Harnessing chemical and toxicological data for the evaluation of food ingredients and packaging

Diane M. Schmit, Tammy Page, Kirk B. Arvidson, Patra Volarath, Leighna Holt

US Food and Drug Administration
Center for Food Safety and Applied Nutrition (CFSAN)
College Park, Maryland
Office Of Food Additive Safety (OFAS)

- OFAS is a program office within CFSAN
  - Ensure the safety of food ingredients and packaging (*and more*) in U.S.
    - Evaluate safety information in industry submissions
      - Direct food additives (*e.g.*, high intensity sweeteners)
      - Generally Recognized as Safe (GRAS – phosphoric acid)
      - Food contact substances (*e.g.*, plastic bottles, sanitizers)
      - Foods from GE plants (*e.g.*, herbicide-ready soybeans)
      - Color additives (for foods, drugs, cosmetics, devices)
Background & History

- **1958** Food additive amendments to the Federal Food, Drug and Cosmetic Act (FFDCA)
  - Petitions for direct additives, indirect additives, GRAS “list”
- **1960** Color additive amendments
  - Petitions for color additive petitions
Background & History

- **1969** President Nixon direction
  - Critical review of GRAS substances

- **1972** GRAS affirmations begin
  - Petitions for GRAS

- **1987** FDA Modernization Act (FDAMA)
  - Food contact notifications

- **1997** GRAS proposed rule
  - GRAS notifications
CFSAN
Chemical Information Management

• **1970s**: CFSAN Thesaurus - controlled vocabulary to be used across all Foods programs; data entered on punch cards and information viewed on paper printouts

• **1979**: The Scientific Information Retrieval and Exchange Network (SIREN) - bibliographic index using codes, interfacing with CFSAN Thesaurus to translate codes; documents were heavily indexed.

• **Late 1990s**: SIREN was replaced by FARM, a document repository system. Full text searching was implemented with a reduction in indexing.
CFSAN Thesaurus

- paper note cards
- punch cards with paper printouts
- database with limited direct access, but frequent printouts on microfiche
- Oracle database with GUI interface, but not user friendly
- STARI (2014)
STARI
Scientific Terminology And Regulatory Information

A user-friendly search and display for the CFSAN Thesaurus (an ontology of chemical, biological, technical, and foods regulatory data)
What’s in STARI?

• There are currently over 290,000 terms accessed through STARI, including
  – over 65,000 “preferred terms”
  – over 49,000 chemical substances (with CAS or CFSAN IDs)
  – over 110,000 synonyms, InChIs
  – over 1400 regulations (primarily 21 CFR 73-189 and 40 CFR 180-186) with over 9500 connections to specific substances
  – Over 37,000 CERES IDs crosslinked to CERES
  – over 12,000 UNII codes crosslinked to FDA SRS
  – relationships: broad/narrow, components

• Notes and comments are searchable.
  – Includes reference sources, additional regulations, definitions, etc.
STARI Chemical Substance Categories

Everything is connected to one or more categories

- Color additive (286)
- Direct food additive (821)
- FEMA GRAS substance (2751)
- Flavoring substance (3360)
- Food additive, not elsewhere classified (718)
- Food contact substance (303)
- GRAS list substance (1012)
- Indirect food additive (3468)
- Prohibited substance (31)
- Agrochemical substance (1199)
- Biological product (195)
- Cosmetic substance (5823)
- Drug for animal use (111)
- Drug for human use (6553)
- Nutritional substance (80)
- Pesticide chemical (1286)
- Toxin (465)
- Chemical, not elsewhere classified (29,807)
Search any term, CAS, code, regulation, partial or whole
More ways to search...

Advanced Search

Search for:
vanillin

In Field:
Term (all)

Contains  Starts With  Exact Match

Include comments/notes in search.

Search within these results

Boolean Search

Fill in one or more of the criteria to search for. Separate multiple words (or character strings) with spaces. Character strings may be whole or partial words or numbers, and may include common punctuation as is found in chemical names.

