PROCESS-INDUCED FOOD TOXICANTS
PROCESS-INDUCED FOOD TOXICANTS

Occurrence, Formation, Mitigation, and Health Risks

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Diets are developed to ensure adequate nutrition with the desire to maintain “good” health. This, in turn, directs attention to the quality and safety of individual foods comprising the diet. Whether justified or not, food safety concerns have increased over the past two decades, primarily due to food- and water-borne disease outbreaks (microbiological causation) and some issues of a chemical nature. This has also been accompanied by consumers becoming more aware—and indeed better informed—concerning the risks that consumption of certain foods and food components have with a potential link to degenerative diseases such as diabetes and cancer. Not only is the choice and balance of the “right” foods an essential part of a healthy lifestyle, but how food is prepared and processed can be an important factor.

It has been known for a long time that formation of certain chemicals during food processing or preparation may pose a risk to human health. Examples are polycyclic aromatic amines (PAHs) in grilled/barbecued meat, N-nitrosamines in cured meats and fish, and heterocyclic aromatic amines (HAAs) in overheated meats and fish, which were identified as food-borne carcinogens and consequently a potential human health concern since the early 1970s. In the past few years, the formation of chemicals, particularly those with a potentially adverse effect on human health, has received increased attention. This is illustrated by the report that surfaced unexpectedly in 2002 of the occurrence of acrylamide in commonly consumed foods. The acrylamide issue has become worldwide in scope.

Several more chemicals have been added to the list of undesired process-induced chemicals, also termed process contaminants or process toxicants. With the increasing sensitivity of analytical methodologies and knowledge concerning the formation of both beneficial and potential toxicants during the...
complex reactions, such as the Maillard reaction, occurring during the processing of foods, the numbers of these chemicals of potential concern will continue to increase. Often these are present in very small amounts in foods consumed in normal diets. An important question then becomes: at what amount does the presence of these toxicants in foods consumed by humans become a potential health problem? Answering such a question normally involves carrying out a quantitative risk assessment.

Readers will notice that the two terms, “contaminant” and “toxicant,” are used interchangeably in this book. This is because today there is no clear distinction between a process contaminant and toxicant. It is, however, the editors’ view that the term “contaminant” may encompass a broader definition not necessarily restricted to toxic substances.

This book is divided into two parts and presents a comprehensive update of the major toxicants that may be generated during food processing and food preparation. Part 1 considers the different processes used in the manufacture of foods, including food prepared in the home, and the risk of formation of food-borne toxicants linked to the different technologies and processes. Common methods encountered in a typical industrial or home cooking environment are included. For each of these, the aspects addressed include (1) occurrence in food, (2) methods of analysis, (3) routes of formation, (4) mitigation options, (5) human exposure, (6) health risks, and (7) risk management.

Information regarding the first five aspects is critical to accomplishing a quantitative risk assessment that will indicate the likelihood of occurrence of a potentially adverse health effect. Thorough evaluation of the toxicological risks of food-borne toxicants is pivotal for developing risk management approaches. From the consumer’s perspective, risk management of the potentially adverse risks is an important issue.

An important step in managing such risks initially occurs in the food manufacturing environment. This begins with the application of well-established food safety procedures such as HACCP (Hazard Analysis Critical Control Point). In terms of microbiological and allergen risks, these are usually relatively well controlled in an industrial setting through the use of such procedures. However, knowledge is, in general, lacking on how to effectively deal with processing contaminants. This involves the need for innovative technologies with both a high level of food safety while yielding the functionalities that maintain the nutritional quality of the food vis-à-vis traditional techniques.

Furthermore, it has become increasingly important to recognize that health beneficial chemicals are also formed during the processing of foods, as indicated by several scientific studies linking cocoa, tea, and coffee consumption to certain health benefits. Mitigation measures may in some cases lead to changes in the nutritional profile of foods; for example, acrylamide reduction in some bakery wares is achieved through the replacement of the baking agent ammonium bicarbonate with the corresponding sodium salt. This raises the question of the potential impact of the mitigation measure on sodium intake
and possible health risks, particularly in susceptible subgroups of the population suffering from elevated blood pressure.

To perform a transparent and understandable quantitative assessment of this type, there is a need for a common or at least comparable denominator of risks versus benefits. This is where a major challenge lies today. Finally, communicating food safety risks is a key component of the risk analysis framework and cannot be over-emphasized. All these important topics are dealt with in Part 2 of this book.

