

Comment Submissions - Proposed Adoption of Exposures to Listed Chemicals in Coffee Posing No Significant Risk

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CERT's Submission No. 12 regarding the Opinions of Dr. Ronald L. Melnick regarding Sound Considerations of Public Health for Exposure to Acrylamide from Consumption of Coffee.

Email:

nvidal@toxic torts.com

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Metzger Law Group

Practice Concentrated in Toxic
Tort & Environmental Litigation

401 E Ocean Blvd., Ste. 800
Long Beach, CA 90802
phone: 562.437.4499
fax: 562.436.1561

www.toxic torts.com

Raphael Metzger
Brian Foster
Abraham Pariser
Robyn Mallon
Monica Frye
Scott Brust

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*Via electronic submission to
<https://oehha.ca.gov/comments>*

Monet Vela
Office of Environmental Health Hazard Assessment
P.O. Box 4010
Sacramento, California 95812-4010

Re: Proposed Adoption of New Section Under Article 7: No Significant Risk Levels
Section 25704: Exposures to Listed Chemicals in Coffee Posing No Significant Risk

CERT'S SUBMISSION NO. 12

Dear Ms. Vela:

Enclosed herewith are the following documents that are being submitted on behalf of our client, the Council for Education and Research on Toxics (CERT) regarding the Opinions of Dr. Ronald L. Melnick regarding Sound Considerations of Public Health for Exposure to Acrylamide from Consumption of Coffee.

1. Exhibit A - Opinions of Dr. Ronald L. Melnick regarding Sound Considerations of Public Health for Exposure to Acrylamide from Coffee Consumption (2017).
2. Exhibit B - Assessing the Benefits and Risks of Acrylamide in Coffee [utilizing the Benefit-Risk Analysis for Foods (BRAFO) methodology] (2017).
3. Exhibit C - Critique of Dr. David Kessler's Report and Testimony (2017).
4. Exhibit D - Testimony of Ronald L. Melnick in *CERT v. Starbucks* trial, October 2, 2017 a.m.
5. Exhibit E - Testimony of Ronald L. Melnick in *CERT v. Starbucks* trial, October 2, 2017 p.m.

6. Exhibit F - Testimony of Ronald L. Melnick in *CERT v. Starbucks* trial, October 3, 2017 a.m.
7. Exhibit G - Curriculum Vitae of Ronald L. Melnick, Ph.D.

Kindly include these materials of Dr. Ronald L. Melnick in the record for this rulemaking proceeding.

Very truly yours,

Raphael Metzger

RM:ip
encls: as specified

EXHIBIT “A”

Opinions of Ronald Melnick, Ph.D.

Background

As I understand it, the major issue for the Court to decide in this phase of the case is whether the coffee companies that are the defendants in this case should be allowed to expose Californians to acrylamide in their coffee products in excess of the No Significant Risk Level (NSRL) based on “sound considerations of public health” according to the provisions of 27 California Code of Regulations § 25703.

27 California Code of Regulations § 25703

The California Code of Regulations § 25703, as provided below, clearly requires a quantitative risk assessment for determining the NSRL, i.e., the daily exposure level that poses a cancer risk that is not greater than 1 per 10⁵. The current OEHHA calculated NSRL for acrylamide is 0.2 µg/day. This value was based on data from the most sensitive animal bioassay studies that were considered to be of acceptable quality and design. Cancer epidemiological data on acrylamide were insufficient to perform a reliable quantitative risk assessment. As specified in the California Code of Regulations § 25703, the NSRL for this genotoxic carcinogen was calculated using a no-threshold dose-response model and body weight scaling factors to derive human cancer potency (expressed in reciprocal milligrams of chemical per kilogram of bodyweight per day) from animal cancer potency.

Any quantitative risk assessment that provides an alternative NSRL value “shall be based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for listing the chemical as known to the state to cause cancer.” The California Code of Regulations § 25703 also allows an exception to the 1 per 10⁵ excess cancer risk where “sound considerations of public health” support an alternative level. One noted example for this exception is the situation in which “chemicals in food are produced by cooking necessary to render the food palatable or to avoid microbiological contamination.” Because this exemption could allow the coffee industry to expose people in California to acrylamide at levels greater than the current NSRL without providing a cancer hazard warning, my subsequent opinions focus on the scientific validity of an alternative quantitative risk assessment and whether it meets the requirement of “sound considerations of public health.”

27 California Code of Regulations § 25703. Quantitative Risk Assessment.

(a) A quantitative risk assessment which conforms to this section shall be deemed to determine the level of exposure to a listed chemical which, assuming daily exposure at that level, poses no significant risk. The assessment shall be based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for listing the chemical as known to the state to cause cancer. In the absence of principles or assumptions scientifically more appropriate, based upon the available data, the following default principles and assumptions shall apply in any such assessment:

(1) Animal bioassay studies for quantitative risk assessment shall meet generally accepted scientific principles, including the thoroughness of experimental protocol, the degree to which dosing resembles the expected manner of human exposure, the temporal exposure pattern, the duration of study, the purity of test material, the number and size of exposed groups, the route of exposure, and the extent of tumor occurrence.

(2) The quality and suitability of available epidemiologic data shall be appraised to determine whether the study is appropriate as the basis of a quantitative risk assessment, considering such factors as the selection of the exposed and reference groups, reliable ascertainment of exposure, and completeness of follow-up. Biases and confounding factors shall be identified and quantified.

(3) Risk analysis shall be based on the most sensitive study deemed to be of sufficient quality.

(4) The results obtained for the most sensitive study deemed to be of sufficient quality shall be applicable to all routes of exposure for which the results are relevant.

(5) The absence of a carcinogenic threshold dose shall be assumed and no-threshold models shall be utilized. A linearized multistage model for extrapolation from high to low doses, with the upper 95 percent confidence limit of the linear term expressing the upper bound of potency shall be utilized. Time-to-tumor models may be appropriate where data are available on the time of appearance of individual tumors, and particularly when survival is poor due to competing toxicity.

(6) Human cancer potency shall be derived from data on human or animal cancer potency. Potency shall be expressed in reciprocal milligrams of chemical per kilogram of bodyweight per day. Interspecies conversion of animal cancer potency to human cancer potency shall be determined by multiplying by a scaling factor equivalent to the ratio of human to animal bodyweight, taken to the one-fourth power.

(7) When available data are of such quality that physiologic, pharmacokinetic and metabolic considerations can be taken into account with confidence, they may be used in the risk assessment for inter-species, inter-dose, and inter-route extrapolations.

(8) When the cancer risk applies to the general population, human body weight of 70 kilograms shall be assumed. When the cancer risk applies to a certain subpopulation, the following assumptions shall be made, as appropriate:

Subpopulation	Kilograms of Body Weight
Man (18+ years of age)	70
Woman (18+ years of age)	58
Woman with conceptus	58
Adolescent (11-18 years of age)	40
Child (2-10 years of age)	20
Infant (0-2 years of age)	10

(b) For chemicals assessed in accordance with this section, the risk level which represents no significant risk shall be one which is calculated to result in one excess case of cancer in an exposed population of 100,000, assuming lifetime exposure at the level in question, except where "sound considerations of public health" support an alternative level, as, for example:

(1) where chemicals in food are produced by cooking necessary to render the food palatable or to avoid microbiological contamination; or

(2) where chlorine disinfection in compliance with all applicable state and federal safety standards is necessary to comply with sanitation requirements; or

(3) where a clean-up and resulting discharge is ordered and supervised by an appropriate governmental agency or court of competent jurisdiction.

Sound Considerations of Public Health

While what constitutes “sound considerations of public health” has not been fully described, the California Code of Regulations § 25703 provides informative examples, these include cooking to make a food palatable or avoid microbial contamination, or to comply with sanitation requirements. While roasting coffee beans is necessary to make coffee products and to reduce microbial contaminants to some extent, the presence of acrylamide in coffee provides no health benefits.

Cancer Statistics and Costs

Cancer is a devastating and costly disease. It is the second leading cause of death in the US following heart disease; however, it is the leading cause of death in 22 states (Siegel, R.L., et al., Cancer Statistics, 2017; CA Cancer J. Clin. 67:7-30, 2017). In 2017, the overall estimate of new cancer cases in the US is approximately 1,700,000, with 176,000 occurring in California. The expected number of cancer deaths in the US in 2017 is approximately 600,000 (59,000 in California). The probability of developing an invasive cancer in one’s lifetime is 41 % among males and 38% among females. The national cost of cancer is substantial, the direct health care costs for cancer in the US was about \$88 billion in 2014. In addition to direct medical costs, there are large economic costs due to lost wages and productivity. The annual productivity cost from cancer mortality (including lost wages and loss due to caregiving and household activity) is expected to increase from \$232 billion to \$308 billion in 2020 (Bradley, et al., Productivity Costs of Cancer Mortality in the United States: 2000-2020, J. Natl. Cancer Inst. 100:1763-1770, 2008). Eliminating the suffering and pain due to cancer is a major public health goal.

Primary prevention

The principle behind primary prevention of environmental cancer (i.e., cancers caused by exogenous agents) is simple: prevent disease occurrence by avoiding or maximally reducing human exposure to agents recognized as human carcinogens or to agents for which there is experimental evidence of carcinogenicity. “Reducing exposure to carcinogens can be implemented in two major ways: by elimination of the carcinogen or its substitution with a non-carcinogen, or by impeding the various means of contact between the carcinogen and people” (Boffetta, P., et al., A Quick Guide to Cancer Epidemiology, Springer, 2014).

“Primary prevention encompasses the elimination or reduction of exposure to recognized risk factors in susceptible populations to prevent a disease. Evidence of effective primary prevention measures in reducing cancer rates are, for example, the observed decrease

in cases of male lung cancer from a fall in tobacco smoking or reduced bladder cancer among dye workers after the elimination of aromatic amines' exposures. Primary prevention is an important means to improve public health, and it is by far the most cost-effective and sustainable intervention for reducing the burden of cancer globally. At least one-third of cancer cases that occur annually throughout the world could be prevented" (World Health Organization, Primary Prevention of Cancer Through Mitigation of Environmental and Occupational Determinants, Int. Conf. Environ. Occup. Determinants Cancer: Interventions for Primary Prevention, Asturias, Spain, 2011).

"In the United States and some other countries, an elaborate web of regulations is in place to protect the public from exposure to selected environmental carcinogens. The underlying principles vary, but all of the regulations have the goal of controlling exposures that arise from sources beyond the individual's control. These regulations typically reflect a complex balancing of risk, feasibility of control, costs, and the force of political and other societal pressures. In spite of the inherent complexity and heterogeneity of these regulations, they have proven to be generally effective with some notable successes, such as drastic reduction of worker exposure to asbestos" (Samet, J.M., et al., *Regulating Carcinogens*, Chap. 72, pp. 1341-1353. In Schottenfeld, D. and Fraumeni, J.F., eds., *Cancer Epidemiology and Prevention*, 3rd ed., Oxford 2006).

Dr. Lorenzo Tomatis, the former Director of the International Agency for Research on Cancer and founder of the IARC Monographs program was one of the leading 20th century proponents for primary prevention of environmental cancer. Some of his statements on the need for primary prevention and on obstacles for implementing primary prevention strategies are relevant to the situation concerning acrylamide in coffee:

"Primary prevention of cancer has stumbled from the very beginning because of the interference of powerful economic interest which perceived that any data indicating a possible cancer risk after exposure to industrial chemicals jeopardizes their profits, the protection of which being more important than the protection of human health" (Tomatis, L., *Role of Experimental and Epidemiological Evidence of Carcinogenicity in the Primary Prevention of Cancer*. *Ann Ist Super Sanita*, 42:113-117, 2006).

"Absent or inadequate epidemiological data cannot be considered equivalent to a negative finding and cannot be considered more relevant for public health than positive experimental findings" (Tomatis, L. and Huff, J., *Evolution of Research in Cancer Etiology. Inadequate Epidemiological Data or False-Negative Results can be Hazardous to Public Health, Especially in the Presence of Positive Experimental Data*. In *The Molecular Basis of Human*

Cancer. Humana Press Inc., Totowa, NJ. Ch.9; Coleman, W.B. and Tsongalis, G.J., 189-201, 2002).

“It is essential to adopt an attitude of responsible caution, in line with the principles of primary prevention, the only one that may prevent unlimited experimentation on the entire human species” (Tomatis, L., Primary Prevention Protects Public Health. Ann. NY Acad. Sci., 982:190-197, 2002).

“It is only prudent to pursue public health measures that are likely to reduce the risk of preventable cancers related to environmental chemicals. The occurrence of large numbers of avoidable cancer cases and associated deaths is a circumstance that society should seek to reduce. Protection of public health is a goal that society should always pursue” (Tomatis, L., Melnick, R.L., Haseman, J., Barrett, J.C., Huff. J. Alleged ‘Misconceptions’ Distort Perceptions of Environmental Cancer Risks. FASEB J., 15:195-203, 2001).

Role of Diet in Human Cancer and Public Health Concerns of Acrylamide in Heated Foods

It has long been known that dietary factors are linked to about 30-35% of human cancers (Doll and Peto, 1981 cited in Key et al., Diet, Nutrition and the Prevention of Cancer, Public Health Nutr. 7:187-200, 2004; Anand et al., Cancer is a Preventable Disease that Requires Major Lifestyle Changes, Pharm. Res. 25:2097-2116, 2008).

The discovery that acrylamide is formed in various cooked foods (Tareke, E., et al. Analysis of Acrylamide, a Carcinogen Formed in Heated Foodstuffs. J Agric Food Chem. 50: 4998-5006, 2002) has led to national and international concerns of increased cancer risk from daily consumption of acrylamide by the general public. Acrylamide is widespread in the food supply; about 38% of calories consumed in the United States come from acrylamide-containing foods (Petersen, B.J., et al., Exposure to Acrylamide: Placing Exposure in Context, Adv. Exp. Med. Biol. 561:63-76, 2005). Although acrylamide is present in many foods with the highest concentrations in potato chips and French fries, the greatest source of acrylamide in the adult diet is coffee, accounting for as much as one-third or more of intake among adults; this is due to the high frequency and amount of coffee consumption. Unlike other acrylamide-containing foods, coffee drinkers typically consume multiple servings (> 3 cups) per day, typically throughout adulthood (Coffee Research Institute, available online at www.coffeeresearch.org/market/usa.htm).

Acrylamide is a cancer-causing chemical that upon ingestion is metabolized by cytochrome P450 2E1 in animals and humans to glycidamide, a reactive-epoxide compound that can form covalent bonds with DNA and cause chromosomal aberrations and gene

mutations that can initiate the cancer process. The NTP conducted separate carcinogenicity studies on acrylamide and glycidamide in rats and mice (NTP Technical Report on the Toxicology and Carcinogenesis Studies of Acrylamide [CAS No. 79-06-01] in F344/N Rats and B6C3F1 Mice [Feed and Drinking Water Studies], National Toxicology Program TR 575, 2012; NTP Technical Report on the Toxicology and Carcinogenesis Studies of Glycidamide [CAS No. 5694-00-8] in F344/N Nctr Rats and B6C3F1 Mice/Nctr [Drinking Water Studies], National Toxicology Program TR 588, 2014), and concluded: “the results of this bioassay [glycidamide], when compared to those previously reported for acrylamide, indicate that acrylamide is efficiently metabolized to glycidamide in both sexes of both species. Based upon the concordance of tumor sites between the two bioassays, the data also indicate that carcinogenic activity of acrylamide is due to its metabolic conversion to glycidamide.”

As a genotoxic carcinogen, the risk of cancer increases linearly with increasing dose or exposure. In experimental animals, exposure to acrylamide induces tumors in both sexes of multiple species and in multiple organs (Johnson, K.A., et al. Chronic toxicity and Oncogenicity Study on Acrylamide Incorporated in the Drinking Water of Fischer 344 Rats. *Toxicol. Appl. Pharmacol.* 85: 154-168, 1986; Friedman, M.A., et al. A Lifetime Oncogenicity Study in Rats with Acrylamide. *Fundam. Appl. Toxicol.* 27: 95-105, 1995; NTP 2012). Based on this type of information, IARC (International Agency for Research on Cancer. Acrylamide. IARC Monogr. Eval. Carcinog Risks Hum., 60: 389-433, 1994) concluded that acrylamide is “probably carcinogenic to humans” and the US EPA (US Environmental Protection Agency. Toxicological Review of Acrylamide (CAS No. 79-06-1) EPA/635/R-07/009F, 2010) concluded that acrylamide is “likely to be carcinogenic to humans;” it induces tumors primarily by a mutagenic mode of action that could operate similarly in animals and humans.

A joint expert committee of the Food and Agricultural Organization of the United Nations and the World Health Organization has evaluated exposure and health risks of acrylamide in foods (FAO/WHO, Joint FAO/WHO Expert Committee on Food Additives, 64th Meeting: Summary and Conclusions, Feb. 8-17, 2005). Based on measured concentrations of acrylamide in various food items and food consumption data available at that time, intake levels of acrylamide were estimated to range from 0.2 to 2.0 µg/kg body weight per day for the general population and up to 5.1 µg/kg body weight per day for the 99th percentile consumers. Using animal cancer data from the studies of acrylamide in rats by Johnson et al. (1985) or Friedman et al. (1995), lower confidence limits for benchmark doses associated with 10% extra risk of tumors (BMDL10) were determined. This analysis showed that the margin of exposure (MOE) between the derived BMDL value and human exposure levels from acrylamide in foods was 300 for average acrylamide intake by the general population and 75 for high intake consumers, i.e., exposures for high intake consumers are only 75 times larger than the dose

associated with a tumor response rate of 10%. These low MOEs were considered by the Committee to signify a high human health concern for this genotoxic carcinogen. According to the European Food Safety Authority (EFSA), a MOE of 10,000 or higher for a genotoxic carcinogen, if based on a BMDL10 from an animal study, would be considered to be a low concern for public health (<https://www.efsa.europa.eu/en/efsajournal/pub/2578>). For sound consideration of public health, it is essential that acrylamide levels in major food sources be drastically reduced.

Acrylamide is a potent carcinogen, its NSRL is lower than oral NSRLs for other well-known human carcinogens, including benzene (6.4 µg/day), formaldehyde (40 µg/day), trichloroethylene (14 µg/day), and vinyl chloride (3 µg/day) (Office of Environmental Health Hazard Assessment, Proposition 65 No Significant Risk Levels (NSRLs) for Carcinogens and Maximum Allowable Dose Levels (MADLs) for Chemicals Causing Reproductive Toxicity, May 2017, <https://oehha.ca.gov/media/downloads/proposition-65/general-info/safeharborlist05162017.pdf>).

Reducing Exposures to Carcinogens in Food is a Sound Public Health Policy

The Food Drink Europe Code of Practice for Managing Acrylamide Formation in Foods (2016) recommends that the food industry reduce acrylamide levels in food to as low as is reasonably achievable (ALARA). Because “there are currently no levels [of acrylamide] that regulators have agreed upon as being ‘safe,’ food business operators (FBOs), including coffee manufacturers, shall make every reasonable effort (based upon current knowledge) to reduce levels in final product and thereby reduce consumers’ exposure.” Also, “as technology develops, new and better mitigation measures for acrylamide reduction may become available. If a FBO chooses not to implement an available mitigation measure then the onus shall be placed on that FBO to demonstrate why its application is believed to be unreasonable or ineffective.” Considerations for not implementing an available mitigation measure include “the potential to increase other contaminants, microbiological stability and the acceptability of the final product to the consumer.”

In the declaration I submitted in 2016, regarding technologies to reduce acrylamide in coffee (which I have since updated and expanded), I noted numerous technologies that have been developed that substantially reduce acrylamide levels in coffee without negatively affecting sensorial properties. In my updated report, in which I further reviewed published literature, patented techniques, and proprietary studies, it is clear that methodologies currently exist that are very effective in reducing acrylamide levels in coffee (by at least 90%) without negatively affecting important sensorial properties of coffee. Therefore, if the coffee industry is

serious about taking “every reasonable measure to reduce the presence of acrylamide in final food products,” then the industry should begin implementing available acrylamide reduction technologies to reduce the levels of acrylamide in coffee consistent with the ALARA principle.

Framework for Applying 27 California Code of Regulations § 25703(b)(1)

(where chemicals in food are produced by cooking necessary to render the food palatable or to avoid microbiological contamination)

a) Does the listed chemical itself provide any health benefit?

In determining whether “sound considerations of public health” should allow a company to expose Californians to a carcinogen in excess of the No Significant Risk Level (NSRL), the first issue to consider is whether the listed chemical itself provides any health benefit, because if the carcinogenic chemical itself provides some health benefit, allowing exposures in excess of the NSRL may actually serve public health. For example, several agents, such as chemotherapeutic drugs used in cancer treatment or cyclosporin which is used to prevent organ transplant rejection, are known human carcinogens. However, these agents provide critical benefits to patients undergoing cancer treatment or organ transplant. Acrylamide, on the other hand, is a toxic and carcinogenic chemical for which no health benefit has been reported in the scientific literature.

b) Is the listed chemical essential to product function and quality?

The second issue to be considered is whether the listed chemical is essential to the functionality and quality of the product. If the chemical is essential to the function and quality of the product and it cannot be eliminated or replaced with a less toxic chemical, then the product cannot be reconfigured to substitute a less toxic chemical for the listed chemical. In my review of the published literature and proprietary documents, I could not find any evidence that acrylamide is essential for the functionality or quality of coffee. While acrylamide is formed as product of the Maillard reaction which produces many aromatic and flavorful chemicals, acrylamide itself is not an essential component of coffee. As I mentioned in my declaration regarding methods to reduce acrylamide in coffee, several technologies have been developed that selectively target and remove acrylamide from coffee without affecting chemical constituents that impart aroma or flavor to coffee beverages. Consequently, acrylamide, which itself is odorless, is not an essential constituent of coffee beverages.

c) Can exposure to the chemical from the product be reduced?

This is an important issue, because if levels of a carcinogen in a product can be reduced without materially affecting product quality, “sound considerations of public health” require reduction of the carcinogen in the product, consistent with the ALARA principle. It is equally obvious that “sound considerations of public health” cannot justify exposing consumers to excess levels of a carcinogen in a product if those levels can be reduced. As set forth at length in my declaration regarding methods for reducing acrylamide in coffee, numerous technologies have been developed that demonstrate substantial reduction in the acrylamide content of coffee, with some studies reporting reductions of up to 90%.

c) Can the listed chemical be reduced without negatively affecting palatability

The next important issue to consider is whether the listed chemical can be removed from the product or its levels reduced without negatively affecting palatability or health and safety aspects of the product. As shown in my declaration regarding reduction of acrylamide in coffee, a number of the technologies have been developed that reduce acrylamide in coffee without significantly affecting important sensorial properties of coffee. It also appears that technologies that are effective in reducing acrylamide levels in coffee can be implemented without increasing the risk of microbiological contamination of coffee or the levels of any other harmful contaminants in coffee.

Assessing the Benefits and Risks of Acrylamide in Coffee

a) BRAFO

BRAFO (Benefit-Risk Analysis for Foods) was funded by the European Commission to develop an approach to compare quantitatively human health risks and benefits of foods using a quantitative common scale of measurement (Hoekstra, J., et al., BRAFO Tiered Approach for Benefit-Risk Assessment of Foods, *Food Chem. Toxicol.* 50: S684-S698, 2012; Boobis, A., et al., Critical Appraisal of the Assessment of Benefits and Risks for Foods, ‘BRAFO Consensus Working Group’, *Food Chem. Toxicol.* 55: 659-675, 2013). The approach involves 4 tiers in which a reference dietary scenario (e.g., consumption of coffee at current levels of acrylamide) is compared to an alternative scenario (e.g., consumption of coffee at markedly reduced levels of acrylamide) for informing health-based policy decisions. Thus, based on the comparison of potential health risks and benefits, the evaluation is intended to provide information on the net health impact of the two dietary scenarios and thereby support either the reference dietary

scenario or change to the alternative dietary scenario for improving public health. Important for the communication of risks and benefits is the characterization of uncertainties.

Tier 1 involves identifying potential risks and benefits separately: if there are risks but no benefits with the alternative scenario, then the assessment can stop and the reference scenario is advised; alternatively, if there are only health benefits with the alternative scenario, then the decision can be made to stop the assessment and the alternative scenario is preferred. If there are both health benefits and risks with the alternative scenario, then the assessment should proceed to Tier 2.

Tier 2 involves a qualitative integration of the risks and benefits with no common metric used. This tier assesses the magnitude of the risks and benefits by considering the number of people affected, the severity of the health effect, the number of years living with the effect, and years of life lost due to the effect. Similar to tier 1, if the overall balance indicates that *risks clearly dominate benefits* the assessment can stop and the reference scenario is advised; alternatively, *if benefits clearly dominate risks*, then the decision can be made to stop the assessment and the alternative scenario is preferred. If both beneficial and adverse effects are present but neither scenario clearly dominates, then the assessment needs to proceed to Tier 3.

Tier 3 involves a quantitative integration of risks and benefits by a deterministic approach (assessment is made with fixed values) using a common metric. Example metrics include willingness to pay to avoid an adverse health outcome, disability adjusted life years, and quality adjusted life years. These metrics are a function of the time in a future health state (i.e., years with the disease) times the health-related quality of life associated with that health state (weighted between 0 for death and 1 for completely healthy). For many health conditions, quality disease weights and data for the parameter values are not readily available; this could result in estimates with large uncertainties. If uncertainties are too large to make a reliable conclusion, more data may be needed. Alternatively, if the differences between the reference and alternative scenarios is close to zero and large uncertainties or variabilities exist, the assessment may need to proceed to tier 4.