This Exact phrase:

ALL of these words: vanill glu

ANY of these words:

NONE of these words:

Include comments/notes in search.
Vanillin

VANILLIN

Notes: NF 18; 21 CFR 135.110, 163.111, 163.112, 163.113, 163.114, 163.117, 163.123, 163.130, 163.135, 163.140, 163.145, 163.150, 163.153, 163.155, 172.515; FCC III; FEMA 3107; MI 12, 10069; CCD 11

First Entered: Apr 24, 1995  Last Update: Jan 12, 2016

CAS Registry Number (or CFSAN ID*): 121-33-5

CERES ID: CRS-1931  Link to CERES (authorized users only)

FDA UNII: CHI530446X  Link to FDA SRS

International Chemical Identifier (InChI)

- InChIKey: MWOOGOJBHIARFG-UHFFFAOYSA-N  Link to Google search

  InChI=1S/C8H8O3/c1-11-8-4-6(5-9)2-3-7(8)10/h2-5,10H,1H3


Physical Properties

- Molecular Formula: C8H8O3
- Molecular Weight: 152.14
# Vanillin, categories, regulations

## Categories
- Cosmetic substance
- Drug for human use
- FEMA GRAS substance
- Flavoring substance
- GRAS list substance

## Related Information

### Regulation
- **21 CFR 182.60**
  - Link to 21 CFR 182.60
  - Synthetic flavoring substances and adjuvants.

- **21 CFR 182.90**
  - Link to 21 CFR 182.90
  - Substances migrating to food from paper and paperboard products.

- Substances migrating to food from paper and paperboard products.
Vanillin, synonyms, system

Other Names

**Synonym**
- 2-METHOXY-4-FORMYLPHENOL
- 3-METHOXY-4-HYDROXYBENZALDEHYDE
- 4-HYDROXY-3-METHOXYPHENYLACETALDEHYDE
- BENZALDEHYDE, 4-HYDROXY-3-METHOXY-
  - Chemical Abstracts 9th Collective Index
- METHYLPROTOCOLATECHUIC ALDEHYDE
- PROTOCOLATECHUALDEHYDE 3-METHYL ETHER
- VANILLALDEHYDE
- VANILLIC ALDEHYDE

System

- PAFA.Chemical

[Link to PAFA Report (authorized users only)]
Vanillin, component of

Component Of
- **ASAFETIDA**
  - FEMA 2107: Herbs of Commerce 2; CTFA ICID 8; MI 13, 828; Encyclopedia of Common Natural Ingredients; Natural Medicines Comprehensive Database; Hortus III; Natural Product Medicine.
- **CHAR SMOKE FLAVOR**
  - 21 CFR 133.181; Encyclopaedia of Food Science, Food Technology and Nutrition, p. 4161.
- **GUAIAC**
  - USAN 94; FCC IV; MI 13, 4566; USD 25; CCD 11: Fenaroli’s Handbook of Flavor Ingredients; 9 CFR 318.7 under Antioxidants and oxygen interceptors; 21 CFR 177.1010a5. CAS DEFINITION--EXTRACTIVES AND THEI
- **GUAIAC EXTRACT**
  - FEMA 2531: CTFA ICID 6. CAS DEFINITION--Extractives and their physically modified derivatives such as tinctures, concretes, absolutes, essential oils, oleoresins, terpenes, terpene-free fractions, dis
- **HICKORY SMOKE DISTILLATE**
  - CAS DEFINITION--HICKORY SMOKE DISTILLATE. PRODUCT MADE BY CONDENSATION OF SMOKE BEARING WATER VAPOR RESULTING FROM THE CONTROLLED BURNING OF HICKORY. IT CONSISTS PRIMARILY OF ACETIC ACID, DIMETHOXYPHE
- **OAK CHIP EXTRACT, WHITE**
  - FEMA 2794: Fenaroli’s Handbook of Flavor Ingredients.
- **VANILLA**
  - Hortus: Herbs of Commerce.
- **VANILLA ABSOLUTE**
  - Poucher’s Perfumes, Cosmetics and Soaps, vol. 1.
- **VANILLA EXTRACT**
  - SPICES AND HERBS FOR THE FOOD INDUSTRY, p. 167; ENCYCLOPEDIA OF COMMON NATURAL INGREDIENTS; 21 CFR 163.111, 163.112, 163.113, 163.114, 163.117, 163.123, 163.130, 163.135, 163.140, 163.145, 163.150, 163.
- **VANILLA OLEORESIN**
Search by regulations…

21 CFR 172.515
745 Preferred Terms found

• **1,1-DIMETHOXYOCTANE**
  ○ FEMA 2798.

