US Food Contact Regulation & Standard

-- Facilitating U.S. Market Entry for Food Contact Materials

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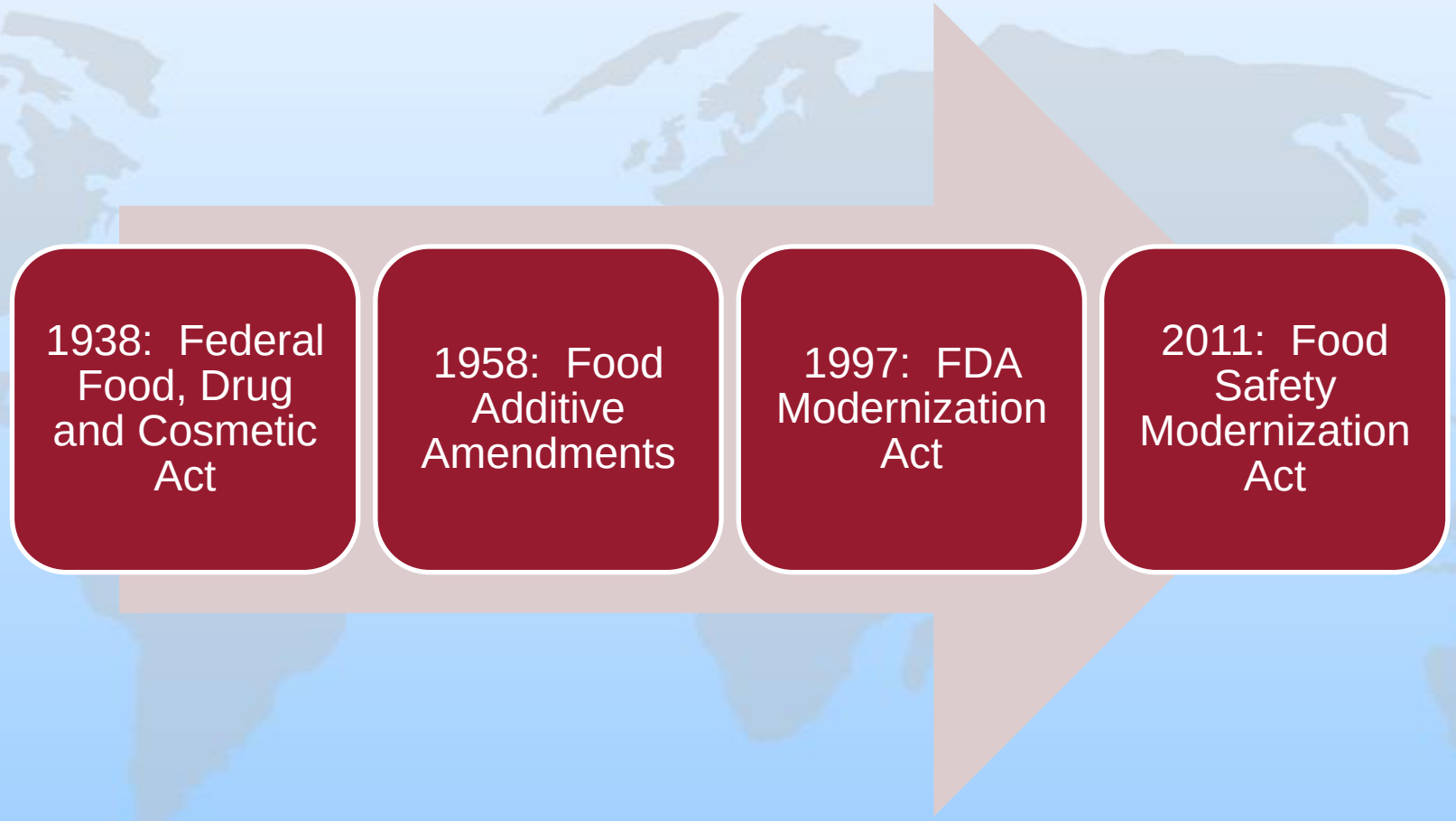
Topics

- Overview of major U.S. laws governing food additives and food-contact substances (FCS)/food-contact materials (FCM)
- Regulatory options and processes for premarket safety review of FCS/FCM
- *FDA's approach to the safety review of FCS – FCN program*