Tier 4 involves a quantitative integration of risks and benefits by a probabilistic approach (assessment is made with input parameters represented by probability distributions) to quantify some uncertainties and variabilities. This assessment,

which is also based on a common metric needs to include “full consideration of the associated assumptions and uncertainties.”

“Benefit-risk assessment is not easy”, “it requires substantial data or assumptions, it is affected by many uncertainties, it requires careful interpretation and communication” (Hoekstra et al., 2012). Thus, all assumptions and uncertainties need to be clearly specified and their impact must be carefully considered when interpreting the results of a benefit-risk assessment. “The source, quantity and quality of data should be stated as well as the nature of the assumptions made at the different steps of the assessment to compensate for insufficient human data, uncertainties in the assessment, including in the extrapolation of animal data to humans and classification of weights for disability and quality of life, respectively” (Boobis et al., 2013). “With respect to benefit assessment [from human studies], meta-analyses of randomized controlled trials provide the highest level of evidence for the documentation of the existence of a benefit” (Boobis et al., 2013). In addition, “the evidence should preferably be supported by the results of observational studies and the effect should be biologically plausible.” “Evidence can be judged as probable when the available epidemiological (observational and intervention) studies show fairly consistent associations between exposure and effect; evidence is judged as possible when it relies on inconsistent results from intervention and observational studies.”

The BRAFO methodology has been applied to several case studies including 2 involving natural foods (e.g., farmed salmon vs oily fish) (Watzl, B., et al., Application of the BRAFO Tiered Approach for Benefit-Risk Assessment to Case Studies on Natural Foods, *Food Chem. Toxicol.* 50: S699-S709, 2012), 3 on heat processing contaminants (Schütte, K., et al., Application of the BRAFO Tiered Approach for Benefit-Risk Assessment to Case Studies on Heat Processing Contaminants, *Food Chem. Toxicol.* 50: S724-S735, 2012), and 5 on dietary interventions (e.g., fortification of bread with folic acid) (Verhagen, H., et al., Application of the BRAFO Tiered Approach for Benefit-Risk Assessment to Case Studies on Dietary Interventions, *Food Chem. Toxicol.* 50: S710-S723, 2012). For most of these case studies, it was possible to assess overall health impacts without proceeding to tiers 3 or 4 because risks or benefits of the alternative scenario were judged to clearly dominate, or because of limited or lack of data to allow for quantitative calculations of risks and benefits. For example, in comparing health benefits and risks associated with consumption of oily fish (reference scenario) versus farmed salmon (alternative scenario) in which contaminants including methyl mercury, dioxin, and dioxin-like PCBs were identified as potential hazardous components, the alternative scenario was recommended because the tier 1 assessment showed that its benefit outweighed the risk of the reference scenario (Watzl et al., 2012). In comparing consumption of soy foods (alternative

scenario) versus no intake of soy (reference scenario), the beneficial effects of the alternative scenario were judged to clearly dominate potential risks (Watzl et al., 2012).

The case studies on heat processing contaminants, especially the one on reducing acrylamide in potato and cereal products (Schutte et al., 2012), are most relevant to the current case concerning benefits of reducing acrylamide levels in coffee. While heat processing produces positive changes to food products, formation of hazardous contaminants such as acrylamide, a genotoxic carcinogen with a low margin of exposure, indicates a human health concern. The BRAFO methodology was applied to the evaluation of cooking practices before acrylamide mitigation measures were introduced (reference scenario) versus foods in which acrylamide mitigation methods have been implemented that could reduce overall acrylamide intake by approximately 30% with limited negative impact on organoleptic properties. With use of asparaginase to reduce the level of the acrylamide precursor asparagine, the evaluation stopped at tier 1, because of the positive safety evaluation of this enzyme, reduced cancer risk from lowered acrylamide consumption, and no expected adverse health effect from this treatment. Because of the beneficial effect of reducing acrylamide in processed foods, “acrylamide-reducing actions should hence be applied as long as the adverse side effects are recognized and minimized to the extent possible.”

The above recommendation is also relevant to coffee. In my opinion, the reduction of acrylamide in coffee with limited negative impact on organoleptic properties can produce a product in which benefits clearly dominate risks; hence, acrylamide-reducing actions should be applied to coffee.

b) Risks and Benefits of Coffee Consumption

Pourshahidi, L.K., et al. (A Comprehensive Overview of the Risks and Benefits of Coffee Consumption, *Compr. Rev. in Food Sci. Food Saf.*, 15: 671-684, 2016) provided a review of 1,277 published human studies on health effects associated with coffee consumption. The authors suggested that this information might be useful for a future quantitative benefit-risk assessment of coffee consumption using published approaches (e.g., Hoekstra et al., 2012; Verhagen et al., 2012; Boobis et al., 2013). However, Pourshahidi et al. (2016) cautioned on the interpretations of studies included in this review because “results and generalizations are complicated by a number of factors, including differences in age, gender, health status, type of coffee preparation, serving size, and source of coffee.” Furthermore, “causality cannot be established for either [benefit or risk] with the research currently available as these are largely based on observational data,” and “heterogeneity between study populations and designs, and also lack of control for many other confounding factors, add limitations to the existing literature.”

Regarding the potential relationship between coffee consumption and cancer risk, Pourshahidi et al. (2016) listed 138 observational studies reporting a beneficial effect, 195 with no effect, and 95 reporting increased risk. A beneficial effect reported from intervention studies was linked to antioxidant consumption and reduced oxidative DNA damage. Regarding this issue, the European Food Safety Authority (EFSA, Scientific Opinion on the Substantiation of a Health Claim Related to Coffee C21, a Coffee Standardised by its Content of Caffeoylquinic Acids, Trigonelline and N-Methylpyridinium, and Reduction of DNA Damage by Decreasing Spontaneous DNA Strand Breaks Pursuant to Article 13(5) of Regulation (EC) No 1924/2006, EFSA Journal 13:4099, 2015,) was asked to provide an opinion on the health claim that consumption of coffee C21, a coffee standardized by its content of caffeoylquinic acids, trigonelline, and N-methylpyridinium, can reduce “the amount of spontaneous DNA strand breaks in white blood cells.” The EFSA panel weighed the available evidence and concluded that a cause and effect relationship between consumption of coffee 21 and reduction in DNA damage had not been established. Based on the inconsistency among studies reviewed by Pourshahidi et al. (2016) for overall cancer effects, it is my opinion that the evidence indicates a possible benefit as well as a possible risk associated with coffee consumption.

Pourshahidi et al. (2016), citing Clavel, J., et al., (Childhood Leukaemia, Polymorphisms of Metabolism Enzyme Genes, and Interactions with Maternal Tobacco, Coffee and Alcohol Consumption during Pregnancy. *Eur. J. Cancer Prev.* 14:531-540, 2005), mistakenly claim that there is a beneficial effect of coffee consumption on childhood acute leukemia. However, in the primary study from that laboratory that investigated the role of coffee drinking on the risk of childhood acute leukemia, Menegaux, F., et al. (Maternal Coffee and Alcohol Consumption during Pregnancy, Parental Smoking and Risk of Childhood Acute Leukaemia. *Cancer Detect. Prev.* 29:487-493, 2005) concluded: “Maternal coffee consumption during pregnancy was associated with childhood acute leukemia, ORs increasing in ALL with coffee consumption (OR=1.1 [0.7-1.8], OR=2.4 [1.3-4.7] and OR=3.1 [1.0-9.5], respectively, for < or =3, 4-8 and >8 cups/day).”

While the frequency of reported benefits compared to reported risks was larger for several health categories examined by Pourshahidi et al. (2016), for many other health categories, the number of studies indicating increased risk was greater than the number of studies indicating increased benefit; these included 1) cardiovascular disease (observational studies: 119 for risk, 48 for benefit, and 88 null effect; intervention studies: 42 risk, 20 benefit, and 30 null), 2) gastrointestinal complaints (observational studies: 14 for risk, 4 for benefit, and 40 null effect; intervention studies: 8 risk, 10 benefit, and 7 null), and 3) bone health (observational studies: 18 for risk, 3 for benefit, and 22 null effect). Based on their reported data, Pourshahidi et al. (2016) concluded “overall, results of this comprehensive review show

that the health benefits (or null effects) clearly outweigh the risks of moderate coffee consumption in adult consumers for the majority of health outcomes considered.” In my opinion, this conclusion is misleading for several reasons: 1) it ignores all of the limitations noted above for interpreting results from observational studies, 2) it assumes causality while recognizing that causality cannot be established from these types of data, 3) it ignores inconsistencies in the number of reported benefits and risks by simply opining an overall judgement, 4) it combines multiple health outcomes without using a common metric or adjusting for quality disease weights, and 5) this review does not identify assumptions made by the authors or characterize uncertainties associated with this conclusion.

In my opinion, the results from the Pourshahidi et al. (2016) study are not suitable for a BRAFO evaluation because two dietary scenarios are not defined. To apply the BRAFO methodology to the current case, a comparison would be needed on the benefits and risks of the reference scenario (e.g., consumption of coffee at current levels of acrylamide) versus the alternative scenario (e.g., consumption of coffee at markedly reduced levels of acrylamide). However, a quantitative comparison cannot be done since there are no data showing health risks of the alternative scenario. Reducing cancer risk by lowering consumption of acrylamide provides a health benefit with no known health risk; this favorable scenario should support the decision to reduce acrylamide levels in coffee.

c) Alternative Cancer Risk Level

As I testified and as the court determined in the Phase I trial, a No Significant Risk Level (NSRL) for a carcinogen in a mixture can only be determined by means of a risk assessment that quantifies the risk of cancer from exposure to the carcinogen in the mixture. Likewise, an Alternative Cancer Risk Level for a carcinogen in a mixture can only be determined by means of a quantitative cancer risk assessment that quantifies health benefits and health risks of coffee containing acrylamide at current levels which are above the NSRL for average consumers versus coffee with substantially reduced levels of acrylamide. This is the approach specified in the regulation titled Quantitative Risk Assessment [27 C.C.R. § 25703]. Thus, to prove the defense the coffee company defendants must quantitatively derive an alternative cancer risk level based on “sound considerations of public health”. The coffee company defendants cannot simply choose an alternative risk to comport with the level of exposure to acrylamide in their products. Rather, they must derive an alternative risk level by means of a quantitative risk assessment “based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for listing the chemical as known to the state to cause cancer” [27 C.C.R. § 25703(a)]. In my view, it is not appropriate to determine an Alternative Cancer Risk Level for acrylamide in coffee, because the acrylamide content of coffee

can be reduced using multiple technologies to a level that would likely not exceed the NSRL for acrylamide in coffee.

Effect of Reducing Acrylamide in Coffee on Other Carcinogenic Constituents

One of the coffee industry's arguments against reducing acrylamide in coffee is that doing so would increase levels of other carcinogenic contaminants in coffee. In making this argument, the coffee industry has focused on furan because, unlike acrylamide, furan levels increase with greater roast degree. Though the furan content in coffee is much higher than other food categories and it is also carcinogenic in rats and mice (classified by IARC as possibly carcinogenic to humans), its margin of exposure for human cancer risk is 3 to 6 times higher than that of acrylamide (Moro, S., et al., Furan in Heat-Treated Foods: Formation, Exposure, Toxicity, and Aspects of Risk Assessment. Mol. Nutr. Food Res. 56:1-15, 2012; Joint FAP/WHO Exert Committee on Food Additives, 2010, <http://www.fao.org/3/a-at868e.pdf>). Mycotoxins, in particular, Ochratoxin A (OTA) is recognized by the coffee industry as another potential carcinogen that can occur in raw and roasted coffee beans. However, several methods for acrylamide remediation can be tailored specifically for acrylamide, for example, reducing the level of the acrylamide precursor with asparaginase or treating roasted coffee with acrylamidase are effective methods in reducing acrylamide levels in roasted coffee without affecting other hazardous agents present in roasted coffee beans. Also, by taking advantage of different physical/chemical properties of these various agents, methods can be adapted to reduce the levels of each of these agents. For example, acrylamide is a solid that is soluble in water, while furan is a highly volatile liquid that is only slightly soluble in water. Thus, methods that separate chemicals based on their physical/chemical properties (e.g., supercritical CO₂ extraction) can be effective in selectively removing undesirable contaminants from roasted coffee. In addition, several technologies that reduce acrylamide in coffee also tend to reduce the levels of these carcinogenic contaminants in roasted coffee.

a) Ochratoxin A

For OTA, "it is generally recognized that the focus of any effort to reduce OTA contamination of coffee must be application of good hygiene practices throughout the chain to avoid the formation of OTA" (MELITTA-00000940 to 00000951). Moisture content and level of bean quality (defects) are the main factors contributing to OTA contamination of coffee beans. Numerous studies have shown reduction of OTA levels in coffee under roasting conditions that also reduce acrylamide levels.

Roasting. The degradation of OTA in coffee increases with increasing temperature and

time of roasting (Ferraz, M.B.M., et al., Kinetics of Ochratoxin A Destruction during Coffee Roasting. *Food Control* 21:872-877, 2010). While thermal degradation during roasting was the major route of elimination of OTA (~84% reduction), green coffee cleaning, eliminating defective coffee beans, and removing the chaff also contribute to the reduction of OTA levels (Blanc, M., et al., Behavior of Ochratoxin A during Green Coffee Roasting and Soluble Coffee Manufacture. *J. Agric. Food Chem.* 46:673-675, 1998; Viani, R. Effect of Processing on Ochratoxin A (OTA) Content of Coffee. In 'Mycotoxins and Food Safety', Ed Trucksess et al., pp. 189-193, 2002). Others have also shown highly significant reduction in OTA levels from contaminated coffee beans with increasing roasting level (La Pera, L., et al., Influence of Roasting and Different Brewing Processes on the Ochratoxin A Content in Coffee Determined by High-Performance Liquid Chromatography-Fluorescence Detection (HPLC-FLD), *Food Addit. Contam.* 25:1257-1263, 2008; van der Stegen, G.H.D., et al., Effect of Roasting Conditions on Reduction of Ochratoxin A in Coffee. *J. Agric. Food Chem.* 49:4713-4715, 2001; Romani, S., et al., Influence of Roasting Levels on Ochratoxin A Content in Coffee. *J. Agric. Food Chem.* 51:5168-5171, 2003; Oliveira, C., et al., Effect of Different Roasting Levels and Particle Sizes on Ochratoxin A Concentration in Coffee Beans. *Food Control* 34:651-656, 2013). The combination of dark roast and coarsely ground coffee gave 97% reduction in OTA concentration (Oliveira et al., 2013).

Gamma radiation. A 10-kGy dose was effective in reducing OTA in green coffee beans "without affecting its sensory attributes" as judged by 15 trained panelists (Kumar, S., et al., Inactivation of *A. ochraceus* Spores and Detoxification of Ochratoxin A in Coffee Beans by Gamma Irradiation. *J. Food Sci.* 77: T44-T51, 2012); OTA degradation increased with increasing moisture content, e.g., 100%, 90%, and 20% reduction in coffee beans with 58%, 23 %, and 12% moisture, respectively. Gamma radiation also significantly decreased the contamination of green coffee beans by the mold species that produce OTA (Alkhalifah, D.H.M., et al., Effect of Gamma Irradiation on Microbiological Analysis, Acrylamide Content of Coffee Beans with Special References to Genotoxicity. *J. Appl. Sci. Res.* 9:3157-3166, 2013).

b) Furan

Furan formation in foods can arise by several pathways: thermal degradation/Maillard reaction of sugars, thermal oxidation of ascorbic acid, thermal oxidation of polyunsaturated fatty acids, and thermal degradation of certain amino acids (Moro et al., 2012; Leuven, K.U., Furan Formation in Heat Treated Food Products. Hightech Europe, 2012; Altaki, M.S., et al., Occurrence of Furan in Coffee from Spanish Market: Contribution of Brewing and Roasting. *Food Chem.* 126:1527-1532, 2011; Santonicola, S. and Mercogliano R., Occurrence and Production of Furan in Commercial Foods. *Ital. J. Food Sci.* 28:155-177, 2016; Anese, M. and

Suman, M., Mitigation Strategies of Furan and 5-Hydroxymethylfurfural in Food. *Food Res. Int.* 51:257-264, 2013). Alanine and glycine appear to be the main amino acid precursors of furan formation (Bi, K.H., et al., Tea Polyphenols as Inhibitors of Furan Formed in the Maillard Model System and Canned Coffee Model. *J. Food Sci.*, 82:1271-1277, 2017). Furan in coffee is generated during the roasting of green coffee beans. Ascorbic acid is probably not a major contributor to furan formation in roasted coffee because it was not detected in green coffee bean samples (Arisseto, A.P., et al., Furan Levels in Coffee as Influence by Species, Roast Degree, and Brewing Procedures. *J. Agric. Food Chem.* 59:3118-3124, 2011). Though furan levels increase with the development of darker roast color and roast time, decreases in furan levels occur during subsequent processing of roasted coffee beans (e.g., grinding and degassing before packaging) and by consumer handling (i.e., the method of coffee brewing) (Guenther, H., et al., Furan in Coffee: Pilot Studies on Formation during Roasting and Losses during Production Steps and Consumer Handling. *Food Addit. Contam.* 27:283-290, 2010; Arisseto et al., 2011). As a volatile liquid, furan levels in brewed coffee samples was significantly reduced (~25%) by holding for 11 to 20 min without a lid at room temperature (Kim, T.K., et al., Effect of Cooking or Handling Conditions on the Furan Levels of Processed Foods. *Food Addit. Contam.* 26:767-775, 2009).

Strategies to reduce furan formation in foods are addition of free radical scavengers or modification of atmospheres in roasting systems (e.g., reduction of atmospheric oxygen), and volatilization by heating in an open vessel (Leuven et al., 2012; Santonicola and Mercogliano, 2016; Anese and Suman, 2013). Indeed, the addition of tea polyphenol antioxidants inhibited furan formation, but also the formation of other aromatic compounds, in a canned coffee preparation during sterilization (Bi et al., 2017). Other strategies for reducing furan formation include slow roasting, gamma radiation, and post-process vacuum treatment.

Reduced roasting temperature and slow roasting. Furan levels in brewed coffee are significantly lower with low temperature and long roasting times (e.g., 140°C for 20 min) compared to higher temperature and shorter roasting times (e.g., 170°C for 12 min or 200°C for 6 min) (Altaki et al., 2011). Reducing roast time during the first two roasting stages and increasing roast time during later roasting stages reduces acrylamide levels in coffee by about 40% (Xu, T., et al., Content and Formation of Acrylamide in Traditional Coffee Roast Programmes. 2nd International Conference on Machinery, Materials Engineering, Chemical Engineering and Biotechnology, pp. 884-887, Atlantis Press, 2016). Because heating temperature has the greatest effect on furan formation, using a lower heating temperature and longer heating time can reduce furan levels produced in foods (Bi et al., 2017).

“In principle, decreasing the thermal input, i.e., the heat amount provided to the sample during heating, represents an effective way of acrylamide, furan and HMF [5-

hydroxymethylfurfural] mitigation. Thermal input reduction can be obtained by applying prolonged heating at lower temperatures, eventually at pressures lower than the atmospheric one (e.g. vacuum frying) or by optimizing the temperature profile of the oven (i.e. higher temperatures at the early stages of heating, when the moisture content is high, followed by lower temperatures in the final ones, when the water content is reduced” (Anese and Suman, 2013). Reduction of the thermal input can also be obtained by microwave heating.

Gamma radiation. Gamma radiation at a dose of 10 kGy reduced the furan content in dark roasted coffee beans by nearly 75%, and by nearly 70% in light roasted coffee beans (Farag Zaied, S.A., et al., Mitigation Strategies of Furan in Coffee Beans by Irradiation Process. Res. J. Pharm. Biol. Chem. Sci. 8:1064-1071, 2017).

Post-process vacuum treatment. “By exploiting their chemical and physical properties, these molecules [acrylamide, furan and HMF] can be removed from the finished product by proper application of temperature, time and pressure conditions” (Anese and Suman, 2013). A hydration step (e.g., spraying with water) before entering the vacuum chamber may be necessary to remove these chemicals from dry foods such as coffee.

There does not appear to be a significant effort by the coffee industry to actually evaluate the effect of acrylamide mitigation on furan formation or to prevent furan formation and apply strategies to remove furan from coffee products.

Summary and Conclusions

- 1) As I understand it, the major issue in this case is whether the defendant coffee companies should be allowed to expose Californians to acrylamide in their coffee products in excess of the NSRL based on “sound considerations of public health.”
- 2) Any propose alternative NSRL value must be “based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for listing the chemical as known to the state to cause cancer,” and an exception to the 1 per 10⁵ excess cancer risk might be allowed where “sound considerations of public health” support an alternative level.
- 3) Acrylamide is a probable human carcinogen that induces tumors primarily by a mutagenic mode of action (by binding to DNA and causing chromosomal aberrations and gene mutations) that could operate similarly in animals and humans.
- 4) Cancer is a costly and devastating disease. Avoiding or reducing exposure to carcinogenic agents (i.e., primary prevention) is an effective strategy to reduce human cancer rates.

- 5) Coffee provides the greatest source of acrylamide in the adult diet.
- 6) The Food and Agricultural Organization of the United Nations and the World Health Organization have determined that the ratio between exposures associated with 10% extra cancer risk and current human exposures to acrylamide are low, signifying a high human health concern for this genotoxic carcinogen. Therefore, for sound consideration of public health, it is essential that acrylamide levels in major food sources be drastically reduced.
- 7) While roasting coffee beans is necessary to make coffee products, the presence of acrylamide in coffee fails all valid criteria for allowing an alternative cancer risk level:
 - a) Acrylamide in coffee provides no health benefit,
 - b) Acrylamide is not essential for the functionality or quality of coffee,
 - c) Acrylamide levels in coffee can be substantially reduced, and
 - d) Acrylamide levels can be reduced without significantly affecting sensorial properties or increasing the levels of any other harmful contaminants in coffee.
- 8) A methodology exists to quantitatively compare human health risks and benefits of foods (Benefit-Risk Analysis for Foods, BRAFO). For the documentation of the existence of a human benefit, meta-analyses of randomized controlled trials provide the highest level of evidence.
- 9) The BRAFO methodology has been applied to the use of asparaginase to reduce the level of the acrylamide precursor asparagine in potato and cereal products. In this case, cancer risk was reduced due to lowered acrylamide consumption and there was no expected adverse health effect from this treatment.
- 10) In my opinion, the reduction of acrylamide in coffee with limited negative impact on organoleptic properties can likewise produce a product in which benefits clearly dominate risks; hence, acrylamide-reducing actions should also be applied to coffee.
- 11) A review of the scientific literature on risks and benefits of coffee consumption has been published (Pourshahidi et al. (2016). While the frequency of reported benefits compared to reported risks was larger for some health categories, for many other health categories, the number of studies indicating increased risk was greater than the number of studies indicating increased benefit; these included cardiovascular disease, gastrointestinal complaints, and bone health. The authors recognized “causality cannot be established for either [benefit or risk] with the research currently available as these are largely based on observational data,” and “heterogeneity between study populations and designs, and also lack of control for many other confounding factors, add limitations to the existing literature.”

- 12) The argument that reducing acrylamide in coffee would increase levels of other carcinogenic contaminants in coffee is not valid because methods can be tailored specifically to the removal of acrylamide (e.g., use of asparaginase), and because methods can be adapted to reduce the levels of other undesirable contaminants based on their physical/chemical properties.
- 13) In conclusion, it is my view that an Alternative Cancer Risk Level for acrylamide in coffee is not appropriate because the acrylamide content of coffee can be reduced to a level that would likely not exceed the NSRL for acrylamide in coffee using existing technologies.

EXHIBIT “B”

Assessing the Benefits and Risks of Acrylamide in Coffee

BRAFO (Benefit-Risk Analysis for Foods) was funded by the European Commission to develop an approach to compare quantitatively human health risks and benefits of foods using a quantitative common scale of measurement (Hoekstra et al., 2012; Boobis et al., 2013). The approach involves 4 tiers in which a reference dietary scenario (e.g., consumption of coffee at current levels of acrylamide) is compared to an alternative scenario (e.g., consumption of coffee at markedly reduced levels of acrylamide) for informing health-based policy decisions. Thus, based on the comparison of potential health risks and benefits, the evaluation is intended to provide information on the net health impact of the two dietary scenarios and thereby support either the reference dietary scenario or change to the alternative dietary scenario for improving public health. Importantly, for the communication of risks and benefits is the characterization of uncertainties.

Tier 1 involves identifying potential risks and benefits separately: if there are risks but no benefits with the alternative scenario, then the assessment can stop and the reference scenario is advised; alternatively, if there are only health benefits with the alternative scenario, then the decision can be made to stop the assessment and the alternative scenario is preferred. If there are both health benefits and risks with the alternative scenario, then the assessment should proceed to Tier 2.

Tier 2 involves a qualitative integration of the risks and benefits with no common metric used. This tier assesses the magnitude of the risks and benefits by considering the number of people affected, the severity of the health effect, the number of years living with the effect, and years of life lost due to the effect. Similar to tier 1, if the overall balance indicates that *risks clearly dominate benefits* the assessment can stop and the reference scenario is advised; alternatively, *if benefits clearly dominate risks*, then the decision can be made to stop the assessment and the alternative scenario is preferred. If both beneficial and adverse effects are present but neither scenario clearly dominates, then the assessment needs to proceed to Tier 3.

Tier 3 involves a quantitative integration of risks and benefits by a deterministic approach (assessment is made with fixed values) using a common metric. Example metrics include willingness to pay to avoid an adverse health outcome, disability adjusted life years, and quality adjusted life years. These metrics are a function of the time in a future health state (i.e., years with the disease) times the health-related quality of life associated with that health state (weighted between 0 for death and 1 for completely healthy). For many health conditions, quality disease weights and data for the parameter values are not readily available; this could result in estimates with large uncertainties. If uncertainties are too large to make a reliable conclusion, more data may be needed. Alternatively, if the differences between the reference and alternative scenarios is close to zero and large uncertainties or variabilities exist, the assessment may need to proceed to tier 4.

