【Session 4】
Case Study of Risk Assessment and Management
- “Pizza Pan Case Study”

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Chile
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- Hazard Identification
- Dose Response
- Exposure Assessment
- Risk Characterization
Risk Analysis – Human Health Paradigm

RISK CHARACTERIZATION

Hazard Identification → Dose - Response in Animals → Equivalent Dose in Humans → Characterize Risk to Human

Human Exposure

Risk Communication

Risk Management Process

Risk/Benefit Decisions Exposure Controls

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Case Study: The Pizza Pan Proposal

- A case study to demonstrate the steps of risk assessment

- The Product: a composite fiber material to be used for making and serving personal size pizzas

- The Product would allow the same pan to be used for cooking and serving for both eating in and taking out

- The primary question: Will the product be safe to use? Or will it cause harmful exposure?
The Pizza Pan: Hazard Identification

- What substances are there that could be released?
  - Analytical work was conducted to identify a suite of chemicals that might be released.
  - Several possible cooking conditions were examined
- Concerned with human receptors only.
  - People consuming the pizza
  - People making the pizza
Background: The Oven for Cooking

Lincoln Impinger Conveyer Oven

Cooks with forced hot air
Background: Impact of Cooking Conditions

- Composite material was tested at several possible cooking conditions
  - 246 ºC for 7.05 minutes
  - 246 ºC for 45 minutes
  - 316 ºC for 35 minutes
  - 267 ºC for 8 minutes
  - 268 ºC for 8.5 minutes

- Analytical testing was used to identify the off-gassing products
Chemicals Identified by the Analytical Testing

**A Long List of Chemicals of Potential Concern**

- Methyl Chloride
- Acetaldehyde
- Acetone
- Methyl Methacrylate
- Furfural
- Acetophenone
- 2-Propenal (Acrolein)
- Methanol
- Ethyl Acetate
- Methyl Formate
- Trimethylamine
- Ethanol
- Furan
- Formic Acid
- Methyl Acetate
- Acetic Acid
- Methyl Ethyl Ketone
- **& 18 other chemicals**
Narrowing the List – What is critical?

• Chemicals that had consistent readings over analytical runs – i.e. they were likely to be present and not analytical “artifacts”
• Chemicals for which standards to evaluate “harmful” effects are available (i.e. toxicity benchmarks)
• Chemicals of special interest to the manufacturer
• Final selected chemicals would act as surrogate for those chemicals not directly evaluated
### Identified Chemicals of Concern

#### Chemicals of Potential Concern

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Test 3 (µg/g)</th>
<th>Test 4 (µg/g)</th>
<th>Test 2 (µg/g)</th>
<th>Test 1 (µg/g)</th>
<th>Average (µg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl Chloride</td>
<td>8</td>
<td>9</td>
<td>8</td>
<td>11</td>
<td>9.00</td>
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<tr>
<td>Acetaldehyde</td>
<td>1</td>
<td>0.3</td>
<td>0.5</td>
<td>0.5</td>
<td>0.58</td>
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<td>Acetone</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3.50</td>
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<td>Methyl Methacrylate</td>
<td>73</td>
<td>68</td>
<td>78</td>
<td>62</td>
<td>70.25</td>
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<tr>
<td>Furfural</td>
<td>4</td>
<td>19</td>
<td>3</td>
<td>3</td>
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<td>Acetophenone</td>
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<td>5</td>
<td>4</td>
<td>4.75</td>
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<tr>
<td>Styrene</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2.00</td>
</tr>
<tr>
<td>2-Propenal (Acrolein)</td>
<td>20</td>
<td>24</td>
<td>21</td>
<td>11</td>
<td>19.00</td>
</tr>
</tbody>
</table>
The Pizza Pan: Dose Response

• Dose response is used to determine the toxicity benchmarks
  » RfD’s/RfC’s for non-cancer endpoints
  » Cancer Slope factors for potential carcinogens.

