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Food Safety Briefs

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Chemical Risk Assessment

Risk Assessment or Assessment of Risk? Developing an Evidence-Based Approach for Primary Producers of Leafy Vegetables to Assess and Manage Microbial Risks

Monaghan JM, Augustin JC, Bassett J, Betts R, Pourkomailian B, Zwietering MH. *J Food Prot*. 2017 Mar 28:725–733. doi: 10.4315/0362-028X.JFP-16-237. Article Link

Significance: This article highlights the need for evidence to be more easily available and accessible to primary producers and identifies the need to develop hygiene criteria to aid validation of proposed interventions.

Over the last 10 years, some high-profile foodborne illness outbreaks have been linked to the consumption of leafy greens. Growers are required to complete microbiological risk assessments (RAs) for the production of leafy crops supplied either to retail or for further processing. These RAs are based primarily on qualitative judgements of hazard and risks at various stages in the production process but lack many of the steps defined for quantitative microbiological RAs by the Codex Alimentarius Commission. This article is based on the discussions of an industry expert group and proposes a grower RA approach based on a structured qualitative assessment, which requires all decisions to be based on evidence and a framework for describing the decision process that can be challenged and defended within the supply chain.

Origin of the TTC Values for Compounds That Are Genotoxic and/or Carcinogenic and an Approach for Their Re-Evaluation

Boobis A, Brown P, Cronin MTD, Edwards J, Galli CL, Goodman J, Jacobs A, Kirkland D, Luijten M, Marsaux C, Martin M, Yang C, Hollnagel HM. *Crit Rev Toxicol*. 2017 May 16:1–23. doi: 10.1080/10408444.2017.1318822. Article Link

Significance: Critical to the application of the TTC approach to substances that are likely to be DNA-reactive mutagens is the reliability of the software tools used to identify such compounds. Current methods for this task are reviewed and recommendations made for their application.

The threshold of toxicological concern (TTC) approach is a resource-effective de minimis method for the safety assessment of chemicals, based on distributional analysis of the results of a large number of toxicological studies. It is being increasingly used to screen and prioritize substances with low exposure for which there is little or no toxicological information. The first step in the approach is the identification of substances that may be DNA-reactive mutagens, to which the lowest TTC value is applied. This TTC value was based on the analysis of the cancer potency database and involved a number of assumptions that no longer reflect the state-of-the-science and some of which were not as transparent as they could have been. Hence, review and updating of the database is proposed, using inclusion and exclusion criteria reflecting current knowledge. A strategy for the selection of appropriate substances for TTC determination, based on consideration of weight of evidence for genotoxicity and carcinogenicity is outlined. Identification of substances that are carcinogenic by a DNA-reactive mutagenic mode of action and those that clearly act by a non-genotoxic mode of action will enable the protectiveness to be determined of both the TTC for DNA-reactive mutagenicity and that applied by default to substances that may be carcinogenic but are unlikely to be DNA-reactive mutagens (i.e. for Cramer class I-III compounds).

An Integrated Chemical Environment to Support 21st-Century Toxicology

Bell SM, Phillips J, Sedykh A, Tandon A, Sprankle C, Morefield SQ, Shapiro A, Allen D, Shah R, Maull EA, Casey WM, Kleinstreuer NC. *Environ Health Perspect*. 2017 May 24;125(5):054501. doi: 10.1289/EHP1759. Article Link

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Access to high-quality reference data is essential for the development, validation, and implementation of in vitro and in silico approaches that reduce and replace the use of animals in toxicity testing. Currently, these data must often be pooled from a variety of disparate sources to efficiently link a set of assay responses and model predictions to an outcome or hazard classification. To provide a central access point for these purposes, the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods developed the Integrated Chemical Environment (ICE) web resource. The ICE data integrator allows users to retrieve and combine data sets and to develop hypotheses through data exploration. Open-source computational workflows and models will be available for download and application to local data. ICE currently includes curated in vivo test data, reference chemical information, in vitro assay data (including Tox21TM/ToxCast™ high-throughput screening data), and in silico model predictions. Users can query these data collections focusing on end points of interest such as acute systemic toxicity, endocrine disruption, skin sensitization, and many others. ICE is publicly accessible at https://ice.ntp.niehs.nih.gov. https://doi.org/10.1289/EHP1759.

