ILSI North America

ILSI North America 2019 Food Packaging Conference: Scientific Advances and Challenges in Safety Evaluation of Food Packaging Materials
April 2-3, 2019

Presentation Abstracts:

Session 1: Analytical Testing and Migration Assessments/Modelling

Analytical Battery Testing Development for Generic Food Packaging Migration Study

Thomas Hartman, PhD, Rutgers University

Most countries have regulations for food packaging and mandate that manufacturers perform migration studies on food contact materials to ensure food safety. Many manufacturers also perform their internal analysis of packaging materials which exceeds the minimum regulatory requirements to ensure their product quality. Nevertheless, regulatory guidance documents generally do not provide detailed analytical protocols to achieve the end points of migration tests. There are many gaps between the testing methods from different companies. This study aims to develop and validate a battery of analytical tests for generic food packaging migration analyses. Representative finished food packaging with different multilayer structures and/or coating species were collected from the industry and extracted with designated food simulants for GC-MS and LC-MS screen analysis. They were also evaluated by Headspace-GC-MS and Purge & Trap-Thermal Desorption-GC-MS techniques as complementary tests for volatile and semi-volatile out-gas products such as retain solvents and off-odor compounds. All migrants and "compounds of high concern" (e.g. compounds listed in CA Prop 65 or perceived negatively by consumers) identified from this study were categorized according to their source and selectively analyzed for method validation. The analytical data and protocols generated from this study will provide important references for the packaging industry.

Trends in Heavy Metal Content for Recycled Polyethylene Terephthalate (RPET) Food Packaging Between 2010 and 2018

Keith Vorst, PhD, Iowa State University

Increasing regulatory and consumer pressure to monitor and reduce overall heavy metals in the environment has resulted in the ongoing evaluation of maximum allowable threshold levels in food packaging. One of the greatest hurdles to regulatory oversight is the lack of historical data to make data driven threshold recommendations. The purpose of this research was to

quantify the concentration of heavy metals (Pb, Cd, Cr, Al, Sb, Fe, Ti) in recycled polyethylene terephthalate (RPET) between January 2010 to May 2018. Cadmium, chromium, and lead are heavy metals of interest, and are currently regulated in food-contact materials. Samples from different RPET feedstock suppliers used in food grade thermoform packaging were grouped into three-month quarters within each year of manufacture. All rigid RPET samples were digested in nitric and hydrochloric acid using a microwave assisted digestion, followed by quantification in a radial inductively coupled optical emission spectrometer (ICP-OES). Results of this study determined that antimony and aluminum levels remained mostly constant between 2010 to 2018, with concentrations ranging from 190 µg/g to 375 µg/g and 150 µg/g to 215 µg/g, respectively. Titanium concentrations ranged between 1 µg/g and 4.5 µg/g, and iron concentrations from 5 µg/g to 21 µg/g. Cadmium, lead, and chromium levels were all below 5 µg/g. Notable exceptions are 2013 Q1, which contained a chromium concentration of 54 µg/g PET, an iron concentration of 42 µg/g, and a titanium concentration of 6 µg/g; and 2014 Q1, which contained reduced antimony concentrations of 90 µg/g. Differences were found in feedstocks of RPET between mechanically processed flake and solid-state pellets with slightly higher antimony values (a 25-100 µg/g increase) in solid-state pellets. These findings provide much needed data to make informed decisions when evaluating threshold levels and exposure to heavy metals in recycled packaging.

Plasticizers in Food Contact Materials and Food Products

Katherine Carlos, PhD, FDA

PVC is a common food contact material that can be plasticized to increase its flexibility. Phthalates are one of many chemical compounds that are used as plasticizers in PVC. They may be used in packaging materials for foods and can also be found in components of certain food processing equipment such as conveyor belts, tubing and/or hoses. In recent years, there has been renewed interest in understanding the potential health effects of phthalates, as well as the possible human exposure levels. However, there is limited information available about the major routes of exposure to phthalates. Transfer of plasticizers from packaging to the surfaces of foods can occur. A recent study investigated the plasticizers currently used in fifty six different samples of PVC food packaging and food processing materials available for purchase in the U.S. Nine different plasticizers including three phthalates, diethylhexyl phthalate (DEHP), diisononyl phthalate (DINP), and diisodecyl phthalate (DIDP), were identified in the products tested. The plasticizer concentrations ranged from 1- 53% depending on the types of food contact materials and the type of plasticizer. Overall, and constant with past testing, manufacturers are switching away from phthalates as their primary plasticizer to alternate compounds such as ESBO, ATBC, DEHT, DINCH, DEHA and DINA.