Major U.S. Food Additive Laws



Major U.S. Food Additive Laws

- **The Federal Food Drug and Cosmetic Act (FDC Act) of 1938:** Giving FDA broad responsibilities to control use of food additives without pre-market clearance authority
- **Food Additive Amendment of 1958:** Establishing **pre-market approval** system for direct and indirect food additives – establish food additive partition process

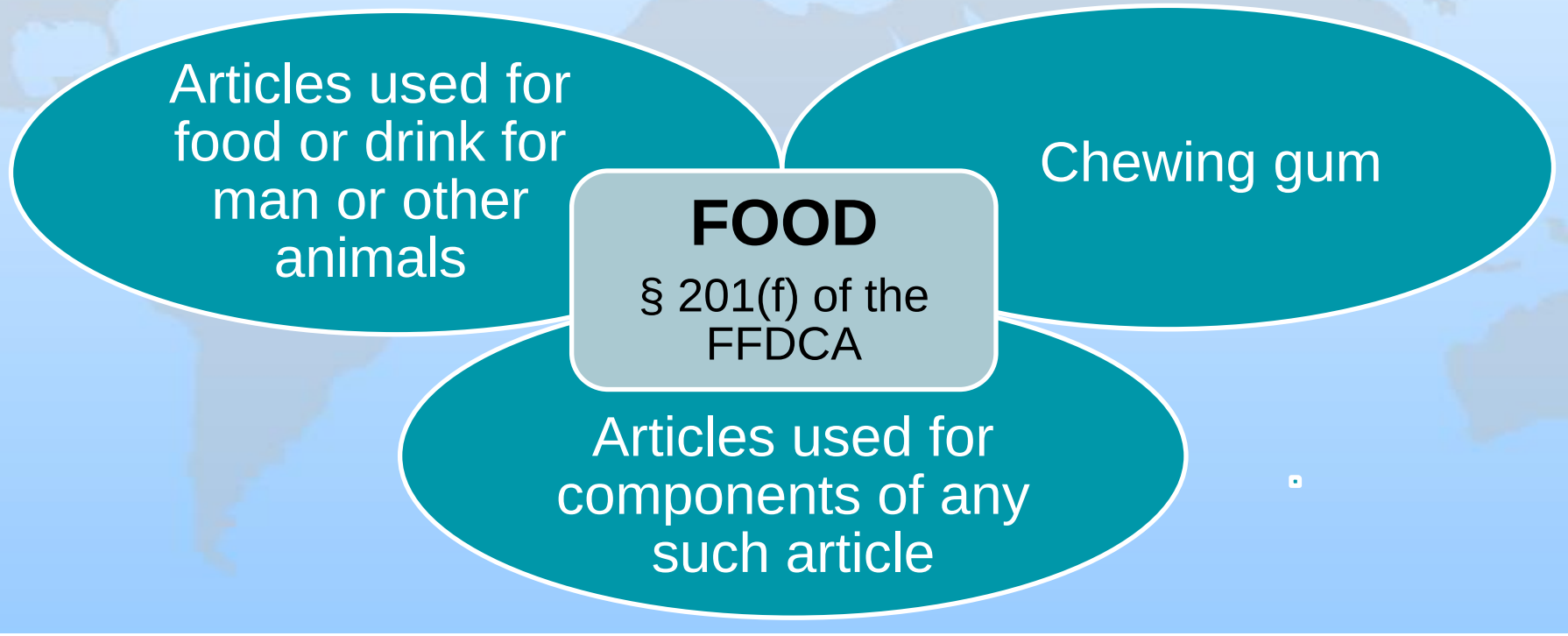
Major U.S. Food Additive Laws

- **Food and Drug Administration Modernization Act (FDAMA) of 1997:** Establishing **Food Contact Notification** process for authorizing the safe use of food contact substances

- **Food Safety Modernization Act of 2011:** Improving safety and security of U.S. food supply through prevention rather than response; "Importer accountability" is a key component; etc.