• The numbers are developed off of various toxicological studies

• For the pizza pan we need this information for each chemical of potential concern
## Available Non Cancer Toxicity Benchmarks

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Repro. MADL (µg/day)</th>
<th>Oral MADL (mg/kg/day)</th>
<th>Oral MRL (mg/kg/day)</th>
<th>Oral TDI (mg/kg/day)</th>
<th>Oral RfD (mg/kg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl Chloride</td>
<td>11,000</td>
<td>2.86E-02</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Acetaldehyde</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2.57E-03</td>
</tr>
<tr>
<td>Acetone</td>
<td>-</td>
<td>8.57</td>
<td>-</td>
<td>1.00E-01</td>
<td></td>
</tr>
<tr>
<td>Methyl Methacrylate</td>
<td>-</td>
<td>-</td>
<td>5.00E-02</td>
<td>1.40E+00</td>
<td>3.00E-03</td>
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<tr>
<td>Furfural</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1.00E-01</td>
</tr>
<tr>
<td>Acetophenone</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>2-Propenal (Acrolein)</td>
<td>-</td>
<td>5.00E-04</td>
<td>-</td>
<td>2.00E-02</td>
<td></td>
</tr>
</tbody>
</table>

MADL – Maximum Allowable Daily Level  
MRL – Minimal Risk Level  
RfD – Reference Dose  
TDI – Tolerable Daily Intake
A Note on Hazard Impacting the Assessment

- The Methyl Chloride MADL is a single day exposure limit.
  - Hence this requires an evaluation of what would occur on a single visit to the pizza shop

- The RfD’s are chronic exposures, i.e. acceptable levels over a long period of time.
  - Hence these are compared to the averages over a single year

- These reflect incorporating exposure duration in the selection of hazard endpoints
A Note on Hazard Impacting the Assessment

• Temporal impact of hazard
  » Acute vs. chronic
  » Pattern of exposure is critical
  » Window of receptor vulnerability

• Physical properties/characteristics
  » Viability of various transport routes
  » Bioavailability
  » How the chemical is absorbed, distributed, metabolized and excreted from the body
  » Binding or capture in a media compartment
# Available Cancer Toxicity Benchmarks

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Cancer NSRL</th>
<th>Inhalation RSC</th>
<th>Oral RSC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>µg/day</td>
<td>mg/m³</td>
<td>mg/kg/day</td>
</tr>
<tr>
<td>Methyl Chloride</td>
<td>-</td>
<td>5.56E-3</td>
<td>1.59E-3</td>
</tr>
<tr>
<td>Acetaldehyde</td>
<td>90</td>
<td>4.5E-3</td>
<td>1.29E-3</td>
</tr>
</tbody>
</table>

NSRL – No Significant Risk Level  
RSC – Risk Specific Concentration at a risk of 1/100,000
Reminder on Exposure Assessment

- Basic Definition: Exposure assessment is the process that quantifies the uptake of an agent resulting from contact with various environmental media.
Exposure Assessment - Questions to ask?

• Is the Exposure Significant?
  » How long does the exposure last?
  » How concentrated is the substance?
  » What is the route?

• Methods to determine Exposure
  » Direct or Indirect measurement
  » Modeling methods

• How do we address these for the pizza pan?
How will the Pizza Pan cause exposure?

- A barrier layer prevents direct contact of the pizza to the pizza pan

- For a worker, there could be exposure to direct off-gassing of substances

- For a customer there could be indirect exposure by chemicals transferred to the pizza
  - Via air in the oven
  - Via direct migration if the barrier is compromised
What are the required Inputs?

• We need information on who will eat the pizza - references and marketing information

• We need information on the chemicals released - analytical information

• We need information on the consumption rates - references and marketing information
Assumptions for Pizza Pan Exposure

- A pizza pan is approximately 18 cm in diameter
- A pizza pan is 31.4 grams
- A pizza is 219.6 grams
- The receptors these need to reflect both the general public and also special subpopulations if appropriate
  - A child at 15 kg
  - A small adult/teenager at 50 kg
  - An average adult at 70 kg
Assumptions for Pizza Pan Exposure

- An adult consumes about 10.5 kg of pizza per year
- A child consumes about 6 kg of pizza per year
- 100% of the chemicals emitted are absorbed by the pizza and consumed.
- All pizza consumed during a lifetime comes from 18 cm diameter pizzas heated on the composite material (about 47.5 pizzas per year for adults and 27 pizzas per year for a child)
Assumptions for Pizza Pan Exposure