The editors of this book have been very fortunate in attracting contributions from leading experts in their field. These individuals come from industry, academia, and regulatory/government bodies, bringing the diversity of backgrounds and viewpoints necessary to adequately address the wide scope of issues inherent in dealing with food process toxicants. We have also attempted to provide both European and North American approaches to dealing with food process contaminants, selecting experts from both geographical regions.

However, many challenges remain. Today, in most cases, clear-cut answers concerning the impact of food process toxicants on human health cannot be given. It is hoped that this book will help clarify important issues and caveats involved in the safety assessment of such substances, and will highlight the endeavors and commitments of all stakeholders at an international level to ensure that the foods we prepare are safe to eat.

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PART I

SPECIFIC TOXICANTS RELATED TO PROCESSING TECHNOLOGY
INTRODUCTION TO FOOD PROCESS TOXICANTS

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1.1 HISTORY AND ROLE OF FOOD PROCESSING

Food processing and preservation, the traditional focus of food science and technology, have played, and continue to play, important roles in achieving food sufficiency (availability, quality, and preservation) for the human race. These practices originated in recognition of a need to improve the edibility of many food sources and to maintain food supplies for longer periods of time than their seasonal availability. With the transition from a hunter–gatherer society to life in villages and early agriculture, this need became even greater and emphasis on food preservation became increasingly important. This, of course, was paralleled by the development of processes/processing of animal, vegetable, and marine raw materials into usually more palatable, portable, and nutritionally dense foods. In many cases, if not most, this occurred in a fortuitous, rather than planned, manner as natural causes of food processing and preservation were observed and adapted to human use.

Food processing involves the actions taken from the time a raw product (crop, animal, fish) is harvested, slaughtered, or caught until it is sold to the consumer. By this process, the parts regarded as most valued are separated from by-products or waste. Equally enhanced is the palatability/digestibility...
of foods, illustrated in the transformation of baking flour into bread, to main-
tain or increase quality attributes and to ensure safety. Increasing understand-
ing of the science involved in food loss, deterioration of quality, and means of
improving the palatability of foods has resulted in development of the sophis-
ticated methods of food processing and preservation now in use. The work of
Pasteur, resulting in identification of the role of microorganisms in food spoil-
age and development of technology leading to canning by Nicolas Appert in
1809, can be considered initial steps in the development of modern food
processing and preservation (1). As the world population continues to grow,
resulting in increasing requirements and demands for food availability and
safety, new and improved methods of food processing and preservation are
needed and in development.

The term “minimal processing” is frequently used to describe foods, such
as vegetables, that are harvested, sorted, and washed (or similar minimal inva-
sive procedures) before distribution and sale. This is done to distinguish these
more “natural” products from those that undergo more extensive processing
procedures. Over the last years the development and distribution of minimally
processed foods has been increasing steadily. This trend has been triggered by
the demand for fresh and convenient products as well as for more natural
products, i.e., less processed or containing less salt, sugar, or preservatives.

Such foods range from fruits and vegetables, which are usually only sub-
mited to washing (with or without biocides), trimming, slicing, or shredding,
to prepared foods processed by applying minimal bactericidal treatments in
combination with different physicochemical hurdles to ensure their stability
and safety. These foods represent certainly a challenge to manufacturers since
no or only minimal killing steps are applied, and, at the same time, require-
ments for more global availability and longer shelf life are increasing. The fact
that these challenges are frequently underestimated or not mastered suffi-
ciently is illustrated by the occurrence of numerous incidents linked to a
variety of products involving different pathogens. Outbreaks related to mini-
mally processed foods often encompass chilled foods such as sous-vide prod-
ucts, pasteurized vegetables, and baked potatoes, which have frequently been
linked to Clostridium botulinum intoxication (2–4).

Early types of processing/preservation evolved from observations of natural
processes, e.g., drying, curing (such as salting), smoking, fermentation, and
reducing storage temperature (refrigeration or freezing). Salting and smoke
processing originated at the beginning of human civilization, mainly employed
to preserve meat and fish. In fact, salting, pickling, and drying continued as the
primary means of preserving foods until the twentieth century and the advent
of mechanical refrigeration (5). More modern means of preservation pre-
cluded the use of copious amounts of salt, exemplified by the far reduced
concentrations of salt in ham today (<2%) versus that in hams produced in
the first half of the twentieth century (>6%). Changes to technologies were
also introduced a few decades ago with regard to cured meats and residual
nitrite content. Nitrite, used to cure meat, acts as a preservative against
Clostridium botulinum and other spoilage bacteria. However, during the 1970s, concern arose due to the role of nitrates in the formation of carcinogenic nitrosamines (Chapter 4.1), as well as its contribution to the body burden. In modern cured meats, the nitrite amounts have decreased and are typically one-fifth of those found some 30 years ago. Moreover, the use of ascorbate—an effective inhibitor of nitrosamine formation—is an additional mitigation measure introduced in the production of most cured meats.