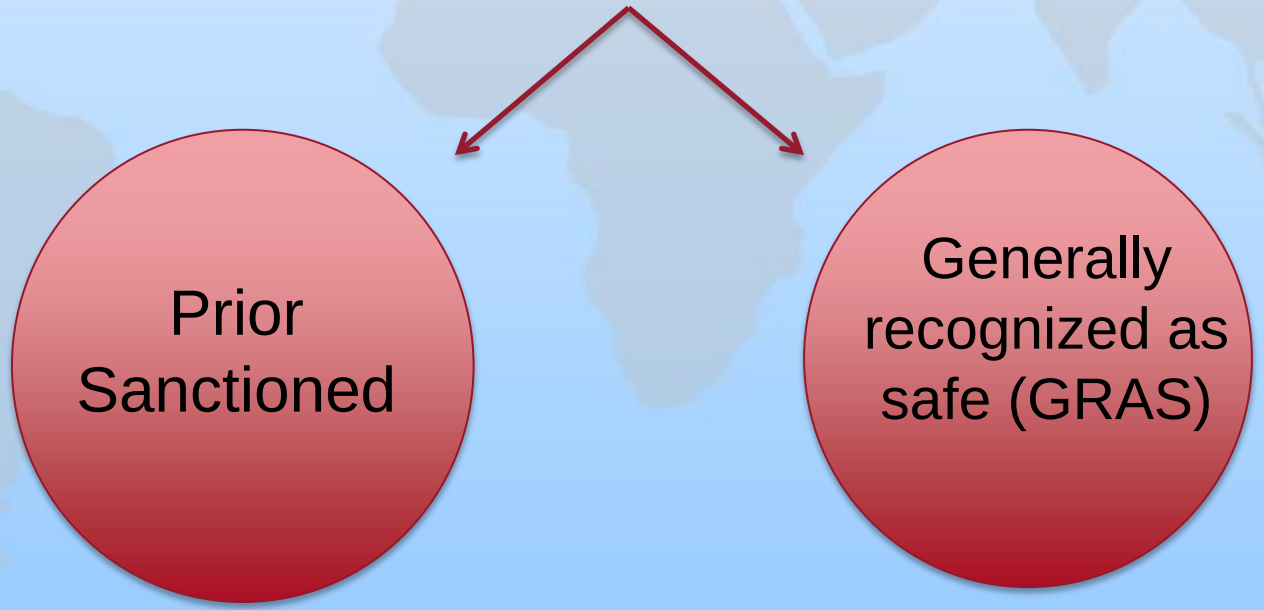
What Is Food?

- 1906: “Food” shall include all articles used for food, drink, confectionery, or condiment by man or other animals, whether simple, mixed, or compound
- From 1938 on:



What Is a Food Additive?

"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 . . .
if such substance is not"



Prior Sanction

- Letters issued by FDA or USDA prior to 1958
  - 21 C.F.R. Part 181
  - A.J. Lehman's 1956 article "Food Packaging Materials"
  - Private company letters
- Prior sanctions viewed narrowly–limitations matter
  - Apply to specific use of a substance delineating level(s), condition(s), and product(s) set forth by explicit pre-1958 FDA/USDA approval
- Caveat: new safety concerns may impact prior sanctions
- Narrowly interpreted

Prior-Sanctioned Substances

21 CFR Part 181, Subpart B

Section 23 – Antimycotics (e.g. sorbic acid)

Section 24 – Antioxidants (e.g. BHA, BHT)

Section 27 – Plasticizers (e.g. dibutyl sebacate)

Section 28 – Release agents (e.g. oleamide)

Section 29 – Stabilizers (e.g. calcium oleate)

Section 30 – Substances used in the manufacture of paper and paperboard products used in food packaging (e.g. PEG 400)

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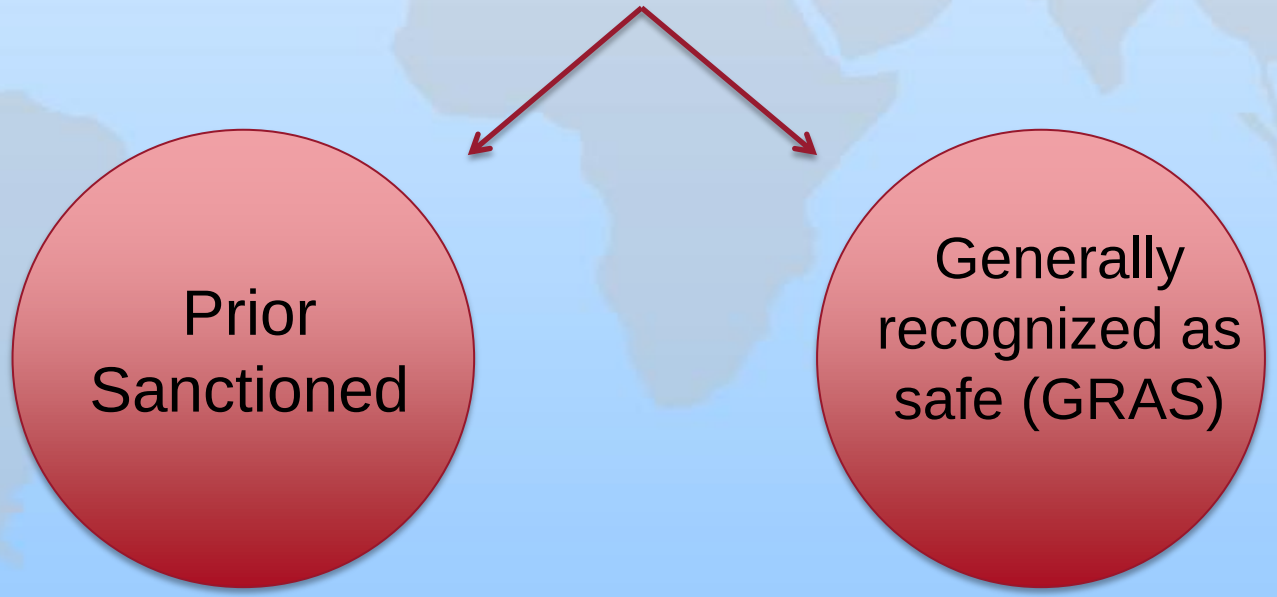