Additional studies are underway investigating the phthalate concentration of non-PVC packaging and food products. Due to the widespread use of plasticized PVC in many commercial applications, background concentrations of phthalates are a concern when doing laboratory analyses. Several different extraction and analysis methods were evaluated for food contact materials such as coated paper and paper board. These methods were used to investigate the concentrations of phthalates present in these sample types. These studies will provide the Agency important information on potential phthalate exposure to consumers via food consumption.

Looking Beyond the Lamppost: High Throughput Measurement and Modeling for Chemical Prioritization

John Wambaugh, PhD, EPA National Center for Computational Toxicology

The U.S. National Academy of Sciences report "Using 21st Century Science to Improve Risk-Related Evaluations" recognized that high-throughput screening and high-throughput exposure prediction tools are both necessary to prioritize thousands of chemicals with respect to public health risk. High-throughput models based upon machine learning can estimate human exposure rates. Models currently exist for four sources of exposure: industrial manufacturing, pesticide use, consumer products, and diet. Of the four current pathways, diet is currently the least well covered by mechanistic exposure models. Machine learning models can only predict sources of exposure when given appropriate training data. These data may be obtained from databases or chemical surveillance of relevant media. Many of these data are limited to occurrence of chemicals in products, which is a prerequisite to, but does not guarantee exposure. To address the thousands of chemical-formulation combinations, models of migration or emission of chemicals are needed. Ultimately, exposure prediction and surveillance should allow prioritization of potential risk posed to public health. *This abstract does not necessarily reflect U.S. EPA policy.*

Session 2: Toxicological Exposure Assessments

Characterization of Genotoxicity and Endocrine Activity of Food Contact Materials by *in-vitro* Bioassays

Christian Kirchnawy, PhD, Team Leader Microbiology & Cell Culture, OFI Technologie & Innovation GmbH

In-vitro bioassays have been recently proposed as an analytical tool for the safety assessment of food contact materials (FCM), for the detection of substances of high toxicological concern, such as genotoxic or endocrine active substances. However, most in-vitro bioassays were originally designed for the analysis of pure substances, and are not yet optimized and validated as an analysis tool for FCM. There is still very limited knowledge on important analytical parameters such as the limit of detection, reproducibility or robustness to FCM sample matrices. Within the research project MIGRATOX, OFI and University of Applied Sciences Vienna have been working on the optimization and validation of in-vitro test methods for the analysis of food contact materials. A set of 31 different FCM samples (Paperboard, plastic and compound materials) have been tested for genotoxicity and endocrine activity with in-vitro bioassay methods. Spiking of all samples with known genotoxic or endocrine active compounds demonstrates that the in-vitro bioassays work in the presence of most FCM sample matrices, however for some sample dilutions were necessary due to cytotoxic or inhibiting effects. In 4 out of 31 tested samples a significant endocrine activity could be detected. 2 out of 31 samples showed indications for a possible genotoxic activity, which has to be further evaluated. 80% of the tested samples, did not show any indication of genotoxic or endocrine activity.

