0.1

FD&C Red 40, Yellow 5 & Yellow 6



Name of color	FD&C Red No. 40 Allura Red AC	FD&C Yellow No. 5 Tartrazine	FD&C Yellow No. 6 Sunset Yellow FCF
In use since	1971	1916	1929
Genetox	Negative	Negative	Negative
Acute/Subchronic	Animals	Mice	R,M/90d
Chronic	Rats/Mice	Rats/Mice	Rats/Mice
Carcinogenicity	Rats/Mice	Rats/Mice	Rats/Mice
Reproductive/ Teratological	Neg/Neg	Neg/Neg	Neg/Neg
Special studies		Allergenicity	Allergenicity
Human studies		Allergenicity	Allergenicity
ADMEK	Dogs, rats	Humans, animals	Humans, animals
JECFA ADI (mg/kg/d)	0-7	0-7.5	0-4

Exempt Colors

Name of color	Annatto Extracts (Bixin, Norbixin)	Grape Skin Extract (Anthocyanins)	Beet Red
In use since	1890		
Genetox	Negative	Negative	Negative
Acute/ Subchronic	Rat	Rat/90-day	Rat/14-day
Chronic	Rats/Mice		Rat
Oncogenicity	Rats/Mice		
Reproductive/ Teratological	Neg/Neg	Neg/Neg	Neg/Neg
Special studies	Allergenicity		
Human studies	Allergenicity		ADMEK
ADMEK		Animals	Animals/ Humans
JECFA ADI (mg/kg/d)	0-12 (Bixin)	None allocated	Not specified

Exempt Colors

Name of color	Curcumin	Carmines	Paprika Extract
In use since	1500 BC	1500	1500 BC
Genetox	Negative	Negative	Negative
Acute/ Subchronic	Rats,Mice/90d	Mice/90d	Mice
Chronic	Rats/Mice	Rats	
Oncogenicity	Rats/Mice	Rats	
Reproductive/ Teratological	Neg/Neg	Neg/Neg	
Special studies		Allergenicity	
Human studies		Allergenicity	
ADMEK	Rats		
JECFA ADI (mg/kg/d)	0-3	0-5	None allocated



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

FD&C (E-Number)	Common Name	Mix A	Mix B
FD&C Yellow 5 (E102)	Tartrazine	Present	Absent
E104	Quinoline yellow	Absent	Present
FD&C Yellow 6 (E110)	Sunset Yellow	Present	Present
E122	Carmoisine	Present	Present
E124	Ponceau 4R	Present	Absent
FD&C Red 40 (E129)	Allura Red AC	Absent	Present
E211 (Preservative)	Sodium benzoate	Present	Present

Children given either Mix A or Mix B during the 'challenge' periods