• **1,1-DIMETHYL-3-PHENYLPROPYL ACETATE**
  ○ FEMA 2735.

• **VANILLIN ACETATE**
  ○ FEMA 3108; Fenaroli’s Handbook of Flavor Ingredients: Perfume and Flavor Chemicals, Arctander.

• **VERATRALDEHYDE**
  ○ FEMA 3109; PERFUME AND FLAVOR CHEMICALS, ARCTANDER; MI 12, 10084; DICTIONARY OF ORGANIC COMPOUNDS, D-05313; FCC IV-first supplement.

• **VERBENOL**
  ○ FEMA 3594.

• **ZINGERONE**
  ○ FCC IV; FEMA 3124; MI 12, 10301; CCD 11; DICTIONARY OF ORGANIC COMPOUNDS, H-02216; Fenaroli’s Handbook of Flavor Ingredients.
Broader Terms

PEG-20 OLEYL ETHER

Notes: CTFA ICID 5.

CAS Registry Number (or CFSAN ID*): 977057-53-6  
CERES ID: CRS-37684  
Link to CERES (authorized users only)

Categories
- Cosmetic substance
- Indirect food additive

Related Information

Regulation
- 21 CFR 175.105  
  Link to 21 CFR 175.105  Adhesives.
- 21 CFR 176.180  
  Link to 21 CFR 176.180  Components of paper and paperboard in contact with dry food.
- 21 CFR 177.1210  
  Link to 21 CFR 177.1210  Closures with sealing gaskets for food containers.

Other Names
- Synonym: 
  - ALPHA-CIS-9-OCTADECANYL-OMEGA-HYDROXYPOLY(OXYETHYLENE-20)
  - POLYETHYLENE GLYCOL 1000 OLEYL ETHER

- Cosmetic Label Name (INCI)
  - OLETH-20

- Trade/Proprietary Name
  - BRU 98  
    - CTFA ICID.
  - EMULPHOR ON-870  

System
- PAFA.Chemical  
  Link to PAFA Report (authorized users only)

Relationships with Other Terms

Broader Term
- PEG OLEYL ETHER

* CFSAN IDs (977------ or 80977------) are used when no CAS RN is found. See the STARI Help (dat
Narrow Terms, Component

curcuminoids

Scope Notes: USP 35.  

First Entered: Mar 21, 2013  Last Update: Apr 1, 2013  

CAS Registry Number (or CFSAN ID*): 80977189-44-8  

» Previous CAS/Temp. Reg. Num.: 80888489-81-4  

Categories  

• Chemical, not elsewhere classified  

Related Information

Narrow Term  

• bisdemethoxycurcumin  

• curcumin  

• demethoxycurcumin  

Relationships with Other Terms

Component Of  

• TURMERIC
  
  • Handbook of U.S. Colorants; MERGY, FOOD FLAVORINGS; USD 25; FENAROLI'S HANDBOOK OF FLAVOR INGREDIENTS, 3rd ed; FEMA 3085; MI 13, 9892; SPICES AND HERBS FOR THE FOOD INDUSTRY, P.79: 21 CFR 582.10;  

* CFSAN IDs (977------ or 80977------) are used when no CAS RN is found. See the STARI Help (data documentation).
## Polymers

### poly(butadiene-co-butyl acrylate-co-methyl methacrylate-co-styrene)

**Scope Notes:** FCN 452; FCN 1508. & Link(s) to FDA website  
**First Entered:** Sep 13, 2004  **Last Update:** Jul 9, 2015

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<th>CAS Registry Number (or CFSAN ID*)</th>
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</table>