Application of an Extended Decision Tree for the Safety Assessment of Food Packaging Materials

Tim Adams, PhD, FDA

The concept of the Threshold of Toxicological Concern (TTC) uses the principles of chemical grouping and read-across to prioritize the relative toxicity of chemical substances and determine levels of intake (TTC) below which a substance is considered safe. Substance with intakes greater than their respective TTC would be prioritized for further safety studies. The approach incorporates an understanding of chemical structure, metabolism, and animal toxicity data to establish exposure thresholds below which there is no appreciable human health risk. The Chemical Groups and exposure thresholds were originally established based on the Cramer et al. (1978) Decision Tree (CDT) and the Munro et al.'s (1996) proposal for establishing a Threshold of Concern. The CDT prioritizes chemical structures based upon their toxic potential using a sequence of 33 mainly structure-based yes or no questions to which the answer either refers the user to another question or assigns the substance to one of three classes of toxic potential. Given the scientific knowledge accumulated since 1978, the DT sequence is overdue for a comprehensive update. More than 15,000 scientific studies were reviewed to determine the effects of species, strain, sex, and target organ on toxicity and

metabolic fate. These studies provided no-observed-effect-levels for more than 1,900 substances that were then organized according to their structure, metabolic fate, and toxic potential. Analysis of this database resulted in the development of refined DT questions leading to an increased number of classes of toxic concern. The toxic potential of each class is quantified by determining the lowest 5th% NOEL from which TTC levels are determined. These classes of toxic potential can be applied to a vast group of chemicals, including food packaging materials, for prioritization for future evaluation or to determine the safety of these chemicals at the current intake levels.

Reevaluation of FDA's Packaging Factors Used to Calculate Consumer Exposure to Food Contact Substances in Food Packaging Materials

Jessica Cooper, PhD, FDA

The FDA's premarket safety assessment of food contact substances (FCSs) relies on evaluating probable consumer exposure to an FCS and its constituents as a result of the intended use of the FCS and ensuring that such exposures are supported by the available toxicological information. Probable consumer exposure is determined by combining migrant levels in food with information on packaging uses. For single use packaging, the FDA uses packaging factors (PFs), which includes consumption factors (CF) and food-type distribution factors (fT), to estimate exposures to the FCS and its constituents. PFs describe the fraction of the daily diet expected to contact specific packaging materials and specific types of food. Many of the FDA's PFs were developed over 40 years ago. Because there have been technological innovations in the food packaging industry, we have reevaluated these PFs. This presentation describes the information sources and tools at our disposal, our approach, and our initial efforts at updating PFs to reflect current food packaging use.

Exposure and Risk Assessment of Printing Inks used in Packaging under California Proposition 65

Sneha Bhatia, Sun Chemical

Today's consumer expects high quality and safe products in a convenient form. Packaging plays a crucial role in protecting the products from physical, chemical and environmental stress. Likewise, poor packaging materials can adversely impact the products and pose danger to human and environmental health. Inks and coatings are an important component of communication and shelf-appeal aspect of packaging. Recognizing the pivotal role of

packaging materials, there are Federal and State regulations designed to protect consumers and the environment from potentially harmful chemicals. The California Proposition 65 Safe Water Drinking Act is a right-to-know statue that requires everyone in the chain of commerce to provide a warning before exposing consumers in California to a chemical listed on the California Proposition 65 list. For packaging articles, the manufacturer who places the product into the marketplace is required to provide a warning notifying the Californian if either the product or the t packaging contains a listed chemical. The only exception is if the anticipated exposure level is below the Safe Harbor Limit (SHL). Printing inks and coatings may contain low-levels (<0.1%) of chemicals listed in California Proposition 65. In the final converted packaging these levels are often not-detectable and may not necessitate a warning. However, without an exposure assessment or testing, businesses carry the risk of not complying with California Proposition 65. Currently, in the literature there is no model available to readily estimate the exposure of chemicals from printing inks in the converted packaging. To fill this void an exposure assessment model was developed to estimate the amount of listed chemical from the printing ink or coatings in the packaging material.