What Is GRAS?

The use of a substance added directly or indirectly to food is a food additive. . . if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use . . .

Generally Recognized As Safe (GRAS)

21 CFR Parts 182, 184 and 186

- **182** – Substances generally recognized as safe
- **184** – Direct food substances affirmed as generally recognized as safe
- **186** – Indirect food substances affirmed as generally recognized as safe

- *GRAS Notices listed on FDA's website:* https://www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices

GRAS Factors: Section 170.30

- Views of qualified scientific experts
- Common knowledge in the scientific community about the safety of the substance
- Same quantity and quality of scientific evidence required for food additive approval
- Based on published studies

GRAS and Other Determinations

- Binding on the manufacturer who makes the determination but not on FDA
- Non - zero risk of FDA action
  - Conduct assessments following FDA guidelines
  - Ensure conflict of interest is addressed
- Greatest risk may not be FDA action
  - NGO activity
- GMPs and intended use

FDA's GRAS Notice Process

- Does Not Result In An FDA Approval
- FDA Reviews a GRAS Notice In 180 Days
- GRAS Determinations Must Be Based On The Same Quality And Quantity Of Information As a Food Additive (Including Food Contact Substance) Approval
- FDA's Review Results In
  - A no questions letter
  - A letter stating that the GRAS notice is not sufficient
  - A letter acknowledging a request to cease review
- Remember GRAS determinations are temporal

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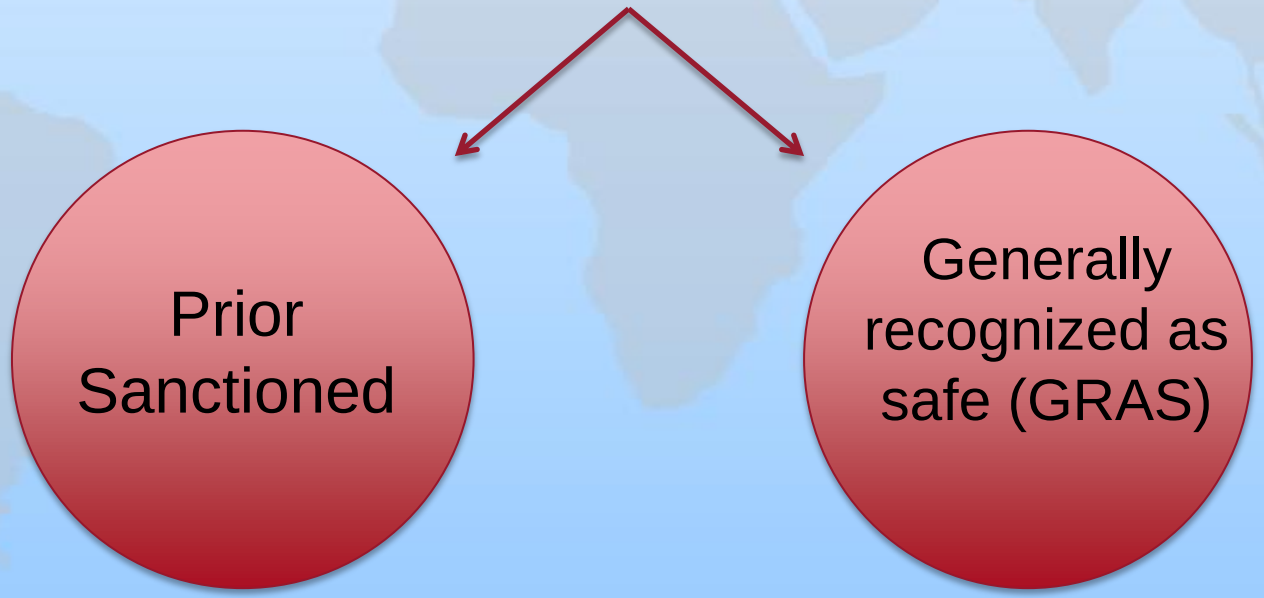