**CERES ID:** CRS-15195  & Link to CERES (authorized users only)

**Categories**
- Food contact substance  
  
Feb 19, 2010

### Related Information

#### Other Names

**Synonym**
- 1,3-butadiene, polymer with butyl acrylate, methyl methacrylate and styrene
  - Chemical Abstracts 8th Collective Index  
- 2-propenoic acid, 2-methyl-, methyl ester, polymer with 1,3-butadiene, butyl 2-propenoate and ethenylbenzene
  - Chemical Abstracts 9th Collective Index  
- butadiene-butyl acrylate-methyl methacrylate-styrene copolymer  
- poly(1,3-butadiene-co-butyl 2-propenoate-co-ethenylbenzene-co-methyl 2-propenoate)  
- poly(1,3-butadiene-co-butyl acrylate-co-methyl methacrylate-co-styrene)

**Components**
- BUTADIENE  
- BUTYL ACRYLATE  
- METHYL METHACRYLATE  
- STYRENE
CERES Knowledgebase

- Chemical-Centric Food-Additives Knowledgebase
  - Desktop access to:
    - Regulatory data
    - Chemical data
      - Human intake values of food additives and their impurities
    - Toxicity data
    - Structure analog searching and data retrieval
    - MoA QSAR Models
    - Data entry tools
    - Electronic memoranda forms
Available Data

- >96,651 Chemicals with CAS RN
- >44,869 Chemical structures
- 22 Toxicity study types
  - *In vitro* assays → clinical studies
  - 11,300 toxicity tests
- >1796 Human intake values
- >9484 Regulatory references
CERES Central Terminal: TRAM

Welcome to CFSAN OFAS CERES
Your gateway to data and tools

Data
- CERES Database
- CFSAN OFAS FARM
- CFSAN OFAS STARI
- US FDA SRS
- CFSAN CEDI Database

Estimation Tools
- CERES Prediction
- CERES Read-across
- CERES TTC

Support Tools
- CERES myMemo
- CERES Chemistry
- CERES Thesaurus
- CERES Toxicity
- Report Issues
Query Results Page
Toxicity Test Results

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<th>Species</th>
<th>Strain</th>
<th>Sex</th>
<th>Route of Exposure</th>
<th>Test Duration</th>
<th>Dose Levels / Range</th>
<th>Endpoints</th>
<th>Comments</th>
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<td>Oral - Feed</td>
<td>2 year</td>
<td>50.0-1000.0 mg/kg/day</td>
<td>LOAEL (Study): 250.0 mg/kg/day</td>
<td>Show...</td>
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<td>Show...</td>
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# Treatment Level Data

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<th>Effect</th>
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<th>Treatment Related</th>
<th>Stat Sig</th>
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# Structure Analog Search

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Predictive Toxicity Endpoints
Toxicity Predictions

Prediction Results for compound #1

In database: Yes
CERES ID: CRS-4496
Name: METHYL SALICYLATE
Registry number(s): 8022-86-4;119-36-8;8024-84-2;648434-07-5
# studies in CERES: 42

Predictions for endpoint: Bacterial Reverse Mutagenicity

NEGATIVE

Probability (POSITIVE) = [0.067, 0.129]
CERES in silico Paradigm

*concern factor = exposure/threshold
eMemoranda

- Web based forms for scientific review staff
  - Prepopulate chem and tox data from CERES
  - Tox and chem memo dynamically linked
    - Automatic transfer exposure values to Tox memo
      - Eliminates recreating exposure tables
  - Updates of CERES data from eMemos
    - No manual data collection or processing
  - Track key chem and tox determinations
OFAS Public Web Inventories
Food Ingredient and Packaging Inventories

Food Contact Substances Inventories
- Food Contact Substances (FCS): Inventory of Effective Food Contact Substance Notifications
- Cumulative Estimated Daily Intake (CEDI) Database for Food Contact Substances
- Indirect Additives Used in Food Contact Substances
- Recycled Plastics in Food Packaging
- Threshold of Regulation (TOR) Exemptions

GRAS Substances Inventories
- GRAS Notice Inventory
- Database of Select Committee on GRAS Substances (SCOGS) Reviews
- Enzyme Preparations Used in Food (partial list)
- Microorganisms and Microbial-Derived Ingredients that are Used in Food (partial list)