• An individual consumes 6 kg of pizza every year during childhood (6 years) and 10.5 kg of pizza every year after childhood for a 70-year lifetime
• For a Lifetime Average Daily Dose (LADD), a person is a child for 6 years, a youth for 14 years and an adult for 50 years
Additional Exposure Scenarios Considered

- A home re-heating scenario
  - The individual takes home pizza and re-heats it on a routine basis
  - This leads to potential increased transfer to the pizza
- A compromise in the barrier integrity
- Potential exposure to workers in the pizza restaurant
- Potential misuse of the product
Reminder on Risk Analysis – Human Health Paradigm

RISK CHARACTERIZATION

Hazard Identification → Dose - Response in Animals → Equivalent Dose In Humans → Characterize Risk to Human

Human Exposure

Risk Communication

Risk/Benefit Decisions Exposure Controls

Risk Management Process
Risk Characterization for the Pizza Pan

- Started with our Chemicals of Concern
- Used the available analytical data to estimate the amounts available
- Used simple models for the transfer from the pizza pan to the pizza
- Estimated the potential exposures and compared them to the toxicity benchmarks
- Bottom-line - don’t eat the pizza???
A Tiered Approach
SCREENING RISK ASSESSMENT (worst-case exposure)

- below standard
- above standard

DONE

REFINE EXPOSURE ASSUMPTIONS
( more realism )

below
above

DONE

- REFINE ASSUMPTIONS
- INSTALL CONTROLS
(best estimate)

below
above

DONE

DONE!!
Key Assumption to Refine

• 100% Transfer is a gross overestimate
• Lab work demonstrated that the oven has an air exchange rate of approximately 1,977 air changes per hour.
• The next step uses a more complex model accounting for air movement and dispersion
• Additional assumptions must be made
Refined Calculations

- Estimate emissions per pizza pan
- Estimate the transfer to the pizza
- Estimate consumption of chemicals based on pizza consumption for each age group
- For Lifetime Average Daily Dose calculations combine the estimates for each life stage
- Compare estimated exposure to toxicity benchmarks.
A Tiered Approach
SCREENING RISK ASSESSMENT
(worst-case exposure)

below standard
above standard

DONE

REFINE EXPOSURE ASSUMPTIONS
( more realism )

below
above

DONE

The refined scenario makes the model more realistic, but it is still very conservative.

DONE

• REFINE ASSUMPTIONS
• INSTALL CONTROLS
(best estimate)

below
above

DONE !!
### Results of the Refined Assessment

#### Estimated Dosages with Oral Non-Cancer Toxicity Benchmarks

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>15 kg child mg/kg/day</th>
<th>Receptor 50 kg adult mg/kg/day</th>
<th>70 kg adult mg/kg/day</th>
<th>Toxicity Benchmarks mg/kg/day</th>
<th>Agency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl Chloride</td>
<td>1.8E-06</td>
<td>9.4E-07</td>
<td>6.7E-07</td>
<td>2.9E-02</td>
<td>ATSDR</td>
</tr>
<tr>
<td>Acetaldehyde</td>
<td>1.6E-05</td>
<td>8.2E-06</td>
<td>5.9E-06</td>
<td>2.6E-03</td>
<td>US EPA</td>
</tr>
<tr>
<td>Acetone</td>
<td>1.5E-07</td>
<td>7.7E-08</td>
<td>5.5E-08</td>
<td>1.0E-01</td>
<td>US EPA</td>
</tr>
<tr>
<td>Methyl Methacrylate</td>
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<td>6.8E-06</td>
<td>4.8E-06</td>
<td>5.0E-02</td>
<td>Health Canada</td>
</tr>
<tr>
<td>Furfural</td>
<td>1.5E-06</td>
<td>7.7E-07</td>
<td>5.5E-07</td>
<td>3.0E-03</td>
<td>US EPA</td>
</tr>
<tr>
<td>Acetophenone</td>
<td>7.3E-07</td>
<td>3.9E-07</td>
<td>2.8E-07</td>
<td>1.0E-01</td>
<td>US EPA</td>
</tr>
<tr>
<td>2-Propenal (Acrolein)</td>
<td>2.6E-06</td>
<td>1.4E-06</td>
<td>9.8E-07</td>
<td>5.0E-04</td>
<td>ATSDR</td>
</tr>
</tbody>
</table>
Results of the Refined Assessment