Tier 4 involves a quantitative integration of risks and benefits by a probabilistic approach (assessment is made with input parameters represented by probability distributions) to quantify some uncertainties and variabilities. This assessment, which is also based on a common metric needs to include “full consideration of the associated assumptions and uncertainties.”

“Benefit-risk assessment is not easy”, “it requires substantial data or assumptions, it is affected by many uncertainties, it requires careful interpretation and communication” (Hoekstra et al., 2012). Thus, all assumptions and uncertainties need to be clearly specified and their impact must be carefully considered when interpreting the results of a benefit-risk assessment. “The source, quantity and quality of data should be stated as well as the nature of the assumptions made at the different steps of the assessment to compensate for insufficient human data, uncertainties in the assessment, including in the extrapolation of animal data to humans and classification of weights for disability and quality of life, respectively” (Boobis et al., 2013). “With respect to benefit assessment [from human studies], meta-analyses of randomized controlled trials provide the highest level of evidence for the documentation of the existence of a benefit” (Boobis et al., 2013). In addition, “the evidence should preferably be supported by the results of observational studies and the effect should be biologically plausible.” “Evidence can be judged as probable when the available epidemiological (observational and intervention) studies show fairly consistent associations between exposure and effect; evidence is judged as possible when it relies on inconsistent results from intervention and observational studies.”

The BRAFO methodology has been applied to several case studies including 2 involving natural foods (e.g., farmed salmon vs oily fish) (Watzl et al., 2012), 3 on heat processing contaminants (Schutte et al., 2012), and 5 on dietary interventions (e.g., fortification of bread with folic acid) (Verhagen et al., 2012). For most of these case studies, it was possible to assess overall health impacts without proceeding to tiers 3 or 4 because risks or benefits of the alternative scenario were judged to clearly dominate, or because of limited or lack of data to allow for quantitative calculations of risks and benefits. For example, in comparing health benefits and risks associated with consumption of oily fish (reference scenario) versus farmed salmon (alternative scenario) in which contaminants including methyl mercury, dioxin, and dioxin-like PCBs were identified as potential hazardous components, the alternative scenario was recommended because the tier 1 assessment showed that its benefit outweighed the risk of the reference scenario (Watzl et al., 2012). In comparing consumption of soy foods (alternative scenario) versus no intake of soy (reference scenario), the beneficial effects of the alternative scenario were judged to clearly dominate potential risks (Watzl et al., 2012).

The case studies on heat processing contaminants, especially the one on reducing acrylamide in potato and cereal products (Schutte et al., 2012), are most relevant to the current case concerning benefits of reducing acrylamide levels in coffee. While heat processing produces positive changes to food products, formation of hazardous contaminants such as acrylamide, a genotoxic carcinogen with a low margin of exposure, indicates a human health concern. The BRAFO methodology was applied to the evaluation of cooking practices before acrylamide mitigation measures were introduced (reference scenario) versus foods in which acrylamide mitigation methods have been implemented that could reduce overall acrylamide intake by approximately 30% with limited negative impact on organoleptic properties. With use of

asparaginase to reduce the level of the acrylamide precursor asparagine, the evaluation stopped at tier 1, because of the positive safety evaluation of this enzyme, reduced cancer risk from lowered acrylamide consumption, and no expected adverse health effect from this treatment. Because of the beneficial effect of reducing acrylamide in processed foods, “acrylamide-reducing actions should hence be applied as long as the adverse side effects are recognized and minimized to the extent possible.”

The above recommendation is also relevant to coffee. In my opinion, the reduction of acrylamide in coffee with limited negative impact on organoleptic properties can produce a product in which benefits clearly dominate risks; hence, acrylamide-reducing actions should be applied to coffee.

Pourshahidi et al. (2016) provided review of 1,277 published human studies on health effects associated with coffee consumption. The authors suggested that this information might be useful for a future quantitative benefit-risk assessment of coffee consumption using published approaches (e.g., Hoekstra et al., 2012; Verhagen et al., 2012; Boobis et al., 2013). However, Pourshahidi et al. (2016) cautioned on the interpretations of studies included in this review because “results and generalizations are complicated by a number of factors, including differences in age, gender, health status, type of coffee preparation, serving size, and source of coffee.” Furthermore, “causality cannot be established for either [benefit or risk] with the research currently available as these are largely based on observational data,” and “heterogeneity between study populations and designs, and also lack of control for many other confounding factors, add limitations to the existing literature.”

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Pourshahidi et al. (2016), citing Clavel et al., (2005), mistakenly claim that there is a beneficial effect of coffee consumption on childhood acute leukemia. However, in the primary study from that laboratory that investigated the role of coffee drinking on the risk of childhood acute leukemia, Menegaux et al. (2005) concluded: “Maternal coffee consumption during pregnancy was associated with childhood acute leukemia, ORs increasing in ALL with coffee consumption (OR=1.1 [0.7-1.8], OR=2.4 [1.3-4.7] and OR=3.1 [1.0-9.5], respectively, for < or =3, 4-8 and >8 cups/day).”

While the frequency of reported benefits compared to reported risks was larger for several health categories examined by Pourshahidi et al. (2016), for many other health categories, the number of studies indicating increased risk was greater than the number of studies indicating increased benefit; these included cardiovascular disease (observational studies: 119 for risk, 48 for benefit, and 88 null effect; intervention studies: 42 risk, 20 benefit, and 30 null), gastrointestinal complaints (observational studies: 14 for risk, 4 for benefit, and 40 null effect; intervention studies: 8 risk, 10 benefit, and 7 null), and bone health (observational studies: 18 for risk, 3 for benefit, and 22 null effect). Based on their reported data, Pourshahidi et al. (2016) concluded “overall, results of this comprehensive review show that the health benefits (or null effects) clearly outweigh the risks of moderate coffee consumption in adult consumers for the majority of health outcomes considered.” In my opinion, this conclusion is misleading for several reasons: 1) it ignores all of the limitations noted above for interpreting results from observational studies, 2) it assumes causality while recognizing that causality cannot be established from these types of data, 3) it ignores inconsistencies in the number of reported benefits and risks by simply opining an overall judgement, 4) it combines multiple health outcomes without using a common metric or adjusting for quality disease weights, and 5) this review does not identify assumptions made by the authors or characterize uncertainties associated with this conclusion.

In my opinion, the results from the Pourshahidi et al. (2016) study are not suitable for a BRAFO evaluation because two dietary scenarios are not defined. To apply the BRAFO methodology to the current case, a comparison would be needed on the benefits and risks of the reference scenario (e.g., consumption of coffee at current levels of acrylamide) versus the alternative scenario (e.g., consumption of coffee at markedly reduced levels of acrylamide). However, a quantitative comparison cannot be done since there are no data showing health risks of the alternative scenario. Reducing cancer risk by lowering consumption of acrylamide provides a health benefit with no known health risk; this favorable scenario should support the decision to reduce acrylamide levels in coffee.

EXHIBIT “C”

Critique of Dr. David Kessler's Report and Testimony

In his expert report (¶ 83), Dr. Kessler opined that “sound considerations of public health support an alternative risk level up to 10^{-4} for acrylamide in coffee,” though in his testimony he stated (page 235) “that an alternative risk level would be between 10 to the minus 4 and 10 to the minus 6.” In formulating this opinion, Dr. Kessler relies largely on the USDA Scientific Report of the 2015 Dietary Guidelines Advisory Committee (DGAC) which he claims “recognized nutritional health benefits associated with the consumption of coffee.” However, that report does not address any concerns about acrylamide in foods or recommend an acceptable risk level for this carcinogen in coffee. Thus, the alternative risk level of up to 10^{-4} proposed by Dr. Kessler for acrylamide in coffee appears to be an arbitrary value with no supporting rationale. Listed below are my critiques of specific statements made by Dr. Kessler in his deposition or expert report that appear to serve as the basis for his opinion on this issue.

1. Dr. Kessler's Opinions for an Alternative Cancer Risk Level for Acrylamide in Coffee are Based on Improper Reliance on Decisions of Federal Agencies.

In his expert report (¶ 21), Dr. Kessler refers to actions of federal regulatory agencies (primarily FDA), to support the use of 10^{-4} to 10^{-6} risk levels for cancer causing chemicals. In my opinion it is inappropriate to rely on decisions of federal regulatory agencies to base decisions under Proposition 65 because of different statutes and regulations that have different purposes and goals.

The purpose of the federal Food Drug and Cosmetic Act (FDCA) is to assure the safety of food, drugs and cosmetics, while the purpose of Proposition 65 (the Safe Drinking Water and Toxic Enforcement Act of 1986) is to inform people about three specific chemical hazards that they encounter in daily life -- cancer, reproductive toxicity, developmental toxicity -- and whether such chemical hazards are encountered in air, soil, water, food, drugs, cosmetics, or consumer products. Regarding cancer risk, FDA applies a strict (protective) standard of 1 excess cancer per 1 million people exposed (1×10^{-6}) (GAO, Chemical Risk Assessment: Selected Federal Agencies' Procedures, Assumptions, and Policies, 2001; <http://www.gao.gov/assets/240/232303.pdf>); while to assure that people in California are informed of cancer risks to which they are exposed, Proposition 65 applies a standard of 1 excess cancer per 100,000 people exposed (1×10^{-5}), which OEHHA considers to be equivalent to a 10^{-6} standard applied to a less conservative risk assessment.

The FDCA was adopted by Congress to protect public health and safety, while Proposition 65 was adopted following a referendum of the people of California who voted for this initiative by a 63 to 37 percent margin (<https://oehha.ca.gov/proposition-65/law/proposition-65-law-and-regulations>). In adopting Proposition 65, the people of the State of California declared their rights (Safe Drinking Water and Toxic Enforcement Act of 1986, Section 1):

- a) To protect themselves and the water they drink against chemicals that cause cancer, birth defects, or reproductive harm.
- b) To be informed about exposures to chemicals that cause cancer, birth defects, or other reproductive harm.
- c) To secure strict enforcement of the laws controlling hazardous chemicals and deter actions that threaten public health and safety.

Proposition 65 expresses the will of the People to protect themselves from hazardous chemicals that cause cancer, birth defects and other reproductive harm because state government agencies had failed to provide them with adequate protection.

Dr. Kessler's reliance on a small number of extraordinary exceptions to the 10^{-6} standard by FDA is inappropriate for a determination of the cancer risk level under Proposition 65. The 10^{-6} standard is the standard that the FDA has deemed to be appropriate to protect Americans from carcinogenic hazards of food, drugs, and cosmetics. In almost all instances the FDA has applied the 1×10^{-6} standard in regulating carcinogenic substances in food, drugs, and cosmetics. In a very few special circumstances the FDA has allowed foods to be sold although they do not meet the 10^{-6} standard. However, these few instances are exceptions rather than the rule, and they should not serve as precedent for deviating from the 10^{-6} standard for FDA or for Proposition 65. Indeed, it appears that the FDA has only allowed deviation from the 10^{-6} standard in a few rare circumstances where (1) the FDA had previously approved of a health claim for the particular food substance and (2) the carcinogen contaminating the food could not be removed.

Rare exceptions cited by Dr. Kessler to justify a 10^{-4} standard for exposure to acrylamide in coffee include PCBs in fish and arsenic in rice.

- a) PCBs in fish: in this case, the FDA determined that the evidence supporting a protective effect of omega-3 fatty acids on coronary heart disease was sufficiently strong to allow a qualified health claim for fish (FDA Summary of Qualified Health Claims Subject to Enforcement Discretion).
- b) Arsenic in rice (a whole grain food): in this case, the FDA had approved health claims associating diets high in fiber-containing grain products with reduced the risk of cancer [21 C.F.R. § 101.76] and with reduced risk of coronary heart disease [21 C.F.R. § 101.77.]

It appears that the FDA allowed deviation from the 10^{-6} standard for fish and rice because the FDA had approved health claims for these particular foods and the carcinogens contaminating them could not be removed. These two extraordinary exceptions are not analogous to acrylamide exposure from coffee consumption, because no governmental agency has ever approved of a health claim for coffee and a number of technologies are available to substantially reduce levels of acrylamide in coffee without compromising the favorable sensorial properties of coffee.

While Dr. Kessler looks to federal regulatory agency determinations regarding carcinogens in food and water as precedent for determining an alternative risk level for

exposure to acrylamide from consumption of coffee, he ignores the EPA's standard for exposure to acrylamide in drinking water.

The Safe Drinking Water Act, passed by Congress in 1974, required the EPA to determine safe levels of chemicals in drinking water, which are called Maximum Contaminant Level Goals (MCLGs). In 1992, EPA set the MCLG for acrylamide at zero (EPA, Support for the Third Six-Year Review of Drinking Water Regulations for Acrylamide and Epichlorohydrin, EPA 810-R-16-019, 2016), because it believed that this was the level of protection necessary to protect people from exposure to this mutagenic carcinogen in drinking water. Since acrylamide is used in drinking water treatment processes, the EPA determined that acrylamide would be controlled in drinking water simply by limiting its use for this purpose. Thus, the EPA required water suppliers to show that when acrylamide is added to water, the amount of uncoagulated acrylamide is less than 0.55 parts per billion (which is equal to 0.55 µg/L) (EPA, 2016). The EPA's standard for limiting the concentration of acrylamide in drinking water to less than 0.55 ppb is quite analogous to the NSRL that OEHHA set at 0.2 µg/day. Thus, if a federal regulatory standard were relevant to derivation of an alternative risk level for acrylamide in coffee, the most analogous federal regulatory standard would be EPA's 0.55 ppb standard for acrylamide in drinking water. Indeed, it makes no sense for California to set an alternative risk level for acrylamide in coffee that is less protective than EPA's standard for acrylamide in drinking water.

2. Dr. Kessler's Argument that Risks of 10^{-6} to 10^{-4} are Acceptable to OEHHA is Wrong.

In his report, Dr. Kessler wrote (¶ 26): "The agency (OEHHA) adopting regulations implementing the "no significant risk" exemption recognized that risk levels of between 10^{-6} and 10^{-4} are acceptable. (Final Statement of Reasons for Articles 7-8, at pp. 24-25 ["Generally speaking, regulatory levels range from 10^{-4} to 10^{-6} or lower," citing Travis, et al., 'Cancer Risk Management: A Review of 132 Federal Regulatory Decisions,' Environmental Science and Technology, Vol. 21, No. 5, p. 415 (1987)."]

Contrary to Dr. Kessler's assertion, the Final Statement of Reasons for Articles 7-8 **does not endorse a 10^{-4} risk level as being acceptable**. The text referred to by Dr. Kessler actually states: "The 10^{-5} risk level is commonly used as an acceptable risk level by many regulatory agencies. Generally speaking, regulatory levels range from 10^{-4} to 10^{-6} or lower. (See, C. C. Travis, et al., "Cancer Risk Management: A Review of 132 Federal Regulatory Decisions," Environmental Science and Technology, Vol. 21, No. 5, p. 415 (1987).) These fluctuations are often imposed due to differences in the methodologies employed in the underlying risk assessment. Under these regulations, it is intended that risk assessments based upon default assumptions will produce fairly conservative results. In effect, applying a 10^{-5} standard to a conservative risk assessment can produce the same result as applying a 10^{-6} standard to an assessment employing less conservative methodologies. Moreover, the application of a 10^{-5} standard for the purposes of the Act appears to be no less protective than the application of a 10^{-6} or lower standard under other regulatory programs. The purpose of the Act is to regulate exposures to specific chemicals. The purpose of most other programs is to control the risk from a particular medium, such as food, water or air. Therefore, these other programs must, in adopting a particular standard, consider issues of mixture, interaction, bioconcentration and

transformation of several chemicals as part of the cumulative risk presented by chemicals in that medium. This often demands that the standards applied under such programs to the chemicals of concern be individually set at more restrictive levels. Accordingly, the Agency believes that setting the level of "no significant risk" for "safe harbor" risk assessments at a 10^{-5} level will in effect provide no less protection than other levels set at 10^{-6} or lower, and is consistent overall with the regulation of cancer-causing chemicals."

Reading the Final Statement of Reasons in context, it is clear that this section is not an endorsement of a 10^{-4} risk standard for carcinogens, but rather is an explanation by OEHHA on why the NSRL was set at 10^{-5} instead of at 10^{-6} , i.e., OEHHA believes that "applying a 10^{-5} standard to a conservative risk assessment can produce the same result as applying a 10^{-6} standard to an assessment employing less conservative methodologies." Thus, contrary to Dr. Kessler's assertion, OEHHA has not endorsed a 10^{-4} risk standard for carcinogens, but rather endorses a 10^{-5} standard.

3. The FDA Hasn't Approved of Industry's Holistic Approach to Risk Assessment.

Dr. Kessler asserts in his report (¶32) that FDA concluded that "a holistic approach that considers risks and benefits is necessary for AA [acrylamide] in foods." Actually, it is the food and coffee industries that have advocated a "holistic approach" to risk assessment in order to avoid regulation of carcinogenic contaminants in foods. Email correspondences in 2005 from Gerrit van der Stegen of Sara Lee Netherlands (a major coffee company) and Sally Vater of Procter & Gamble [KRAFT-00027322 to 00027324] clearly reflect the strategy of the coffee industry in promoting the "holistic approach" to avoid requirements for acrylamide reduction in coffee:

Gerrit van der Stegen to members of the coffee industry including the National Coffee Association: "EU authorities are discussing acrylamide strategies, as many other authorities do. Coffee is very prominently on their list of food items under concern. . . . The European industry is advocating to do more holistic kind of safety assessments particularly for complex foods instead of assessments of individual chemical components one by one. Part of the governmental officials have adopted the idea, but clearly not yet all. For complex products like coffee such holistic approach is far more attractive than having to go through all the individual assessments of something like 25 out of 1000 components in coffee, which are already somewhere on an IARC or other official list."

Sally Vater: "Thanks very much for this helpful perspective. Do you think that this holistic perspective will reduce concerns for coffee, and avoid the imposition of acrylamide reduction measures?"

Gerrit van der Stegen: "Indeed it is expected that a risk/benefit or holistic assessment will reduce the pressure on coffee."

In support of his assertion that the FDA approves of industry's "holistic approach," Dr. Kessler cites only one article: Doerge D.R., et al., "Using Dietary Exposure

and Physiologically Based Pharmacokinetic/Pharmacodynamic Modeling in Human Risk Extrapolations for Acrylamide Toxicity," *J. Agric. Food Chem.* 56:6031-6038, 2008). However, this article contains a disclaimer that states: "The views presented in this paper do not necessarily reflect those of the U.S. Food and Drug Administration." Dr. Kessler cites no other FDA publication that either proposes, recommends, approves of, or adopts the food industry's "holistic approach" to regulating foods; thus, it is disingenuous of Dr. Kessler to claim that the FDA has approved industry's "holistic approach."

4. The FDA Has Not Concluded that Difficulties in Removing Risks Must be Weighed Against the Benefits of Foods with Reduced Microbial Contamination

In his report, Dr. Kessler wrote (¶33) "FDA also stated that 'substantial reductions in AA [acrylamide] consumption from typical cooked foods comprising the modern diet will be difficult to achieve and that theoretical cancer risks might be significant at the population level.' In light of that, FDA stated that 'the difficulties in effectively removing or accepting risks must be weighed alongside the many real benefits from consuming nutritious cooked foods with reduced microbial contamination.'" These statements do not represent an official FDA position, as they were taken from the article by Doerge et al. ("Using Dietary Exposure and Physiologically Based Pharmacokinetic/Pharmacodynamic Modeling in Human Risk Extrapolations for Acrylamide Toxicity," *J. Agric. Food Chem.* 56:6031-6038, 2008) in which the authors wrote "the views presented in this paper do not necessarily reflect those of the U.S. Food and Drug Administration."

While the above statements acknowledge potential cancer risk in the general population from acrylamide in cooked foods, the rationale for not reducing these cancer risks runs counter to FDA policy. In fact, it has long been FDA policy that the agency does not consider a manufacturer's difficulty in eliminating carcinogenic chemicals in food or the costs to the manufacturer of doing so. As noted by Kessler (1984), FDA's "general safety clauses allow only for consideration of potential harm. However, the FDA may indirectly take benefits into account by, for instance..... when confronted with an additive that has important health and economic benefits." Acrylamide in coffee provides not health or economic benefits for coffee consumers. Also, through the Food, Drug and Cosmetic Act, "Congress has directed the FDA . . . to consider only whether an added food ingredient is "safe" when making decisions about allowing it to be used," and that "costs are not allowed to be considered by the agency either in the case of drugs or of food ingredients" (Rodricks JV. The management of risk. In "Calculated Risks: The Toxicity and Human Health Risks of Chemicals in our Environment," 2nd edition, Cambridge University Press, 2006).

Because methods are available to reduce acrylamide levels in coffee, it appears, contrary to Dr. Kessler's assertion, that the FDA cannot properly consider the difficulties or costs of reducing acrylamide in coffee in determining the appropriate risk standard for exposure to this carcinogen from drinking coffee.

5. Dr. Kessler’s Opinion That Reducing Acrylamide in Coffee Isn’t Necessary Because the FDA Has Not Recommended Doing So Is Contrary to the Evidence and Lacks Relevance to this Case

First of all, the Proposition 65 statute does not specify that decisions on reducing levels of carcinogens in foods served in California should align with FDA recommendations, or lack thereof. Since the FDA recognizes that reducing acrylamide in foods may mitigate potential health risks, the decision by the FDA to not set any action level for acrylamide in coffee or other food items does not justify similar inaction in California under Proposition 65.

To support his opinion, Dr. Kessler notes:

- a) (¶ 35) in its Guidance to Industry, the FDA recognized that “reducing acrylamide levels in foods may mitigate potential health risks,” but did not recommend specific removal approaches and did not set any maximum recommended level or action level for acrylamide in foods.
- b) (¶ 36) that the “FDA provided no recommendation or guidance for the reduction of acrylamide levels in coffee,” although it did provide guidance for some other acrylamide-containing foods.
- c) and (¶ 37) that “FDA found that risks of exposure to AA must be ‘weighed alongside the many real benefits’ of cooked foods” and, “as a result of this balance, FDA has not set any action level for AA in food.”

However, a search of the FDA Guidance for Industry: Acrylamide in Foods (March 2016) does not show Dr. Kessler’s quoted statement: “weighed alongside the many real benefits.” That statement was also not present in the FDA document *You Can Help Cut Acrylamide in Your Diet* (March 2016). I therefore conclude that those quotations that Dr. Kessler attributes to the FDA are spurious and leave it to Dr. Kessler to explain his misquotations of the document to the court.

The FDA Guidance document provided some guidance for reducing acrylamide in some foods, but not for coffee; according to the Guidance document, this was because “FDA is not aware of any proven mitigations measures” for coffee. I believe that the FDA was unaware of proven mitigation measures for reducing acrylamide in coffee, because the coffee industry did not submit to the FDA numerous confidential reports of methodologies that members of the industry had investigated to remove acrylamide from coffee, in response to the FDA’s request to industry to submit such documents to the agency. I only became aware of these industry reports because they were produced in this litigation pursuant to a protective order.

I also believe that the FDA may have been unaware of proven mitigation measures for reducing acrylamide in coffee, because Richard Stadler (Director of the Nestlé S.A. Food Contaminants Group) and John Mwangi (then Manager of Technical and Regulatory Affairs at Nestlé USA, and now with Starbucks) concealed important information regarding acrylamide in coffee from the FDA when they met with Nega Beru (Director of the Office of Food Safety in the Center for Food Safety and Applied Nutrition) at the FDA on May 20, 2010. The purpose of this meeting was to persuade the FDA to not set regulatory limits for acrylamide in coffee. In a self-assessment of his achievements at Nestlé in 2010, Mr. Mwangi described his success on behalf

of Nestlé in deterring the FDA from regulating acrylamide in coffee: “Our Visit to the FDA was succes[s]ful in influencing the FDA to use the tool box approach and against setting guidance values. Nega Beru at the FDA mentioned that FDA was going to issue a guidance document for the management of acrylamide which was not issued. We initially had offered to provide more data on Acrylamide to the FDA but on the advice of legal and of Nancy Rachman at GMA we were advised not to provide more data to the FDA because of the risk of the data being discovered in the event of a lawsuit under Prop 65.” “The visit to the FDA is a good example of courage because the Company especial[ly] QA wa[s] reluctant for Nestle to have a meeting with the FDA. So reached out to Richard Stadler who is a recognized global expert on acrylamide and asked for a meeting with Dr Nega Beru head of the FDA contaminant group. Richard presented the work that Nestle has done in mini[mi]zing acrylamide levels in food [w]hich gave the FDA confidence that we are the global leaders on this issue. Also we were able to influence the FDA against following the EU direction of using guidance values” “On acrylamide there was a lot of concern in the Company about making a trip to the FDA to make a presentation on progress Nestle has made on reducing levels of Acrylamide in foods. I held a number of conversations with Bruce Kohnz and with Mark [Nelson] and with Paul Casaletto and Rick Jarman in Nestle Nutrition to convince everyone that . . . we would not divulge any data that would be damaging to us . . .” “ILSI hired a summer post doctorate student to write a paper on a acrylamide. The original draft contained data that would have played into the hands of the anti acrylamide lawyers. I reviewed the paper and then shared my comments with Richard Stadler and then related the Nestle comments to the ILSI Food safety committee and we were able to correct the [e]rroneous impression created by the data” [NESTLE-00000036 to 00000046].