The U.S. Food's "Additive" Universe

Direct Food Ingredients

Sweeteners; Preservatives; Nutrients; Fat substitutes; Texturizers (thickeners, emulsifiers, etc.); Flavors

Color Additives

In food, animal feed, drugs, cosmetics, and medical devices (i.e., sutures and contact lenses)

"GRAS" Ingredient uses

Enzymes; Fibers; Proteins; Lipids; Sugars; MSG; Antimicrobials; Phytosterols/stanols; Flavors; Infant formula ingredients

Foods/Ingredients produced using modern biotechnology

Plants w/ herbicide resistance or insect resistance; delayed ripening, etc.

Processing Aids

Antimicrobials (meat and poultry processing); Defoamers; Ion exchange resins

Food Irradiation Equipment

To process food

To inspect food

Food Packaging / Food Contact Substances.

Coatings (paper, metal, etc.); New/recycled plastics including both polymers and monomers; Paper; Adhesives; Ingredients in pkgs. (i.e., colorants; antimicrobials; antioxidants, etc.); Packaging materials for use during food irradiation; Food packaging "formulations"

Regulatory Options for Premarket Safety Review of Food Additives and Food Contact Substance/materials

- Food Additive Petition (**FAP**)
- Threshold-of-Regulation exemption(**TOR**)
- Food Contact Notification (**FCN**)

Food Additive Amendment of 1958

- **Definition of food additive:** "Any substance the intended of which results or reasonably expected to result – ***directly or indirectly*** – in its becoming a component …. To be safe under the **conditions of its intended use** ….."
- **Food Additive Petition** process: All new food additives or new uses of regulated food additives subject to premarket review and approval by FDA

General Safety Standards

- Definition – “Safety requires proof of a ***reasonable certainty*** that no harm will result ……. It ***does not- and cannot-*** require proof beyond any possible doubt that no harm……”
- **Absolute safety** of any substance can ***never be proven***.

Delaney Anti-Cancer Clause

- General safety standards inapplicable to carcinogenic food additives
- Use of a food additive that ***has been shown to induce cancer in humans or animals upon oral ingestion*** *can not be approved*
- **No level of exposure** to a carcinogenic food additive can be considered safe under the **FDC Act**.

Food Additive Petition (FAP)

- Packaging material **not legal** until FDA publishes a **regulation** to permit its use
- Regulation written to be **generic**. Applicable to everyone who has the same product for the same use
- Regulations to be composed of 3 parts: identity of the additive, chemical and physical specifications, and limitations on the condition of its use
- 21 CFR (Code of Federal Regulations), Parts 175-179: FDA's "**positive lists**"

21 CFR Parts 175-179

- **Part 175** – Adhesives and components of coatings
- **Part 176** – Paper and paperboard components
- **Part 177** – Polymers
- **Part 178** – Adjuvants, production aids and sanitizers
- **Part 179** – Irradiation in the production, processing and handling of food

Examples of Subparts and Sections

Part 177 – Polymers

Subpart B – Substances for use as basic components of single and repeated use food-contact surfaces

Section 1520 – Olefin polymers

i.e. 177.1520(a)(3)(i)(*c*)(*2*)

Subpart C – Substances for use only as components of articles intended for repeated use

Threshold of Regulation Exemption (TOR) Process and Criteria

- **Regulation listing exempted** for food-contact substances that meet TOR requirements (Part 170.39 in 21 CFR)
- **A faster process** than food additive petitions
- Estimated **consumer exposure** to the food -contact material not exceeding **0.5 ppb** in the daily diet
- **No evidence** that the material is **carcinogenic** in man or animal
- No **structural basis** for suspecting the material to be a carcinogen or potent toxin