Smoke processing is still used today to preserve meat, especially in tropical countries. Smoke imparts appealing organoleptic properties, with concomitant preservation of nutrients. However, concern has been raised about the presence of both polycyclic aromatic hydrocarbons (PAHs) and nitrosamines in smoked foods. PAHs are covered in Chapter 2.8, with special attention to their formation, mitigation, and toxicology. Although the exposure risks in modern manufacture of meats and fish are considered minimal, alternatives to traditional smoking have been developed. Liquid smoke flavorings have gained popularity as they provide the same traits, i.e., desirable organoleptic properties, and preservation through antioxidation and bacteriostasis. Additional benefits include increased product consistency and absence of detectable animal carcinogens. In fact, approximately 75% of hot dogs produced in the United States contain aqueous liquid smoke flavorings (5).

Food preservation can be considered part of or an extension of food processing, since it involves the use of procedures to prevent or reduce spoilage of foods. Examples include the inactivation of enzymes and microorganisms by heating or reduction of moisture content, use of antimicrobial compounds, pasteurization (heat or irradiation), freezing, modified atmospheric packaging, and fermentation.

Techniques that have been used in food processing and preservation include:

- Drying/dehydration
- Curing
- Smoking
- Fermentation
- Canning
- Pasteurization (heat or irradiation)
- Freezing and refrigeration
- Additives
- Controlled atmosphere storage
- Aseptic packaging

Until the last quarter of the twentieth century, canning was widely used in homes throughout the rural United States. Inadequate heat treatment during the canning process occasionally resulted in severe illness or death caused by Clostridium botulinum that was not inactivated during the heating process and
resulted in subsequent formation of the toxin. Commercial canning, while having some outbreaks of botulinum poisoning, became used much more widely due to improved quality, safety, and increased urban populations.

1.2 GENERAL APPROACHES TO FOOD PROCESSING

The rapid growth and development of commercial food processing in the twentieth century has continued and now dominates food processing, particularly in developed countries. However, food processing in the home, such as canning, decreased with increasing urbanization. Although some aspects of food processing still occur frequently in home situations, particularly in developing nations. Food preparation/processing in the home is primarily related to heat treatment, which plays an important role in the formation of desirable flavors, colors, aromas, and textures. In fact, exposure of food to heat can be considered the most used processing step in modern society, involving frying, baking, grilling, roasting, toasting, microwaving, and broiling, using ovens (convection, microwave), stoves, toasters, grills (gas, wood, and charcoal), and fat-based fryers.

There are, however, considerable differences between practices in the home and in commercial industrial settings. Home appliances tend to have less accurate temperature controls, resulting in actual oven temperatures differing considerably from what is indicated by the oven setting or temperature gauge. In general, there is also less rigid timing due to interruptions and delays in homes as contrasted to an industrial environment. High-quality standards are pivotal for industrialized processes, and food manufacturers have identified early on the need for quality control tools and stringent targets to achieve consumer preference in terms of nutritional quality, shelf life, and organoleptic properties at all times. Ideally, quality is addressed early on in the product and process design phase, identifying those process steps that impact (key) quality parameters. For this purpose, modern industrial lines are equipped with appropriate measuring systems/sensors (temperature profiles, moisture content, texture, color, pH, etc.) to deal with raw material variability and process complexity.

1.3 CONCERNS ABOUT FOOD SAFETY DURING FOOD PROCESSING

1.3.1 Types of Hazards

The major hazards considered in food safety are allergens, and those that are microbiological, physical, and chemical in nature.

Microbiological contamination with pathogens such as enterohemorrhagic *Escherichia coli* strains, *Listeria monocytogenes*, and *Salmonella* spp. represents a major problem in modern food safety (pathogen identification, control,
and prevention). It is considered the most important aspect of improving food safety globally, displacing the emphasis on chemical contaminants of previous decades. For further reading, various books and reviews on this topic can be consulted (see References 6 and 7).