Session 3: Risk Assessment and Regulatory Science Interpretation/Practical Significance

Challenges in Safety Evaluation of Food Contact Materials in Europe

Cristina Nerin, PhD, University of Zaragoza

Food contact materials (FCM) shouldn't transfer any substance to the food in contact with them that could endanger the human health. Although this is the general requirement to guaranty the safety of such materials, there are many questions to solve and many difficulties to overcome. The first one is to identify any single substance migrating from the FCM to the food or food simulant used. Many substances can be leached but their effect on human health is concentration dependent. Thus, after identification they need to be quantified. In this frame, the sensitivity of the analytical technology used for the purpose is critical. Many unknowns appear and need accurate identification. Non-intentionally added substances (NIAS) are often leaching from FCM and there is not information about them. Some substances can be dangerous at ppb level and others at ppm. With this information, which is difficult to get, time consuming and expensive, risk assessment of the FCM should be applied. Which are the criteria for that? Should the risk assessment applied to individual substances or to the mixtures? Are the toxicity values applied to mixtures? Can a theoretical approach such as the application of TTC (Threshold of Toxicological Concern) helps in this task? Are bioassays

the right solution for that? All these points will be discussed with some examples of FCM in the presentation.

Dietary Exposure and Toxicological Review of Epoxidized Soybean Oil (ESBO) from use in Food-Contact Materials

LaShonda Cureton, PhD, FDA

Plasticizers have a long history of use in the industrial manufacture and processing of polymers for the purpose of increasing the flexibility and strength of the material. Approximately 80–90% of the plasticizer market is devoted tomalmal the production of polyvinyl chloride (PVC), a highly versatile thermoplastic used to produce both rigid and flexible articles. Many types of plasticizers, including ortho-phthalate esters (OPE), can be added to PVC to impart flexibility. Recently, alternatives to OPEs, such as epoxy esters and aliphatic adipates, are becoming more prevalent for use in PVC-based food-contact articles. Epoxidized soybean oil (ESBO) is used as a plasticizer in flexible PVC for many food-contact articles, including food packaging and food processing equipment, from which it can potentially migrate into food and become a component of an individual's daily diet. The purpose of this review is to provide an update on the U.S. dietary exposure and toxicological information on ESBO used in PVC-based food-contact articles. The cumulative dietary concentration (CDC) and cumulative estimated daily intake (CEDI) for ESBO from its use as a plasticizer in PVC-based food-contact articles (i.e., gaskets for glass jar lids and film wraps) was calculated to be 2.6 mg/kg (i.e., ppm) and 0.13 mg/kg bw/d, respectively, for the general population. Some regulatory agencies have reported safety levels for ESBO, and the most conservative no observed adverse effect level (NOAEL) was identified to be 100 mg/kg bw/d (i.e., 2000 ppm) based on a two-year feeding study in rats. The current CEDI is well below these levels, supporting the safe use of ESBO in food-contact applications.

Chemicals in Plastic Packaging: Prioritization of Hazardous Substances

Jane Muncke, PhD, Food Packaging Forum Foundation

One of the main challenges for assessing the risks of chemicals originating from plastic packaging is the absence of information on the materials' exact chemical composition. To provide a first overview of the available information, we compiled the Chemicals associated with Plastic Packaging Database (CPPdb), which comprises 4283 unique substances with additional substance-specific information such as toxicity data, physico-chemical properties

and uses, where available. The CPPdb includes plastic monomers, additives, and other substances used during plastics manufacturing, such as solvents, and some non-intentionally added substances (NIAS). Using harmonized hazard classifications assigned by the European Chemicals Agency within the Classification, Labeling and Packaging (CLP) regulation implementing the United Nations' Globally Harmonized System (GHS), we ranked the substances in the CPPdb according to their hazard for human health and the environment. In addition, we also included endocrine disrupting properties and PBT (persistence, bioaccumulative and toxic) characteristics. Further, we present a case study where hazardous chemicals identified in the CPPdb were prioritized for human health and the environment, to facilitate substitution. Due to the lack of empirical hazard data for many of the substances in the CPPdb and the scarcity and reliability of chemical use information, we propose a data commons approach for filling data gaps.

Realistic Intake Assessment and Fully Informed Hazard and Risk Assessment: From Monomers to NIAS

Mitchell Cheeseman, PhD, Steptoe & Johnson LLP

The regulation and approval of food contact materials has always been based on precautionary assumptions and testing approaches to ensure reasonable certainty of public health protection. The presenter will explore such assumptions from the standpoints of both intake assessment and toxicological assessment. The presenter will contrast current intake assessments In addition, previous and entirely new probabilistic approaches will be presented to address the toxicological (hazard) portion of risk assessment for food contact materials, including NIAS.