Information for a TOR Submission

- Identity and composition
- Conditions of use – temperature, type of food contact, repeated or single use, etc.
- Chemistry data needed by FDA to assess the probable consumer exposure to the additive or other migrating materials (i.e. impurities)
- Results of analyses of the existing toxicological information on the additive and its impurities
- Environmental impact information
- TOR Exemptions listed on FDA's website: https://www.accessdata.fda.gov/scripts/fdcc/?set=TOR

FDA Modernization Act (FDAMA) of 1997

- Established the FCN program as a more efficient and preferred new process
- Defined a food contact substance (FCS)

- Made approval proprietary
- Mandated confidentiality during review process
- Maintained same safety standard as FAP's
- Mandated a decision in 120 days

The FCN Program

From Food Additive Regulations

- Found at 21 C.F.R. Part 174 – 186
- Resulted from the submission of Food Additive Petitions
- Process could take 2-4 years (or longer)
- Generic approval

To Food Contact Notifications

- Food and Drug Administration Modernization Act of 1997, § 409(h)
- Program effective January 18, 2000
- FDA regulations at: 21 C.F.R. §170.100 *et seq*.
- 120 day review
- Online inventory lists all effective FCNs
- Manufacturer specific

Data Required for Safety Evaluation

- **Chemistry data** for confirming identity of a food-contact substance and for assessing potential consumer exposure to the substance and its impurities
- **Toxicology data** for use as basis for establishing a safe level of consumer exposure to the substance and its impurities
  (Chemistry and toxicology data should be on substances ***expected to migrate to food*** under the conditions of intended use)
- **Environmental data** for consideration of impact on human environment

What's Needed for an FCN (Or Any Food Contact Evaluation)

Chemistry information

- Chemical identity and composition of FCS
- Properties and specifications
- Manufacturing process
- Impurities and breakdown products

Conditions of intendent use

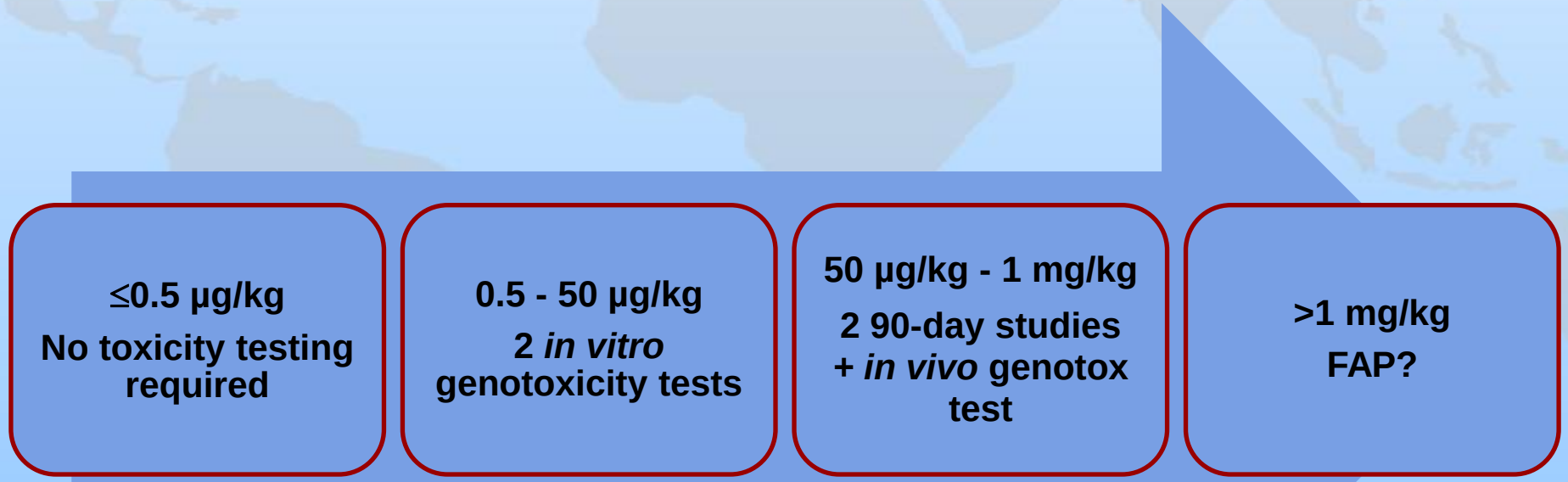
- Use level
- Single/repeat use
- Food types
- Conditions of Use