Physical hazards are considered acute hazards if not adequately addressed and controlled and may pose a serious threat to human health (e.g., glass, hard plastic and metal pieces, bones, wood, stones). There are different sources of physical hazards, and the origins of the potential risks must be clearly understood (raw materials/ingredients or the operations in the manufacturing of food per se may be a source of a physical hazard, e.g., potential glass breakage along a glass filling line). Within the frame of Hazard Analysis Critical Control Points (HACCP), measures are identified that remove or reduce such hazards to an acceptable level in the final product (e.g., filtration, sieving, centrifugation). Procedures must be put in place by the manufacturer to verify that the measures to control such hazards are indeed effective (e.g., metal detectors, X-ray machines).

Food allergens are generally recognized as a serious food safety issue and manufacturers are responsible for controlling them and providing concise information to consumers. Through good manufacturing practice (GMP), identifying possible sources of cross contact, integration of allergen hazards into HACCP studies, and appropriate ingredient labeling, the health risks can be minimized.

The chemical hazards in foods can be multiple, and as depicted in Fig. 1.1 may enter the food and feed supply chain at many different points. Traditionally, the environment has been thought to be the origin of many chemical food hazards, such as heavy metals and persistent organic pollutants (POPs). An increased risk of pathogenic microorganisms may also be attributed to the contamination of the agricultural water supply caused by human and animal waste, and use of manure as fertilizer.

Essentially, the potential chemical contaminants in food can be broadly classified into:

1. natural toxins, e.g., mycotoxins, higher plant toxicants, and marine biotoxins;
2. environmental contaminants, e.g., heavy metals, dioxins, and radionuclides;
3. chemicals used as aids in food manufacture and, in the event of a failure, which may contaminate food, e.g., through leakage, spillage, or misuse of lubricants, cleansing agents, or disinfectants;
4. agrochemical residues, e.g., fungicides, pesticides, and veterinary drugs;
5. packaging migrants, e.g., isopropylthioxanthone, semicarbazide, and styrene;
6. processing toxicants, e.g., heterocyclic aromatic amines, acrylamide, and furan.
INTRODUCTION TO FOOD PROCESS TOXICANTS

The latter class of substances is the focus of this book, and the reader is referred to further sources of information on general chemical risks in food (see References 8 and 9).

1.3.2 Definition of a Process Toxicant

Processing toxicants (process-induced toxicants, process-formed toxicants) as used in this book are defined as those substances present in food as a result of food processing/preparation that are considered to exert adverse physiological (toxicological) effects in humans, i.e., substances that create a potential or real risk to human health. Food in this definition also includes beverages and nonalcoholic drinks such as coffee and tea, and thus both parts of the diet are included.

Ingredients commonly occurring in food formulations (recipes) are excellent substrates for chemical reactions occurring under the conditions encountered in food processing. The reaction products formed depend on the processes and conditions used, such as fermentation, irradiation, and heat processing.
Products from such reactions can have beneficial properties and/or adverse physiological effects on consumers. Examples of the former include compounds such as antioxidants, anticarcinogens, and those resulting in or contributing to nutritional properties, desirable flavor, aroma, texture, and color in food products. Examples of the latter include carcinogens, genotoxins, neurotoxins, anti-nutrients, and undesirable flavors or aromas. Many of these coexist as a result of being formed during common food processing technologies, particularly those involving heating, e.g., toasting, roasting, frying, broiling, baking, grilling and microwaving.

1.3.3 Progress in Technological Developments

The development of new food processing technologies continues at a rapid pace, with some of these, such as high-pressure processing (HPP), already in commercial use (see Chapters 5 and 8). In fact, the application of HPP is not a new concept, and was already described in certain foods in the late nineteenth century (10). The use of HPP is not uncommon in foods such as whole shell oysters, salsa, ready-to-eat (RTE) meats, and jams. New technologies are aimed at delivering products with superior organoleptic quality, minimal changes to nutrients, safety, and shelf life (product life, preservation of quality), and ideally the minimal formation of undesirable compounds. Pulsed electric field, ohmic heating, jet impingement, infrared radiation, and new biotechnological applications are just a few that can be considered new processing techniques. Innovative nonthermal processing technologies (photosensitization, pulsed electric field technologies, high-pressure homogenization, and HPP coupled to packaging under inert atmosphere) to improve the quality and safety of RTE meals are being investigated within the European “HighQ RTE” project, with the goal to improve the safety and quality of three representative categories of European RTE foods, i.e., salads, fluid foods, and vegetable-based meals (11).

