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# Food Contact Materials – A Company's Perspective

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# Introduction

- This presentation presents some real-world issues facing manufacturers of food contact materials
  - Impact of FFDCA rather than TSCA
  - Getting FDA approvals
  - Good manufacturing practices
  - The new frontier: nano-based food packaging

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# Dow Sells FDA-Regulated Products

- Personal care product components (cosmetics)
- Food packaging materials (indirect food additives)
- Bulking agents, chewing gum base, etc. (direct food additives)
- Ion-exchange resins (secondary direct food additives)
- Food components
- Animal feed components
- Dietary ingredients used in dietary supplements
- Excipients and active pharmaceutical ingredients for both OTC and prescription drugs
- Veterinary drug components
- Medical device components
- Much of what Dow sells is regulated by FDA or its counterparts in other countries

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# Food Contact Materials vs. TSCA

- TSCA § 3(2)(B)(vi) excludes from the definition of “chemical substance” any “food additive ... when manufactured, processed, or distributed in commerce for use as a ... food additive ....”
- “Intermediates and catalysts intended solely for use as a component of a ... food additive ... are excluded from regulation under TSCA.” 42 Fed. Reg. 64572 (Dec. 23, 1977)
- EPA: “If a substance has multiple uses, only some of which are regulated under FFDCA, the manufacturing, processing, distribution, and use of the substance for the remaining uses comes within the jurisdiction of TSCA.” Id.
- Do not report food additives or their catalysts and intermediates for PMNs or IUR or TSCA §12(b) export notification to the extent used for food additives

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# Perspective

- Food contact materials require a different mind set than that needed for industrial chemicals
  - Unlike with PMNs, applicant for a new product must generate data
  - Manufacturer has burden of proving safety for new products
  - Focus is on preventing more than minute levels of migration into food
  - Manufacturing, handling, and distribution are regulated to assure adequate purity

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# What Does “Safe” Mean?

- 21 CFR § 170.3(i): “Safe” means “there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use”

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# Factors to Consider About “Safe”

## 21 CFR § 170.3(i)

- The probable consumption of the substance and of any substance formed in or on food because of its use
- The cumulative effect of the substance in the diet, taking into account any chemically or pharmacologically related substance or substances in the diet
- Safety factors which, in the opinion of experts qualified by scientific training and experience to evaluate the safety of food and food ingredients, are generally recognized as appropriate

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# GRAS Status

- GRAS substance is not a food additive, thus not subject to premarket review and approval by FDA
- GRAS – “generally recognized as safe”
- “generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures ... to be safe under the conditions of its intended use” – FFDCA § 201(s)
- Typically, GRAS only for certain uses and subject to limitations
- FDA listed some 12 food contact materials as GRAS in 21 CFR Part 186 – not exhaustive

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# Getting GRAS Status

- Need scientific evidence sufficient for food additive regulation
- Scientific evidence must be generally available (i.e., published)
- Must show a consensus among qualified experts
- FDA GRAS affirmation process (resulting in CFR listing) no longer being staffed
- Since 1997, FDA will review GRAS notifications (self-determinations) – 238 submitted so far
- Manufacturers can self-determine without FDA notification, but customers may want stronger assurance

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# GRAS Notifications

- Submit substance description, conditions of use, notifier's reasons for concluding that the substance is GRAS for its intended use
- FDA posts on its website a listing of GRAS notifications with indication that:
  - FDA has “no questions at this time”
  - The notifier requested FDA cease to evaluate the notice”
  - FDA's evaluation is “pending”

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# Dow's Recent GRAS Notification

- GRAS Notice GRN 213 for hydroxypropyl methylcellulose (for direct use in food)
- Dow spent months developing the draft notice
  - Substantial evidentiary base had to be assembled
  - Manufacturing description and product analysis critical
  - Used consultants
- Dow convened a panel of experts who reviewed and commented on the draft notice
- Notice filed Sept. 2006
- FDA response Mar. 2007 (6 months) – “no questions at this time” – 5 page summary of notice
- Cost was significant

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# Food Additive Regulations

- Extensive listing in CFR of indirect food additives – 21 CFR Parts 174-178
- Questions of interpretation arise (if not listed or GRAS or prior sanction, need new FDA approval)
- With FDA approval, manufacturers can submit food additive petitions to FDA for new food additive regulations (or amendments to existing ones)
  - Request for FDA to conduct rulemaking
  - No time limit on FDA action – takes FDA resources
  - Get CFR listing if successful – can cite to customers

