FDA's Approach to Process Filings
(& Validation)

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Outline

- Pathways to compliance
- Technology considerations
- FSMA: Validation
- Process Filings

Acts of Congress

Federal Regulations

Policies

Guidance Documents

COMPLIANCE

Food Drug and Cosmetic Act
Food Safety Modernization Act

- Food Additives
- Labeling
- GMPs
  - Preventive Controls Rules
  - Juice and Seafood HACCP
  - LACF
  - PMO

FD&C Act
Adulteration under Section 402

Food shall be deemed **adulterated** if…

- Bears or contains an added poisonous or deleterious substance which may render it injurious to health [402(a)(1)]
- Bears or contains any food additive that is unsafe within the meaning of sec 409 [402(a)(2)(C)]

Use of Emerging Technologies

- A new regulatory submission may be necessary to **clearly establish the conditions** under which the food substance is safe and lawful
- The agency encourages early/often industry consultation about the impact on the safety and regulatory status of the food using the new process

Safety Assessments

- The manufacturing process is considered because it may impact the safety and/or regulatory status
- Should be based on data relevant to the food substance

Juice HACCP—Example

- Juice processors must include in their HACCP plans control measures that will consistently produce, at a minimum, a 5 log reduction in a "pertinent microorganism."

(21 CFR 120.24)

Technologies Evolve

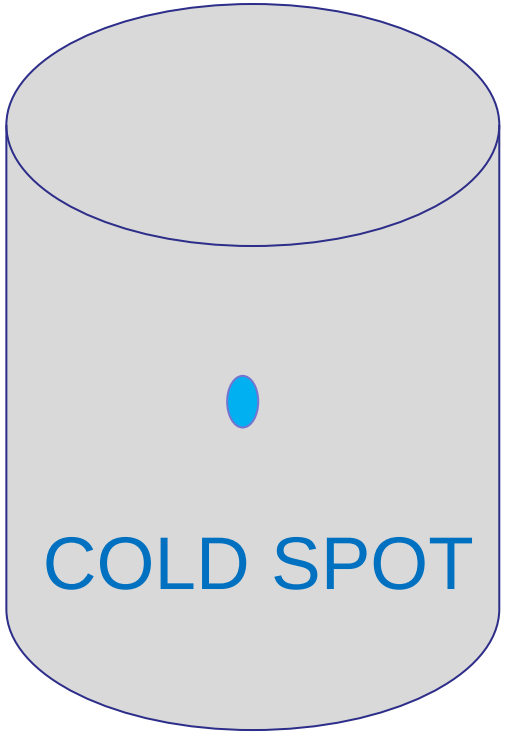
- Variations of thermal
- Non-thermal
- Irradiation
- Filtration
- Combinations

The basic validation questions remain the same……

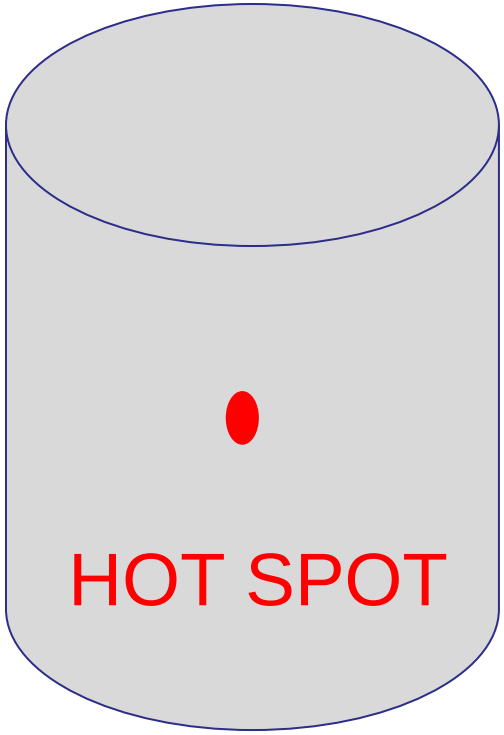
The Processor becomes the Expert

- Regulatory agencies need to understand that all relevant **Critical Factors** were discussed and identified
- With results/data to back them up…….
- Is the Process/System proven for your product in your package for the intended storage conditions and shelf life???

