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The Basics of the U.S. FDA's Food Contact Materials Regulations

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Agenda

- Brief Overview of FDA's Regulation of Food Contact Materials
- FDA's Food Contact Notification Program
- Questions and Answers

FDA's Regulation of Food Contact Materials

Overview-
Food, Drug, and Cosmetic Act of 1938

- 402(a) of the Act:
- Created the statutory imperative within the food industry to protect against the adulteration of food
- Packaging materials employed could not contaminate food
- Food industry began to insist on assurances
- Packaging manufacturers and their suppliers sought informal opinions from FDA and USDA ("No-objection" Letters)

Overview – Food Additives Amendment of 1958

“The Turning Point”

Legislation enacted to require FDA pre-clearance of food additives

Section 201(s) of the Act Defines

“Food Additive” as:

Any Substance Reasonably Expected to Become a Component of Food When Used as Intended Unless...

Prior Sanctioned

Generally Recognized as Safe (GRAS)

Overview - Three Types of Food Additives

- **Direct**

Food Ingredients

(technical effect in food)

- **Secondary Direct**

Added to Food During Processing But Removed

(No technical effect in food)

- **Indirect**

Food-Contact (Packaging) Materials

(No technical effect in food)

A Few Options to Consider - Clearing a New Packaging Component

- Food Additive Regulation under parts 170-199 of 21 CFR
- Generally Recognized as Safe position
- Prior Sanction letter from FDA or USDA prior to 1958
- “No migration/no food-additive” position
- As of January 18, 2000, an effective **Food Contact Notification**

A Few Options to Consider - Clearing a New Packaging Component

- **Food Additive Regulation under parts 170-199 of 21 CFR**

FDA's Food Additive Regulations 21 C.F.R. Parts 170 to 199

- Part 175 – Adhesives and Coatings
- Part 176 – Paper and Paperboard
- Part 177 – Polymers (single-use and repeated-use)
- Part 178 – Adjuvants, Production Aids, and Sanitizers
- Part 181 – Prior-Sanctioned Substances
- Parts 182, 184, and 186 – GRAS Substances

A Few Options to Consider - Clearing a New Packaging Component

- Food Additive Regulation under parts 170-199 of 21 CFR
- **Generally Recognized as Safe position**

"Generally Recognized as Safe"

- A GRAS position can be premised on:
  - A listing in Part 182, 184, or 186 of 21 CFR
  - Self-determination:

    1) Common use in food prior to 1958

    2) Scientific procedures – the necessary published toxicological data supporting the conclusion

    Data demonstrating *de minimis* dietary exposure (Canadian Center for Toxicology papers)

A Few Options to Consider - Clearing a New Packaging Component

- Food Additive Regulation under parts 170-199 of 21 CFR
- Generally Recognized as Safe position
- **Prior Sanction letter from FDA or USDA prior to 1958**

Prior Sanctions

- FDCA exempts any substance that is the subject of a *prior sanction* letter issued by FDA or USDA prior to 1958
  - Some listed in Part 181
  - Some listed in A.J. Lehman's 1956 article *Food Packaging Materials*, published in Association of Food and Drug Officials of the United States
  - Private letters

Must look at limitations of prior sanction

e.g., if prior sanction is for use of a compound in PET bottles, then cannot rely on prior sanction to use compound in polyolefin films

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- **“No migration/no food-additive” position**

"No Migration-No Food Additive" Position

Monsanto v. Kennedy: Substance must migrate into food in more than insignificant amounts to consider it a food additive

- "No migration" conclusion is usually based on:
  - Migration testing
  - 100% migration calculations
  - Diffusion calculations that model extraction testing
- Default - 50 parts per billion analytical sensitivity
- High-end-use applications (soda, beer, milk, and infant formula containers): ≤10 ppb
- Toxicologically significant substances: ≤10 ppb

Other Exemptions To Consider

- Housewares Exemption
- Functional Barrier
- Basic Resin Doctrine

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FDA's Food Contact Notification Program

FCN - System Overview

- Food and Drug Administration Modernization Act of 1997
  - Effective January 18, 2000

- Significant change in 40-year old FDA system of regulating food packaging materials

FCN – Faster FDA Action

Old System

Food additive petition process

2-4 years

New System

Food contact notification process

120 days

FCN – Notifications Are Proprietary

Old System

Anyone could rely on a regulation

New System

Effective only for company that filed the notification and its customers

Competitors must file their own notifications

FCN – What is a Food Contact Substance?

- Any substance intended for use as a component of materials used in manufacturing, packing, packaging, transporting, or holding food

- If such use is not intended to have a technical effect in food

FCN – What Can be the Subject of an FCN?