Food and Color Additive Petitions
- Petitions Under Review or Held in Abeyance
- Final Rules Issued from 2000 to present
- Summary of Color Additives Listed for Use in Foods, Drugs, Cosmetics and Medical Devices in the US

Direct Food Additives & GRAS Substances
- EAFUS (Everything Added to Food in the United States): A Food Additive Database
## Inventory of Food Contact Substance (FCS) Notifications

<table>
<thead>
<tr>
<th>FCN No. (sorted Z-A)</th>
<th>Food Contact Substance</th>
<th>Manufacturer</th>
<th>Effective Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1604</td>
<td>Isotridecanol phosphate condensation product with butylidenetris(2-(1,1-dimethylethyl)-5-methyl-4, 1-phenylene).</td>
<td>ADEKA Corporation</td>
<td>Jan 9, 2016</td>
</tr>
<tr>
<td>1592</td>
<td>Copolymers of acrylamide, diallyldimethylammonium chloride, 2-methylen eketanedioc acid and propenoic acid.</td>
<td>Palsmine Technology, Inc./Hanna Chemicals, Inc.</td>
<td>Dec 9, 2015</td>
</tr>
</tbody>
</table>
## Indirect Additives (with 21 CFR)

<table>
<thead>
<tr>
<th>CAS Reg. No.* (or other ID)</th>
<th>Substance* (sorted A-Z)</th>
<th>21 CFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1338-08-5</td>
<td>GLYCERIN-MALEIC ANHYDRIDE</td>
<td>177.1200</td>
</tr>
<tr>
<td>25395-31-7</td>
<td>GLYCEROL DIACETATE</td>
<td>177.1200</td>
</tr>
<tr>
<td>27902-24-5</td>
<td>GLYCEROL DIRICINOLEATE</td>
<td>178.3130</td>
</tr>
<tr>
<td>25791-96-2</td>
<td>GLYCEROLPOLYOXYPROPYLENE TRIOLE</td>
<td>175.105 177.1680</td>
</tr>
<tr>
<td>2540-54-7</td>
<td>GLYCEROL TRICINOLEATE</td>
<td>178.3130</td>
</tr>
<tr>
<td>42220-19-9</td>
<td>GLYCERYL BORATE</td>
<td>175.105 177.2900</td>
</tr>
<tr>
<td>1338-10-9</td>
<td>GLYCERYL LACTOSTEARATE</td>
<td>176.170</td>
</tr>
<tr>
<td>1323-68-8</td>
<td>GLYCERYL MONOBUTYL RICINOLEATE</td>
<td>175.105 176.170</td>
</tr>
<tr>
<td>26402-22-2</td>
<td>GLYCERYL MONOCAPRATE</td>
<td>176.180</td>
</tr>
<tr>
<td>1323-42-8</td>
<td>GLYCERYL MONOHYDROXY STEARATE</td>
<td>175.105</td>
</tr>
<tr>
<td>1323-43-9</td>
<td>GLYCERYL MONO-12-HYDROXYSTEARATE</td>
<td>176.170 176.200 177.1200 177.1210 177.2800</td>
</tr>
<tr>
<td>68553-08-2</td>
<td>GLYCERYL MONOHYDROXY TALLOWATE</td>
<td>175.105 176.216</td>
</tr>
<tr>
<td>1323-38-2</td>
<td>GLYCERYL MONORICINOLEATE</td>
<td>176.170 178.3130</td>
</tr>
</tbody>
</table>
### Search Food Ingredient and Packaging Inventories

To search across all datasets listed below, enter a term(s) in the basic or advanced search below.

To search a specific dataset, or to learn more about a specific dataset, click on the dataset name below.

(Note: Additional search features and examples are listed with individual datasets.)

Additional datasets are listed at Food Ingredients and Packaging Inventories.

#### Basic Search

Fill in one or more of the criteria to search for. Separate multiple word (or character string) entries with spaces.

(Character strings may be whole or partial words or numbers, and may include common punctuation as is found in chemical names.)