Packaging

An Effect-Directed Strategy for Characterizing Emerging Chemicals in Food Contact Materials Made From Paper and Board

Rosenmai AK, Bengtström L, Taxvig C, Trier X, Petersen JH, Svingen T, Binderup ML, Barbara Medea Alice VV, Dybdahl M, Granby K, Vinggaard AM. *Food Chem Toxicol*. 2017 May 29;106(Pt A):250–259. doi: 10.1016/j.fct.2017.05.061. Article Link

Significance: A tool for identifying emerging chemicals in food packaging has been developed.

Food contact materials (FCM) are any type of item intended to come into contact with foods and thus represent a potential source for human exposure to chemicals. Regarding FCMs made of paper and board, information pertaining to their chemical constituents and the potential impacts on human health remains scarce, which hampers safety evaluation. Authors describe an effect-directed strategy to identify and characterize emerging chemicals in paper and board FCMs. Twenty FCMs were tested in eight reporter gene assays, including assays for the AR, ER, AhR, PPARγ, Nrf2 and p53, as well as mutagenicity. All FCMs exhibited activities in at least one assay. As proof-of-principle, FCM samples obtained from a sandwich wrapper and a pizza box were carried through a complete step-by-step multi-tiered approach. The pizza box exhibited ER activity, likely caused by the presence of bisphenol A, dibutyl phthalate, and benzylbutyl phthalate. The sandwich wrapper exhibited AR antagonism, likely caused by abietic acid and dehydroabietic acid. Migration studies confirmed that the active chemicals can transfer from FCMs to food simulants. In conclusion, the authors report an effect-directed strategy that can identify hazards posed by FCMs made from paper and board, including the identification of the chemical(s) responsible for the observed activity.

Food Allergens

Peanut Allergen Threshold Study (PATS): Novel Single-Dose Oral Food Challenge Study to Validate Eliciting Doses in Children With Peanut Allergy

Hourihane JO, Allen KJ, Shreffler WG, Dunngalvin G, Nordlee JA, Zurzolo GA, Dunngalvin A, Gurrin LC, Baumert JL, Taylor SL. *J Allergy Clin Immunol*. 2017 May;139(5):1583–1590. doi: 10.1016/j.jaci.2017.01.030. Article Link

Significance: The novel single-dose oral food challenge appears clinically safe and patient acceptable, regardless of the outcome. It identifies the most highly dose-sensitive population with food allergy not otherwise identifiable by using routinely available peanut skin prick test responses or specific IgE levels, but this single-dose approach has not yet been validated for risk assessment of individual patients.

Eliciting doses (EDs) of allergenic foods can be defined by the distribution of threshold doses for subjects within a specific population. The ED05 is the dose that elicits a reaction in 5% of allergic subjects. The predicted ED05 for peanut is 1.5 mg of peanut protein (6 mg of whole peanut). Researchers sought to validate the predicted peanut ED05 (1.5 mg) with a novel single-dose challenge. Consecutive eligible children with peanut allergy in 3 centers were prospectively invited to participate, irrespective of previous reaction severity. Predetermined criteria for objective reactions were used to identify ED05 single-dose reactors. 518 children (mean age, 6.8 years) were eligible. 378 children (206 male) completed the study. 58 (15%) children experienced signs of a mild and transient nature that did not meet the predetermined criteria. Only 8 (2.1%; 95% CI, 0.6%-3.4%) subjects met the predetermined criteria for an objective and likely related event. No child experienced more than a mild reaction, 4 of the 8 received oral antihistamines only, and none received epinephrine. Food allergy–related quality of life improved from baseline to 1 month after challenge regardless of outcome ($\eta 2 = 0.2$, $P < .0001$). Peanut skin prick test responses and peanut- and Ara h 2–specific IgE levels were not associated with objective reactivity to peanut ED05. A single administration of 1.5 mg of peanut protein elicited objective reactions in fewer than the predicted 5% of patients with peanut allergy.

