



SOT FDA Colloquia on Emerging Toxicological Science Challenges in Food and Ingredient Safety

Overview of Regulatory Science of Food Contact Substances

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Conflict of Interest Statement

- None



About FDA

FDA is responsible for over \$2 trillion in medical products, food, cosmetics, dietary supplements and tobacco.

FDA-regulated products account for about 20 cents of every dollar of annual spending by U.S. consumers.

The agency has approximately 16,200 full-time employees located around the world.

FY 2017 budget is \$4.99 billion.



About the Office of Food Additive Safety (OFAS)



Responsible for the safety of food ingredients, food packaging and food processing equipment, including sources of radiation used to treat or inspect food, and foods derived from bioengineered plants.

Premarket safety reviews of food and color additive petitions, GRAS notices, and food-contact notifications.



More OFAS

- Responsible for:
 - Food additives
 - Color additives
 - Food contact materials
 - GRAS (generally recognized as safe) ingredients
 - Food products using biotechnology
- 138 full-time employees
- FY 2017 budget is \$6.1 million



Focus: Food Contact Substances

- This talk presents a brief overview of the approval process for food contact substances (FCS).
 - Roles and responsibilities
 - Review and safety standards
 - Concept of harm
 - General overview of the process
- Most of the details of the process will be presented by Dr. Jessica Cooper.



What is a Food Contact Substance?

- Food and Drug Administration Act of 1997 defined food contact substances as “***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 such food.***”



Examples of Food Contact Substances

- Adhesives
- Coatings
- Paper and paperboard components
- Polymers, monomers
- Colorants
- Antioxidants
- Production aids
- Sanitizers



The Notification Process

- The Food Contact Notification (FCN) process is the primary means by which FDA authorizes new uses of food additives that are food contact substances (FCSs).
- This FCN process replaces the previous food additive petition (FAP) process for indirect additives.
- FDA can decide if the FAP process is more appropriate
 - When the exposure to the FCS under the proposed use conditions is high.
- FCN is exclusive to the manufacturer/supplier.



When Should an FCN be Submitted?

- FCNs are required only for:
 - New FCS
 - New use of a FCS
 - New manufacturing process
 - New manufacturer/supplier
- Before submitting an FCN, the notifier may submit a prenotification consultation (PNC) request to discuss the eligibility of the FCS, and the adequacy of the information supporting the proposed use of the FCS.



Roles and Responsibilities

- The **notifier** has the burden to demonstrate a “***reasonable certainty of no harm***” from the intended use of the ingredient.
- This requires that the **FDA** assess whether it has received adequately documented answers to appropriate questions of probative value.



REASONABLE CERTAINTY OF NO HARM

- “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.”
- Harm: “an effect is harmful if it affects health, not if it is simply an undesirable or unexpected effect that has no adverse health consequences.”



FCN Program in General

- Same safety standard and basic data recommendations as FAP
 - Chemistry, Toxicology, and Environmental information prepared per our guidance for industry.
- FCN is effective 120 days after an FCN is accepted unless FDA objects.
- If FDA concludes that there is a reasonable certainty of no harm caused by the intended use, the agency will allow the FCN to become effective.
- Effective FCNs are listed on [CFSAN website](#) (transparent to the public).



Review and Safety Standards

- Standard of review
 - Fair evaluation of all of the data
 - Made in the absence of complete knowledge
 - Decisions are time-dependent
 - Must withstand scientific, procedural, and legal challenge from all sides
- Standard of safety
 - Safety-based approval (not risk:benefit analysis)
 - Reasonable certainty of no harm

These standards are the same for food and color additives, GRAS substances, and food contact substances.



Food Contact Substance (FCS) Safety Assessment

- **What exactly is the food ingredient and how much is there in food?** (Details provided by J. Cooper)

Identity

- Chemical Name and CAS Number
- Structure and Molecular Weight
- Physical Characteristics

Manufacturing Process

- Full description of process
- List of chemicals/reagents used

Specifications

- Typically proposed by petitioner or reference published specs (FCC)
- Should include description of the additive, identification tests, purity assay, and limits for impurities/contaminants

Stability

- Data demonstrating the stability
- Discussion of the fate of the additive

Technical Effect and Use

- Type of food and use level
- Data to show that the use level is the minimum needed to achieve the technical effect

Analytical Methodology

- If a use limitation of the additive is required for safe use, the petition must include a method able to quantify the substance for the purpose of enforcing the limit

Dietary Intake

Technical Review of an FCN

Chemistry	Toxicology	Environmental
<ul style="list-style-type: none">• Identity• Manufacture• Specifications• Intended use & technical effect• Stability• Use level• Migrant levels in food• Exposure assessment	<ul style="list-style-type: none">• Data/information supporting the safety of the proposed use of the FCS• Safety Narrative• Comprehensive Toxicological Profile (CTP)-summary and critical evaluation of all available toxicology data used in the safety assessment	<ul style="list-style-type: none">• A claim of categorical exclusion <p>OR</p> <ul style="list-style-type: none">• An Environmental Assessment (EA)

Interaction with USDA: If the FCS is intended for use with meat and poultry, they review its suitability.



References

- Code of Federal Regulations
 - [21 CFR 170 Subpart D-Premarket Notifications](#)
- [FDA Ingredients, Packaging, and Labeling web page](#)
- [Inventory of Effective FCNs](#)
- We have a form for that!
 - Premarket Notification for New Use of a Food Contact Substance (FCN), a Pre-notification Consultation (PNC), and a submission of a Food Master File (FMF).
 - [FDA Form No. 3480: \(PDF - 311KB\)](#)
 - [Letter to Stakeholders: Older Versions of Form 3480 No Longer Accepted \(PDF - 27KB\)](#)
 - [FDA Form No. 3480 \(Instructions\): \(PDF - 95KB\)](#)
 - Amendment to an FCN, PNC, or FMF.
 - [FDA Form No. 3480a: \(PDF - 64KB\)](#)
 - [FDA Form No. 3480a \(Instructions\): \(PDF - 153KB\)](#)