Indirect additives

- Polymers
- Starting substances (monomers, polymerization aids, etc.)
- Adjuvants
- Packaging compounds subject to irradiation

Secondary direct additives

- Defoamers
- Ion exchange resins

(Technical effect in food during processing only)

FCN – What Cannot be the Subject of an FCN?

- Materials that cannot be cleared by an FCN:
  - Direct additives (by definition have a technical effect in finished food)

FCN – Replacing Petitions and Regulations

No more Food Additive Petitions for packaging materials

EXCEPT: Where FDA requires one

Food Additive Regulations will remain in effect, but will not be expanded

FCN - Key Components

- Form 3480 http://www.cfsan.fda.gov/~dms/opa-fcn.html)
- Copies of relevant data/reports/studies
- Comprehensive Toxicology Profile
- Environmental Assessment (if needed)

FCN - Data Requirements

Virtually the same as for a food additive petition

- Chemical identity
- Manufacturing process
- Intended conditions of use
- Migration data
- Dietary exposure (CEDI)
- Toxicity data
- Environmental impact assessment (if required)

FCN -Toxicity Data Recommendations

Tiered approach:

- Potential health risk likely to increase as exposure increases
- Therefore, data requirements increase as exposure increases

FCN – Toxicity Data Recommendations

CEDI	TOXICITY DATA
<0.5 ppb	No data needed (relevant known data);
0.5-50 ppb	Genotoxicity studies: Ames test + in vitro cytogenetic damage or mouse lymphoma
50 ppb–1 ppm	Above, plus in vivo cytogenetic damage assay, plus 2 subchronic studies: 90-day rodent (rat) 90-day non-rodent (dog)
>1 ppm	Chronic (2 yr) rodent studies, 1 yr feeding study in dogs and multigeneration reproductive studies in rats Note: FAP usually required

FCN – The 120-day Clock

FDA's "receipt" of a "complete" FCN triggers the 120-day review period

- Receipt = receipt by FCN review office
- Complete = no substantial data missing

If deemed incomplete, FDA will send a deficiency notice

- 10-Day response deadline
- For substantial deficiencies or late responses, receipt date is the date the remaining data is submitted

FCN – Customer Assurances

FDA will send a letter stating the FCN is “effective”; the letter will identify:

- Food-contact substance
- Notifier
- Manufacturer/supplier
- Intended use
- Limitations/specifications

FDA’s Inventory of Effective FCNs

http://www.cfsan.fda.gov/~dms/opa-fcn.html

FDA's Inventory of Effective FCNs

FCN No.	Food Contact Substance (FCS)	Notifier / Manufacturer of the FCS	Intended Use	Limitations/ Specifications	Effective Date	Environmental Review
1	Silver sodium hydrogen zirconium phosphate, rhombohedral framework structure, of the general formula $Ag_xNa_yH_zZr_2(PO_4)_3$ x=(0.1-0.5); y=(0.1-0.8); z=(0.1-0.8)	Milliken & Company Toagosei Company, Ltd.	Antimicrobial additive for polymeric food-contact materials	Limitations/ Specifications	Mar 1, 2000	EA/ FONSI
2	GENOX TM EP, chemically identified as Amines, bis (hydrogenated rape-oil alkyl) methyl, N-oxides (CAS Reg. No. 204933-93-7)	GE Specialty Chemicals GE Plastics	An antioxidant and/or stabilizer	Limitations/ Specifications	Mar 9, 2000	EA/ FONSI
3	Styrene-acrylic copolymers produced by polymerizing a minimum of 72 parts by weight of styrene with a minimum of 4 parts of methyl methacrylate and with up to 10 parts total of any one or more of the following monomers: butyl methacrylate, methacrylic acid, butyl acrylate, acrylic acid and allyl methacrylate	Rohm and Haas Company Rohm and Haas Company	As components of coatings for paper and paperboard in compliance with 21 CFR 176.170(b)	Limitations/ Specifications	Mar 9, 2000	EA/ FONSI
4	Isophthalic acid or dimethyl isophthalate	BP Amoco BP Amoco	As a monomer in the manufacture of ethylene terephthalate - isophthalate copolymers	Limitations/ Specifications	Mar 15, 2000	EA/ FONSI
5	Polybutadiene - graft - poly(methyl acrylate- co-acrylonitrile) (CAS Registry No. 27012-62-0)	BP Amoco Chemicals, Inc. BP Amoco Chemicals, Inc.	Fabricating beverage containers	Limitations/ Specifications	Mar 14, 2000	EA/ FONSI
6	Completely hydrolyzed copolymer of acrylonitrile and trivinylcyclohexane ion-exchange resin (CAS Registry No. 109961-42-4)	Rohm and Haas Company Rohm and Haas Company	Treating potable water	Limitations/ Specifications	Mar 17, 2000	EA/ FONSI