Only very few studies have been performed on the use of alternative or new processing technologies to mitigate process toxicants. Work has recently been reported on the application of infrared radiation to baking with the goal to reduce the amount of acrylamide (12) while maintaining the sensorial properties of the food. Steam baking and steam roasting have also been assessed to reduce acrylamide, and in the case of coffee beans the steam roast had a major impact on the sensorial properties of the coffee, with only a marginal reduction in acrylamide (13).

1.4 FOOD-BORNE PROCESSING TOXICANTS: SETTING PRIORITIES

The processing of ingredients into food products can lead to the formation of a number of chemical compounds having properties desired in the flavor,
aroma, and color of the food. One of the most important sources of these compounds is the Maillard reaction (14). This complex reaction, involving reducing sugars and amino acids, has been, and continues to be, the subject of intensive research for many years due to its importance in the formation of characteristic flavors, aromas, and colors (browning) in foods prepared by heating. A major emphasis has been on the identification of the compounds involved in these attributes as formed during the Maillard cascade and in understanding the chemical pathways involved. The Maillard reaction is known to produce more than 550 volatile compounds of which more than 330 have been identified in the volatiles of cooked foods (15). Many of these contribute to the flavors and aromas in these foods. Nonvolatile products such as the melanoidins contribute to the browning colors.

However, compounds having adverse physiological effects or potential health risks are often formed also. The number of studies involving detection, identification, and measurement of such compounds continues to increase as more sensitive analytical methodologies become available and are applied to foods. One example is the discovery in early 2002 of acrylamide in foodstuffs (16), present in the μg/kg (part per billion) range in a wide variety of common foods that are heated at temperatures >120°C, such as potato chips, French fries, bread, cereal-based products, and coffee (17). Acrylamide has received unprecedented attention since it was first reported in food, with several books and reviews summarizing the research efforts across the disciplines, and reflected by more than 600 research publications to date (15, 18).

Development of new analytical methods to detect and determine acrylamide was required for the very low concentrations encountered in foods. As analytical methodologies continue to become even more sensitive, more of such compounds undoubtedly will be found in foods. When these compounds are determined or known to have adverse effects or potential health risks, toxicological studies can become difficult since these usually are accomplished in animals at concentrations much higher than may be observed in foods. This has become an issue with acrylamide, since definitive toxicological studies are not yet available (anticipated to be complete and reported beginning 2009).

A key question raised by food safety authorities, by academics in the field, and in particular by food producers, is which toxicants are of greatest concern in foods from a dietary health perspective? Numerous compounds have been identified over the past years in foods that show carcinogenic, mutagenic (genotoxic), or neurotoxic properties at high doses in animal studies. Such toxicants can be classified by chemical (structural) type or by the processing methods in which they occur. There will be some overlap in either case. In this book, the issue is approached from the processing method involved and includes (i) thermal treatments, e.g., frying, baking, grilling, roasting, broiling, toasting, and microwaving (Chapter 2); (ii) fermentation (Chapter 3); (iii) preservation (Chapter 4); (iv) high hydrostatic pressure (Chapter 5); and (v) other selected processes such as acid and base treatment (Chapter 6).

When one begins to seek substances that have the potential to be toxic when present in foods, an entirely different set of issues is raised. The HEATOX
The HEATOX inventories for Maillard and heated lipid reaction products are in a spreadsheet format and list compounds that may be formed in model systems and/or are known to occur in food, the latter also featuring the food where the concentration has been reported to be higher than 1 mg/kg (different literature sources).

A key question, however, is the ranking of these compounds in terms of risk level. One approach that is employed to help prioritize risks of food-borne genotoxic carcinogens is the margin of exposure (MoE). The MoE is usually calculated as a range, taking in most cases the BMDL_{10} value (the lower confidence limit on the benchmark dose associated with a 10% cancer incidence) and the upper- and lower-bound human exposure estimate. Table 1.1 illustrates the principle, and shows selected food-borne toxicants and an approach to estimate the margin of safety or MoE. A MoE band >10,000 is interpreted as unlikely to be of concern. Such a procedure would provide a first indication of the degree of risk. However, the interpretation of any MoE is complex and comparisons are not straightforward without knowledge of the methodologies used to analyze the data and data quality (for both the animal carcinogenicity data and dietary exposure estimates).