<table>
<thead>
<tr>
<th>This Exact phrase:</th>
<th>whey protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL of these words:</td>
<td></td>
</tr>
<tr>
<td>ANY of these words:</td>
<td></td>
</tr>
<tr>
<td>NONE of these words:</td>
<td></td>
</tr>
</tbody>
</table>

#### Results

<table>
<thead>
<tr>
<th>Results</th>
<th>Dataset Name</th>
<th>Updated</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 Hits</td>
<td>Biotechnology Consultations on Food from GE Plant Varieties</td>
<td>Feb 22, 2015</td>
</tr>
<tr>
<td>0 Hits</td>
<td>Food Additive and Color Additive Petitions Under Review or Held in Abeyance</td>
<td>Jan 4, 2016</td>
</tr>
<tr>
<td>2 Hits</td>
<td>GRAS Notices</td>
<td>Nov 30, 2015</td>
</tr>
<tr>
<td>0 Hits</td>
<td>Indirect Additives used in Food Contact Substances</td>
<td>Jan 15, 2016</td>
</tr>
<tr>
<td>5 Hits</td>
<td>Inventory of Effective Food Contact Substance (FCS) Notifications</td>
<td>Jan 29, 2016</td>
</tr>
<tr>
<td>0 Hits</td>
<td>Inventory of Environmental Impact Decisions for Food Contact Substance Notices</td>
<td>Dec 31, 2015</td>
</tr>
<tr>
<td>0 Hits</td>
<td>New Protein Consultations (Early Food Safety Evaluation)</td>
<td>Sep 17, 2015</td>
</tr>
<tr>
<td>0 Hits</td>
<td>SCOCS (Select Committee on GRAS Substances)</td>
<td>Jan 7, 2016</td>
</tr>
<tr>
<td>0 Hits</td>
<td>Submissions on Post-Consumer Recycled (PCR) Plastics for Food-Contact Articles</td>
<td>Feb 12, 2015</td>
</tr>
<tr>
<td>0 Hits</td>
<td>Threshold of Regulation (TOR) Exemptions</td>
<td>Mar 4, 2016</td>
</tr>
</tbody>
</table>
FCN No. 531
GE Healthcare

According to Section 409(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act, food contact substance notifications (FCNs) are effective only for the listed manufacturer and its customers. Other manufacturers must submit their own FCN for the same food contact substance and intended use.

Food Contact Substance: Agarose, polymer with (chloromethyl)oxirane, 2-hydroxy-3-(2-hydroxy-3-(trimethylammonio)propoxy)propyl ethers, sulfate salts (CAS Reg. No. 846053-13-2).

Notifier: GE Healthcare
Manufacturer: GE Healthcare
Intended Use: As an ion exchange resin.

Limitations/Specifications:
For repeated use in extracting individual proteins or substances present in similar low concentrations from liquid, water-based food materials, such as milk, whey, fruit juice, beer and wine. For continuous use, the process conditions will be between pH 3 and 12 and temperatures below 40°C. Use at pH 12 up to 40°C is limited to a maximum of 2000 hours over the resin lifetime. Cleaning at 20°C may take place at up to pH 14, cleaning at 40°C conducted at up to pH 13.7, and cleaning at 60°C conducted at up to pH 13.3.

Effective Date: Oct 26, 2006
National Environmental Policy Act (NEPA)** Submission: Categorical Exclusion 25.32(j)
FDA Decision: Categorical Exclusion Memo
## GRN No. 37

<table>
<thead>
<tr>
<th>Substance:</th>
<th>Whey protein isolate and dairy product solids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intended Use:</td>
<td>Whey protein isolate - use in foods in general, including meat, for multiple technical effects; dairy product solids - use in foods in general, including alcohol, for multiple technical effects</td>
</tr>
<tr>
<td>Basis:</td>
<td>Scientific procedures</td>
</tr>
<tr>
<td>Notifier:</td>
<td>American Dairy Products Institute</td>
</tr>
<tr>
<td></td>
<td>300 West Washington Street #400; Chicago, IL 60606</td>
</tr>
<tr>
<td>Date of filing:</td>
<td>Jan 14, 2000</td>
</tr>
<tr>
<td>GRAS Notice (releasable information):</td>
<td>37</td>
</tr>
<tr>
<td>Date of closure / FDA’s Letter:</td>
<td>Apr 21, 2000</td>
</tr>
<tr>
<td></td>
<td>FDA has no questions (additional correspondence available)</td>
</tr>
<tr>
<td>Additional correspondence:</td>
<td>Additional correspondence clarifying the term &quot;dairy product solids&quot;: Jan. 30, 2001</td>
</tr>
<tr>
<td>GRP:</td>
<td>1G0371</td>
</tr>
</tbody>
</table>
### Coming…