FDA's Inventory of Effective FCNs

FCN No.	Intended Use	Limitations/ Specifications
1	Antimicrobial additive for polymeric food-contact materials	For use only at levels not to exceed 2% by weight of the polymer. Conditions of use are limited to those for which the polymer has been established as safe with a silver content not to exceed 10% by weight of the compound.
2	Antioxidant in polypropylene	For use only at levels not to exceed 0.1 weight percent polypropylene complying with 21 CFR 177.1520. The finished copolymers may be safely used in single-use as well as repeated-use applications involving contact with food of types I, II, IV-B, VI, VII-B, and VIII, under Conditions of Use B through H, as described in 21 CFR 176.170 (c), Tables 1 and 2
3	Use of styrene...	For use at levels not to exceed 20 percent by weight of the total coating solids.
4	As a monomer in the manufacture of ethylene terephthalate-isophthalate copolymers.	The finished copolymers must contain from 3 to 17 weight percent ethylene isophthalate units. The finished copolymers must also meet specifications in 21 CFR 177.1630(f) - (j) appropriate to their intended use.
5	Fabricating beverage containers	Nitrile rubber modified acrylonitrile-methyl acrylate copolymers consist of 8 to 10.5 percent by weight of butadiene-acrylonitrile copolymers containing approximately 70 percent by weight of polymer units derived from butadiene. Adjuvant substances permitted for use in copolymers complying with 177.1480 may be used in the subject copolymers. The finished copolymers must meet any applicable specifications prescribed in 21 CFR 177.1480 and may be safely used as components of articles intended for food-contact use only under Conditions of Use E and F as described in 21 CFR 176.170(c) Table 2. Paragraph 177.1480(d) not withstanding, the finished copolymers are authorized for use in fabricating bottles intended as containers for beverages as defined in 21 CFR 170.3(n)(3), (7) only under Conditions of Use E and F, (16), (35) and (36), with exception of soft drinks and coffee substitutes. The finished copolymers are to meet the following specifications: 1. residual acrylonitrile monomer content not more than 4 parts per million as determined by gas chromatography, 2. melt index in the range 2 to 6 grams per 10 minutes as determined by ASTM method D 1238-95 under the conditions 200 degrees C, 27.5 pounds, 0.0824 inches diameter x 0.3145 inches length.
6	Treating potable water	Adjuvant substances permitted for use in ion-exchange resins complying with 21 CFR 173.25 may be used in the subject ion-exchange resin subject to any limitations in the authorizing regulation or notification. The finished ion-exchange resin must meet any applicable specifications prescribed in 21 CFR 173.25

FCN – Revocation of an Effective FCN

If FDA determines that the intended use of the FCS is no longer safe, it will contact the notifier in writing stating this determination

- Notifier is given an opportunity to rebut this determination by an assigned deadline

If FDA still finds that the FCS is unsafe, a notice will be published in the Federal Register

- Final Agency action

FCN – "Me Too" FCNs

FCNs are proprietary to the notifier, but others can file an FCN for the same food contact substance

A "me too" FCN often requires substantially less data:

- Obtain original FCN through FOIA
- Can often reference and rely upon migration and toxicology data in original FCN
- Must supply information on manufacturing process, impurities, specifications, etc.

FCN – Changes after the FCN is Effective

Substantive changes to the FCS specifications or manufacturing process require submission of a new FCN

- Changes within GMP are not considered substantive, e.g., cleaner impurity profile

Changes in the intended use (use level, food types, conditions of use) require submission of a new FCN

FCN – Meeting with FDA

Prenotification Conferences (PNC)

- Obtain FDA advice/input prior to filing
- Helps avoid questions during the review period
- FDA assigns a PNC number which should be referenced in the FCN

How Well is the FCN System Working?

- As of May 2007, over 600 effective FCNs posted on FDA's Web site
- Most FCNs become effective 120 days after submission (FDA does not typically "reset" the clock)
- Overall: A Success!

FCN – Documents You Should Know About

FDA guidance documents:

- Administrative
  http://www.cfsan.fda.gov/~dms/opa2pmna.html
- Chemistry
  http://www.cfsan.fda.gov/~dms/opa2pmnc.html
- Toxicology
  http://www.cfsan.fda.gov/~dms/opa2pmnt.html
- Environmental
  http://www.fda.gov/ohrms/dockets/98fr/03d-0379-gdl00001.pdf
- FDA regulations found at: http://www.cfsan.fda.gov/~lrd/fr020521.html

Questions and Answers

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Thank you!

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