From Packaging Safety Exposure Modelling to a Decision Support System for Food Packaging Innovation – including Safety and Environmental Assessment (GLOPACK)

Cronan McNamara, Creme Global

Creme Global is the data science technology partner in the GLOPACK (EU H2020) project. Building on Creme Global's work in the EU FP7 project FACET, the goal of GLOPACK is to develop environmentally friendlier and safer alternatives to the current range of food packaging. The project focuses on three complementary technologies: active, intelligent and bio-circular packaging.

The Creme™ Global team is curating food packaging related datasets and developing models (including chemical migration and consumer exposure models) and decision support tools. These are being deployed on a data science collaboration platform called Expert Models. This will result in a user-friendly yet holistic decision support system for industry and regulators.

In this talk, Cronan will discuss how data science and modelling are used in the above projects to assess safety and to enable the development of new, safer and cost-effective food packaging solutions.

Poster Abstracts:

Analysis of Data on Food-Contact Surface Area-to-Food Mass Ratios for the Estimation of Migration Levels of Food Contact Substance in Food.

Andres Gonzalez Bonet, FDA

When evaluating the exposure of a food contact substance subject of a premarket submission, FDA typically assumes that 10 grams of food contacts 1 square inch of single-use food contact article (FCA) (10 g/in2), equivalent to a food-contact surface-to-food mass ratio (SA/mF) of 6.45 dm2/kg, when estimating FCS migration to food. However, with the current trends toward consumer preference for convenience foods and technological advances in packaging materials, this value might not be representative of the SA/mF ratios for the wide range of packaged food currently consumed in the U.S. Therefore, we conducted a literature search for publications specifically reporting the food mass and SA for a variety of food and packaging scenarios. We identified publications, all from food and packaging collected in Europe, that reported the food mass (mF) and surface area (SA) values for the various food and packaging scenarios. Using these values, we calculated SA/mF ratios for different food types and packaging materials. We also conducted food intake analyses to estimate intakes of the different food types. Here, we will describe an approach for calculating a weighted mean SA/mF ratio for all packaged food consumed in the US using the SA/mF ratios and food intakes for all foods and each food type.

Real-Time Detection of Volatile Organic Compounds and Heavy Metals in Laminated Films

Lingling Liu, PhD, Iowa State University

Volatile organic compounds (VOCs) and heavy metals (HMs) contaminants in laminated films are big concerns for food packaging corporations since they are under regulations in the US. There are needs to develop rapid or near real-time detection systems for laminated packaging films as conventional benchtop laboratory analyses are time-consuming and expensive. The lag time associated with the time required for sample collection, shipment and analysis could be detrimental if the contaminant levels are beyond the safety regulation limits. Thus in this study, a real-time detection system of VOCs and HMs with network interface was established during high speed laminated film production. The real-time detection system with real-time data interface and threshold gauge was installed on a designated line in a local food packaging company. Specifically, multiple sensor units with high sensitivity, including photoionization (PID), infrared (IR) and semiconducting metal oxide (SMO) sensors, were purchased, installed and used for rapid detection of various VOCs. Energy dispersive X-ray fluorescence (ED-XRF), which has been validated based on our previous study, was used for fast detection of HMs. Online data were collected in conjunction with off-line, benchtop analysis to be optimized by system capability of 1, 5 and 10 minute sampling rates. Specifically, film samples were collected and analyzed with gas chromatography (GC)-mass spectrometry (MS) and inductively coupled plasma optical emission spectrometry (ICP-OES). Correlations were found between the VOCs detected by the sensors and those tested by GC-MS. Similarly, correlations were found between ED-XRF and ICP-OES regarding the detection of HMs. Results from this study show the potential to decrease cost of labor and laboratory analysis, increase market share through traceability and marketing of 100% inspection packaging substrates while demonstrating real-time customer and regulatory compliance for laminated packaging.