Dr. Kessler also writes that even though the FDA recognized that the risk of dietary exposure to acrylamide was “significant,” “FDA’s non-action was based on the agency’s recognition, in part, that “dietary exposure modeling suggests that because AA is found in so many common foods, even big changes in concentration for single foods or groups of foods would probably have a small impact on overall population-based intake and risk” (¶ 38). However, the only reference that Dr. Kessler cites in support of this assertion is not a publication by the FDA, but is rather the nearly 10-year-old article by Doerge, et al. (2008), which states that “the views presented in this paper do not necessarily reflect those of the U.S. Food and Drug Administration.” Even if this statement was true for mean population intake and risk, it does not address the impact of reducing acrylamide levels in coffee on exposure and risk for coffee consumers. The NSRL is based on excess cancer risk in individuals exposed to the chemical; it is not based on cancer risk in the overall population.

6. Acrylamide in Coffee Should Not be Regulated at the 10^{-4} Standard Because OEHHA Proposed (though never adopted) Regulating Acrylamide in Bread & Cereal at that Standard 12 years ago

Dr. Kessler contends (¶ 39 of Kessler report) that his proposed 10^{-4} risk standard for exposure to acrylamide from coffee should be adopted because, in 2005, OEHHA proposed regulating acrylamide in bread and cereal at the 10^{-4} risk standard. Dr. Kessler notes that

OEHHA issued an Initial Statement of Reasons to support regulating bread and cereal at that standard. However, Dr. Kessler acknowledges that, upon receiving comments from the public, “OEHHA did not finalize these proposals, and on March 27, 2006, withdrew them without responding to comments.” Dr. Kessler opines that although OEHHA did not adopt the 10^{-4} risk standard for exposure to acrylamide from bread and cereal, that standard should nevertheless apply to exposure to acrylamide from coffee (¶ 40, ¶ 72, and ¶ 85).

It is odd that Dr. Kessler maintains his opinion that exposure to acrylamide from coffee should be regulated at the 10^{-4} risk standard, even though OEHHA decided not to do so for acrylamide in bread and cereal at that risk level after receiving comments regarding that proposed change. Does Dr. Kessler view that an agency’s rejection of its proposed regulation to be an endorsement of the proposed regulation? Dr. Kessler’s conclusion makes no sense because 12 years have passed since OEHHA initially proposed to regulate acrylamide exposure from bread and cereal at the 10^{-4} standard, but has never since suggested that exposure to acrylamide from any food should be regulated at that standard. It seems to me that OEHHA’s rejection of the 10^{-4} risk standard for exposure to acrylamide in bread and cereal suggests disapproval, rather than approval.

Several years after OEHHA rejected a 10^{-4} risk standard for exposure to acrylamide from bread and cereal, a risk assessment that compared benefits and risks of acrylamide in potato and cereal products was published (Schütte, K., et al., “Application of the BRAFO Tiered Approach for Benefit-Risk Assessment to Case Studies on Heat Processing Contaminants,” *Food Chem. Toxicol.* 50: S724-S735, 2012). This study and the methodology it employed are discussed in detail below (Item 11). I mention the study here because the investigators demonstrated that the benefits of reducing acrylamide in potato and cereal products outweighed the risks of not doing so. The investigators concluded that “the beneficial effect of reducing acrylamide in processed foods through various intervention methods in the food production is desirable” and that “acrylamide-reducing actions should hence be applied as long as the adverse side effects are recognized and minimized to the extent possible.” Thus, this study shows that OEHHA reached the correct conclusion in not adopting a 10^{-4} risk standard for exposure to acrylamide in cereal.

7. Acrylamide is Not the Inevitable Byproduct of Roasting Coffee Beans

In his report (¶ 50) Dr. Kessler writes that acrylamide, produced by roasting coffee beans to render them palatable, “is the inevitable byproduct of that cooking.” As I explained in my 2016 declaration regarding published studies concerning reduction of acrylamide in coffee, multiple technologies have been the subject of peer-reviewed publications and patent applications for reducing acrylamide levels in coffee, and a number of these technologies have been shown to substantially reduce acrylamide levels in coffee without compromising important sensorial properties of coffee. Since submitting my declaration to the court in 2016, I have received numerous confidential documents regarding experiments that members of the coffee industry undertook to investigate various technologies for reducing acrylamide levels in coffee. These documents also show that the coffee industry had identified technologies that

substantially reduce acrylamide levels in coffee without negatively impacting coffee's sensorial properties, but that the industry did not inform regulatory authorities of its successes in removing acrylamide from coffee in order to avoid regulation of acrylamide levels in coffee. Dr. Kessler's conclusion that acrylamide is "the inevitable byproduct" of roasting coffee beans is contrary to the published scientific literature and confidential industry documents. Dr. Kessler may not have read or been fully aware of this information when he rendered his incorrect opinion.

8. Dr. Kessler's Opinion that Coffee May Confer Health Benefits is Conjectural and Not Proven

Dr. Kessler wrote (¶ 62 of Kessler report) that the DGAC (USDA Scientific Report of the 2015 Dietary Guidelines Advisory Committee) found "consistent evidence [] that coffee consumption is associated with reduced risk of type 2 diabetes and cardiovascular disease in adults" and "moderate evidence [of] a protective association between caffeine intake and risk of Parkinson's disease." This statement omits several key modifiers from the DGAC report; the actual statement is "consistent **observational** evidence indicates that **moderate** coffee consumption is associated with reduced risk of type 2 diabetes and cardiovascular disease in **healthy** adults." The three bolded and italicized words are critical omissions by Dr. Kessler:

a) The word "observational" is an important limitation in the interpretation of epidemiological studies (cohort or case-control studies, because "in contrast to intervention studies, even the best-designed observational studies cannot establish cause and effect between an intervention and an outcome" (FDA, "Guidance for Industry: Evidence-Based Review System for the Scientific Evaluation of Health Claims-Final," 2009). Even for meta-analyses, the DGAC notes that "the substantial heterogeneity observed in the meta-analyses shows that interpretation of the results should be cautious." Similarly, Pourshahidi et al. (A Comprehensive Overview of the Risks and Benefits of Coffee Consumption, *Compr. Rev. Food Sci. Food Safety* 15:671-684, 2016) cautioned on the interpretations of epidemiological studies of the risks and benefits of coffee consumption because

i) "results and generalizations are complicated by a number of factors, including differences in age, gender, health status, type of coffee preparation, serving size, and source of coffee,"

ii) "causality cannot be established for either [benefit or risk] with the research currently available as these are largely based on observational data," and

iii) "heterogeneity between study populations and designs, and also lack of control for many other confounding factors, add limitations to the existing literature."

b) The word "moderate" is an important limitation on "coffee consumption," because it suggests that reported statistical associations of reduced risk were observed only at lower levels of coffee consumption, and that consumption of coffee at higher levels may well be detrimental to human health.

c) The word “healthy” is an important limitation on “adults”, because it indicates that the statistical associations of reduced risk for coffee consumption have been found only in healthy adults and not in others, such as pregnant women and their children, and unhealthy adults. Indeed, at his deposition Dr. Kessler testified that he himself recommends abstinence or limitation of caffeine intake (from coffee and other caffeine sources) among pregnant women, infants, children, and “sensitive individuals.”

Dr. Kessler also wrote that “The Committee [DGAC] concluded “moderate coffee consumption can be incorporated into a healthy dietary pattern, along with other healthful behaviors” (¶ 66 of Kessler report).

a) This statement does not indicate that there are health benefits of coffee. Rather, the DGAC simply recommends healthy diets and suggests that **moderate** consumption of coffee by **healthy** individuals “can be incorporated” into healthy dietary patterns. The acceptance of health claims for foods requires scientific agreement among qualified experts in the field that available scientific evidence demonstrates that risk reduction of a human disease condition is due to consumption of a food or food component. However:

i) Neither the DGAC nor any governmental agency has ever concluded that consumption of coffee prevents cancer or any chronic disease.

ii) The FDA has never authorized any health claim for coffee.

iii) The European Food Safety Authority (EFSA) has evaluated, but rejected, three separate applications for coffee health claims. EFSA considered the health claim that chlorogenic acids in coffee protect DNA, proteins and lipids from oxidative damage, maintain normal blood glucose concentrations, and contribute to the maintenance or achievement of a normal body weight. EFSA concluded that cause and effect relationships had not been established between the consumption of chlorogenic acids from coffee and each of these health claims (EFSA, Scientific Opinion on the substantiation of health claims related to coffee, including chlorogenic acids from coffee, and protection of DNA, proteins and lipids from oxidative damage (ID 1099, 3152, 4301), maintenance of normal blood glucose concentrations (ID 1100, 1962), and contribution to the maintenance or achievement of a normal body weight (ID 2031, 4326) pursuant to Article 13(1) of Regulation (EC) No 1924/2006, *EFSA Journal* 9:2057, 2011].

In a second health claim application EFSA concluded that a cause and effect relationship had not been established between the consumption of coffee C21 and a reduction of spontaneous DNA strand breaks (EFSA, Scientific Opinion on the substantiation of a

health claim related to coffee C21 and reduction of spontaneous DNA strand breaks pursuant to Article 13(5) of Regulation (EC) No 1924/2006, *EFSA Journal* 9:2465, 2011).

In a third application that was based on six intervention studies, EFSA again concluded that a cause and effect relationship had not been established between the consumption of coffee C21, a coffee standardised by its content of caffeoylquinic acids, trigonelline and *N*-methylpyridinium, and a reduction of DNA damage by decreasing spontaneous DNA strand breaks (EFSA, Scientific Opinion on the substantiation of a health claim related to coffee C21, a coffee standardised by its content of caffeoylquinic acids, trigonelline and *N*-methylpyridinium, and reduction of DNA damage by decreasing spontaneous DNA strand breaks pursuant to Article 13(5) of Regulation (EC) No 1924/2006, *EFSA Journal* 13:4099, 2015).

b) Thus, to date neither the FDA, EFSA, nor any other governmental agency has approved any health claims for consumption of coffee.

9. Coffee's Long Use by Hundreds of Millions of People Does Not Assure Safety.

In his report, Dr. Kessler notes that coffee has been “used by hundreds of millions of people” (¶73) and states that “in my opinion, based on coffee’s long history of use . . . , there are sound considerations of public health to support an alternative risk level in the case of acrylamide in coffee” (¶75). Dr. Kessler’s opinion that because coffee has been used by many millions of people a higher cancer risk level for acrylamide in coffee should be applied is contrary to sound science. Indeed, an equally unscientific assertion is that because many millions of people who drink coffee get cancer and other chronic disease, coffee must cause these diseases. In an analogous scenario, benzene had a long history of use as a solvent in chemical laboratories worldwide; however, epidemiological studies subsequently demonstrated that benzene causes leukemia in people. In 1982, the International Agency for Research on Cancer determined that “there is sufficient evidence that benzene is carcinogenic to man,” which indicates a causal relationship between exposure and cancer (IARC, 1982, *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Some Industrial Chemicals and Dyestuffs*, vol. 29, Lyon, France). A similar consideration could be made for cigarette smoking, i.e., long use does not indicate safety.

Recent studies have shown that a food flavoring agent that has been consumed by many millions of people causes a disabling, fatal lung disease. In 2002, the same year that acrylamide was discovered in food, medical researchers discovered that the butter flavoring chemical, diacetyl, was responsible for an epidemic of a rare lung disease called bronchiolitis obliterans at a popcorn manufacturing plant (Kreiss K., et al., “Clinical Bronchiolitis Obliterans in Workers at a Microwave-Popcorn Plant,” *New Engl. J. Med.* 347:330-338, 2002). Like acrylamide, diacetyl was shocking news to the food industry, because diacetyl was classified by the FDA as Generally

Recognized as Safe (GRAS) and, as an ingredient in many foods for many decades, had been consumed by hundreds of millions of people worldwide. In the years following this discovery, studies conducted by the National Institute for Occupational Safety and Health showed that diacetyl was causing this rare lung disease not only among chemical workers who produced diacetyl (van Rooy, F.G., et al., “Bronchiolitis Obliterans Syndrome in Chemical Workers Producing Diacetyl for Food Flavorings,” *Am. J. Respir. Crit. Care Med.* 176:498-504, 2007), but also among flavoring plant workers exposed to diacetyl among many other food flavorings (Kanwal, R., “Bronchiolitis Obliterans in Workers Exposed to Flavoring Chemicals,” *Curr. Opin. Pulm. Med.* 14:141-146, 2008). Subsequently, cases of the rare disease were even reported among consumers of microwave popcorn (Egilman, D.S., et al., “Bronchiolitis Obliterans and Consumer Exposure to Butter-flavored Microwave Popcorn: A Case Series,” *Int. J. Occup. Environ. Health* 18:29-42, 2012), and, most recently, among coffee roasting plant workers exposed to diacetyl in coffee (Bailey et al., “Respiratory Morbidity in a Coffee Processing Workplace with Sentinel Obliterative Bronchiolitis Cases,” *Am. J. Ind. Med.* 58: 1235-1245, 2015).

Thus, the history of environmental and occupational carcinogenesis and the contemporaneous discovery of diacetyl – an extremely toxic food flavoring agent that had been generally recognized as safe by the FDA and had been consumed by millions of people contradict Dr. Kessler’s unscientific assertion that because coffee has been used by many millions of people for many years coffee and acrylamide in coffee must be safe.

10. The International Agency for Research on Cancer Has Concluded the Scientific Evidence is Insufficient to Determine Whether or Not Coffee Causes Cancer

Dr. Kessler writes (¶75 of Kessler report) that a major reason for supporting an alternative risk level for acrylamide in coffee is because IARC concluded that “there is inadequate evidence in humans for the carcinogenicity of coffee drinking.” An IARC evaluation of “inadequate evidence of carcinogenicity” in humans indicates that “available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association between exposure and cancer, or no data on cancer in humans are available” (IARC preamble). The IARC evaluation of 2016 did not conclude that coffee does not cause cancer nor did it make any comment about the cancer risk of acrylamide in coffee. Although the IARC monograph on coffee has not yet been published, in an announcement of the overall results of the 2016 evaluation, IARC concluded that coffee drinking is “unclassifiable as to its carcinogenicity to humans (Group 3)” (Loomis, et al., “Carcinogenicity of drinking coffee, mate, and very hot beverages,” *Lancet Oncol.* 17:877-878, 2016).

IARC’s classification does not mean that coffee has been proven to be “safe” or that it does not cause human cancer. Rather, it means that “existing scientific data do not enable a conclusion to be made about whether it causes cancer” (IARC “Q & A on Monographs Volume 116: Coffee, maté, and very hot beverages,” 2016, available online at https://www.iarc.fr/en/media-centre/iarcnews/pdf/Monographs-Q&A_Vol116.pdf).

11. Dr. Kessler's Opinion that No Method Exists to Weigh Risks/Benefits is Wrong.

In his report (¶174), Dr. Kessler states: "In my opinion, while it is theoretically appealing on the surface to weigh risks versus benefits, as I have written, there is no calculus that allows this to be readily accomplished and has serious limitations (Kessler 1984 at p. 1037)." Dr. Kessler further writes: "There is no way to add up all the benefits, and risks and feed them into a computer and come up with a precise quantification of the point at which the benefits outweigh risks."

While the cited page in *Science* (223:1034-1040, 1984) describes FDA's regulation for lifetime cancer risk at one-in-one-million, in subsequent pages (1038-1039) he describes the FDA authority of not comparing risk and benefits of food additives ("no consideration of benefits is permitted"). In that article, Dr. Kessler lists several limitations of risk-benefit analyses that are relevant to the current case, for example, "those who reap the benefits are not necessarily those who assume the risks," "balancing risks and benefits would require the FDA to make social value judgments that are appropriately within the jurisdiction of the Congress," and "the inability to quantify benefits."

Dr. Kessler's assertion that there is no methodology "to weigh risks versus benefits," is incorrect and outdated. As I wrote in my opinions document, BRAFO (Benefit-Risk Analysis for Foods) was developed with funding by the European Commission to compare quantitatively human health risks and benefits of foods using a quantitative common scale of measurement (Hoekstra, J., et al., "BRAFO Tiered Approach for Benefit-Risk Assessment of Foods," *Food Chem. Toxicol.* 50: S684-S698, 2012; Boobis, A., et al., "Critical Appraisal of the Assessment of Benefits and Risks for foods, 'BRAFO Consensus Working Group,'" *Food Chem. Toxicol.* 55: 659-675, 2013). The approach involves 4 tiers in which a reference dietary scenario (e.g., consumption of coffee at current levels of acrylamide) is compared to an alternative scenario (e.g., consumption of coffee at markedly reduced levels of acrylamide) for informing health-based policy decisions. Thus, based on the comparison of potential health risks and benefits, the evaluation is intended to provide information on the net health impact of the two dietary scenarios and thereby support either the reference dietary scenario or change to the alternative dietary scenario for improving public health. Important for the communication of risks and benefits is the characterization of uncertainties.

The 4 tiers are described in more detail in my opinions document. The BRAFO methodology has been applied to several case studies, the one on reducing acrylamide in potato and cereal products (Schütte, K., et al., "Application of the BRAFO Tiered Approach for Benefit-Risk Assessment to Case Studies on Heat Processing Contaminants," *Food Chem. Toxicol.* 50: S724-S735, 2012), is most relevant to the current case concerning benefits of reducing acrylamide levels in coffee. While heat processing produces positive changes to food products, formation of hazardous contaminants such as acrylamide, a genotoxic carcinogen with a low margin of exposure, indicates a human health concern. The BRAFO methodology was applied to the evaluation of cooking practices before acrylamide mitigation measures were introduced (reference scenario) versus foods in which acrylamide mitigation methods have been implemented that could reduce overall acrylamide intake by approximately 30% with

limited negative impact on organoleptic properties. With use of asparaginase to reduce the level of the acrylamide precursor asparagine, the evaluation stopped at tier 1, because of the positive safety evaluation of this enzyme, reduced cancer risk from lowered acrylamide consumption, and no expected adverse health effect from this treatment. Because of the beneficial effect of reducing acrylamide in processed foods, the authors concluded “acrylamide-reducing actions should hence be applied as long as the adverse side effects are recognized and minimized to the extent possible.”

The above recommendation is also relevant to coffee. In my opinion, the reduction of acrylamide in coffee with limited negative impact on organoleptic properties can produce a product in which benefits clearly dominate risks; hence, acrylamide-reducing actions should be applied to coffee.

12. Dr. Kessler’s Opinion that Reducing Acrylamide in Coffee Also Reduces levels of Antioxidants Which Confer Substantial Health Benefits is Unsubstantiated.

At his deposition, Dr. Kessler testified (page 230) that coffee companies should not reduce acrylamide in coffee, because he has seen studies that suggest that reducing levels of acrylamide might also reduce levels of antioxidants in coffee which he claims benefit human health.

Dr. Kessler’s assertion of a health benefit from consumption of antioxidants in coffee has not been established. In fact, as noted in Item 8 above, EFSA rejected three proposed claims of health benefits from antioxidants in coffee, concluding, in each case that “a cause and effect relationship had not been established between the consumption of coffee” and “reduction of DNA damage by decreasing spontaneous DNA strand breaks” (*EFSA Journal* 9:2057, 2011; *EFSA Journal* 9:2465, 2011; *EFSA Journal* 13:4099, 2015 (full citations provided above).

The assessment of antioxidants in coffee is complex, primarily because levels of some antioxidants decrease, while other antioxidants increase during roasting. Chlorogenic acids are the predominant antioxidants in green coffee and light roast coffee, while Maillard reaction products (primarily melanoidins) predominate in dark roast coffee (Leloup, V., et al., “Antioxidative Activity of Coffee Extracts Depending on Roasting and Extraction Conditions,” *Proc. 22nd Int. Conf. Coffee Science* pp. 118-126, 2008; Budryn, G., et al., “Correlation Between the Stability of Chlorogenic Acids, Antioxidant Activity and Acrylamide Content in Coffee Beans Roasted in Different Conditions,” *Int. J. Food Properties* 18:290-302, 2015).

Asparaginase is one of the most promising technologies for reducing acrylamide levels in coffee and for maintaining sensorial properties of coffee (Xu, F., et al., “Effect of Asparaginase on Flavour Formation in Roasted Coffee,” in *Flavour Science: Proceedings of the XIV Weurman Flavour Research Symposium*, Sept. 15-19, 2014, Queen’s College Cambridge, pp. 563-566, 2015; Xu, F., et al., “The Use of Asparaginase to Reduce Acrylamide in Cooked Food,” *Food Chem.* 210:163-171, 2016). Since the food enzyme asparaginase targets the acrylamide precursor asparagine in coffee beans, and antioxidant activity in roasted coffee derives from constituents other than asparagine (chlorogenic acids in green coffee and melanoidins in

roasted coffee), maintenance of adequate antioxidant levels in brewed coffee should not be affected by the use of asparaginase. Supercritical CO₂ extraction, which has been used to extract caffeine from coffee beans is also effective in reducing acrylamide levels in roasted coffee beans (Banchero, M., et al., Supercritical Fluid Extraction as a Potential Mitigation Strategy for the Reduction of Acrylamide level in Coffee," J. Food Eng. 115:292-297, 2013). The selective extraction of acrylamide with minimal effect on sensorial properties or antioxidant levels in brewed coffee is possible by this method because the solubilities of extracted compounds in supercritical CO₂ vary with pressure. Any claims to the contrary (e.g., by the coffee industry that reducing levels of acrylamide would also reduce levels of antioxidants in coffee) should be tested and validated by those making such unsubstantiated claims.

EXHIBIT “D”

1 SUPERIOR COURT OF THE STATE OF CALIFORNIA

2 FOR THE COUNTY OF LOS ANGELES

3 DEPARTMENT 323

HON. ELIHU M. BERLE, JUDGE

4

5 CERT,)
6)
7) Plaintiff,)
8) vs.) SUPERIOR COURT
9) CASE NO. BC 435759
10) BC 461182
11)
12) STARBUCKS CORP, ET AL.,)
13)
14) Defendants.)
15)
16)

17 REPORTER'S TRANSCRIPT OF PROCEEDINGS

18 Monday, October 2, 2017

19 (A.M. Session)

20 APPEARANCES OF COUNSEL:

21 FOR THE PLAINTIFFS: METZGER LAW GROUP
22 BY: RAPHAEL METZGER, ESQ.
23 ABRAHAM I. PARISER, ESQ.
24 401 East Ocean Boulevard
25 Suite 800
26 Long Beach, California 90802
27 (562) 437-4499
28 sbrust@toxictorts.com
rmetzger@toxictorts.com
apariser@toxictorts.com

21 FOR THE ROASTER AND DOE DEFENDANTS:
22 MORRISON/FOERSTER
23 BY: JAMES M. SCHURZ, ESQ.
24 425 Market Street
25 San Francisco, California 94105-2482
26 (415) 268-7124
27 jschurz@mofo.com

28 (Appearances continued on next page.)

DAVID A. SALYER, CSR, RMR, CRR
Official Pro Tem Court Reporter
License No. 4410

1 APPEARANCES OF COUNSEL: (CONTINUED)

2 FOR KEURIG: SKADDEN, ARPS, SLATE, MEAGHER
& FLOM, LLP
3 BY: RAOUL D. KENNEDY, ESQ.
4 525 University Avenue
Palo Alto, California 94301
5 (650)470-4550
rkennedy@skadden.com

6 FOR HN FERNANDEZ, ET AL.:

7 NORTON ROSE FULBRIGHT, LLP
8 BY: JEFFREY B. MARGULIES, ESQ.
555 South Flower Street
9 41st Floor
Los Angeles, California 90071
10 (213)892-9286
jmargulies@nortonrosefulbright.com

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1 CASE NUMBER: BC 411192/BC435759
2 CASE NAME: CERT CASES
3 LOS ANGELES, CALIFORNIA MONDAY, OCTOBER 2, 2017
4 DEPARTMENT 323 ELIHU M. BERLE, JUDGE
5 REPORTER: DAVID A. SALYER, CSR 4410
6 TIME: 9:15 a.m.

7 -o0o-

8 THE COURT: All right. In CERT versus Starbucks,
9 counsel ready to proceed?

10 MR. METZGER: Yes, your Honor.

11 THE COURT: All right. I'm not in the comfort zone.
12 I was worried I didn't get any new briefs on this case this
13 morning. We don't want to have a morning without briefing.

14 MR. MARGULIES: It's here.

15 THE COURT: Okay. Mr. Metzger, are you ready to call
16 your next witness?

17 MR. METZGER: Yes.

18 The plaintiff calls Dr. Ronald Melnick.

19 THE COURT: Just one second. I want to set up the
20 LiveNote.

21 Just one moment, please.

22 Okay. All right.

23 I'll ask the clerk to swear the witness.

24

25 RONALD MELNICK,
26 having been called as a witness and sworn testified as
27 follows:

28 THE WITNESS: I do.

1 THE CLERK: And would you please state and spell your
2 name for the record.

3 THE WITNESS: Ronald Melnick, R-O-N-A-L-D,
4 M-E-L-N-I-C-K.

5 THE CLERK: Thank you.

6 THE COURT: Good morning, Dr. Melnick.

7 Mr. Schurz, you were standing for some reason?

8 MR. SCHURZ: I was, your Honor.

9 I thought before we proceeded with Dr. Melnick, there
10 was one issue of housekeeping that your Honor had asked us to
11 address, and I believe we have done so.

12 We've been directed to do this on the record. It
13 relates to the exchange of a document that's been identified,
14 Exhibit 73540.

15 Counsel have met and conferred and agreed that the only
16 change here is the branding of this exhibit with page numbers.
17 And we would, at this time, ask permission to exchange
18 Exhibit 73540 with the one that has been branded with page
19 numbers.