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# Food Contact Notifications

- Food and Drug Administration Modernization Act of 1997 (FDAMA) created a faster, less burdensome alternative to food additive petitions for food contact substances in light of lower risk
- “Food contact substance” = “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” – FFDCA § 409(h)(6)
- Not rulemaking but notification with FDA approval required – no public input
- FCN process is required in lieu of food additive petition unless
  - FDA determines a food additive petition is necessary to provide adequate assurance of safety, or
  - FDA and manufacturer agree that food additive petition is okay

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# Food Contact Notifications

- 21 CFR Part 170, Subpart D – FCN procedures
  - FDA requires use of food additive petition if migration > 1 ppm (200 ppb for biocides)
  - FCN must contain prescribed information – detailed guidance on chemistry, toxicology, manufacturing, etc.
  - No public disclosure of FCN until after approval
  - 120-day review period
  - FCN approvals are listed on FDA website, not in CFR
  - FCN approvals apply only to FCN submitter for that product
  - FDA can determine that FCN is no longer effective if evidence appears that the intended use is no longer safe

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# Filing FCNs

- At least 757 FCNs have been filed through Nov. 2007, fewer approved
- 9 approved FCNs submitted by Dow
- Dow's most recent: FCN 741 (effective Sept. 28, 2007)
  - Ethylene/hexene copolymers containing up to 25 weight percent polymer units derived from hexene
  - Higher hexene polymer level than allowed in the food additive regulation for olefin polymers, 21 CFR § 177.1520(a)(3)
  - Broad usage allowed
  - 6 months of work including migration study

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# Good Manufacturing Practices

- 21 CFR § 174.5: GMP requirements for food contact materials
  - In addition to any regulations allowing use, must meet GMPs
  - Quantity added to food shall not exceed prescribed limits or, if none, amount reasonably required to achieve the intended physical or chemical effect in the food contact article; and
  - “Any substance used as a component of articles that contact food shall be of a purity suitable for its intended use”
- Also – not impart odor or taste to the food such as to render it unfit

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# Dow's Indirect Food Additive GMPs

- Dow has adopted internal guidance on GMPs for indirect food additives
  - Adapted from FDA's voluntary cosmetic GMPs
  - Also takes into consideration IPEC GMPs for excipients (inactive components of drugs)
- Training slides
- Audit requirements
- Less rigorous than for drug chemicals, but still adds meaningful standards

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# Dow's Indirect Food Additive GMPs

- Address the following topics:
  - Scope
  - Quality organization
  - Buildings and facilities
  - Equipment
  - Personnel
  - Raw materials
  - Utilities
  - Production, including procedures

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# Dow's Indirect Food Additive GMPs

- Also address:
  - ❑ Laboratory controls
  - ❑ Records
  - ❑ Labeling
  - ❑ Complaints
  - ❑ Auditing
  - ❑ Change control
  - ❑ In-process product

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# Nano Food Additives

- Ambitious plans to incorporate engineered nanomaterials in food packaging to:
  - Provide superior barrier properties, keeping food fresher longer
  - Provide sensors for spoilage (active packaging)
  - Antimicrobial activity to prevent spoilage
- FDA has already approved at least one nano food additive (FCN 716) – titanium nitride – as an additive in food-contact polyethylene terephthalate (PET) bottles
- Key questions include what chemistry and toxicology data are necessary for FDA to review?

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# Nano Food Additives

- Nano food additives also raise questions about whether premarket approvals for macroscale materials cover nanoscale versions
  - Food additive regulations are not size-specific
  - FCNs are product-specific
- GRAS – is there a consensus on safety of the nanoscale material?
- These and related issues are addressed in:
  - FDA's own Nanotechnology Task Force report (2007)
  - GMA/PEN case studies project (near completion)
  - ABA Nanotechnology Project paper under development

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# EPA vs. FDA on Nano

- EPA has reviewed ~ 20 nano PMNs, no nano pesticides
- FDA has reviewed a few nano drugs, devices, food additives
- Both agencies face unknowns in how to regulate, leading to case-by-case regulation until experience grows (little guidance for now)
- EPA has NMSP; FDA Task Force Report calls for voluntary action