Understanding Detection of Perfluoroalkyl Substances (PFASs) in Food Packaging

Rkia Moutiq, PhD, Iowa State University; presented by Greg Curtzwiler, PhD, Iowa State University

Recent studies have raised awareness and concern of residuals and intentionally added fluorine in packaging materials, on the environment and human health. Data has shown that while fluorine may be present, it does not necessarily indicate the presence of PFASs. Additionally, proper laboratory technique and method validation can significantly influence results and thus raised concern by regulatory bodies for method selection and proper

detection when establishing exposure limit values. Much work has been done on specific detection of PFOS and PFOA due to consumer and environmental awareness with limited information on appropriate exposure levels in food packaging. Many studies have reported the inability to detect PFOA and PFOS due to poor method sensitivity with low recovery with intentionally spiked samples. The purpose of this study was to evaluate recovery rates when using liquid extractions followed by analysis with liquid chromatography. Various recovery methods were evaluated for detection of PFOA and PFOS in paper packaging. Results of this study found significant differences in method selection and sample preparation. A modified method with newly developed sample extraction apparatus for sample preparation, outlined by Moreta and Tena, yielded the highest recovery for PFOS and PFOA with greater than 70% recovery with a repeatable limit of detection of 4.0 ng/g. The selected modified method utilized focused on ultrasound liquid extraction (PULSE) coupled with LC-MS/MS or UHPLC-(QTOF) MS/MS. Results of this research can be used for selection of standardized methods and sample preparation for increased accuracy and precision when determining regulatory thresholds for public and private testing laboratories.

Ensuring the Safety of Food Contact Materials by Addressing the Challenges in FCM Risk Assessment

Jane Muncke, PhD, Food Packaging Forum Foundation

Food packaging is essential for the food supply chain as it protects food from physical damage and external contamination during storage, transportation and distribution. However, chemicals can migrate from food packaging and food contact articles (FCAs) into foods, therefore warranting chemical risk assessment as human health may be affected. A review of the regulatory requirements for risk assessment of food contact materials (FCMs) in the United States and Europe has identified scientific challenges. In this talk, we will review these challenges and discuss how they can be overcome.

Firstly, chemical exposures from FCAs are often unknown or insufficiently addressed, thus making cumulative exposure estimates impossible. Secondly, risk assessment of FCMs focuses on monomers and additives used during manufacture, but intentional and nonintentional reaction products are often not considered. Thirdly, the structures of many chemicals migrating from FCMs are unknown; therefore, risk assessment using the current approach is not feasible. Fourthly, mixture toxicity of migrates is not assessed, although this would reflect real-life exposures. Fifthly, hazards associated with many highly prevalent non-communicable diseases in the human population are not routinely tested.

To improve the safety of FCMs and FCAs, adequate toxicological testing could be further developed and implemented to risk assess all FCCs migrating from finished FCAs, since humans are exposed to these chemical mixtures. Limiting the selection of available starting substances to tested chemicals which have been shown not to possess hazard properties is another possibility to reduce potential risk. We will discuss these and other options for ensuring FCAs are safe.

Method Selection to Measure Migration of NIAS in Multi-Laminate Polyolefin / Polyurethane, Poyol Isocyanate Structures

Ryan Ramey, MS, Clemson University

NIAS (Non-Intentionally Added Substances) are a subject of concern to the food packaging industry. Testing methods to measure NIAS have not yet been standardized due to the variety of equipment used, sampling methods, food simulants, and detection methods as well as complexity in chemical compounds to be measured. While it may not be possible to standardize detection of NIAS by one specific method, the objective of this work will be to dose a multi-laminate structure with a known adhesive ratio and determine if any amount of NIAS in the packaging laminate can be detected using a method which is yet to be determined for this study. Primary Aromatic Amines (PAA's) are one component NIAS that can form during a reaction in the lamination process where unreacted isocyanate monomers from PU adhesive react with moisture. This poster will discuss future research where acidic based food simulates will be utilized to test for migration of PAA's with in-house made laminate structure pouches, made on pilot equipment where different ratios of PU adhesive will be added. Analysis could be conducted using a combination of spectrophotometric methods (NEDA) and UHPLC-MS/MS. It is hoped that discussions taking place at the ILSI North America Food Packaging Conference will help determine a "best" method to use for this study.