20 THE COURT: Any objection?

21 MR. METZGER: No, your Honor.

22 THE COURT: The Court will order the substitution.

23 Thank you.

24 MR. SCHURZ: Thank you.

25 THE COURT: Mr. Metzger, you may proceed.

26 ///

27 ///

28 ///

DIRECT EXAMINATION

1
2 BY MR. MELNICK:

3 Q. Good morning, Dr. Melnick.

4 A. Good morning.

5 Q. I think it's been about three years since you
6 sat in that chair.

7 A. Yes, it's been three years almost exactly.

8 Q. Well, welcome back.

9 So let's see. In the first phase trial, you testified
10 about risk assessment and some other subjects. And now you've
11 done more work on the case; is that correct?

12 A. Quite a bit of work.

13 Q. Okay.

14 A. A lot more.

15 Q. All right. First, a few housekeeping things.
16 Would you confirm that what I'm handing you,
17 Exhibit 60076, is your current curriculum vitae?

18 A. It's close to current.

19 Q. Okay.

20 A. I attended another meeting of the International
21 Agency for Research on Cancer in June of this year, and
22 typically when I participate in those I add those to my CV.

23 So I believe this doesn't include that.

24 Q. All right. And in attending that meeting, were
25 you an actual member of the IARC Working Group?

26 A. Yes. I was invited by IARC to participate in
27 that meeting as a member of the Working Group.

28 Q. All right. And what was that meeting regarding?

1 A. There were approximately seven different agents,
2 most of them which are somehow found in foods.

3 And the report, the initial report hasn't come out, the
4 monograph, but a publication was put out in the Lancet
5 Oncology, and in that the title of it is described as
6 chemicals that cause urinary tract tumors.

7 Q. All right. Regarding your education, would you
8 refresh the Court as to what your degrees are in.

9 A. Okay. I have a BS and MS and Ph.D in food
10 science.

11 And in my graduate studies, and this was at the
12 University of Massachusetts at Amherst, I also was providing
13 an emphasis in biochemistry.

14 Q. Okay. You spent many years at the National
15 Toxicology Program involved with animal cancer bioassays; is
16 that correct?

17 A. Yes. I joined the National Toxicology Program
18 in 1980, and I retired from that program in January of 2009.

19 So it's approximately -- almost 29 years.

20 Q. Okay. And you also worked at the National
21 Institute for Environmental Health Sciences; is that correct?

22 A. Yes.

23 The National Toxicology Program is composed of several
24 components within the Department of Health and Human Services.

25 The major component is located at the National
26 Institute of Environmental Health Sciences in North Carolina.
27 This is the one institute of the National Institutes of Health
28 which is not located in Bethesda.

1 Q. Okay. I see that you won a National Institute
2 of Health Plain Language Award for developing a brochure
3 entitled Cancer and the Environment. What You Need to Know.
4 What You Can Do; is that correct?

5 A. Yes. I remember that.

6 Q. Okay. Approximately how many working groups
7 have you been invited by the International Agency for Research
8 on Cancer to attend and participate as a Working Group member?

9 A. Well, I've been invited to IARC, if I can use
10 that acronym, 13 times.

11 Ten of those times were related to monograph meetings
12 which evaluate the carcinogenicity data for a large number of
13 chemicals.

14 The other times related to mechanisms.

15 In fact, there will be a book coming out fairly shortly
16 from some of that work which relates to after having conducted
17 100 volumes of IARC monographs, a number of chemicals were
18 identified as human carcinogens. So it was what have we
19 learned during that course of time with respect to the
20 mechanisms of carcinogenesis as well as site concordance
21 between animals and humans.

22 Q. Would you inform Judge Berle of some of your
23 publications that you considered to be relevant to this phase
24 of the trial.

25 A. Okay. Well, I've spent a lot of effort related
26 to chemicals which metabolize to epoxide intermediates. One
27 that I've now published numerous studies on is 1,3-Butadiene.
28 This is a chemical used in the synthetic rubber industry

1 making styrene butadiene rubber, for example.

2 And as a consequence of working with butadiene, I
3 nominated to the NTP that we should also study chloroprene and
4 isoprene.

5 The work on butadiene was a combination of studies.

6 For example, the animal bioassay determining what are
7 the sites of cancer induction as well as redesigning the study
8 after the first to better characterize the dose-response
9 relationships. So the larger study up to that time was my
10 butadiene study with five exposure levels.

11 In addition to that, we also developed oncogenetic
12 models on butadiene to try to characterize the dosimetry,
13 which I'll probably explain later, of the epoxide
14 intermediates that are formed from butadiene. And those are
15 the ones that are considered to be involved in the
16 carcinogenicity of that chemical.

17 Q. What is the relationship or import of your work
18 regarding epoxides and mechanisms of carcinogenesis for
19 epoxides with respect to acrylamide?

20 A. Okay. Well, acrylamide is metabolized the same
21 way as 1,3-butadiene, the same way as vinyl chloride to an
22 epoxide intermediate chlorpropamide. The epoxide intermediate
23 is glycidamide. And it reacts with DNA, similarly to the
24 oxide intermediates of butadiene and the epoxide intermediate
25 of vinyl chloride.

26 Ethylene oxide is an epoxide as purchased and it also
27 behaves similarly.

28 Q. Okay. I believe that one of the topics that

1 you're going to talk about today is primary prevention of
2 cancer; is that correct?

3 A. Yes, I would.

4 Q. And I see that you have published in the
5 peer-reviewed literature some articles regarding that one
6 entitled "Primary Prevention of Cancer," published in The
7 Scientist, 2002.

8 Do you remember that?

9 Look at the bottom of page 20 of your curriculum vitae.

10 A. Let me just say that the work of the National
11 Toxicology Program is designed to identify agents in the
12 environment or workplace which pose a carcinogenic potential.

13 That information is intended for use by regulatory
14 agencies to eliminate or reduce human exposure to chemicals
15 which are hazardous to human health.

16 That is what we consider primary prevention. The
17 prevention of the development of the disease and in this case
18 by reducing or eliminating exposure to the agent which would
19 induce cancer.

20 Q. Okay. I see you also have an article in
21 Environmental Health Prospectus entitled "Declaring Chemicals
22 Not Carcinogenic to Humans Requires Validation, Not
23 Speculation."

24 Could you tell us generally what that's about.

25 A. I believe -- could you give me the number again?

26 Q. It's number 100.

27 A. Okay. At this time there was a number of
28 studies that we had conducted, others had conducted, relating

1 to kidney cancer in rats caused by agents which induces a
2 certain protein. It's called alpha-2-globulin. And there was
3 attempts by certain people to claim that if you see
4 alpha-2-globulin neuropathy, the disease in the kidney, that
5 that would be sufficient evidence to claim that it is not a
6 human carcinogen because that would be the mechanism of
7 carcinogenesis and humans don't produce alpha-2-globulin.

8 It's a hypothesis. And what we believed was that
9 rather than speculating that that is the case, we need
10 scientific evidence to test a hypothesis before implementing
11 it for public health reasons.

12 Q. Okay. And let's see.

13 I'm looking at the bottom of page 25 of your curriculum
14 vitae.

15 Is this item number 17, Bond and Melnick,
16 "Electrophilic Compounds in Tumor Concordance and Mechanisms
17 of Carcinogenesis," an IARC scientific publication in press --
18 is that the publication that you were speaking of earlier that
19 is coming out?

20 A. Yes. That one has been in press for at least
21 six or seven months, so it's due out anytime.

22 When I was at IARC in June, I asked that same question,
23 and I was told it would be another month or two.

24 Q. Okay.

25 A. But I still haven't seen it.

26 Q. So I don't want to spend a lot of time on your
27 experience and qualifications because you've already testified
28 in the phase one trial.

1 But is there anything in particular that you would wish
2 to share with the Court regarding your experience that you
3 think relates, in particular, to the issues that you'll be
4 testifying about today?

5 A. Well, like some of the questions that you asked
6 me, I've written papers about mechanisms of carcinogeneses for
7 epoxide-forming chemicals. I've worked on pharmacokinetic
8 modeling of chemicals, including those that form epoxide
9 intermediates.

10 I've conducted -- led the efforts for numerous animal
11 bioassays for the National Toxicology Program.

12 I have served on, like I mentioned, ten IARC Working
13 Group evaluations of carcinogenicity.

14 I've also served on a number of review groups for EPA
15 in their IRIS evaluations on risk assessment of chemicals.

16 I've served as a reviewer for journal articles, a
17 reviewer for contract proposals.

18 I'm not sure how extensive you want me to go, but a lot
19 of this is -- and I might say that much of this is still
20 ongoing even though I've retired from NTP.

21 Q. Okay. Turning to acrylamide, when did you first
22 begin research regarding acrylamide?

23 A. Well, I think I was always aware of acrylamide
24 being a carcinogen, because it had been studied numerous years
25 ago.

26 In 2002 it was identified as a chemical present in
27 foods.

28 And in 2006 I was asked by the California State

1 Attorney General's Office if I would consult with them on the
2 case that they were working on related to acrylamide and
3 acrylamide reduction in french fries and potato chips.

4 Q. Okay.

5 A. So the history -- my history related to
6 acrylamide was awareness of it as a chemical carcinogen back
7 in the nineties, but the intensity of my interest increased as
8 I served as a consultant for the California Attorney General.

9 Q. All right. And we met through your service for
10 the California Attorney General on the prior acrylamide
11 litigation regarding french fries and potato chips, correct?

12 A. Yeah, I was deposed several times on that, and I
13 believe you were in the room one or two of those.

14 Q. All right.

15 MR. METZGER: Your Honor, I would offer at this time in
16 evidence trial Exhibit 60076, Dr. Melnick's almost current
17 curriculum vitae.

18 THE COURT: Any objection?

19 MR. KENNEDY: No objection, your Honor.

20 THE COURT: The exhibit is admitted.

21 (Exhibit 60076 received in evidence.)

22 Q. BY MR. METZGER: Let's see.

23 Dr. Melnick, is one of the things that I asked you to
24 do regarding this case to research the published technologies
25 regarding reduction of acrylamide, especially in coffee?

26 MR. KENNEDY: Objection, your Honor. Irrelevant that
27 there's any duty to mitigate under the applicable statutes.

28 THE COURT: Overruled.

1 THE WITNESS: Yes. That's one of the many things you
2 asked me to do.

3 Q. BY MR. METZGER: And did you initially prepare a
4 declaration regarding those technologies that have been
5 published in the peer-reviewed literature?

6 MR. KENNEDY: Same objection, your Honor. Also object,
7 lack of foundation.

8 There's been no showing that he's an expert in
9 acrylamide, that he's actually done any research in the area
10 or that he's done anything other an literature search.

11 THE COURT: Overruled.

12 THE WITNESS: The question was did I prepare it?

13 Q. BY MR. METZGER: Yes.

14 A. Yes, I did.

15 Q. Okay. And then at some point did you receive
16 confidential documents that had been produced by certain of
17 the defendants in this case regarding acrylamide reduction?

18 MR. KENNEDY: Your Honor, object under People versus
19 Sanchez.

20 We're now getting into case-specific hearsay. So we
21 know the Supreme Court has ruled that doesn't qualify under
22 801(b) unless it's been independently established by a
23 competent witness.

24 We object to any questions along these lines unless
25 they're either in hypothetical question form or there's
26 specific identification of where the materials he's relying on
27 were offered in evidence by a competent witness.

28 THE COURT: The hypothetical is assume you received

1 documents from the defendants?

2 He asked him did he receive documents.

3 MR. KENNEDY: He certainly has. Many of those contain
4 multiple levels of hearsay.

5 THE COURT: He hasn't gotten there yet. He just asked
6 if he received documents.

7 MR. KENNEDY: I just want to make sure -- it seems to
8 me it's irrelevant whether he did or not unless we're talking
9 about documents for which there is a hearsay exception and are
10 competently admitted. Otherwise the fact he's received
11 case-specific material is irrelevant.

12 THE COURT: Thank you.

13 Objection is overruled.

14 MR. METZGER: All right.

15 THE WITNESS: Yes, I did receive confidential
16 documents, lots of them.

17 Q. BY MR. METZGER: Regarding --

18 A. Regarding acrylamide in coffee and means of
19 reducing acrylamide in coffee.

20 Q. Okay. And did this include confidential studies
21 that had been done by various coffee companies?

22 A. The documents indicated the companies that had
23 provided this information. So much of it had been done by the
24 coffee companies, yes.

25 Q. Okay. And did you review those documents?

26 A. Yes, I did.

27 Q. All right. And based on your review of those
28 documents, did you expand your previous declaration to include

1 information regarding reduction of acrylamide that you had
2 ascertained from your review of the industry confidential
3 documents?

4 A. Yes, I did.

5 I received those in January and then added that
6 information to my declaration from -- previously submitted.

7 Q. I'm going to show you what has been marked as
8 Exhibit 59957 and ask you if this is the updated and expanded
9 declaration that you prepared regarding reduction of
10 acrylamide in coffee.

11 A. Yes, I believe it is.

12 Q. All right. I'm going to show you a few more
13 things.

14 One is Exhibit 60076(sic), a document entitled
15 "Opinions of Ronald Melnick."

16 I'll ask you, is this a report that you prepared
17 setting forth some of your opinions for this second phase of
18 the trial?

19 A. Yes, it is.

20 Q. Oh, 60077.

21 THE COURT: 60077.

22 MR. METZGER: Did I misspeak earlier?

23 Oh, I apologize.

24 Q. And as part of your work in this case, did you
25 read the deposition as well as the trial testimony of
26 Dr. William Ristenpart?

27 A. I also read his report. So I read his report,
28 the transcript of his deposition and the transcript of his

1 trial testimony.

2 Q. And did you prepare a critique of
3 Dr. Ristenpart's report in testimony?

4 A. It's of his report and deposition.
5 I prepared a report in response to that.

6 Q. Right.

7 And is Exhibit 60081 that report critiquing Dr. William
8 Ristenpart's report and testimony that you prepared?

9 A. Yes, it is.

10 Q. And did you also read the report and the
11 deposition and trial testimony of Dr. David Kessler?

12 A. Yes, I have.

13 Q. And did you prepare a critique of Dr. David
14 Kessler's report and his deposition testimony?

15 A. Yes, I did.

16 Q. And is Exhibit 60079 the report that you
17 prepared critiquing Dr. Kessler's report and testimony?

18 A. Yes, it is.

19 Q. All right. And did you also read the deposition
20 and the trial testimony of Dr. Lorenz Rhomberg?

21 A. Yes, I did.

22 Q. And did you prepare a report critiquing
23 Dr. Rhomberg's report and his deposition?

24 A. Yes, I did.

25 Q. Is that Exhibit 60080?

26 A. Yes, that is it.

27 Q. Okay. You've done a lot of work on this case,
28 and some of this is quite complex, is it not?

1 A. It could be for a number of people.

2 Yes, it is complex. There's many aspects that
3 contribute to understanding the issues related to acrylamide,
4 its reduction and its risk.

5 Q. And did you take it upon yourself to prepare
6 some demonstrative aids to help with the presentation and the
7 understanding of the testimony that you intend to give today?

8 A. Yes, I have prepared them.

9 MR. METZGER: What is the next exhibit in order?

10 MR. INFANTE: 61950.

11 Q. BY MR. METZGER: All right. Is Exhibit 61950 a
12 printout of the slides that you prepared?

13 A. This looks like the ones.

14 Q. All right. And would you inform the Court, give
15 us the overview of the different topics that you are prepared
16 to talk about today.

17 A. If we could go to the next slide.

18 MR. KENNEDY: Your Honor, I want to make sure the
19 record is protected here.

20 Bullet point 3 talks about selection of tumor sites and
21 application of a pharmacokinetic factor.

22 In his deposition Dr. Melnick was asked the extent of
23 his criticisms of Dr. Rhomberg and he talked about the PK
24 factor and said absolutely nothing about tumor sites.

25 We have not been told subsequently he was planning to
26 do that.

27 I suspect it will be more fine-tuned on the objecting
28 when we actually get there, but I just don't want any

1 misunderstanding that we didn't object from the outset
2 regarding any critique concerning the tumor sites.

3 THE COURT: All right. Thank you.

4 The testimony is subject to, always, cross-examination
5 and motion to strike.

6 Mr. Metzger, you may continue.

7 MR. METZGER: All right.

8 Q. So, Dr. Melnick, what are the topics that you
9 would like to discuss with the Court today regarding the work
10 that you've done?

11 A. Okay. I've broken this down into six topics.

12 The first one on the principles for the determination
13 of an NSRL are ones which have been reviewed numerous times
14 within this Court and its involvement in performing a
15 quantitative cancer risk assessment. But I want to just
16 present a couple slides on that topic just to ensure that my
17 opinions and valuations are consistent with those
18 recommendations on how to perform a determination of an NSRL
19 as well as the defendants.

20 Q. Incidentally, did you testify regarding tumor
21 site selection and risk assessment in the first phase trial?

22 MR. KENNEDY: Objection. The record speaks for itself.

23 THE COURT: Overruled.

24 THE WITNESS: If I was asked the question, I'm sure I
25 would have. But I don't recall --

26 Q. BY MR. METZGER: Three years ago.

27 A. -- whether that question came up.

28 Q. I'll join Mr. Kennedy that the record speaks for

1 itself.

2 A. I would have to review it, the testimony.

3 Q. I didn't mean to tax your memory. Sorry.

4 What are the other topics that you have worked on and
5 that you think are important to relate?

6 A. The second is the mitigation of acrylamide in
7 coffee to show that there are available and effective methods
8 to substantially reduce acrylamide in coffee.

9 I want to talk about the quantitative cancer risk
10 assessment of acrylamide in coffee that was presented in this
11 court with emphasis on tumor sites.

12 Q. When you say in this court, are you referring to
13 Dr. Rhomberg?

14 A. Yes, presented by Dr. Rhomberg.

15 Q. Okay.

16 A. With respect to tumor sites and application of
17 pharmacokinetic factor.

18 The issue of tumor sites is one I've been dealing with
19 since 1980 with respect to identifying cancer sites in animal
20 studies and in terms of my work for IARC as well as for EPA,
21 the sites that should be included in the cancer risk
22 assessments.

23 The issue of quantitative benefit-risk assessment to
24 show that there is a methodology available.

25 And a big topic is what do we mean by sound
26 considerations of public health and how do those sound
27 considerations of public health influence the concept of a
28 cancer risk at 1 per 100,000 versus 1 per 10,000, which is one

1 times 10 to the minus 5.

2 Q. Let me interrupt you for just one second.

3 You mentioned a quantitative benefit-risk assessment of
4 coffee. Is that different from a quantitative risk assessment
5 of coffee?

6 A. Yes, it is.

7 Q. What is the difference?

8 A. In one case the quantitative cancer risk
9 assessment is of acrylamide which is present in coffee, so
10 what is the risk level from acrylamide in coffee.

11 The benefit-risk assessment is an evaluation of the
12 benefits and risks of coffee with consideration of whether or
13 not acrylamide is present.

14 Q. Okay.

15 A. And then I will present, after my last bullet,
16 my overall conclusions on the issues of acrylamide in coffee.

17 Q. All right. So let's start, if we could, with
18 the principles also for the determination of the NSRL,
19 quantitative cancer risk assessment.

20 And what are the principles that you considered to be
21 important?

22 A. If we can go -- thank you.

23 MR. KENNEDY: Objection, your Honor, to bullet points 3
24 and 4. They're pure legal interpretations, and they aren't
25 even accurate legal interpretations.

26 THE COURT: All right. Counsel, you can argue it
27 later.

28 Let's move forward.

1 Q. BY MR. METZGER: Go ahead, Dr. Melnick.

2 A. Okay. So the lifetime exposure for an NSRL is
3 one which results in not more than one excess cancer in an
4 exposed population of 100,000.

5 This is specified as the non-significant risk level, or
6 the NSRL.

7 Currently for acrylamide the safe harbor level is
8 0.2 micrograms per day. If you look this up on OEHHA's sites,
9 that's what you will find.

10 I know the presentation by Dr. Rhomberg indicated that
11 19 micrograms was a risk that would be appropriate.

12 And I just want to point out that the ratio of
13 19 micrograms to 0.2 micrograms is approximately a 100-fold
14 increase over the current non-safe harbor level.

15 However, an alternative --

16 Q. Excuse me. When you said would be appropriate,
17 are you speaking of your opinion or Dr. Rhomberg's opinion?

18 A. The opinion that he put forward.

19 Q. Okay.

20 A. However, an alternative level is one which could
21 be considered, but it must be supported by sound
22 considerations for public health. And they're specified as
23 where chemicals are produced by cooking necessary to render
24 the food palatable or to avoid microbiological contamination.

25 Those are examples that are provided. They are not
26 necessarily all of the factors, but those are the ones that
27 were cited.

28 THE COURT: Any numerical limitations on that?

1 Whatever the ultimate number is, somebody comes in and
2 says, well, cooking is necessary to make food palatable and
3 therefore we can pick any number. We would like to eat wild
4 mushrooms found in the forest. One out of two is okay.

5 THE WITNESS: Well, in my view that might be arbitrary
6 in terms of the selection of the number.

7 THE COURT: In other words, where do you draw the line?
8 What's the number?

9 THE WITNESS: An appropriate risk level is actually a
10 policy decision.

11 The policy decision I think was put forward in the
12 Prop 65 rule. The definition of non-significant risk level is
13 1 per 100,000.

14 To deviate from that -- I've seen in this court it's
15 been mentioned as an alternative significant risk level, an
16 ASRL, which I sort of object to that term because it's an
17 alternative risk level.

18 So it is implying that the citizens of California can
19 be exposed to a chemical without warning in which the risk is
20 greater than 1 per 100,000.

21 THE COURT: Right. And then what's the limit?

22 THE WITNESS: This would have to be one in which people
23 would be willing to accept.

24 So, for example, if the state wanted to put out a rule
25 and ask the citizens would you accept a ten-fold higher cancer
26 risk --

27 THE COURT: We're not in front of the legislature here,
28 and we're not putting any propositions on the ballot.

1 I mean, I read stories occasionally about some exotic
2 foods that may be dangerous to consumption, but people do eat
3 it. They're taking a risk by preparing it properly, but
4 nevertheless there's risk.

5 I'm just asking what is the limit when you say
6 alternative level to make the food palatable?

7 THE WITNESS: I think the acceptance of risk is
8 personal.

9 For example, we all assume certain risks when we leave
10 our home and drive on highways. So what is an acceptable
11 level is really up to either the people or the legislature to
12 decide what is appropriate.

13 EPA and FDA have an acceptable risk of 1 per 100,000.

14 I know I'm not asking your question.

15 THE COURT: But we don't have a legislature here. We
16 have a regulation and it says alternative risk.

17 So what is it?

18 MR. METZGER: We're going to get to that.

19 Q. Does it require a calculation, Dr. Melnick?

20 A. You can do a benefit-risk analysis and see --

21 THE COURT: Is that a policy decision or a legal
22 decision?

23 I guess I'll let the lawyers argue that.

24 Go ahead, counsel.

25 THE WITNESS: And the last point here was from the
26 final statement of reasons, whereas if the beneficial effects
27 do not outweigh the risks, then the 10 to the minus 5 standard
28 applies.

1 Q. Is that an important concept for your opinion in
2 this case?

3 A. Yes, it is. Because in order to move away from
4 that 10 to the minus 5 standard, beneficial effects must be
5 demonstrated.

6 THE COURT: Is there a mathematical calculation of the
7 benefit?

8 You say, okay, it's not 10 to the minus 5. Maybe it's
9 10 to the minus 4, 10 to the minus 3, and that's counteracted
10 by the beneficial effects.

11 Is that purely subjective or is there some mathematical
12 calculation?

13 THE WITNESS: I haven't seen a calculation that would
14 say we can fine tune it to 10 to the minus 4 or 2 times 10 to
15 the minus 4 or 5 times 10 to the minus 5. I haven't seen any
16 type of calculation like that.

17 Q. BY MR. METZGER: Well, Dr. Melnick, let me ask
18 you --

19 MR. KENNEDY: Objection. The witness hasn't had a
20 chance to finish his answer yet.

21 THE COURT: Yes.

22 Finish your answer.

23 So you haven't seen any mathematical -- is there any
24 way to calculate human satisfaction?

25 THE WITNESS: Yes. That is possible by a method which
26 we'll talk about a little bit later called BRAFO, which is a
27 benefit-risk assessment for foods where you can quantify the
28 benefits or the risks if it's necessary to go to that extent.

1 THE COURT: Go ahead, Mr. Metzger.

2 Q. BY MR. METZGER: So, first of all, from your
3 understanding, does determination of an NSRL require a
4 quantitative risk assessment?

5 A. Yes.

6 Q. Okay.

7 A. I'm sure it's specified.

8 Q. And what are the important aspects of that that
9 need to go into that quantitative risk assessment?

10 A. Well, first they must be of comparable
11 scientific validity to be evidence of standards which led to
12 the listing of the chemical.

13 Q. And by that you mean the listing of acrylamide
14 as a chemical known to the State to cause cancer?

15 A. Yes, exactly.

16 Q. Okay.

17 A. In determining and performing a quantitative
18 risk assessment, it's based on the most sensitive study which
19 is of sufficient quality, and those exist.

20 Secondly, this is not all of the principles, but I
21 think these are the principles which impact this discussion.

22 Assume no threshold. In other words, the response, the
23 tumor response is linear, down to zero exposure.

24 If there is insufficient human data to do a
25 quantitative risk assessment, then the human cancer potency
26 estimate is derived from the animal cancer potency, which is
27 that response versus dose and applying a body weight scaling
28 factor.

1 The potency is expressed in a certain way. It's a
2 value of risk relative on a per milligram/per kilogram per day
3 exposure.

