



Overview of FDA's Program for Reviewing New Food Contact Substances

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Nutrition Facts
Serving Size 1 Cup (28g)
Serving Per Container about 3

1958 Food Additives Amendment to the Federal Food, Drug, and Cosmetic Act (FD&C Act)

- Requires pre-market approval of new uses of food additives.
 - “any substance the **intended use** of which results or may **reasonably be expected** to result, **directly or indirectly**, in its becoming a **component** or otherwise affecting the characteristics of any food”
 - “including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food”
- Established the standard of safety, the standard of review, and formal rulemaking procedures for food additives.



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Standard of safety: Reasonable Certainty of No Harm

(Legislative History of the FD&C Act)

“The concept of safety used in this legislation involves the question of whether a substance is hazardous to the health of man or animal. Safety requires proof of a **reasonable certainty that no harm** will result from the proposed use of an additive. It does not -- and cannot -- require proof beyond any possible doubt that no harm will result under any conceivable circumstance.”



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Formal rulemaking procedures: petitions and CFR

- Interested party petitions the agency
 - The petition process is the scientific, administrative, and legal basis for issuing food additive regulations
- FDA reviews the data submitted and makes a determination of safety
- Results in a regulation in Title 21 of the Code of Federal Regulations (21 CFR)
 - Regulations are generic and anyone or company in compliance with the conditions outlined in the authorizing regulation may use the additive
 - For example, 21 CFR 175.300 (Resinous and polymeric coatings)



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1997 FDA Modernization Act

- Amendment to FD&C Act to establish a premarket notification process for food contact substances (FCSs)
 - “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 any technical effect in such food”
- This notification process is intended to replace the petition process as the primary means for authorizing new uses of food additives that are food contact substances
- Standard of safety and standard of review are the same for direct food additives and food contact substances



Features of a Food Contact Substance Notification (FCN)

- 120-Day review period after receipt of a complete submission
- Listed in our [Inventory of Effective Notifications](#)
- Exclusive for the manufacturer or supplier



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The FCN: Demonstrating Human Safety

- The FCN has the following parts:
 - Identity of Substance
 - Substances, not formulations
 - Intended use (Chemistry review)
 - Exposure information (Chemistry review)
 - Safety Narrative (Toxicology review)
 - An Environmental Assessment or Claim of Categorical Exclusion (Environmental Review).



FCN Chemistry Information

- **Chemistry data** is reviewed to establish the identity of a food-contact substance and for assessing potential consumer exposure to the substance.
- The sponsors or notifiers must provide supporting analytical data.

<http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm081818.htm>



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FCN Chemistry Information

- Identity
- Physical/chemical specification
- Manufacturing Information
- Impurities
- Conditions of Use
- Technical Effect
- Stability

What is the FCS?

What has the potential to migrate?

- Migration Levels in Food
- Exposure Estimates

How much is migrating?

How much are we consuming?



Migration Levels in Food

- Migration data is used by FDA to assess potential **consumer exposure** to a substance
- Migration levels in food may be estimated by:
 - **Migration Testing**
 - **Calculation**
 - **100% migration assumption**
 - **Diffusion theory calculation**



Typical Migration Testing

- **Accelerated temperature/time conditions** intended to simulate thermal processing and extended storage
- Consistent with the intended conditions of use with respect to **use level, food types and temperatures**
- Use of food **simulating solvents** rather than real foods



Exposure Assessment

- To estimate probable **consumer exposure** in terms of **concentration** (ppb or ppm) of the FCS in the **daily diet** or **Estimated Daily Intake** (EDI, mg/person/day) of the substance
- **Combine** migration levels determined from migration studies with **packaging information** on uses of food contact articles that contain the FCS



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Packaging Factors

- **Food-type distribution factor (f_t)** – distribution of packaging use among food types

- **Example:** polymer coated metal

$$f_{(aq)} = 0.16, f_{(acidic)} = 0.35, f_{(al)} = 0.40, f_{(fatty)} = 0.09$$

- **Consumption factor (CF)** – fraction of the daily diet expected to contact specific packaging materials

- **Example:**

Metal (polymer coated)	0.17
Metal (uncoated)	0.03



Concentration of FCS and its impurities in the Daily Diet

- **Total migration of the FCS ($\langle M \rangle$)**

$$\langle M \rangle = F_{aq} (M_{aq}) + F_{acidic} (M_{acidic}) + F_{alcohol} (M_{alcohol}) + F_{fatty} (M_{fatty})$$

- **Dietary Concentration (DC)**

$$DC = \langle M \rangle \times CF$$

= μg migrant/g food or ppb in the daily diet

- **Estimated Daily Intake (EDI)**

$$EDI = 3000 \text{ g food/person/day} \times DC$$



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Exposure Estimate Calculation Example

- FCS is copolymer intended for use as component in can coatings
- Food types : aqueous, acidic, and fatty foods
- Maximum temperature of 121 °C (250 °F)
(High temperature, heat sterilized or retorted)
- Possible migrants:
 - FCS oligomers, monomer A, monomer B, Impurity C



Exposure Estimate: Example

Migration Testing

- Test sample: Coating containing FCS
- Food simulants: 10% ethanol – aqueous and acidic foods,
miglyol – fatty foods
- Test conditions: High temperature, heat sterilized or retort
- Test samples analyzed for possible migrants



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Exposure Estimate: Example

Migration Testing

Exposure Calculation

Chemical	Migration 10% Ethanol (µg/g)	Migration Miglyol (µg/g)
FCS oligomer	500	600
Monomer A	50	60
Monomer B	40	80
Impurity C	< 5.0	< 5

For FCS oligomer:

$$\langle M \rangle = \sum F_i (M_i)$$

$$\langle M \rangle = F_{aq}(M_{aq}) + F_{acidic}(M_{acidic}) + F_{fatty}(M_{fatty})$$

$$\langle M \rangle = (0.16)(500\text{ppb}) + (0.35)(500\text{ppb}) + (0.09)(600)$$

$$\langle M \rangle = 309 \text{ ppb}$$

$$DC = CF \langle M \rangle = 0.05 (309 \text{ ppb}) = 15.5 \text{ ppb} = 15.5 \mu\text{g FCS/g food}$$

$$EDI = DC (3\text{kg/p/d}) = 46.5 \mu\text{g/p/d}$$



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Exposure Estimate: Example

Chemical	Migration 10% Ethanol (µg/g)	Migration Miglyol (µg/g)	<M> (ppb)	DC (ppb)	EDI (µg/p/d)
FCS oligomer	500	600	309	15.5	46.5
Monomer A	50	60	31	1.6	4.7
Monomer B	40	50	27.6	1.4	4.1
Impurity C	< 5.0	< 5	<3	<0.2	<0.5



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Thank you