Testing Protocol for Determining Exposure to Radiolysis Products from Packaging Materials Irradiated in Contact with Food

Kristina E. Paquette, Ph.D.
U.S. FDA
Center for Food Safety and Applied Nutrition
Office of Food Additive Safety

Recent Developments in the Regulation of Irradiated Packaged Food
American Chemical Society National Meeting
New York, NY
September 9, 2003
Why All the Interest Now?

- 1960s Many materials approved for use during irradiation of prepackaged food
- 1982 *E. coli* O157:H7 first linked to serious illness from eating undercooked meat
- 1990 Irradiation of poultry approved
- 1993 Jack-in-the-Box incident
- 1997 Irradiation of meat approved
- 2001 Radiation sources deemed equivalent

- Oxygen barrier needed to prevent off-odors, off-flavors
Legal Considerations

- Food, Drug, and Cosmetic Act, Section 409
- 21 CFR 179.25(c) General provisions for food irradiation
- §179.26 Ionizing radiation for the treatment of food
- §179.45 Packaging materials for use during the irradiation of prepackaged foods
- Approvals for new materials
  - Food Contact Notification (FCN) §170.100 – §170.106
  - Threshold of Regulation (TOR) §170.39
Radiolysis Products (RP) from Polymers

- Irradiation of polymers in O₂ is known to generate measurable levels of polymer RPs
  - Aldehydes, ketones, alcohols, carboxylic acids
- RP exposure must be determined for irradiated uses of
  - Polymers
  - Adjuvants such as antioxidants
  even if already approved for unirradiated uses
Highlights of the Protocol

- Proposed protocol for determining RPs in polymers and estimating exposure
  - Why/how is it being developed?
  - Low-MW vs. non-volatile RPs
  - Step-wise vs. direct migration approach
- Special considerations for determining RPs formed from polymer adjuvants
- Validation of analytical methods
- Dosimetry
Low-MW Compounds: Headspace, Thermal Desorption

Sample Preparation
- For headspace (HS): ASTM D 4526-96
- Polymer test article placed in HS vial filled with air or modified atmosphere and sealed
- 3 replicates for each set of testing conditions: dose, atmosphere, time after irradiation
- Irradiation: control, low-dose, high-dose
- Report temperature at which samples are irradiated
- After irradiation, maintain samples at 40°C until ready to be analyzed
Headspace, Thermal Desorption Method, contd.

- Check Samples
  - Vials containing NIST standard reference material, e.g., polystyrene or LDPE
  - Same irradiation, analytical conditions as test article
  - Analyze in duplicate
  - Chromatograms compared to standard chromatograms developed by CFSAN
  - Process ensures that key RPs are not missed
Headspace, Thermal Desorption Method, contd.

- Qualitative Analysis
  - Identify chemicals whose concentrations increase with irradiation or that are newly formed upon irradiation (RPs)
  - Introduce sample HS vapor to GC/MS via
    - Static HS sampling
    - Dynamic technique such as direct TD
  - Demonstrate capability of GC system to measure a variety of volatile, semi-volatile chemicals
Headspace, Thermal Desorption Method, contd.

◆ Quantitative Analysis
  ◆ Internal standardization using standards similar to identified RPs in terms of
    ◆ Functional groups
    ◆ Retention times
  ◆ Demonstrate precision, validity, LODs of method
  ◆ At 24 and 240 hr after irradiation, analyze, in triplicate by GC/MS, samples of HS vapor from control, low-, high-dose vials for volatile organic compounds (18 analyses)
E-beam Irradiation of EVOH
GC-MSD Chromatograms of Head Space

Time (min)
Non-Volatiles: Analysis by Polymer Dissolution, Extraction

- Same sample preparation as for HS method
- After irradiation, maintain samples at 40°C until ready to be analyzed
- At 24 and 240 hr after irradiation, place sections of test articles into solvent that will dissolve or swell article
- Analyze, in triplicate, solvent extract by GC/MS and/or LC/MS, as appropriate (18 analyses)
- Analyze for non-volatile and low-MW compounds
  - Overlap with HS results = crosscheck of two methods
- Demonstrate precision, validity, LODs of method
- Identify, quantify RPs
Irradiation of Nylon-6 at 0, 25 and 50kGy
Analysis by LCMS-APCI