4 That's how the law, the rule, Prop 65 wants the potency
5 to be expressed.

6 In terms of body scaling, I believe it had previously
7 been a human body weight to animal body weight to one-third
8 the power, but now it's raised to the one-fourth power.

9 This is a method for enabling the determination of the
10 human cancer potency from animal cancer potency.

11 However, a pharmacokinetic adjustment may be made when
12 available evidence can be taken into account with confidence.

13 That's why this is going to be discussed in a lot more
14 detail later on to see whether we can consider that
15 pharmacokinetic factor with confidence.

16 That's why I have it italicized.

17 Q. At this point would you define for us what a
18 pharmacokinetic adjustment or a pharmacokinetic factor or
19 model is? What is all of that?

20 A. This is something I was going to discuss later,
21 but I can go into it a little bit now.

22 Q. Give us just a quick.

23 A. The body weight scaling is intended to take into
24 effect two factors.

25 One is pharmacokinetics. This is how the body handles
26 a chemical that enters. And this includes factors such as the
27 absorption of the material, how it distributes in the body,
28 how it's metabolized and how it's eliminated.

1 This is important for providing information on
2 dosimetry, which is a concentration in a tissue over a certain
3 period of time. Okay?

4 So for a pharmacokinetic adjustment, rather than using
5 the scaling factor, the pharmacokinetic factor might be used
6 which would be a ratio of the dosimetry in a tissue in humans
7 relative to the dosimetry of that same compound in animals.

8 So it may not be the same as what you would obtain from
9 a scaling factor.

10 Pharmacodynamics, which isn't really addressed at this
11 point because we don't have information, is how the cell
12 responds to that active material when it is present.

13 So you have the dosimetry that says this is the
14 concentration of, for example, glycidamide in a tissue over a
15 certain amount of time. What's the response that we might
16 expect relative to that.

17 That becomes the pharmacodynamics. Do animals and
18 humans behave the same? We don't have enough information. So
19 the scaling factor seems to be most appropriate, because it's
20 scales for factors, physiological differences.

21 Q. Thank you for explaining that.

22 So now let's start with the reduction or mitigation of
23 acrylamide in coffee.

24 Could you tell -- before we get into the individual
25 studies, could you give us kind of an overview of the
26 different -- how these different technologies within this
27 puzzle of reducing acrylamide in coffee.

28 A. I'm sorry. How they --

1 Q. Just the overview of the different types of
2 technologies.

3 MR. KENNEDY: Object. Narrative answer.

4 THE COURT: Overruled.

5 THE WITNESS: Some are physical removal and some are
6 biological removal, by influencing, for example, the formation
7 of precursors for acrylamide in the tissue of the bean or
8 plant or whatever.

9 Q. BY MR. METZGER: All right. And have you
10 prepared a series of slides which illustrate the different
11 technologies and the results?

12 A. I've prepared a series of slides, yes, on that.

13 Q. Okay. And the first one here is acrylamide
14 levels in Arabica versus Robusta roasted coffees.

15 And what did you find regarding the differences for
16 acrylamide in Arabica versus Robusta?

17 A. There are numerous articles that have looked at
18 these two strains of coffee, and it is rather consistent that
19 the Arabica has a lower level than the Robusta.

20 These are two publications which show that type of
21 difference. You can see in the Lantz paper it was 35 percent
22 reduced in Arabica, and in the Bagdonaite paper it was
23 47 percent.

24 The plus or minus is the standard deviation, so it
25 gives you the sense there is a deviation within measurements.
26 But in spite of that, these differences are significant and
27 are reflective of the difference between the two strains, that
28 Arabica in almost all cases that I've seen where the

1 comparisons were made roasting to the same level was lower in
2 its acrylamide levels.

3 Q. You earlier mentioned some technologies that
4 prevent the formation of the precursors.

5 Could you tell us what that's about?

6 A. Okay. This is shown in the next slide. It's
7 going to require a little bit of explanation on some of this.

8 First of all, the precursors for acrylamide -- there we
9 go -- it's asparagine reacting with reducing sugars, glucose
10 and fructose, with the application of heat in the Maillard
11 reaction forming acrylamide at the very bottom.

12 So the approaches that are used -- this is now in the
13 biological sense -- is how can you lower the amount of
14 precursor compound, as I mentioned, asparagine and glucose and
15 fructose.

16 The use of an enzyme called asparaginase can reduce
17 asparagine in plants, tissues substantially.

18 If you reduce asparagine, you get less acrylamide.

19 I will be showing this slide as a typical example where
20 it shows that treatment to remove asparagine pre-roasting can
21 reduce acrylamide levels by somewhere in the range of 70 to
22 90 percent.

23 So one approach is treatment with enzymes to remove the
24 precursor.

25 Now, as I mentioned in 2006 I was a consultant for the
26 State Attorney General, and this related to reducing
27 acrylamide in potato chips and french fries.

28 And that case settled because there was an agreement

1 made --

2 MR. KENNEDY: Objection, your Honor. Lack of
3 foundation that he knows why a case settled.

4 THE COURT: Overruled.

5 THE WITNESS: It was settled because there was some
6 agreement to reduce the levels. I don't know the full
7 details, but there was agreement to reduce the levels of
8 acrylamide in potato products.

9 MR. KENNEDY: Move to strike the answer.

10 THE COURT: Let me ask you this.

11 To your knowledge, has any coffee manufacturer
12 attempted this process of reducing the amount of asparagine in
13 coffee?

14 THE WITNESS: Yes.

15 THE COURT: And who that is?

16 THE WITNESS: We'll be getting into some of that very
17 shortly.

18 THE COURT: Okay.

19 THE WITNESS: But what I want to talk about --

20 MR. KENNEDY: Your Honor, this is just a narrative at
21 this point.

22 THE COURT: Overruled.

23 THE WITNESS: What I really want to talk about is the
24 development that the potato industry made in terms of trying
25 to reduce acrylamide.

26 THE COURT: No.

27 What you want to talk about is not relevant.

28 Mr. Metzger, please move on.

1 Q. BY MR. METZGER: We'll get to the potato
2 industry in just a moment, Dr. Melnick.

3 THE COURT: We have enough trouble with coffee. I
4 don't want to get into potatoes and potato chips.

5 THE WITNESS: Part of my reason for doing this is to
6 show --

7 MR. KENNEDY: Objection. There is no question pending.
8 He's trying to earn his money, I know.

9 THE COURT: Dr. Melnick, please listen to the question.
10 Mr. Metzger is a well-experienced attorney. He knows how to
11 ask questions.

12 MR. METZGER: Thank you, your Honor.

13 Q. All right. Regarding the formation and
14 enzymatic mitigation of acrylamide that you have on this flow
15 chart or whatever one calls it, is there anything else that
16 you would like to inform the Court regarding the use of
17 enzymes to reduce acrylamide in coffee?

18 You mentioned asparaginase. Anything else?

19 A. Okay. There are other approaches that are
20 available, and these approaches make use of some advances in
21 molecular biology.

22 The enzymes that are shown in red, as well as
23 invertase, in fact all the arrows that have a word next to
24 them are enzymes.

25 Enzymes are proteins. Enzymes catalyze reactions.
26 They make the rate of reaction faster.

27 What has been done is to silence some of the genes that
28 make asparagine or silence the gene invertase in potatoes that

1 makes glucose and fructose.

2 So silencing the gene -- for example the asparagine
3 synthetase -- is a mechanism for reducing asparagine formation
4 of which that is a precursor for the Maillard reaction that
5 leads to acrylamide.

6 I can try to explain a little bit, if you would like,
7 in terms of how this is being done. But you would have to ask
8 me the question.

9 I'm used to giving a talk rather than having a
10 presentation where someone asks me a question.

11 THE COURT: It's a different forum. You're guided by
12 rules of procedure, doctor.

13 All right. Mr. Metzger.

14 Q. BY MR. METZGER: All right. We'll talk about
15 gene silencing in a moment.

16 I see there is another enzyme there which I think is --
17 is that acrylamidase?

18 A. Yes, it is.

19 Q. And will you tell us what that is.

20 A. That is an enzyme which will break down
21 acrylamide to acrylic acid plus ammonia. So it is also
22 another enzyme means of reducing acrylamide once it has
23 formed.

24 Q. So asparaginase prevents the formation of
25 acrylamide, but once acrylamide is formed, acrylamidase gets
26 rid of it; is that it, in essence?

27 A. Correct.

28 They are acting in different ways. One prevents the

1 formation. One removes it once it has formed.

2 Q. Okay. All right.

3 So now I would like you to tell the Court how
4 asparaginase has been used successfully to reduce acrylamide
5 in the potato industry.

6 MR. KENNEDY: Objection, irrelevant.

7 THE WITNESS: Okay.

8 THE COURT: Overruled.

9 You may answer.

10 THE WITNESS: Actually, it was through the gene
11 silencing technique which I didn't describe.

12 Q. All right. So tell us about the gene silencing
13 technique, then.

14 A. The DNA molecule codes for proteins. There's --
15 the structure of the DNA molecule was determined in the 1950's
16 by Watson and Crick.

17 It is a double-stranded molecule which has connections,
18 four bases that pair with each other to make the DNA molecule.
19 These are adenine, thymine, guanine and cytosine.

20 This is the code. The code is read by an enzyme that
21 makes RNA.

22 RNA, then, is the message and it's called -- it
23 synthesizes a messenger RNA. Messenger RNA is single
24 stranded. It is read in the ribosomes, where three of these
25 bases define what amino acid can be added on to a growing
26 chain -- it's called a polypeptide chain -- leading to the
27 formation of a protein.

28 Now, one technique that has been used is to create

1 what's called an inhibitor, mRNA, because the strands bind
2 complementary to each other. Like I mentioned, adenine,
3 thymine, guanine and cytosine and guanine.

4 So now you have the same structures on a single strand
5 of RNA.

6 They develop constructs in which a short chain RNA
7 binds to the actual messenger RNA and that gets cleaved. So
8 the enzyme never gets synthesized. That's one technique.

9 The other is to take the gene out, modify it, put it
10 back in such that it is no longer active.

11 That has been done by the potato industry, and I might
12 say it's been very successful.

13 Q. And what happens when you inactivate that
14 invertase gene? What does that do?

15 A. It prevents -- to an extent on the conversion of
16 sucrose to glucose and fructose, but they have also
17 inactivated asparagine synthetase, so that prevents the
18 formation of the asparagine which is also a precursor for
19 acrylamide.

20 Q. Okay. Well, what has the potato industry done?
21 What is the status of that in terms of regulation?

22 MR. KENNEDY: Objection to the demonstrative and lack
23 of foundation.

24 We're talking about a press release from a potato
25 company here. No showing that this is something that real
26 scientists rely for purposes of 801(b).

27 THE COURT: Overruled.

28 THE WITNESS: The patents were developed in the 2000,

1 2009 for reducing acrylamide.

2 In February of this year, the FDA and EPA gave
3 clearance for growing and selling potatoes with this gene
4 alteration in the United States.

5 Part of the reason that they're also excited about it
6 is because sensory evaluation said it was indistinguishable
7 from heat-processed products.

8 So they have a product which, if I can read, says there
9 is a reduction in the chemical asparagine and the reduced
10 asparagine shows that the levels of acrylamide can be reduced
11 up to 90 percent in potatoes that are cooked at high
12 temperatures.

13 So there has been success by this type of approach. It
14 does take years. It's not something that can be done
15 overnight. But this goes back to -- I was mentioning in 2006
16 the potato industry agreed to make a -- work on mitigation.
17 And they developed techniques that are now enabling potatoes
18 to be grown which will have much lower acrylamide levels than
19 conventional potatoes.

20 MR. KENNEDY: Move to strike. No foundation that he
21 knows what causes excitement in the potato industry or any of
22 the details as to what they were doing.

23 THE COURT: Overruled.

24 Let's get back to coffee.

25 MR. METZGER: Yes, your Honor.

26 Q. All right. So now let's talk about asparaginase
27 treatment for coffee which I think his Honor asked you about
28 earlier.

1 And what has been done regarding that?

2 MR. KENNEDY: Object, narrative answer.

3 THE COURT: Overruled.

4 THE WITNESS: Okay. This is work done by Novozymes,
5 who have produced the asparaginase.

6 And they have demonstrated that treatment of coffee
7 pre-roasting can reduce acrylamide levels, and You can see it
8 reduces asparagine levels.

9 Asparagine are the graph, block graphs. Acrylamide is
10 the line values.

11 And the acrylamide, you can notice, decreases from
12 800 micrograms per kilogram down to approximately
13 200 micrograms per kilogram. In other words, a 75 percent
14 reduction.

15 So this is one example. Others have reported on the
16 use of asparaginase as a treatment. This is one example just
17 showing what the data looked like.

18 Q. Okay. And this is in coffee.

19 Is this roasted coffee, brewed coffee or what?

20 A. This is in -- this is in roasted coffee. These
21 are micrograms per kilograms, so it's in the roasted coffee,
22 but the treatment is prior to roasting.

23 Q. Okay. So would you explain to the judge how
24 this works, how you get the asparagine in there?

25 A. Well, they steam and soak the beans in the
26 presence of an enzyme. I believe it's done at approximately
27 60 degrees centigrade, which may seem high but the enzyme that
28 they used is active.

1 They've determined that it was peak activity at that
2 temperature. They've also worked out what is the optimal PH
3 for the enzyme, so you work through these kinds of conditions.

4 It breaks down the asparagine, and then the fluids are
5 allowed to reinfuse into the beans. They are dried and then
6 the beans are roasted.

7 Q. Okay.

8 THE COURT: Is this during the roasting process or the
9 brewing process?

10 THE WITNESS: Pardon me?

11 It's done prior to roasting, and this is the level in
12 the roasted coffee.

13 THE COURT: Has any manufacturer attempted this
14 process?

15 THE WITNESS: Yes.

16 THE COURT: And who is that?

17 THE WITNESS: Novozymes worked with a company in
18 Germany to produce -- I believe it was 200 tons of treated
19 coffee that had been treated with asparaginase.

20 THE COURT: Is this the coffee that is distributed to
21 the public?

22 THE WITNESS: It was made available, yes. It was sold
23 to the market.

24 THE COURT: Sold to the market.

25 And what is the success rate in selling this to the
26 market?

27 THE WITNESS: I haven't seen that type of information.

28 THE COURT: What percentage of that market in Germany

1 does this company enjoy?

2 THE WITNESS: For its total production, I don't know.
3 It's just -- it's a demonstration of a scale-up to an
4 industrial level as opposed to a strict laboratory
5 demonstration that they can do it.

6 THE COURT: That's what I'm trying to find out, how
7 they do it? How much did they do of what they did?

8 THE WITNESS: I don't know what their present
9 production levels are.

10 THE COURT: What year did they commence this
11 production?

12 THE WITNESS: What year?

13 I believe it was around five years ago, four years ago.
14 But I would have to look back to the records to see. I don't
15 have that off to top of my head.

16 THE COURT: Are they still doing that today?

17 THE WITNESS: That I don't know.

18 THE COURT: Has it been accepted by the consuming
19 public?

20 THE WITNESS: I haven't seen information to that
21 effect.

22 THE COURT: All right. Thank you.

23 Mr. Metzger?

24 MR. KENNEDY: Move to strike.

25 Total lack of foundation.

26 May I voir dire on this?

27 THE COURT: Let Mr. Metzger finish the examination.

28 Q. BY MR. METZGER: Dr. Melnick, have you seen any

1 information that any of those 200 tons of coffee,
2 acrylamide-reduced coffee, that was prepared by that company
3 in Europe, that any of that was not accepted by the public and
4 returned?

5 A. No, I haven't seen that either.

6 THE COURT: When you say 200 tons, what percentage of
7 the German coffee market is that?

8 THE WITNESS: I don't know what percentage. But I
9 don't think they would --

10 THE COURT: How many tons of coffee are consumed by the
11 American public?

12 THE WITNESS: Oh, it's probably hundreds of thousands.

13 THE COURT: Hundreds of thousands of tons?

14 THE WITNESS: Yes.

15 THE COURT: Thank you.

16 Mr. Metzger?

17 Q. BY MR. METZGER: All right. Dr. Melnick, could
18 you explain to the Court, perhaps using the next graph that
19 they prepared, how the acrylamide is formed and degrades in
20 the process of roasting coffee.

21 A. Well, as I mentioned, it's formed by the
22 reaction of asparagine with the reducing sugars, glucose or
23 fructose.

24 And this is a typical graph showing the formation of it
25 on a time scale. I know this type of information has been
26 presented before.

27 Q. What is the significance to you about this?

28 A. So what you see on the first part is the rise

1 that's occurring between 50 and maybe 110 seconds under this
2 condition. It's for a medium roast.

3 It reaches a peak, after which the rate of its
4 degradation or loss increases such that it comes -- reduces
5 down to approximately 20 to 30 percent remaining in the final
6 product.

7 The reason I show this is because this, then, provides
8 information on opportunities for removing acrylamide when you
9 know what the apparent -- that there is a formation and a
10 degradation reaction occurring.

11 Some of the studies subsequent show how they've made
12 use of this type of information to reduce acrylamide levels.

13 Q. Okay. So have you read articles in the
14 peer-reviewed literature regarding the effect of roast time on
15 acrylamide levels in coffee?

16 A. In the next slide. This is from the
17 confidential report.

18 Q. Oh, so this is not from the peer-reviewed
19 literature. This is from a confidential internal report
20 prepared by one of the coffee companies?

21 THE COURT: Can we go back to the last slide for a
22 moment.

23 What's your understanding as to how much time coffee is
24 processed in the general coffee market?

25 In other words, what do most manufacturers do? How
26 long do they roast?

27 THE WITNESS: It varies substantially depending on --
28 it's time-temperature relationships.

1 Actually in the next slide we can look at four
2 different times of roasting times.

3 THE COURT: Is there a difference in terms of taste as
4 far as the consumer reaction or the consumer acceptability
5 with coffee having different roasting times?

6 THE WITNESS: Definitely. Because some people like
7 light-roasted coffee. Some people like medium-roasted coffee.
8 Some people like dark-roasted coffee.

9 So there is a preference. And as I'll show later,
10 dark-roasted coffee, because you're continuing down that
11 chart, has lower acrylamide levels than medium- or
12 light-roasted coffee.

13 But there are preferences among coffee consumers for
14 different degrees of roast.

15 THE COURT: All right. Thank you.

16 MR. METZGER: All right.

17 Q. So regarding the report from Kraft in 2007 that
18 you reviewed, what did you take away from that confidential
19 report that Kraft did?

20 A. So in this chart they have roasted coffee beans
21 for different amounts of time, one and half minutes, two and a
22 half minutes, five minutes or eight minutes. But they show
23 with that dotted line -- the vertical dotted lines where the
24 beans were all at the same roast color.

25 And in this what you can see, if I can find a
26 pointer -- it may be hard to see.

27 For example, on the one-and-a-half minute, that dotted
28 line is crossing at approximately 350 micrograms per kilogram.

1 If you can go up to where that dotted line crosses to
2 the right -- you went too far. Just a little bit over to the
3 right. To the right. Right there.

4 The dotted line is showing with a roast of
5 one-and-a-half minutes achieving the same roast color, the
6 acrylamide level is approximately 150.

7 If you then follow where that dotted line crosses the
8 descending part of the graph, you can see that it constantly
9 decreases.

10 In fact, by the time you get up to eight minutes or
11 five minutes, you've reduced the amount of acrylamide by
12 approximately 50 percent.

13 So you can see that Kraft acknowledged there was a
14 decrease in acrylamide levels with longer roasting times even
15 at the same color.

16 Q. So how do you or how did Kraft get a decrease in
17 acrylamide when roasting to the same roast color? How did
18 they do that?

19 A. It appears that with the increasing roasting
20 time during the descending phase particularly causes a
21 decrease in acrylamide levels.

22 So I showed you a typical graph, the up and down. Now
23 they're manipulating, looking what happens to acrylamide as
24 you start to change some of the process conditions.

25 Q. Well, how did they get the same roast color with
26 a longer time with lower acrylamide? What else was changed?

27 A. The effect would be due to the heat. There's
28 differences in temperature to enable the longer time to

1 produce the same roast color.

2 Q. So a lower temperature with a longer roast time
3 yielded less acrylamide?

4 A. Exactly.

5 Q. Roasted to the same color?

6 A. Exactly.

7 Q. All right. Did any of the articles that you
8 reviewed use standard roast profiles to see how they varied
9 and the resultant acrylamide?

10 A. This is an example of that where --

11 Q. Is that Xu, 2016?

12 A. Yes, it is.

13 And what I've tried to present are two of the different
14 programs for roasting where you can see there's temperature
15 changes for different intervals of time between program 1 and
16 program 2.

17 And the net effect is that by reducing the heating time
18 of the first two stages but increasing the time of the later
19 two stages, they were able to show a reduction in acrylamide
20 levels in coffee, in the roasted coffee.

21 Q. So there was a 39 percent reduction of
22 acrylamide from roast program 1 in comparison to roast program
23 number 2, correct?

24 A. That's correct.

25 Q. Was roast program number 1 a standard roast
26 profile that was used in industry as opposed to just some
27 experimental program?

28 A. It's defined as a traditional coffee roast

1 program.

2 Q. All right. So what do you conclude from this
3 study?

4 A. Well, one approach to reduce acrylamide would be
5 to focus on the time of the later stages to reduce acrylamide.
6 To extend the later stages does have an effect on reducing
7 acrylamide.

8 Q. Okay. And have you reviewed studies regarding
9 the effect of the degree of roast on the formation or the
10 level of acrylamide in coffee?

11 A. Yes, I have.

12 I think I mentioned this to his Honor a couple minutes
13 ago, but this a slide that, in fact, will show that type of a
14 difference.

15 Q. All right.

16 A. Between light, medium and dark roasted coffees
17 for both Robusta and Arabica.

18 Q. And is this data you have here from the Alves
19 2010 study?

20 A. Yes, that's where I obtained this data.

21 Q. And would you explain what you observed from
22 this study.

23 A. So if you focus first on just Robusta coffee,
24 you can see the differences between light, medium and dark,
25 that the medium is 67 percent lower in acrylamide compared to
26 the light, and the dark is 72 percent lower in acrylamide than
27 the light.

28 Similarly for the Arabica, the medium-roasted coffee

1 was 77 lower in acrylamide than the light and the dark was
2 83 percent lower than the light.

3 So, in essence, the degree of roasting, as you go from
4 light, medium to dark -- and this makes sense -- reduces the
5 level of acrylamide. Because that's based on that first curve
6 that I showed the formation and the destruction, elimination
7 of acrylamide, that as you get darker the acrylamide levels
8 decrease.

9 Now, you don't want to overcook the coffee, but this is
10 coffee which is consumable, acceptable, palatable.

11 This is actually fairly well established in the coffee
12 industry.

13 Q. Okay. Have you also reviewed articles regarding
14 or for that matter industry studies regarding the effect of
15 pressure on acrylamide formation?

16 A. Yes.

17 Did you skip a slide? Okay.

18 Q. And this study, this says in the bottom
19 left-hand corner, "Kraft, 2006." Is this a Kraft confidential
20 report you reviewed for you this case?

21 A. Yes. These data were obtained from a Kraft
22 confidential report.

23 And what I have done is tried to provide the essence of
24 their study on the steaming and pressure effects on acrylamide
25 levels in coffee that had been roasted for 120 seconds to
26 different color levels.

27 And what you can see here is that with steaming there
28 is a reduction in acrylamide. This is all Robusta coffee.

1 As they increase the pressure from atmospheric 2.7, 3.7
2 and 4.7 bar -- one bar is the equivalent of one atmospheric
3 pressure or approximately 14 and a half pounds per square
4 inch -- that it was effective in reducing acrylamide levels
5 such that the steam that the high pressure provided, the
6 percentage decreased compared Robusta was 47 percent lower.

7 The 16 would be the lighter color.

8 The others showed 36 and 30 percent reductions.

9 So it was showing approximately a 30 to 45 percent
10 reduction by applying steam and pressure during the roasting
11 process.

12 Q. And has vacuum roasting been evaluated for its
13 effect on reducing acrylamide in roasted coffee?

14 A. Yes, it has.

15 This is a paper by -- I believe it's pronounced Anese.

16 Q. Anese, 2014?

17 A. Yes.

18 Q. All right.

19 A. And what they are comparing is conventional
20 roast at 200 degrees centigrade. What they call combined is
21 ten minutes of conventional roast followed by a vacuum roast,
22 as well as then vacuum roasting at the same temperature,
23 200 degrees, under a vacuum.

24 And what they're showing is that where you're seeing
25 high levels of acrylamide, if you apply the vacuum early on,
26 this will remove the acrylamide by approximately 15 percent.

27 And one thing I want to point out is that on the
28 F minutes -- those aren't minutes. That's what's called a

1 thermal effect that they achieved within the coffee bean.

2 Under vacuum roasting, if you can read the boxes that I
3 highlighted, at the 3.8 F minutes was actually a 15-minute
4 roasting time. So it was -- they were roasted not for just
5 four minutes.

6 And you can see as you increase the roasting time, they
7 start to approach each other, the vacuum as well as the
8 conventional or the combined.

9 And the conclusion from this is that for people who
10 appreciate light-roasted coffee -- and this is true in
11 Northern Europe and in many places in America -- where I just
12 showed the information that light roasted has the higher
13 levels of acrylamide, that it's possible to reduce the
14 acrylamide levels for light-roasted coffee by applying a
15 vacuum when the acrylamide levels are at their highest levels.