**Estimated Dosages with Oral Cancer Toxicity Benchmark**

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>LADD Estimate for 50 kg adult</th>
<th>LADD Estimate for 70 kg adult</th>
<th>Proposition 65 NSRL</th>
<th>US EPA Cancer Benchmark</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mg/kg/day</td>
<td>mg/kg/day</td>
<td>mg/kg/day</td>
<td>mg/kg/day</td>
</tr>
<tr>
<td>Methyl Chloride</td>
<td>7.91E-4</td>
<td>6.41E-4</td>
<td></td>
<td>1.59E-3</td>
</tr>
<tr>
<td>Acetaldehyde</td>
<td>5.06E-5</td>
<td>4.10E-5</td>
<td>1.3E-3 / 1.8E-3</td>
<td>1.29E-3</td>
</tr>
</tbody>
</table>

RSC – Risk Specific Concentration at a risk of 1/100,000
Re-heating Scenario

- Any substances entering the pizza during original cooking remain in the pizza
- 25% of every 18 cm pizza ordered is brought home and re-heated on the original pan
- Half is re-heated by the use of a microwave oven, half is re-heated by conventional oven
- A conventional oven it is used at 177º C for 15 minutes
- Based on a thermogravimetric analysis the amount of emissions from the pizza pan at 177º C would be 1.6% the level at 246º C
Re-heating Scenario

- The ratio of pan to pizza on re-heating “is 4 times greater than the original cooking conditions

- Combining the ratio factors indicates the potential exposure for the re-heating scenario is approximately 101% of the original scenario

- Based on the margin of clearance for the consumption in a restaurant no additional risk is expected
Misuse/Foreseeable Failures

• The following are possible misuses
  » Defect in the barrier layer
  » Alternate cooking conditions
  » Cleaning the pizza pan and re-using it for cooking

• Each is based on a comparison to the primary assessment for evaluation
Caveats

• Explicit assumptions were selected to be health protective

• It was assumed all of the pizza would be cooked on the composite material.

• It was initially assumed that all of the chemicals of concern went into the food; this was later refined to account for air movement and dispersion.
Caveats

- Interactions of the chemicals of concern with organics released from the food were not considered.

- The re-heating scenario assumes an individual always takes home 25% of all of their pizza.

- The misuse scenarios examined in this report are deemed to be the most realistic and most likely to occur.
Caveats

- The best available science was used in estimating potential exposure from the re-heating scenario, but no actual measurements were taken under these conditions.

- Each assumption can be interpreted as being high but within the range of plausibility. However, the combination of the conservative assumptions is unlikely.
Pizza Pan Conclusions

- None of the estimates provided within this document should be interpreted to represent, in any form, an actual estimate of risk.

- Under the conditions of this assessment there is NO indication that the use of the product, under its intended use or foreseeable misuse is likely to lead to a potential health risk.

- **ENJOY THE PIZZA!!!!!!!!!!!!!!!**
Pizza Pan and Risk Management

- How was risk management implemented with the Pizza Pan case study?
  - Based on the initial results, before refinement, the decision would have been to not allow this particular application with this product
  - Refinement indicated that the risk was not unacceptable and that it was management by the cooking process
  - The entire evaluation reflects a product stewardship to manage potential risk from the product application

- How might this change?
  - If the cooking method changes than risk management/product stewardship would indicate a re-evaluation may be necessary
  - Alternative types of cooking applications (e.g. for cooking eggs or cakes, etc.) might also call for a re-evaluation
The Pizza Pan: Risk & Value Chain Communication

• Risk Communication
  » This was mostly internal as the product was in development
  » Steps along the way indicated potential risk and resulted in additional laboratory work
  » The development team was communicated with so they understood the assumptions and the issues to make informed decisions

• Value Chain Communication
  » During development a potential downstream customer was communicated with that an evaluation for safety was in process
  » Information was supplied by the customer to help refine the assumptions
  » This was an important link!
Summary

• The Pizza Pan case study demonstrates the 4-step risk assessment process
• It demonstrates that simple conservative assessments may not work and refinement may be necessary
• The Pizza Pan case study also shows that risk assessments of this nature require teams with various expertise – toxicology, analytical chemistry, engineers, etc.
• It also required good communication,
  » Internally so the team could work together
  » Externally with the potential customer to understand
    • The application
    • Ways to refine the assessment