**Regulatory Status of Color Additives**

<table>
<thead>
<tr>
<th>CAS Reg. No. (or other ID code)</th>
<th>Color</th>
<th>Status</th>
<th>Use (Restrictions)</th>
<th>End Notes</th>
<th>21 CFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>9004-92-0</td>
<td>D&amp;C Yellow No. 10</td>
<td>Permanently listed, certification required</td>
<td>Drugs, Cosmetics, Devices (Drugs generally. Modification of uses and restrictions. Cosmetics generally. Contact lenses.)</td>
<td>3, 4, 5, 6, 7</td>
<td>74.1710</td>
</tr>
<tr>
<td>8003-22-3</td>
<td>D&amp;C Yellow No. 11</td>
<td>Permanently listed, certification required</td>
<td>Drugs, Cosmetics (Externally applied drugs. Externally applied cosmetics.)</td>
<td>4, 5, 6</td>
<td>74.1711</td>
</tr>
<tr>
<td>2321-07-5</td>
<td>D&amp;C Yellow No. 7</td>
<td>Permanently listed, certification required</td>
<td>Drugs, Cosmetics (Externally applied drugs. Externally applied cosmetics.)</td>
<td>4, 5, 6</td>
<td>74.1707</td>
</tr>
<tr>
<td>516-47-8</td>
<td>D&amp;C Yellow No. 9</td>
<td>Permanently listed, certification required</td>
<td>Drugs, Cosmetics (Externally applied drugs. Externally applied cosmetics.)</td>
<td>4, 5, 6</td>
<td>74.1708</td>
</tr>
<tr>
<td>8417-85-2</td>
<td>D&amp;C Yellow No. 9</td>
<td>Delisted, formerly subject to certification</td>
<td>None, formerly Drugs, Cosmetics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>130-20-1</td>
<td>7,16-dichloro-6,15-dihydro-5,3,14,16-anthrazoneetrone</td>
<td>Permanently listed, exempt from certification</td>
<td>Devices (Contact lenses.)</td>
<td>3</td>
<td>73.3119</td>
</tr>
<tr>
<td>86316-86-1</td>
<td>2-[2,5-diethoxy-4-[1-2]-methylphenyl]-thio(phenylazo)-1,3,5-benzene</td>
<td>Permanently listed, exempt from certification</td>
<td>Devices (Formed in situ in soft contact lenses to mark L and R NTE 1.1x10^-7 glens.)</td>
<td>3</td>
<td>73.3115</td>
</tr>
<tr>
<td>82-18-8</td>
<td>N.N'-(9,10-Dihydro-9,10-dioxo-1,5-anthracenediyl)bisbenzamide</td>
<td>Permanently listed, exempt from certification</td>
<td>Devices (Contact lenses.)</td>
<td>3</td>
<td>73.3118</td>
</tr>
</tbody>
</table>
D&C Violet No. 2
Permanently listed, certification required