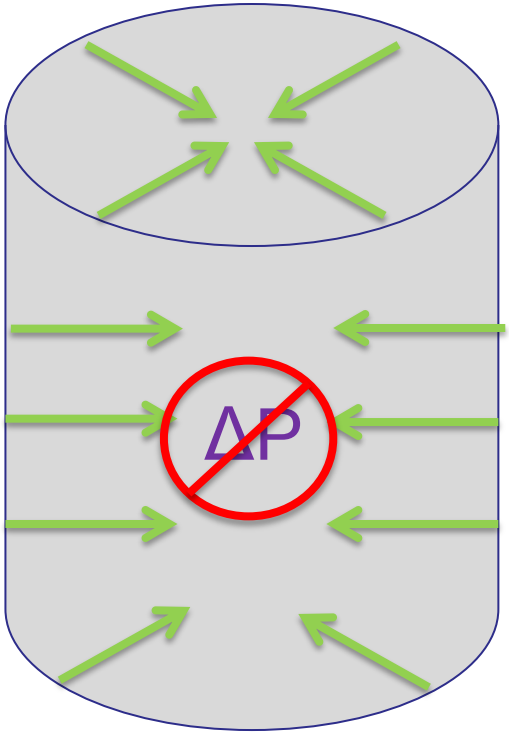
Thermal Process



MW Process



HPP Process



What about package sterilization?

- Aseptic
  - Integrated with design
- Conventional
  - Integrated with process
  - Could depend on GMPs
  - Storage conditions
- Novel
  - Fitments on pouches

Regulatory Status
New Irradiation Systems

- Does the manufacturing process for the food substance comply with the regulation?

Example: The use of a source of radiation that does not comply with current regulations requires an amendment:

  - **Submission of a food additive petition OFAS**

Radiation and Radiation Sources

- 21 CFR 179 – Irradiation in the production, processing and handling of food
  - Covers **radiation sources**, general provisions, ionizing radiation, radio frequency (and microwave), ultraviolet, pulsed light *and* petitioned amendments.
    - Sec. 179.30 Radiofrequency radiation for the heating of food, including Microwave frequencies. (Frequency approved for Heat)
    - Sec. 179.39 Ultraviolet: The radiation sources consist of low pressure mercury lamps emitting 90 percent of the emission at a wavelength of 253.7 nanometers (Juice: turbulent flow thru tubes)

Guidance

June 2014

Guidance for Industry

Assessing the Effects of Significant Manufacturing Process Changes, Including Emerging Technologies, on the Safety and Regulatory Status of Food Ingredients and Food Contact Substances, Including Food Ingredients that are Color Additives

Additional copies are available from:
Office of Food Additive Safety, HFS-205
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740
(Tel) 240-402-1200
http://www.fda.gov/Food/Guidances

You may submit either electronic or written comments regarding this guidance at any time. Submit electronic comments to http://www.regulations.gov. Submit written comments on the guidance to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the Federal Register.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Food Safety and Applied Nutrition

June 2014

Food Safety Modernization Act

Validation

Preventive Controls

- Processes that significantly minimize or prevent known or reasonably foreseeable hazards
- Preventive controls will need to be **validated**
  - 21 CFR 117.160
- Validation must include collecting and evaluating scientific and technical information (or … conducting studies)……21 CFR 117.160 (b)(1), (b)(2)

What is validation?

- **Validation** means obtaining and evaluating scientific and technical **evidence** that a control measure, combination of control measures, or the food safety plan as a whole, when properly implemented, is capable of effectively controlling the identified hazards.
  - 21 CFR 117.3 Definitions

Why do we need to validate?

- To establish documented evidence
- High degree of assurance
- **Specific process or system**
- Consistently produce a product meeting predetermined safety specifications and quality attributes

Adapted from NFPA Bulletin 43-L

Approaches to Validation

- Government/Industry guidance
- Safe harbors
- Published scientific literature
- Mathematical models
- Data from microbial inactivation studies

Validation Studies

- Equipment operating within established control limits
- Microbiological validation that provides documented evidence
- Process delivers microbiological inactivation to acceptable and safe levels

Validation Studies

- Determine the appropriate critical factors, limits and design specifications for the desired process
- Critical factors **may** include:
  - radiation (e.g., UV, pulsed light)
  - physical (e.g., time, distance from lamp)
  - thermal conditions(e.g., temperature)
  - mechanical (e.g., conveyor speed)
  - chemical (e.g., ozone concentration)