Migration and exposure

- Level of migration, as determined by calculations, modeling, or testing
- Estimation of dietary exposure, including cumulative exposure

FDA's Safety Review

- Cumulative exposure values are compared to available toxicity data on the FCS
  - The main exposures are generally to oligomers and monomers
    - Oligomer exposure to species below MW of 1000
    - Safety data specifically on oligomers is acceptable
    - Safety data on monomers may be acceptable depending on structural analysis
- Toxicity data recommendations (based on DC):



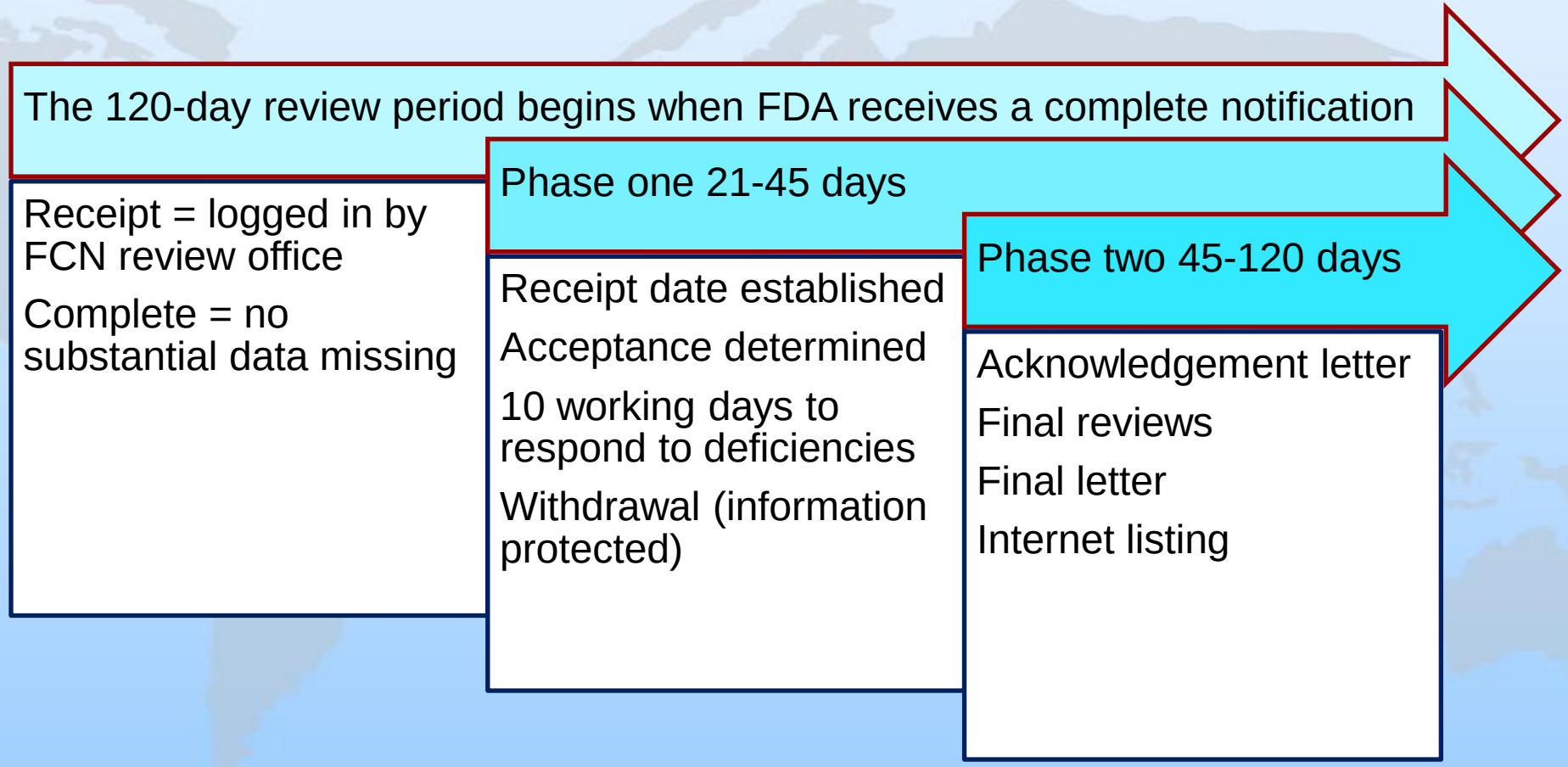
FDA's Environmental Review

- Allowing an FCN to become effective is an agency action and the FCN must contain:
- An Environmental Assessment (EA)

  or

- A warranted claim of categorical exclusion from the requirement to prepare an EA (21 CFR 25.15)
- Statement regarding no extraordinary circumstances

The Phases of FDA's Review



Key Steps in FCN Review Process

Phase 1 review:

Within 3-4 weeks from official receipt date of FCN to determine, through a cursory review of the various components of a submission, whether any major deficiencies or obvious problems exist which will affect the acceptability of the submission as a notification.