For a majority of the compounds, however, toxicity data may simply be lacking. In this case, a first screening will be required using existing data (considering also the limitations and uncertainties of the predictive toxicity models), and preferably probabilistic modeling, followed where warranted by in-depth research including method development, analytical measurement, and chronic animal studies. Other databases such as the carcinogenicity potency database (CPDB), which contains information on the toxicity of more than 1400 chemicals, some of which are naturally present in foods such as coffee, may also be a useful source of data (22). This, combined with occurrence databases or other published data on amounts of the selected chemicals in food, may allow a first ranking based on the margin of safety, provided that the compounds are retrievable in the database.

When considering process-induced toxicants and their potential health risks, a number of additional factors come into play in establishing the context...
within which concerns are raised and decisions made, particularly those relating to risk analysis. In this book, these are included in Part II: General Considerations. One of the most commonly used approaches to food safety during food processing is the HACCP concept. Some countries mandate application of this approach, which recognizes that safety should be built into a product during the early development phase, rather than depending on final product testing to detect safety defects. This subject is presented in Chapter 7. A pivotal factor in food processing, including development of new process technologies, is the impact of the processing technology on nutritional aspects (gain/loss during processing, bioavailability, formation of allergens). Chapter 9 deals with this very important area.

In recent years it has become apparent that decisions, particularly those involving regulatory action, need to be risk-based. This is often encompassed in the concept that the amount of regulation should be in direct proportion to the health risk in the food product. As a result, risk analysis (risk assessment, risk communication, risk management) is playing an increasingly important role in this general area. Importance of risk communication is addressed in

### TABLE 1.1 Risk assessment of selected food-borne toxicants.

<table>
<thead>
<tr>
<th>Food-borne toxicant</th>
<th>Estimated dietary uptake, ng/kg bw/d*</th>
<th>Tox. dose: point of departure, ng/kg bw/d</th>
<th>MoE/Safety factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,3-DCP/2,3-DCP (***)</td>
<td>3 – 200</td>
<td>6,300,000$</td>
<td>2,100,000 – 32,000</td>
</tr>
<tr>
<td>Heterocyclic aromatic amines (PhIP)</td>
<td>4.8 – 7.6 (***)</td>
<td>1,250,000$</td>
<td>260,000 – 164,000</td>
</tr>
<tr>
<td>Polyaromatic hydrocarbons [Benz(a)pyrene]</td>
<td>4$^{(a)}$ – 10$^{(b)}$</td>
<td>100,000$</td>
<td>25,000 – 10,000</td>
</tr>
<tr>
<td>N-nitrosamines (NDMA)</td>
<td>3.3 – 5.0</td>
<td>60,000$</td>
<td>18,200 – 12,000</td>
</tr>
<tr>
<td>Ethylcarbamate</td>
<td>33$^{(c)}$ – 55$^{(d)}$</td>
<td>300,000$</td>
<td>9,000 – 5,460</td>
</tr>
<tr>
<td>Furan</td>
<td>260$^{(e)}$ – 610$^{(f)}$</td>
<td>1,000,000$</td>
<td>3,900 – 1,600</td>
</tr>
<tr>
<td>3-MCPD$^{(g)}$</td>
<td>360$^{(h)}$ – 1,380$^{(i)}$</td>
<td>1,100,000$</td>
<td>3,055 – 800</td>
</tr>
<tr>
<td>Acrylamide</td>
<td>1,000$^{(j)}$ – 4,000$^{(k)}$</td>
<td>300,000$</td>
<td>300 – 75</td>
</tr>
</tbody>
</table>

*Data sources vary and are shown here for illustrative purposes only; a = mean intake; b = high-level intake; c = lower-bound mean; d = upper-bound mean; e = mean for 2+-year-old children; f = 90th percentile for 2+-year-old children; g = non-genotoxic mode of action; h = highest mean of participating country for adult population (23); i = highest 95th percentile of participating country for adult population (23); j = average intake for general population; k = high consumers. ** (24). *** (25). ¶ LOAEL. $\#$ BMDL$^{10}$ (lower conservative end of the range was chosen).

DCP = dichloropropanol; NDMA = N-nitrosodimethylamine; PhIP = 2-Amino-1-methyl-6-phenylimidazo-[4,5-b]pyridine.