Green = 50 kGy
Red = 25 kGy
Blue = 0 kGy
Irradiation of Nylon-MXD-6 at 0, 25 and 50 kGy
Analysis by LCMS

Green = 50 kGy
Red = 25 kGy
Blue = 0 kGy
Exposure Estimate

- Use highest quantitative low-MW and non-volatile data from samples to calculate exposure to RPs
- Assume amount of RPs found = amount in volume of food that would typically contact surface area of test article
- Calculate exposures
  - 100% migration
  - Migration modeling
- If dietary concentration > 0.5 ppb, migration studies may need to be done
Optional Migration Studies

- Sample Preparation
  - Pouches made of packaging material filled with air or modified atmosphere and sealed
  - 3 replicates for each set of testing conditions: dose, atmosphere, time after irradiation
  - Irradiation: control, low-dose, high-dose
  - Report temperature at which samples are irradiated
  - Without delay after irradiation, open the pouches, fill with appropriate food simulant, and reseal
  - After irradiation, maintain samples at 40°C until ready to be analyzed
Migration Studies, contd.

- Quantitative Analysis
  - At 24, 48, 120, and 240 hr after irradiation, analyze, in triplicate by GC/MS and/or LC/MS, food simulant from the samples (36 analyses)

- Data Treatment, Validation, Exposure Estimate
  - See the “Recommendations” at http://www.cfsan.fda.gov/~dms/opa2pmnc.html

- RPs pre-identified by HS and total polymer dissolution/solvent extraction
  - Spike-and-recovery validation is feasible
Direct Migration Approach

- Skip HS, polymer dissolution/extraction steps; go directly to migration study
- Not very informative
  - No “pre-identification” of RPs
  - Very difficult to identify/quantify unknown RPs at very low concentrations against high background of food simulants
- Stability of RPs in food simulants
- Easy to miss RPs completely
- Very difficult to validate analytical results
E-beam Irradiation of EVOH
GC-MSD Chromatograms of Head Space

Time (min)

Relative Abundance

50 kGy

NIR

2-Butanal

Acetaldehyde
Butane
EtOH
MEK

Acetic
Propionic
Butanoic
Pentanoic
Acid
Typically, high levels of adjuvant RPs form (preferentially degrade over polymer)

Possible to predict RPs from structure, literature articles

Additional control samples in testing:
- Irradiated adjuvant
- Irradiated polymer without adjuvant
- Unirradiated polymer with adjuvant

Further polymer/adjuvant combinations tested if the polymer or adjuvant is not approved for unirradiated uses
Effect of Irradiation on Antioxidants in HDPE by LCMS

Tentative structures of degradation products

Antioxidants ‘disappear’ almost completely

25 kGy NIR

Time (min)

8 9 10 11 12 13
Dosimetry

- Description of dosimetry system
  - ISO/ASTM 51261
- Procedure for calibration
- Description of analysis of dosimeters
- Certificate of Irradiation, stating maximum and minimum doses absorbed within group of irradiated samples
- Ensure that absorbed-dose measurements are for the dose absorbed by the test material and not by other materials used to construct the sample vial or cell
Conclusions

- Determine RPs in polymer via HS and polymer dissolution/extraction
- Calculate exposure
- Do migration studies on pre-identified RPs if more realistic exposures are needed
  - Food simulants NOT irradiated
- Direct migration approach not informative
- Polymer adjuvant RPs can be predicted, but analysis may require more control samples
- Describe dosimetry
Obtaining Approval for New Polymers, Adjuvants for Irradiated Foods

- Meet with FDA -- Pre-Notification Consultation (PNC)
- Submit a Food Contact Notification (FCN)
- Guidance documents:
  - [http://www.cfsan.fda.gov/~dms/opa-toc.html](http://www.cfsan.fda.gov/~dms/opa-toc.html)