Criteria for Process Evaluation

- Able to effectively control the hazard
- Scientific evidence that the process is capable of consistent treatment
- Determination that treatment is effective for at least as long as the shelf-life of the food
- Identify the appropriate pathogen/surrogate

Criteria for Process Evaluation

- Complete documentation of the process including:
  - description of the system,
  - list of critical factors/limits,
  - results from biological challenge tests, and
  - list of factors **monitored and recorded**

Challenge Tests/Data

- Process Conditions
  - Described appropriately
- Variability of data
- Min vs Max vs Average
- How many tests conducted/needed?
- What happens to product next? Cross Contamination/Contact

Recordkeeping

- Verify preventive controls
- Monitor critical factors
- Take corrective actions if not properly implemented
- Keep records of these activities

Conclusion

- Novel processing technologies must meet all of the regulatory requirements specified in the FD&C Act, FSMA, pertinent regulations
  - Describe system
  - Determine Critical Factors
  - Show data

Process Filing

- New Forms and Database
- Some initial observations from FDA
- Novel Technology/New Systems

New Forms and Database

- New forms were published in October 2015
- Instead of 2 forms (2541a and 2541c), 4 forms were created to streamline the forms
  - 2541d: Low-Acid Retorted Products
  - 2541e: Acidified Products
  - 2541f: Water Activity/Formulation Control Products
  - 2541g: Low-Acid Aseptic Products
- Paper and electronic forms are identical

Top Reasons for a SID Inquiry

- Acidified
  - LSV is filed as a Fo instead of Other F value
  - LSV does not reflect the filed scheduled process.
    - For example, filed process is a hot fill hold, but the LSV is for the kettle cook prior to hot filling
  - No challenge study or inadequate challenge study for cold fill hold products
- Voluntary
  - Did not provide a flow chart for fermented foods or not providing list of ingredients with pH and weight %
  - Do not submit acid foods, aw ≤ 0.85, refrigerated/frozen, USDA, etc.

Top Reasons for a SID Inquiry

- Low-Acid
  - Missing TD studies to verify CUT and HD studies to verify uniform heating medium for steam-air
    - TD studies start CUT profile after the steam has been turned on (truncate start by 5-10 minutes) and profile starts at 180F
    - TD study has product IT at a higher value than what is being filed for. Filed IT could extend CUT beyond what was tested during TD
    - TD study has a larger container size than what was filed (not worst case)
  - Missing HP studies
  - Indicating N/A when a factor is critical

Top Reasons for a SID Inquiry

- Aseptic
  - Filing products that are not aseptically processed on aseptic forms (tuna, beans, acidified, etc.)
  - Incorrect flow correction factor
  - Filed turbulent but could not verify turbulence
  - Filed time and Fo cannot be verified

Top Reasons for a SID Inquiry

- Across all types
  - Documents not in English
  - Unclear or conflicting information

Initial Observations

- Read instructions first……(written & electronic)
- Contact us before sending Novel Technology or Unique filing
- Adequate description of system and Critical Factors (all filings)

Novel Technology/New Systems

- What is FDA's position on _____ technology?
- Using LONO with filing….
- Validation Methodology

What is FDA's position on ___ technology?

- Form FDA 2541d – Low Acid Retorted

E. Processing Method: Thermally Processed Non-Aseptic System

1. What is the finished equilibrium pH of the product after processing? _ _ . _ _

2. Heating Medium *(Select one)*

a) ☐ High pressure assisted ☐ Microwave ☐ Ohmic (electrodes) ☐ Steam

☐ Steam-air *(Attach a heat distribution study. Provide name or a brief description of attachment below.)*

☐ Water cascade ☐ Water immersion ☐ Water spray

☐ Other *(Enter heating medium)*

Continue to Section F.

What is FDA's position on ___ technology?

- Technologies listed have filings
- Case by case basis
- Contact us ahead of time
- Use the Other box

LONO

- FDA received and reviewed information on the filler/technology prior to filing
- NOT a requirement, but OK to add to filing
- FDA calls it an **NQL** – No Question Letter

Validation Methodology

- No prescribed methods
- IFTPS Aseptic Guidance is a good place to start
- Appropriate use of Statistical Methods
- Re-Validation
  - Did anything change? (i.e. that affect CF's)
  - Have we learned more about the hazards?
  - If SID changes…..**Re-file everything**

Thank you!

Questions?