16 Q. And what was the percentage reduction in
17 acrylamide that was achieved in this study using vacuum
18 roasting?

19 A. It was approximately 50 percent.

20 Q. 5-0?

21 A. Yes.

22 Q. Oh, okay.

23 I wasn't sure if you said 15 or 50?

24 A. It was 50.

25 Q. F-I-F-T-Y. I got it.

26 Just from using vacuum roasting?

27 A. Yes.

28 Q. All right. Are there other Kraft confidential

1 studies that you reviewed that provided yet other means of
2 reducing acrylamide in roasted coffee?

3 A. All right. So these are examples of roasting
4 processes, now, if we consider post-roasting, the events to
5 reduce acrylamide.

6 And in this case in the Kraft studies they reported on
7 the reduction during heat curing of coffee at -- either under
8 nitrogen or in an air environment at temperatures of
9 40 degrees, 70 degrees and 100 degrees centigrade.

10 Q. What is heat curing. Can you explain that?

11 A. Well, the beans have been roasted. They're now
12 applying another heat treatment on the beans to see if that
13 would be effective in reducing acrylamide levels.

14 And the heat, 40 degrees centigrade, isn't particularly
15 high. It's a little higher than body temperature, but
16 70 degrees and 100 degrees.

17 What you can see is at 100 degrees and 70 degrees were
18 effective in reducing acrylamide levels by applying this
19 relatively mild heat treatment on the roasted coffee beans.

20 Q. What was the reduction of acrylamide in the
21 roasted coffee using this post-roasting heat curing process
22 that Kraft determined?

23 A. Well, the graph is showing that the reduction
24 went to -- from approximately 450, 425 to maybe 100
25 micrograms.

26 So that would indicate a decrease of approximately
27 75 percent.

28 But they also did some taste testing. And that's

1 what's shown on the following graph, which shows where the
2 acceptable level was found in their taste testing studies to
3 be up to approximately a 45 percent reduction of acrylamide.

4 So if you over-reduce, obviously the tasting is
5 decreasing in its value. But it is acceptable, from their
6 determination, up to approximately 45, 50 percent reduction in
7 acrylamide.

8 Q. By using this post-roast heat curing process?

9 A. Yes.

10 Q. All right. And in this process could you
11 explain what the difference is, whether you do the heat curing
12 in the ambient air or whether you use a nitrogen atmosphere?

13 Explain that, please.

14 A. Well, they did it under both conditions, and
15 evidently there's not a big difference between the nitrogen
16 atmosphere versus ambient air.

17 I imagine it's probably done under nitrogen to prevent
18 any oxidative damage they might have anticipated. But it
19 doesn't seem that that really has much of an influence since
20 the roasting at 70 degrees or a 100 degrees wasn't that
21 different between nitrogen and ambient air.

22 Q. You mentioned oxidative damage and using
23 nitrogen in a nitrogen atmosphere to prevent that.

24 Would you explain that to the Court, what oxidative
25 damage is, first.

26 A. Yes.

27 Within foods, coffee, there are fatty acids, lipids,
28 which include fatty acids. Triglyceride is a lipid with three

1 fatty acid chains on them.

2 And when there is unsaturated fatty acids, this means
3 that there's double bonds as opposed to single bonds
4 connecting these carbon chains.

5 These carbon chains run 16, 18 carbons in length.

6 Where there are unsaturated bonds -- these would be
7 double bonds -- these are prone to attack by oxygen.

8 And with oxidative damage you can start to form
9 products that would be undesirable -- aldehydes, acids, et
10 cetera -- that the nitrogen environment would prevent because
11 it would replace the oxygen which would have allowed the
12 oxidative damage to occur.

13 Q. And in this study, even just using an
14 environment of air, ambient air, they were still able to
15 achieve this acrylamide reduction through this post-roast heat
16 curing process?

17 A. Yes.

18 Q. All right. Let's talk a little bit about
19 decaffeination.

20 How is decaffeination done?

21 A. Well, it used to be done by adding solvents.
22 One solvent in particular that had been used was methylene
23 chloride.

24 However, when methylene chloride was demonstrated to be
25 carcinogenic, the industry looked towards alternative ways of
26 decaffeinating.

27 One that became particularly popular was use of
28 supercriticals, carbon dioxide extraction.

1 Q. What is that?

2 A. Carbon dioxide, you know, is a gas. If you put
3 it under pressure, it will have fluid-like properties.

4 So it can penetrate and act in a fluid-like manner to
5 move materials in or out.

6 Supercritical CO2 is used in numerous other processes,
7 but it has been used now in the coffee industry for removing
8 caffeine by extracting it into this stream, this supercritical
9 CO2.

10 It's particularly done under particular conditions
11 which they work out which would be optimized for the compound
12 that they are trying to extract.

13 Q. Excuse me. Is supercritical extraction used
14 today in the coffee industry to decaffeinate coffee?

15 A. Oh, yes, it is.

16 Q. Has supercritical extraction been investigated
17 as a means of reducing acrylamide in coffee?

18 A. Yes. That's what's shown in this graph.

19 Q. And is this the Banchemo 2013 study?

20 A. Correct.

21 I might point out that Banchemo had a co-author who was
22 from Lavazza, a coffee manufacturing company in Italy.

23 So if we consider back to that graph in terms of where
24 the acrylamide is formed early on in the process, what they
25 did in this case was to optimize a condition for acrylamide
26 formation.

27 So they pre-roasted at 151 degrees for 20 minutes and
28 then applied the supercritical CO2 extraction.

1 And what you're looking at, then, is the percentage of
2 acrylamide which was extracted as a function of the CO₂.

3 And the reason for this at that time was to remove the
4 acrylamide when it is at a high level prior to the formation
5 of the majority of these aromatic and taste compounds which
6 form at the higher temperatures.

7 So they worked out a condition in which the acrylamide
8 could be extracted prior to the real final roasting of coffee
9 beans.

10 Q. And what was the effect or the percentage of
11 reduction of acrylamide that Banchero found using
12 supercritical carbon dioxide extraction?

13 A. Well, in this case, as you can see, the graph
14 goes up to 80 percent at the 100 degrees, 200 bar. That's the
15 pressure, 200 atmospheres.

16 Q. And the last question before the break. I can
17 see -- is this a technology that can be implemented by
18 companies that are already using supercritical extraction to
19 decaffeinate their coffee?

20 MR. KENNEDY: Lack of foundation.

21 THE COURT: Overruled.

22 THE WITNESS: Definitely.

23 They have the -- places to have the facility. Because
24 if they're extracting caffeine, they could easily apply it
25 towards the removal of acrylamide. That's the purpose of them
26 conducting this kind of experiment.

27 THE COURT: All right. Thank you. We'll stop at this
28 point, and we'll have the morning recess.

1 I'll be off the record in this case for 15 minutes.

2 (Recess.)

3 THE COURT: All right. Back on the trial, CERT versus
4 Starbucks.

5 Dr. Melnick is on the stand. Mr. Metzger was
6 questioning him.

7 Counsel, you may proceed.

8 MR. METZGER: Thank you, your Honor.

9 Q. Dr. Melnick, I would like to go back to slide
10 12, which was the effect of roast time on acrylamide levels,
11 the Kraft 2007 study.

12 And did you read Dr. Ristenpart's testimony that beans
13 that are roasted the same color have the same acrylamide
14 level?

15 A. I did see that in his testimony, yes.

16 Q. And in your opinion is Dr. Ristenpart correct in
17 that testimony?

18 A. Well, not according to these data. Because
19 these data demonstrate that the acrylamide levels decrease
20 with longer roast times when roasted to the same color.

21 Q. Okay. And would you -- I would like to go to
22 the latest slide, number 17, the heat curing treatment.

23 Did you read Dr. Ristenpart's testimony that heat
24 curing occurs at high temperatures, around 120 to 160 degrees
25 centigrade, and that sensory testing of the cured coffee was
26 invariably negative because it creates a baked flavor?

27 A. Yes, I did read that.

28 Q. And in your opinion is Dr. Ristenpart's

1 testimony on that point correct?

2 A. No. Because as shown in the slide, the curing
3 was effective at 70 degrees as well as 100 degrees centigrade,
4 not 120 to 160 degrees.

5 This is not a baking temperature. And therefore, I
6 believe his statements are inaccurate, unless he has data
7 showing that curing occurs at 150 degrees.

8 But the data that Kraft has provided shows that curing
9 is effective at lower temperatures.

10 Q. All right. So now I would like to ask you about
11 a chemical called cysteine.

12 Can you tell us, first, what that is.

13 A. Well, cysteine is an amino acid. So is lysine
14 and arginine, which are shown in this slide. But cysteine is
15 one of the amino acids involved in protein synthesis. So all
16 of our bodies contain cysteine, and it's part of our protein.

17 Q. Did you read this study by Narita in 2014
18 regarding the use of cysteine as a use of reducing acrylamide
19 in coffee?

20 A. Yes, I did.

21 Q. Could you tell us what that involved.

22 A. This was a study for ready to drink coffee.

23 Now, what they did was they tried adding these three
24 different amino acids separately to the canned coffee and
25 examined for its effect on acrylamide levels when it was
26 heated to 120 degrees centigrade for six minutes.

27 So this is brewed coffee.

28 Now, let me explain just quickly why this is effective.

1 Acrylamide has a carbon called a double bond next to a
2 carbonyl group.

3 Similarly to the way acrylamide is detoxified in the
4 body by glutathione, a compound like acrylamide which is an
5 electrophile, meaning it wants electrons. It's looking for
6 electrons; it likes them. That's what electrophile means.

7 Cysteine has a sulfhydryl group, an SH group, and it's
8 a donator.

9 What happens is cysteine will react with acrylamide,
10 form a covalent bond. And by forming that covalent bond, when
11 the acrylamide cysteine complex gets ingested, it cannot
12 undergo oxidation to glycidamide, the epoxide that you want to
13 try to avoid.

14 Q. And why are you trying to avoid glycidamide?

15 A. Glycidamide -- we'll talk about later -- is a
16 DNA-reactive compound which is a mutagen which causes
17 chromosomal damage and is linked to the carcinogenicity of
18 acrylamide.

19 Q. In this study by Narita, what did they do?

20 A. So they added various amounts of these three
21 different amino acids to the canned coffee, heated it to
22 120 degrees for six minutes, and followed the effect of the
23 additive on acrylamide levels.

24 As you can see, they got, with cysteine, over
25 90 percent reduction in acrylamide levels, which is quite, in
26 my view, impressive.

27 Q. All right. And this is in coffee, roasted
28 ground coffee in a can?

1 A. Yeah, it's brewed. It's ready to drink.

2 Q. So the amino acids were put in the can of the
3 roasted ground coffee and then it was just brewed? That's all
4 that was done?

5 A. Correct.

6 Q. All right. So now let's talk about storage.

7 And the first thing I would like you to do is explain
8 to Judge Berle the difference between storing coffee in the
9 open air and storing coffee in sealed bags or cans.

10 A. Well, as I mentioned earlier before the break,
11 that coffee can undergo lipid oxidation and create all flavors
12 as a result of that oxidation.

13 Oxidation, as the name implies, is oxygen involved in
14 reacting with the double bonds of the lipid, causing it to
15 undergo various breakages and form new compounds.

16 So the difference between how you store the coffee is
17 critical for maintaining high quality. Because if you store
18 it with access to atmospheric oxygen, it will undergo staling
19 in relationship to the oxidation of the lipids which are
20 present.

21 Q. How quickly?

22 A. Well, I would -- one week, two weeks in open
23 air, depending temperature, room temperature, it's not
24 something which people tend to enjoy.

25 Q. Okay. And what about storing coffee in sealed
26 bags or cans? How does that differ?

27 A. Okay. Well, there are companies, Illy in
28 particular -- I'm familiar with their cans -- that they

1 provide a pressurized inert gas with a very tight seal on
2 them.

3 And they indicate that that coffee is stable for up to
4 two years.

5 Q. So that coffee can sit in that can and doesn't
6 go stale and then you can open that can and brew that coffee
7 up to two years later?

8 A. Well, that's what their website indicates.

9 However, they also say once opened, the coffee will go
10 bad within one or two weeks.

11 Starbucks also lists their coffee as being stable for
12 up to 60 weeks.

13 I know from personal experience, because I've drunk
14 Illy coffee, where we -- where I've seen the date stamp on the
15 bottom. Never did I wait to the end of the date stamp to try
16 the coffee, but I've tasted it personally after it's been
17 stored for three months. This is in relationship to how I
18 travel back and forth between two locations.

19 When we order something, we don't use it up while we're
20 there. And it's -- in my own experience it's still as good as
21 it was if I opened a fresh can.

22 So the companies indicate that their coffee is stable
23 because of their specialized means of storing the can, and a
24 critical part of that is avoiding opening to the oxygen in the
25 air.

26 Q. All right. So I'm gathering that storing
27 acrylamide -- I'm sorry -- that storing coffee in the open air
28 is not a viable means of getting rid of acrylamide, letting it

1 evaporate in the open air, because you're going to have foul
2 coffee; is that right?

3 A. That sounds pretty close to what you wouldn't
4 want to do.

5 Q. All right. But have there been studies that
6 have researched storing coffee, after it's been roasted, in
7 sealed bags or other sealed containers as a means of reducing
8 acrylamide?

9 A. I haven't seen that data, per se.

10 All I have seen is what Illy and Starbucks say about
11 their storing of coffee and my own experience.

12 This particular slide --

13 Q. All right. Let's look at -- what is this?

14 This is the Baum 2008 study?

15 A. Yes.

16 Q. And this about storage of coffee?

17 A. Yes. This is what happens to acrylamide during
18 storage.

19 Q. And when you say storage, is this storage in
20 sealed situations or not?

21 A. Yes.

22 Q. Okay. All right.

23 So in 2008 -- that's almost ten years ago -- what did
24 these investigators find regarding -- or what did they do to
25 do the study regarding storage of coffee and its effect on
26 acrylamide?

27 A. Okay. What they did was inject a radio-labeled
28 form of acrylamide. That's what's indicated as C14

1 acrylamide. This is a label so you can identify the presence
2 of that acrylamide and where it ends up as a consequence of
3 storage.

4 Q. You label it so you can follow it?

5 A. Exactly.

6 Q. Okay.

7 A. Okay. So what they have done here is stored
8 coffee at two different temperatures. One is room
9 temperature, and one is at 37 degrees. This is the roasted
10 coffee with injected radio-labeled acrylamide.

11 They then followed the course of the radio-label over
12 time, storage time, and looked to see where the label was with
13 respect to the brew or the filter.

14 So this would be coffee, roasted coffee brewed by
15 filtration.

16 So when you filter, the grounds remain in the filter
17 paper and the brew comes through. They therefore followed
18 where the radio label was going and what it --

19 Q. The radio-labeled acrylamide?

20 A. The radio-labeled acrylamide. Correct.

21 What they found was the amount in the brew -- that's
22 what people drink -- decreases with time of storage, both at
23 room temperature and 37 degrees storage.

24 But in the filter paper -- now, this is going to be
25 radio-labeled. Because what's happening is that the
26 acrylamide is binding to the matrix material in the filter and
27 not made available into the brew.

28 So what you can see, then, is that these curves are

1 showing a decrease in the brew and an increase in the filtered
2 paper, because it's in that matrix which is trapped by the
3 filter paper.

4 So what is concluded from this -- and they couldn't
5 extract it very easily with solvents -- is that this is what
6 happens, as I mentioned, with cytosine, what happens with
7 acrylamide in the body.

8 There are components to which acrylamide will bind and
9 form a stable covalent bond and hence be retained in that
10 material, which is the filtered material, that matrix
11 material. And that's the explanation for what's happening in
12 acrylamide in roasted coffee during storage time.

13 Q. So how long was the coffee stored in sealed
14 containers after being roasted in this study?

15 A. Well, in this particular study it was up to
16 approximately 50 weeks.

17 Q. All right. And when that coffee was brewed,
18 what did that show regarding the acrylamide that ended up in
19 the brewed coffee?

20 A. Well, in this case it was reduced by
21 approximately 45 percent during that storage period.

22 Q. So --

23 A. And you can see the curve, so that you have
24 different time intervals where you can follow the decrease in
25 acrylamide in a brew.

26 What this also indicates is that acrylamide will wind
27 up in the brew in filtered coffee unless it has bound to that
28 matrix material.

1 Q. Okay. So is simply storing coffee for a period
2 of time -- say 50 weeks -- in sealed containers in your
3 opinion a viable means of reducing acrylamide in coffee?

4 A. Yes, it is a viable means. But it depends,
5 again, on to what extent you want to see the reduction in
6 acrylamide.

7 So, for example, even at 37 degrees at approximately
8 15, 16 weeks, you're approaching 50 percent reduction.

9 So that it may not be necessary to even wait the full
10 one year. This provides the information in terms of the
11 effectiveness of removing the acrylamide in relationship to
12 two different temperatures.

13 Q. Okay.

14 A. And it's not going to remove it all. In this
15 study it didn't remove it all, but it does show its
16 effectiveness in removing acrylamide from the eventual brew.

17 Q. So after about 15 weeks of storage, the
18 resultant acrylamide concentration was reduced by about
19 45 percent?

20 A. Let's see. Let me see if I can show you which
21 point I'm looking at here.

22 Do you see that right in there?

23 Q. Right.

24 A. That's the data I'm looking at. That's
25 approximately 15, 16 weeks.

26 And this is 60 percent. It's less than 60 percent.

27 So it is effective.

28 Q. All right. To do this, would industry need to

1 build new coffee roasting plants?

2 A. Not new roasting plants but maybe storage
3 plants.

4 Q. A storage room?

5 A. Yes.

6 Q. Okay. That's it?

7 A. Yeah, that's it.

8 Q. Low tech?

9 A. Compared to what we know now about technology,
10 that would be about as low as you can go.

11 Q. You just put it in a storage room for 16 weeks
12 and you get rid of about 45 percent of the acrylamide?

13 A. Yeah. It is a function of the temperature, too.

14 Q. All right. Incidentally, Dr. Ristenpart
15 testified that after roasting coffee stales quickly unless
16 used within a week.

17 Is that testimony of his correct?

18 A. That's definitely not correct because -- I
19 believe he got that statement from an individual, an author
20 who writes several books. It was in the introduction to a
21 book about coffee history which gave no information in terms
22 of the conditions in which the coffee was stored.

23 And if it staled within a week, it was certainly not
24 stored under an inert gas or nitrogen during that period.

25 Q. The way Illy does it?

26 A. The way Illy does it, yes.

27 Q. Okay. So now let's look at the end of the
28 process where one actually brews coffee using a filter.

1 Have researchers investigated the use of that enzyme
2 that you mentioned earlier, acrylamidase, to get rid of the
3 acrylamide once it's formed?

4 A. Right. So the early studies are preventing
5 acrylamide formation. At this stage the acrylamide is
6 present. So now we're considering the possibilities of
7 removing the formed acrylamide.

8 And in this case data reported by Smucker's
9 demonstrated that in Folgers roast coffee, by incorporating
10 acrylamidase into the filter paper was effective in reducing
11 acrylamide to below the detection limit.

12 And I might point out that the enzyme that they used
13 was from bacteria Bacillus, a species.

14 And it's obviously bad bacteria, but Bacillus are --
15 there's a number of bacteria that cause lactic acid
16 fermentation or strains of Bacillus that conduct that. But
17 this is the enzyme was incorporated, not the bacteria,
18 incorporated into the paper and was effective in reducing the
19 acrylamide levels as a consequence of its breakdown of
20 acrylamide.

21 Q. So incorporated into the filter paper was an
22 enzyme, not a fungus?

23 A. Not a fungus, no. Just an enzyme from bacteria,
24 but it was an enzyme, yes.

25 Q. So when Dr. Ristenpart testified that people
26 don't want fungus in their coffee from this method, did that
27 make any sense to you?

28 A. It makes sense that you wouldn't want fungus,

1 but this isn't fungus. This is an enzyme from bacteria in
2 filter paper. So in that sense it doesn't make sense.

3 Now, I should point out something which I find
4 interesting, is that --

5 MR. KENNEDY: Objection, your Honor. He's now
6 volunteering an answer to an unasked question.

7 THE COURT: Next question.

8 Q. BY MR. METZGER: What else did you find of
9 interest regarding the Smucker 2015 study, doctor?

10 A. So coffee when it's filtered is warm, very hot.

11 This study was done at 80 degrees. And you might think
12 that why would the enzyme degrade, but there are places where
13 bacteria can grow at very high temperatures.

14 In fact, a person won a Nobel Prize for identifying an
15 enzyme that was used in DNA identification and sequencing,
16 isolated this enzyme from Yellowstone Park, where there was
17 bacteria growing at very high temperatures.

18 So proteins will degrade -- undergo denaturation at
19 typical high temperatures, but there are some that are stable.
20 And this was obviously a stable enzyme such that it could be
21 used when hot water is poured over the ground coffee.

22 Q. Okay. And the acrylamide reduction in this
23 study was what?

24 A. Well, depending the amount of enzyme that was
25 used, the fourth bar shows a 54 percent reduction. And if
26 it's below the limit of detection, it's approaching
27 100 percent.

28 Q. All right. And have attempts been made to

1 reduce acrylamide in instant coffee?

2 A. Yes, it has.

3 Q. And what study is that?

4 A. This is the study by Cha of 2013.

5 Q. And what did Cha do?

6 A. Okay. It wasn't the pure enzyme, but it was a
7 cell-free extract.

8 That means they lysed the bacteria.

9 Q. L-Y-S-E-D?

10 A. Yes.

11 Q. What does that mean?

12 A. They burst it.

13 Q. Okay.

14 A. Okay. They burst the cell, and the material
15 which they could obtain from within is the extract.

16 So it's no longer a cell that can divide. It's just
17 the extract from the cells.

18 And you can precipitate down some of the cell debris
19 and have an extract remaining, a liquid extract.

20 So what they did was, in this case, add different
21 amounts of that cell-free extract to brewed instant coffee. I
22 think he allowed it to work for various amounts of time and
23 examined the effects on the concentration of acrylamide.

24 In this case, you can see they've added acrylamide to
25 see its effectiveness. And it reduced the acrylamide almost
26 100 percent with 80 microliters of their extract.

27 It's a demonstration of an effectiveness of the
28 cell-free extract which contains acrylamidase.

1 Q. This is still acrylamidase?

2 A. Yes. In breaking down acrylamide even in
3 instant coffee.

4 Q. And what was the percentage reduction of
5 acrylamide in instant coffee for this study?

6 A. From this study -- it depends on the amount of
7 enzyme and how long you incubate, but it's approaching
8 100 percent.

9 Q. Okay. Now, Dr. Ristenpart testified that to
10 remove acrylamide by acrylamidase that that would require a
11 two- to four-hour treatment.

12 Was Dr. Ristenpart correct about that?

13 A. Well, from the data presented by Cha, 20 minutes
14 will reduce it more than 80 percent.

15 So I would think he's a little off on his estimation of
16 the time necessary.

17 Q. All right. Dr. Melnick, have you prepared a
18 summary regarding the different acrylamide reduction
19 technologies for coffee indicating the percentages of
20 reduction of acrylamide?

21 A. Yes, I have. That's shown in the next slide.

22 Q. All right. So tell us what you conclude from
23 this.

24 A. Okay. So we've walked through most of these --
25 maybe all of them -- methods for reducing acrylamide.

26 I'm showing some of the data which indicates the
27 percentage reduction that can be achieved by various
28 techniques.

1 These go back to some of the slides that I showed
2 earlier, such as the selection of the coffee bean, the
3 asparaginase treatment, as you said near 90 percent.

4 I might point out that those authors, Navarini from
5 Illy, and Dria is from Procter & Gamble. So it's based on
6 patent work.

7 There are roasting techniques which show certain amount
8 of effectiveness in removing acrylamide.

9 There's post-roasting techniques which are also
10 effective. Some of these we discussed recently. Curing,
11 supercritical carbon dioxide extraction or adding cysteine.
12 Storage is also a means of effectively reducing acrylamide.
13 And the post-brewing techniques of acrylamidase treatment.

14 Now, you can see that there are a number of techniques
15 that have effectiveness. And in many examples you can combine
16 multiple techniques for removing them.

17 So, for example, asparaginase treatment can reduce
18 acrylamide effectively. If you add some additional storing,
19 storage time, you can get even further reduction, so that an
20 effort should be very easily accomplished by using techniques
21 which already exist and combining some of those to reduce
22 acrylamide, in my view, by at least 90 percent.

23 Q. Okay. I want to note just one thing here.

24 On this table you also have altered gene expression.
25 It says 90 percent in potatoes.

26 A. Right.

27 Q. Has anybody yet done the study altering the gene
28 expression to reduce acrylamide in coffee the way it's been

1 done in potato plants?

2 A. I haven't seen any evidence of that. That's why
3 I put -- the title of this slide was "Acrylamide in coffee,"
4 but because there is a methodology that exists for potatoes,
5 that methodology could be applied to coffee.

6 In fact, the Simplot people make that kind of
7 statement, that it could be effective in coffee as well.

8 I don't know if they produced any data on that because
9 they're focused on potatoes. But altered gene expression was
10 where I was talking about silencing genes involved in
11 producing precursors.

12 These techniques are relatively new within the past 20
13 years. And these could be pursued -- could have been pursued,
14 as well.

15 Q. So other than the altered gene expression is all
16 of the -- are all of the studies and the techniques and the
17 percentage reductions of acrylamide that you've summarized on
18 the slide, are those all for coffee?

19 A. Yes. Just the gene expression was not for
20 coffee, but all the others were data obtained from coffee
21 analyses and treatments.

22 Q. Right.

23 And were there some studies that provide a means of
24 reducing acrylamide in light roast coffee?

25 A. Yes.

26 The vacuum roast was effective in removing it from
27 light roast. Light roast is one of the bigger concerns,
28 because that has the highest acrylamide levels.