Processing Effects on Tree Nut Allergens: A Review

Vanga SK, Raghavan V. *Crit Rev Food Sci Nutr.* 2017 Nov 22;57(17):3794–3806. doi: 10.1080/10408398.2016.1175415. Article Link

Significance: This review gives an update on the recent findings on how conventional and novel processing methods influence the tree nut allergens.

"Tree nut" is a broad term for classification of nuts that include cashews, almonds, hazelnuts, etc. Reports of mild to adverse immune reactions following the consumption of these nuts has been on a rise in recent years. Currently, about 1.2–2% of the world's population suffer from sensitivity to tree nuts. The only solution is complete abstinence from the allergy causing tree nut which is not feasible in most cases due to issues like cross contamination or their presence in the form of hidden ingredients in processed foods. Various studies have shown that food processing can effectively vary the secondary structures of the allergenic protein which in turn influences their functional properties. But, the impact of these processing methods on tree nuts allergens is mixed.

Pathogen Detection

Next Generation Sequencing-Based Multigene Panel for High Throughput Detection of Food-Borne Pathogens

Ferrario C, Lugli GA, Ossiprandi MC, Turroni F, Milani C, Duranti S, Mancabelli L, Mangifesta M, Alessandri G, van Sinderen D, Ventura M. *Int J Food Microbiol.* 2017 Sep 1;256:20–29. doi: 10.1016/j.ijfoodmicro.2017.05.001. Article Link

Significance: This novel detection method may represent an alternative and/or a complementary approach to PCR-based techniques, which are routinely used for FBP detection, and could be implemented in (parts of) the food chain as a quality check.

Contamination of food by chemicals or pathogenic bacteria may cause particular illnesses that are linked to food consumption, commonly referred to as foodborne diseases. Bacteria are present in/on various foods products, such as fruits, vegetables and ready-to-eat products. Bacteria that cause foodborne diseases are known as foodborne pathogens (FBPs). Accurate detection methods that are able to reveal the presence of FBPs in food matrices are in constant demand, in order to ensure safe foods with a minimal risk of causing foodborne diseases. Here, a multiplex PCR-based Illumina sequencing method for FBP detection in food matrices was developed. Starting from 25 bacterial targets and 49 selected PCR primer pairs, a primer collection called foodborne pathogen - panel (FPP) consisting of 12 oligonucleotide pairs was developed. The FPP allows a more rapid and reliable identification of FBPs compared to classical cultivation methods. Furthermore, FPP permits sensitive and specific FBP detection in about two days from food sample acquisition to bioinformatics-based identification. The FPP is able to simultaneously identify eight different bacterial pathogens, i.e. Listeria monocytogenes, Campylobacter jejuni, Campylobacter coli, Salmonella enterica subsp. enterica serovar enteritidis, Escherichia coli, Shigella sonnei, Staphylococcus aureus and Yersinia enterocolitica, in a given food matrix at a threshold contamination level of 101cell/g.

Scientific Integrity

Peer Review: A System Under Stress

Gropp RE, Glisson S, Gallo S, Thompson L. *BioScience.* 2017;67(5):407–410. Article Link

The American Institute of Biological Sciences (AIBS) convened a meeting in Washington, DC, on 6 December 2016 to explore The Role of Peer Review in Informed Decision-making. The participants included representatives from AIBS member organizations, government agencies, research funders, scholarly publishers, and scholars of peer review.