| CAS Registry Number (or other ID code): | 81-48-1 |
| Status: | Permanently listed, certification required |
| Use: | Drugs, Cosmetics, Devices |
| Restrictions: | Externally applied drugs. Externally applied cosmetics. NTE 0.2% by wt in glycolic-lactic acid polyester absorbable sutures; NTE 0.3% in polydioxanone synthetic absorbable sutures; NTE 0.25% in epsilon caprolactone/glycolide copolymer absorbable sutures; NTE 0.1% in poly epsilon caprolactone absorbable sutures; NTE 0.2% in glycolide/dioxanone/methylene carbonate tripolymer absorbable sutures; NTE 0.2% in absorbable sutures from homopolymers of glycolide; contact lenses; NTE 0.2% of intraocular lens haptics; NTE 0.15% by wt of meniscal tacks. |
| Other names: | 1-HYDROXY-4-((4-METHYLPHENYL)AMINO)-9,10-ANTHRACENEDIONE |
| | 1-HYDROXY-4-(F-TOLYLAMINO)ANTHRACINONE |
| | 1-HYDROXY-4-P-TOLUIDINOANTHRACINONE |
| | 9,10-ANTHRACENEDIONE, 1-HYDROXY-4-((4-METHYLPHENYL)AMINO)- |
| | ALIZUROIL PURPLE |
| | ANTHRACINONE, 1-HYDROXY-4-P-TOLUIDINO- |
| | C.I. 80725 |
| | C.I. DISPERSE BLUE 72 |
| | C.I. SOLVENT VIOLET 13 |
| | CALCO OIL VIOLET 2/R |
| | DISPERSE BLUE 72 |
| | MACROLEX VIOLET B |
| | SOLVENT VIOLET 13 |
| See also: | D&C Blue No. 3 |
| Color additive regulations in 21 CFR: | 74.1602 |
| | 74.2602 |
| | 74.3602 |
| | 81.30 |
| | 82.1002 |
# D&C Violet No. 2

Permanently listed, certification required

<table>
<thead>
<tr>
<th>Citation</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 FR 3391; Sep 16, 1939; Specifications</td>
<td>Drug and cosmetic use. Converted D&amp;C Blue No. 3.</td>
</tr>
<tr>
<td>25 FR 9759; Oct 12, 1960; Provisional Regulation</td>
<td>Provisional drug and cosmetic use.</td>
</tr>
<tr>
<td>30 FR 4534; Apr 8, 1965; Postponement of closing dates for provisional listing</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Citation</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>55 FR 5898; May 7, 1990; Final Rule</td>
<td>For coloring intraocular lens haptics.</td>
</tr>
<tr>
<td>55 FR 31423; Aug 8, 1990; Final Rule, confirmation of effective date</td>
<td></td>
</tr>
<tr>
<td>58 FR 50105; Nov 15, 1993; Final Rule</td>
<td></td>
</tr>
<tr>
<td>59 FR 3998; Jan 29, 1994; Final Rule, confirmation of effective date</td>
<td></td>
</tr>
<tr>
<td>60 FR 6171; Mar 14, 1994; Final Rule</td>
<td>For coloring sutures for general surgery.</td>
</tr>
<tr>
<td>59 FR 56420; May 19, 1994; Final Rule, confirmation of effective date</td>
<td></td>
</tr>
<tr>
<td>60 FR 20096; Apr 23, 1995; Final Rule</td>
<td>For coloring poly (ε-caprolactone) absorbable sutures for general surgery.</td>
</tr>
<tr>
<td>63 FR 45943; Aug 28, 1998; Final Rule, confirmation of effective date</td>
<td>Not to exceed 0.2% by weight of the suture material for coloring glycolide/dioxanone/trimethylene carbonate tripolymer absorbable sutures for use in general surgery.</td>
</tr>
<tr>
<td>63 FR 32803; Jun 18, 1990; Final Rule</td>
<td>For absorbable meniscal tack made from poly(L-lactic acid).</td>
</tr>
<tr>
<td>64 FR 57974; Oct 28, 1999; Final Rule, confirmation of effective date</td>
<td></td>
</tr>
<tr>
<td>65 FR 36234; Jul 10, 2000; Final Rule</td>
<td>In absorbable sutures prepared from homopolymers of glycolide for general surgery.</td>
</tr>
</tbody>
</table>
Future Directions

• Enhance data updates
  – Increase efficiency and accuracy of data
    • Two-way links between OFAS databases
    • eMemos
      – Collect data within scientific review workflow

• Increase data sharing/transparency
  – Center (CFSAN), Agencies, International and Public
  – Design databases so it is easy to share
Contacts

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Tammy Page – tammy.page@fda.hhs.gov

CERES
Kirk Arvidson – kirk.arvidson@fda.hhs.gov

US Food and Drug Administration
Center for Food Safety and Applied Nutrition (CFSAN)
College Park, Maryland

ACS CINF 129, March 16, 2016