- Acknowledgement letter - if the FCN is accepted at phase 1 meeting
- Deficiency letter - minor deficiencies, require a response within 10 working days
- Withdraw letter - if the FCN is not acceptable for further review

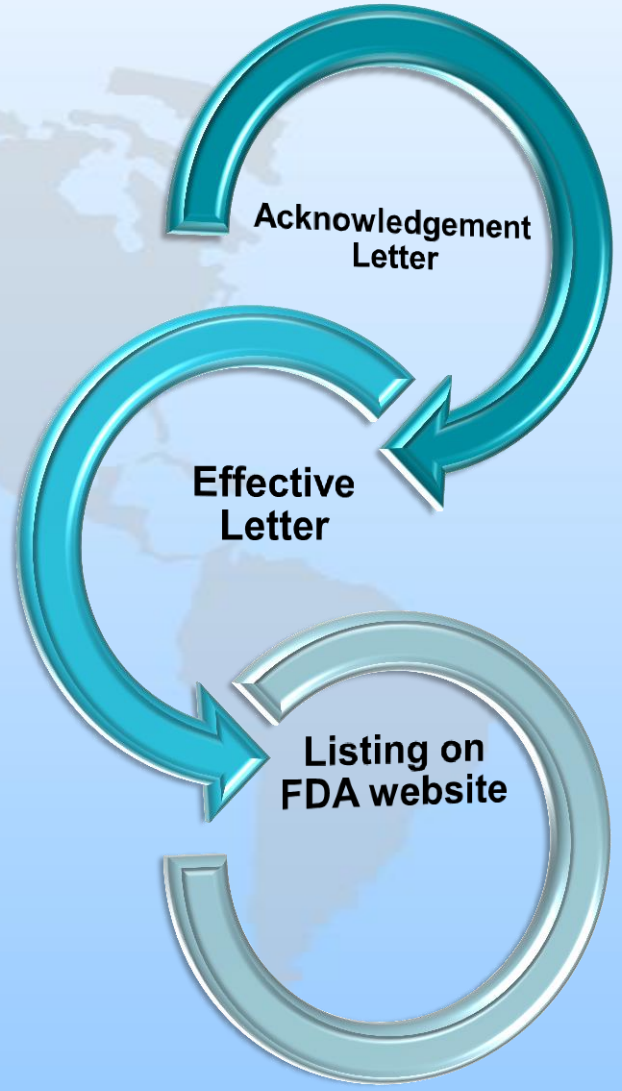
Key Steps in FCN Review Process-2

Phase 2 review:

Final determination of an accepted FCN and complete within 120 days

- Final letter - if FDA does not object to the FCN after phase 2 review
- Withdraw letter/Objection letter – if FDA object to the FCN during phase 2 review
- Effective FCNs listed on FDA's website: https://www.accessdata.fda.gov/scripts/fdcc/?set=FCN

What You Get For a Successful FCN



- Identity of the Food Contact Substance
- Name of the notifier
- Name of the manufacturer/supplier
- Intended use of the FCS
- Limitations/specifications

Summary of Regulatory Options

Factor	FAP	FCN	TOR Exemption
Requirements	21 CFR 171.1	21 CFR 170.101	21 CFR 170.39
Review period	≥180 days	120 days	Variable
Authorization	FR publication; Listed in CFR	Notification letters; Listed in inventory	Letter; Listed in inventory
Legality	Not until regulation publishes	After 120 day review if no object	When letter is received
Ownership	Generic	Proprietary	Generic
Confidentiality	Disclosure of non-CI during review	Disclosure of non-CI after 120 days	Same as FAP
Qualifying exposure	None	CDC < 1000 ppb	DC ≤ 0.5 ppb

CFR: Code of Federal Regulations; CDC: Cumulative dietary concentration; CI: Confidential information;

Thank you

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Any questions?

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