MS Determination of Photolytic Decomposition Products (PDP's) of Photoinitiators (PI's) and Migration Studies of PI's and PDP's in Food Packaging

Joseph Scarsella, MS Student at Rutgers University

Resins in food packaging coatings are increasingly cured by UV radiation of photoinitiators (PI's) with minimal energy requirements and without harmful solvents. When exposed to UV,

PI's produce free radicals that catalyze polymerization of monomers and pre-polymers into resins. Upon UV-exposure, PI's can decompose to form photodecomposition products (PDP's), which remain as residuals that can migrate into foods, becoming dietary components. As interest in additive toxicity has increased, food safety organizations have developed regulations to monitor migration of PI's and PDP's from food packaging. While intact PI's have been investigated, research on formation and migration of PDP's is sparse.

This research characterized and quantified PDP's of 24 PI's commonly used in food packaging. PI's were applied as films onto foil, UV-irradiated using an energy level representing maximum typically used commercial parameters, and extracted from the foil. PDP's formed were determined by GC-MS and ESI-MS. Tentative mechanisms of formation were proposed. PI reference standards were analyzed as controls.

In total, 107 PDP's were identified, 93 of which have not been previously reported as PDP's of PI's. The compilation of PDP's will aid industry in tracing the sources of compounds identified in food packaging migration studies.

To assess the frequency and extent of migration of PI's and PDP's in actual materials, migration data from 258 UV-cure food packaging samples analyzed in previous studies were re-examined. Most commonly observed PI's: Darocur 1173 (139 samples, max 1557ng/cm2) and benzophenone (88 samples, max 948ng/cm2). Most commonly observed PDP's: 2,4,6-trimethylbenzaldehyde from TPO (130 samples, max 1938ng/cm2) and 1-phenyl-2-butanone from Irgacure 369 (83 samples, max 441ng/cm2).

These results show the importance of tracking PDP's in food packaging and provide a base for developing analytical libraries to identify them.

Non-Targeted Analysis of Leachable Residues from Food Contact Materials (FCMs) using HPLC-QTOF-MS

Lei Tian, McGill University, Department of Food Science and Agricultural Chemistry

Food safety regulations for food contact materials (FCMs) usually rely on the assessment of chemical migration in order to reduce human exposure to chemical residues that could leach from FCMs into the food. In this field, there is a need to develop non-targeted analytical tools which can identify unknown (e.g. non-intentionally added substances) or unexpected residues leaching out of the materials. In this work, a method based on high performance liquid chromatography coupled to quadrupole time of flight mass spectrometry (HPLC-QTOF-MS) was developed and optimized to detect and identify leachable contaminants in FCMs. Firstly,

the method was optimized for known compounds to investigate systematically the effect of post-acquisition data processing filters on the feature extraction in non-targeted analysis. Several parameters significantly reduced the number of correct identifications of some target trace residues, which confirms that data post-processing has to be carefully optimized to decrease the risk of false negatives. Optimized parameters were applied to study leachables in a range of FCMs, and several unknown/unexpected residues were identified.

Evaluation of Estrogenic Activity of Novel Bisphenol A Alternatives, Four Bisguaiacol F Compounds, by *in vitro* Assays

Changqing Wu, PhD, University of Delaware

Alternatives to Bisphenol A (BPA), such as lignin-inspired bisguaiacol F (BGF), for packaging and bottling applications are of interest due to increasing evidence of estrogenic activity (EA) and exposure correlated to the adverse health effects of BPA. However, the endocrine disruption potential of BGF is relatively unknown. In this study, the EA of four BGF samples with different regioisomer ratios was quantified relative to 17b-estradiol at nine ten concentrations through the use of two sensitive and accurate *in vitro* assays: MCF-7 cell proliferation and VM7Luc4E2 transactivation. The results of both assays suggest that BGF mixtures with higher molar ratios of p,p′-BGF and o,p′-BGF regioisomers exhibited lower EA activity than BPA, while BGF samples containing higher molar ratios of m,p′-BGF had no detectable EA. These findings demonstrate through synergistic *in vitro* tests that BGF mixtures with higher molar concentrations of m,p′-BGF may contribute to BGF having undetectable EA, and further suggest the potential of BGF as a viable alternative to BPA for the realization of more environmentally friendly materials.

Raman Spectroscopy for Screening Tubing for Phthalates

Betsy Yakes, PhD, FDA

Phthalate and non-phthalate plasticizers are used in a wide variety of food contact materials in order to increase the flexibility of the material. Recent scrutiny has occurred on the use of plasticizers in milk processing tubing and the potential for transfer of these compounds into this commodity. In order to understand the prevalence of use of phthalate versus non-phthalate tubing in the industry, there is a need for a robust, rapid, portable analytical method. FDA has recently begun acquiring and evaluating portable devices for field and or inspection use, including Raman and infrared spectroscopy which potentially could detect and

identify plasticizers in tubing. This presentation will highlight our initial research using one Raman device and illustrate the potential of this technology as a field screening technique for industry surveys.

Dietary Risk Assessment on Chemicals used in Food and Beverage Processing and Packaging

Xinyu Yang, PhD, Nalco Water, Ecolab

Chemicals contact with food during production, processing and packaging prior to consumption. We will highlight some of the methodologies used to assess the risk of dietary exposure to numerous chemicals used in food and beverage processing, and paper packaging industries using the guidelines from US Federal Agencies, i.e. USFDA, regarding human dietary exposure and safety. These methods can be used to evaluate the safety of these chemicals prior to either registration with regulatory agencies or commercial applications. We will provide examples on how we apply deterministic approach to exposure assessment of chemicals used in the manufacturing of paper for food packaging. In addition, we will walk through the typical process to gather toxicological information through read-across, understand the mechanism of toxicity and used appropriate uncertainty factors to extrapolate data from animal studies to humans. FDA use dietary risk assessments to evaluate the hazards posed by direct and indirect food contact substances (FCSs) and follow the principles of standard risk assessment paradigm. Therefore, it is key for regulatory toxicologists in food and beverage, and packaging industries to apply such paradigm into the dietary risk assessments.

Migration and Metabolic Studies of Low Molecular Weight Cyclic Polyester Oligomers (Lactones) from Food Packaging Lamination Adhesives

Alice Zhang, Rutgers University

Laminate structures are widely used for food packaging applications. Polyester urethane based adhesives are very common materials for bonding the layers of such laminates together. Unintended by-products of polyester synthesis include low molecular weight (mw) cyclic oligo-esters (lactones) that lack the required hydroxyl functionality to react with isocyanates to form the intended high mw polyurethane polymer and remain as impurities with high migration potential. Our investigation conducted migration studies of 537 commercial and/or developmental food packaging laminate structures using food simulants with gas chromatography-mass spectrometry (GC-MS) analyses of the extracts. A subset of the extracts were also analyzed by high performance liquid chromatography-mass spectrometry

(HPLC-MS). This report presents electron ionization mass spectra and molecular structures of 106 cyclic oligoesters including a series of novel as well as previously identified species. 56 cyclic oligoesters migrated from the 537 laminate samples analyzed were evaluated for frequency of occurrence and migration concentration range. The data consist of a series of novel as well as previously identified cyclic oligo-esters. We synthesized and purified three of the most commonly observed lactone migrants, cyclic diethylene glycol adipate (DEG-AA), cyclic diethylene glycol phthalate (DEG-PA) and cyclic neopentyl glycol adipate dimer (NPG-AA 2+2), representing aliphatic type, aromatic type and dimer type respectively for further *in vitro* and *in vivo* metabolic study. The results showed that all three cyclic oligoesters can break down to linear monoesters, diol monomers and diacid monomers under enzyme hydrolysis. Our study will provide important references for identification and risk assessment of the cyclic polyester oligomer migrants.