1 Q. And some of these studies, did they show
2 effectiveness in reducing acrylamide in instant coffee?

3 A. Yes. Those were the studies done with
4 acrylamidase, that, yes, once it's formed it still can be
5 removed.

6 Q. And did some of the studies even show the
7 ability to reduce the acrylamide levels in dark roast coffee?

8 A. In dark roast?

9 Well, the asparaginase treatment is selective for
10 asparagine. So it's going to be effective regardless of the
11 roast level because it's taking away a precursor.

12 So it would be effective at any level of roasting if
13 you reduce the precursor compound which is required for
14 forming the acrylamide.

15 Q. Okay. Well, let me ask you a little, then,
16 about asparagine.

17 You've indicated it's an amino acid.

18 A. That's correct.

19 Q. Okay. Is asparagine essential for flavor
20 formation in coffee?

21 MR. KENNEDY: Lack of foundation.

22 THE COURT: Overruled.

23 THE WITNESS: Well, one way to evaluate that is to run
24 sensory tests on asparaginase-treated coffee, and that has
25 been done.

26 Q. BY MR. METZGER: So now let's talk about that.

27 What studies did you find that it actually evaluated
28 flavor or other sensorial properties of techniques used to

1 reduce acrylamide in coffee?

2 A. Okay. So this is a listing of eight examples
3 where the impact of acrylamide reduction was evaluated for
4 flavor and consumer acceptance.

5 For asparaginase, the Illy Company indicated that the
6 organoleptic properties remained unaltered.

7 Stadler, who was at Nestle company, indicated that with
8 70 percent reduction of acrylamide there was no significant
9 impact on organoleptic properties.

10 The Xu paper examined a number of aroma compounds, and
11 there were only minor changes that they observed when they
12 reduced acrylamide by 84 percent.

13 So it does not appear -- it does not seem like removing
14 asparagine is going to have a large impact on flavor.

15 I might point out that asparagine is one of 20 some odd
16 amino acids which still can participate in the Maillard
17 reaction. And, in particular, lysine is an amino acid which
18 is very prone to undergo the Maillard reaction with reducing
19 sugars.

20 So there are other amino acids that are available, and
21 the taste-testing evaluations that have been done indicate
22 that they're not seeing significant changes.

23 Q. What about the vacuum roasting technique.

24 Was there any sensory evaluation for that study?

25 A. Yes. Anese reported that there was no perceived
26 difference by the assessors.

27 So as I mentioned, this would be a light-roasted coffee
28 which you have to assess it for light-roasted coffee, not

1 dark-roasted coffee in case people have a preference for a
2 different level of roasting.

3 Q. And what was observed by the Kraft scientists
4 for the heat curing technique post-roast?

5 A. Well, again, now, the curing, as I mentioned,
6 was done both under nitrogen or under atmospheric conditions
7 of air being present.

8 Under the nitrogen it was effective in preventing the
9 formation of all flavors. And they did do sensory evaluations
10 for that.

11 Q. And what did Illy in its studies observe
12 regarding the storage of roasted coffee in sealed containers?

13 A. Well, they advertise that the flavor and
14 freshness are preserved for up to two years if the can is
15 unopened.

16 Q. Okay. Dr. Ristenpart testified that asparagine
17 is needed for the Maillard reaction that yields products
18 crucial for flavor.

19 Is asparagine essential for coffee flavor?

20 A. The reduction of asparagine does not cause
21 significant effects on flavor.

22 Q. How do you know that?

23 A. From these sensory reports.

24 But if a claim such as that is made, then do the
25 experiment.

26 You know, I always believe in proposals. Hypotheses
27 are valuable, but they need to be tested rather than just
28 arbitrarily claim that you need asparagine for the flavor.

1 Q. Are the published peer-reviewed studies
2 regarding reduction of acrylamide in coffee and the industrial
3 confidential studies that you reviewed, are those hypotheses
4 or do those result in conclusions from experiments?

5 MR. KENNEDY: Compound.

6 THE COURT: Overruled.

7 THE WITNESS: Well, most of them are based on some
8 sensory evaluation.

9 Some are based on statements made in patents, and I
10 didn't see the data from the patents to see how they did it.
11 All I can infer is that they were either telling the truth or
12 misleading in their patent application, and I can't
13 distinguish between the two.

14 Q. BY MR. METZGER: All right. Regarding the
15 patent applications, there were patent applications by what
16 coffee companies?

17 A. Illy and Procter & Gamble.

18 Q. And what did you conclude from your analysis of
19 those patent applications?

20 A. Well, that the statements, I believe, are
21 accurate. But they didn't provide the actual data in the
22 patent of their sensory tests, so I --

23 Q. You would like to see that?

24 A. I would like to see it. I believe in seeing
25 data, both ways.

26 But the intention is to produce acrylamide-reduced
27 coffee that is acceptable. And those patent applications were
28 developed because they had enough evidence to file them.

1 Q. Okay. So, Dr. Melnick, would you tell the Court
2 what is your overall conclusion regarding the feasibility of
3 reducing acrylamide in coffee and still ending up with
4 palatability?

5 A. Well, that's what I state over here in this
6 slide, that in my opinion it can be reduced selectively by at
7 least 90 percent without significantly affecting sensorial
8 properties of coffee.

9 As I indicated before, it may be best to explore
10 combination techniques if -- for example, when I was showing
11 some curves where it seemed like the acceptability was
12 starting to deteriorate, so you work under the levels of
13 acceptable and perhaps include a secondary process to reduce
14 further without affecting palatability.

15 In my opinion this is very doable effort.

16 Q. And would you tell the Court which of the
17 techniques -- perhaps we could go back to the summary slide.

18 Which of these techniques can be implemented without
19 having to tear down and rebuild coffee roasting plants or
20 processing plants?

21 A. Well, asparaginase doesn't require rebuilding
22 coffee plants.

23 The supercritical CO2 extraction method, those are
24 available for companies that are making decaffeinated coffee.

25 Storage wouldn't require tearing down any kind of
26 facility.

27 And acrylamidase treatment is also -- or adding
28 cysteine are very simple methodologies that could be

1 implemented for reducing coffee without much modification of
2 any processing facility.

3 Q. All right.

4 MR. METZGER: Your Honor, would it be appropriate to
5 take a lunch break now?

6 THE COURT: Okay. At this time we will be in recess
7 until 1:30 this afternoon.

8 Have a pleasant lunch.

9 (At 12:00 noon, a recess was taken until 1:30 p.m.
10 of the same day.)

11

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EXHIBIT “E”

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SUPERIOR COURT OF THE STATE OF CALIFORNIA

FOR THE COUNTY OF LOS ANGELES

DEPARTMENT 323

HON. ELIHU M. BERLE, JUDGE

CERT,)	
)	
)	PLAINTIFF,
)	CASE NO. BC 435759
VS.)	
)	BC 461182
STARBUCKS CORP, ET AL.,)	
)	
)	DEFENDANTS.
_____)	

REPORTER'S TRANSCRIPT OF PROCEEDINGS

MONDAY, OCTOBER 2, 2017

P.M. SESSION

APPEARANCES OF COUNSEL:

FOR THE PLAINTIFFS: METZGER LAW GROUP
 BY: RAPHAEL METZGER, ESQ.
 AVI PARISER, ESQ.
 401 East Ocean Boulevard
 Suite 800
 Long Beach, California 90802
 (562)437-4499
 sbrust@toxictorts.com
 rmetzger@toxictorts.com
 apariser@toxictorts.com

FOR THE ROASTER AND DOE DEFENDANTS:
 MORRISON/FOERSTER
 BY: JAMES M. SCHURZ, ESQ.
 425 Market Street
 San Francisco, California 94105-2482
 (415)268-7124
 jschurz@mofo.com

(Appearances continued on next page.)

MARK SCHWEITZER, CSR, CRR, RPR
OFFICIAL PRO TEM COURT REPORTER
LICENSE NO. 10514
213-663-3494

1 APPEARANCES OF COUNSEL: (CONTINUED)

2 FOR KEURIG: SKADDEN, ARPS, SLATE, MEAGHER
3 & FLOM, LLP
4 BY: RAOUL D. KENNEDY, ESQ.
5 525 University Avenue
6 Palo Alto, California 94301
7 (650)470-4550
8 rkennedy@skadden.com

9 FOR HN FERNANDEZ, ET AL.:
10 NORTON ROSE FULBRIGHT, LLP
11 BY: JEFFREY B. MARGULIES, ESQ.
12 LAUREN SHOOR, ESQ.
13 555 South Flower Street
14 41st Floor
15 Los Angeles, California 90071
16 (213)892-9286
17 jmargin@nortonrosefulbright.com
18 lshoor@nortonrosefulbright.com

19 FOR 7-ELEVEN, ET AL.: ARNOLD & PORTER KAYE SCHOLER
20 BY: SEAN A. MCCORMICK, ESQ.
21 One Embarcadero Center
22 22nd Floor
23 San Francisco, California 94111-3711
24 (415)471-3303
25 sean.mccormick@apks.com

26 FOR KERRY, INC.: BRYAN CAVE, LLP
27 BY: MEGAN IRWIN, ESQ.
28 (949)223-7000

FOR WHOLE FOODS: BLAXTER/BLACKMAN, LLP
BY: J.T. WELLS BLAXTER, ESQ.
475 Sansome Street
Suite 1850
San Francisco, California 94111
(415)500-7700
wblaxter@blaxterlaw.com

(Appearances continued on next page.)

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24
25
26
27
28

APPEARANCES CONTINUED:

FOR WALMART STORES, ETC.:

BARTKO, ZANKEL, TARRANT & MILLER
BY: MICHAEL D. ABRAHAM, ESQ.
One Embarcadero Center
Suite 800
San Francisco, California 94111
(415)956-1900
mabraham@bzbm.com

FOR COSTCO, ETC.:

ROGERS, JOSEPH, O'DONNELL
BY: RENEE D. WASSERMAN, ESQ.
311 California Street
San Francisco, California 94104
(415)956-2828
rwasserman@rjo.com

FOR THE KROGER COMPANY:

NIXON, PEABODY, LLP
BY: LAUREN M. MICHALS, ESQ.
GREGORY P. O'HARA, ESQ.
One Embarcadero Center
Suite 1800
San Francisco, California 94111
(415)984-8261
lmichals@nixonpeabody.com
gohara@nixonpeabody.com

FOR STATER BROS, ETC.:

VARNER & BRANDT, LLP
BY: BRENDAN W. BRANDT, ESQ.
3750 University Avenue
Suite 610
Riverside, California 92501-3323
(951)274-7777
brendan.brandt@varnerbrandt.com

FOR SARA LEE:

SHOOK, HARDY & BACON, LLP
BY: FRANK C. ROTHROCK, ESQ.
NAOKI S. KANEKO, ESQ.
5 Park Plaza
Suite 1600
Irvine, California 92614-2546
(949)475-1500
frothrock@shb.com
nkaneko@shb.com

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M A S T E R I N D E X

October 2, 2017; P.M. Session

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1 CASE NUMBER: BC411192/BC435759
2 CASE NAME: CERT CASES
3 LOS ANGELES, CALIFORNIA MONDAY, OCTOBER 2, 2017
4 DEPARTMENT 323 ELIHU M. BERLE, JUDGE
5 REPORTER: MARK SCHWEITZER, CSR 10514
6 TIME: 1:45 P.M.

7 -o0o-

8 THE COURT: Good afternoon, Counsel. Back on the
9 record in CERT versus Starbucks. All counsel are present.
10 And Dr. Melnick is on the stand.

11 You may be seated. Do you understand you are still
12 under oath?

13 THE WITNESS: Yes.

14

15 **RONALD MELNICK, PREVIOUSLY SWORN.**

16

17 THE COURT: Mr. Metzger, you may proceed.

18 MR. METZGER: Thank you, your Honor. Before we
19 begin, I wanted to make a quick announcement and inform the
20 Court that there was one defendant that identified 105
21 witnesses for the remedies phase of the trial. And to spare
22 us all, CERT has settled with that defendant. That is
23 7-Eleven.

24 THE COURT: All right, thank you.

25

26 **DIRECT EXAMINATION (CONTINUED)**

27 BY MR. METZGER:

28 Q. Good afternoon, Dr. Melnick.

1 Let's talk about cancer risk assessment, if we can.

2 Now, as part of your work in this case, did you
3 review probably several years ago and as well more recently
4 the published risk assessment regarding acrylamide of various
5 governmental agencies and authoritative bodies?

6 A. Yes, I have.

7 Q. And have you prepared a summary of how they
8 went about selecting tumors for those?

9 A. Yes, I have.

10 MR KENNEDY: Objection, your Honor. We filed a
11 short brief with the Court this morning. As I said earlier,
12 when Mr. -- Dr. Melnick prepared his critique of Dr. Rhomberg,
13 it's Exhibit 6 to his deposition, he focused in entirely on
14 pharmacokinetic factors. In his deposition on July 28th, he
15 testified at length about PK factors. Page 169, we asked him
16 does this critique contain all of your present criticisms of
17 Dr. Rhomberg's work?

18 His answer was: "Yes, at this point in time, that
19 is the extent of my criticisms, critique of Dr. Rhomberg's
20 report and deposition. If something more is stated, for
21 example, if he were to write back a critique about me, I would
22 take a look at it and look at the basis of it, but at this
23 point that's where I stand."

24 And that was the last we heard about the subject
25 until yesterday, when we were served with the demonstratives
26 in this case, including, I think it's either 12 or 13 dealing
27 with the new topic of tumor selection, and we would object to
28 it at this point.

1 THE COURT: Mr. Metzger, what's your response?

2 MR. METZGER: Well, yes, I believe that Dr. Melnick
3 testified about this back in 2014. And in addition, there's
4 some information here -- this is not even necessarily
5 regarding Dr. Rhomberg but in part regarding Dr. Melnick and
6 these tumor sites. Dr. Melnick was, of course, one of the top
7 people at the national toxicology program that did these
8 studies, and Dr. Rhomberg, in fact, when asked who are the
9 experts in doing these, he mentioned Dr. Melnick.

10 THE COURT: Well, I'll let the witness testify
11 subject to a motion to strike.

12 You may proceed.

13 MR. METZGER: Thank you, your Honor.

14 Q. So how many risk assessments did you find of
15 acrylamide for cancer risk from your review, Dr. Melnick?

16 A. There were four assessments that I identified.

17 Q. And the earliest was what?

18 A. In 2005.

19 Q. That's the FA -- what is that, Food and
20 Agricultural Association/World Health Association. And what
21 type of tumors did they include in their risk assessment?

22 A. Just for a little background, if I may.

23 Q. Sure. Go ahead.

24 A. The NTP conducted studies of acrylamide in rats
25 and mice, and it was published approximately 2012.

26 Prior to that, there were studies in rats that were
27 conducted by Freedman and Johnson. There's two separate
28 papers. Those were the tumor incidence data that were used in

1 the risk assessments up until the EFSA, the fourth one
2 indicated here. So yes, in the FAO/WHO risk assessment, they
3 looked at mammary gland tumors in female rats, and they
4 included the fibroadenomas and adenocarcinomas and
5 peritesticular mesothelioma, the thyroid, and the central
6 nervous system.

7 I highlight in the red the tumors which were
8 excluded by Dr. Rhomberg.

9 Q. Okay. And the next was OEHHA in 2005. And
10 what tumors did OEHHA include?

11 A. OEHHA in their assessment -- this is the
12 assessment that was never finalized. But in that assessment
13 it was all sites and that included the mammary gland, which
14 were the fibroadenomas and adenocarcinomas, as well as the
15 thyroid gland and the tunica mesotheliomas. That's the same
16 as the peritesticular mesothelioma.

17 Q. Okay. And in 2010, the U.S. EPA risk
18 assessment.

19 A. The U.S. EPA included the mammary gland
20 fibroadenomas and adenocarcinomas in thyroid tumors in female
21 rats, and the tunica vaginalis mesothelioma and thyroid gland
22 in male rats. They didn't exclude any of those particular
23 tumors.

24 Q. Okay. So up until the time that the NTP
25 published its studies on acrylamide in 2012, all of the
26 earlier risk assessments included all of these different
27 tumors?

28 A. That is correct.

1 Q. Now, the European Food Safety Association in
2 2015, is that the most recent cancer risk assessment for
3 acrylamide by a major agency?

4 A. That is the only one I have identified.

5 Q. Okay. And what tumors did EFSA include?

6 A. EFSA did what's called a margin of exposure.
7 And they base that margin of exposure on the harderian gland
8 tumors in mice.

9 Q. Okay. So the risk assessment was based just on
10 the harderian gland tumor; is that correct?

11 A. Yes, their margin of exposure values were based
12 on the harderian gland tumors.

13 Q. And would you explain to Judge Berle what a
14 margin of exposure is?

15 A. The margin of exposure is the relative dose in
16 animals that produces a certain percentage of a tumor
17 response, such as a 10 percent response, compared to the
18 exposure that humans experience from that same agent.

19 Q. So is it essentially looking at how far apart
20 the dose is that produces an effect in animals compared to
21 what humans are actually exposed to?

22 A. That is correct.

23 Q. And is the lower the margin of exposure the
24 greater the health concern?

25 A. That is correct. And the typical standard for
26 that, as stated by both EFSA and the Food and Agricultural
27 Association World Health Association work, is 10,000, and that
28 is the type of margin of exposure that they want to see

1 without concern.

2 THE COURT: What does that mean? 10,000.

3 MR. METZGER: Let me ask this this way.

4 Q. Is that the difference between where the
5 animals show an effect and what humans are actually exposed
6 to, a 10,000 fold difference?

7 A. Yes, it's where the animals show a 10 percent
8 response rate compared to the human exposure. What is the
9 dose that is associated with a 10 percent response rate
10 compared to the exposure in humans.

11 THE COURT: All right. So you're saying that a 10
12 percent exposure rate in an animal is equivalent to a risk
13 rate in a human being?

14 THE WITNESS: No. I'm saying that the dose that
15 creates the 10 percent response compared to the exposure that
16 humans experience. So looking at a 10 percent response rate
17 in animals, what dose causes that and what is the exposure in
18 humans.

19 Q. BY MR. METZGER: And how far apart those two
20 values are. Is that it?

21 A. Yeah. What is that ratio.

22 THE COURT: And where does the 10,000 play here?

23 THE WITNESS: Well, 10,000 is the typical value in
24 which they consider it not a concern.

25 Q. BY MR. METZGER: And what is the value for
26 acrylamide?

27 A. It was approximately 70.

28 Q. 70?

1 A. Yes. And therefore, they said this is a
2 concern.

3 Q. So is that essentially saying that adverse
4 effects, responses in animals are seen at a dose that's just
5 70 times what humans are exposed to?

6 A. Yes. The 10 percent response rate is only 70
7 times higher than human exposure, which they consider to be,
8 and I do as well, consider to be a health concern.

9 Q. Okay. Now, regarding the EFSA 2015 risk
10 assessment, how is it that EFSA did its risk assessment based
11 exclusively on the harderian gland, which people don't even
12 have?

13 A. I've written an article on this particular
14 issue of epoxides and sites on which epoxides induce cancer
15 and in that article -- this was back in 2002 -- I noted that
16 harderian gland was a common target for a number of
17 epoxide-forming chemicals.

18 Q. Like acrylamide?

19 A. Well, I didn't take food acrylamide in that,
20 but there were a number of other epoxide-only chemicals that
21 were -- induced harderian gland tumors in mice. In fact, I
22 sort of considered that to be like the canary in the coal mine
23 for epoxides, where this is the warning that the harderian
24 gland represents a site for cancer induction by
25 epoxide-forming chemicals.

26 Q. So what is the significance in terms of risk
27 assessment that the harderian gland tumors in mice are
28 commonly seen in mice exposed to epoxide chemicals?

1 A. It's indicating that epoxides have that
2 capability of forming a tumor response. This is biology.
3 That the biology demonstrates tumor induction in this
4 particular site which is common among epoxide forming
5 chemicals.

6 Q. Does that tend to indicate that it is not a
7 fortuitous occurrence?

8 A. No. This is something which seems to concern
9 or demonstrate a concern for epoxide-forming chemicals.

10 Q. Okay. And here is the EFSA 2015 document, and
11 if we look at this paragraph on Page 191, let's see, it says
12 the Contam panel --

13 MR. KENNEDY: Objection. This wasn't included in
14 the demonstrative. I'm not sure it was even produced in the
15 case.

16 MR. METZGER: It was.

17 THE COURT: Subject to a motion to strike. Counsel
18 can discuss where the document can be found.

19 MR. MARGULIES: Do you have an exhibit number?

20 MR. METZGER: It was identified earlier. I don't
21 see my copy of it.

22 THE COURT: Okay. Let's stop this chitchat.
23 Discuss it during the break. Next question.

24 Q. BY MR. METZGER: Yes, it says the Contam panel
25 considered that even though the harderian gland is not present
26 in humans, this rodent organ represents a sensitive end point
27 for detecting compounds that are both genotoxic and
28 carcinogenic. And it cites three studies. And then it says

1 harderian gland tumors and tumors in other rodent organs,
2 including the lung in mice, the brain in rats, and the mammary
3 gland and forestomach in both species are prone to tumor
4 formation upon exposure to epoxides or epoxide-forming
5 carcinogens, citing Melnick 2002, such as acrylamide.

6 Is that you?

7 A. I'm that Melnick, yes.

8 Q. And if we look at your Curriculum Vitae on
9 Page 20, is the article identified as No. 95 by Ronald L.
10 Melnick, Carcinogenicity and Mechanistic Insights on the
11 Behavior of Epoxides and Epoxide-Forming Chemicals published
12 in the Annals of New York Academy of Sciences? Is that what
13 EFSA relied on?

14 A. Yes, that's the article they are referring to.

15 Can we go back to that page again?

16 Q. Sure. On the EFSA. If you can read the
17 paragraph that begins therefore.

18 THE COURT: Wait, wait. This is not a reading
19 exercise. Next question.

20 Q. BY MR. METZGER: All right. So do you agree
21 with EFSA's conclusion that therefore, the results on the
22 harderian gland in mice cannot be disregarded in the risk
23 assessment of acrylamide?

24 A. That is correct. And that's what I feel and
25 that's what the panel concluded, that the results on the
26 harderian gland in mice cannot be disregarded in the risk
27 assessment.

28 Q. Okay. All right.

1 Have you assessed what the effects of excluding the
2 various tumors that Dr. Rhomberg excluded on the NSRL?

3 A. Yes, I've made that comparison.

4 Q. And what did you find?

5 MR. KENNEDY: Objection, your Honor. This is
6 Dr. Bayard's work. I understand it has tried to be
7 introduced, and your Honor kept it out during Dr. Rhomberg's
8 exam. We object to it at this point. He's just trying to
9 read Bayard's stuff into evidence.

10 THE COURT: The witness can testify based on hearsay
11 subject to a motion to strike, cross-examination.

12 Q. BY MR. METZGER: Dr. Melnick, what did you
13 find?

14 A. I did these calculations and found that the
15 NSRL was increased as a consequence of excluding particular
16 tumor sites. The tunica mesothelioma in male rats was
17 increased approximately 30 percent, 1.3. Mammary gland
18 tumors, excluding those from female rats, increased the NSRL
19 by nearly a factor of three. Excluding the harderian gland,
20 tumors in male mice increased the NSRL by nearly fivefold, and
21 excluding the harderian gland tumors in female mice increased
22 the effect on the NSRL by a little over a factor of two.

23 So if you run a risk assessment and you pick the
24 male rat or female rat or male mouse or female mouse, these
25 are the values that are increased in the NSRL for that
26 particular species by excluding those tumor sites.

27 Q. So as these different tumors and tumor sites
28 are excluded from the risk assessment, does that reduce the

1 risk?

2 A. The risk is increased by excluding sites.

3 Q. Okay. The no significant risk level is
4 increased.

5 A. That is correct.

6 Q. Okay.

7 A. The potency is decreased.

8 Q. That was the term. I used the incorrect term.
9 So the potency is decreased, when you exclude the tumors,
10 because you don't have this potent effect, but that increases
11 the no significant risk level because you can have higher
12 exposures.

13 A. That is correct.

14 Q. Okay. All right. So now I think we're at the
15 topic of pharmacokinetics, which you mentioned at the very
16 beginning, and I know this is going to get complex. So let's
17 take this slowly.

18 First, have you prepared a diagram of the human body
19 to show essentially how chemicals are distributed and
20 metabolized?

21 A. Yes, I have.

22 Q. All right. So there we have this nice
23 gentleman with a cup of coffee I see in front of him, and AA.
24 Is AA for acrylamide?

25 A. Yes, that's what the AA represents.

26 Q. All right. So would you just tell us what
27 you've intended to convey by means of this diagram?

28 A. Okay. Since we all just finished our lunch a

1 little while ago, this is what happens to chemicals that
2 your body may not necessarily want to see. It wants to
3 eliminate them. So if we consider in this case a cup of
4 coffee containing acrylamide, the exposure of this individual
5 is an oral exposure. Drinking a cup of coffee. As a
6 consequence of drinking coffee and having acrylamide in it,
7 the acrylamide passes into the stomach of the individual.

8 Unfortunately, this diagram I picked didn't have an
9 esophagus, but eventually it passes down the esophagus into
10 the stomach, and you can see represented in the stomach the
11 AA.

12 Q. Okay.

13 A. From the gastrointestinal tract there is a
14 direct vein that feeds materials to the liver. This is called
15 the portal vein. And as a result, the chemical passes into
16 the liver before it gets systemically distributed. Okay?

17 Q. Um-hm.

18 A. In the liver -- the liver has a major role in
19 metabolism of foreign agents for the purpose of trying to get
20 rid of them from the body.

21 Q. So we call that detoxification?

22 A. Yes, well, it wants to get rid of them, okay?

23 Q. All right.

24 A. Whether or not it's toxic at that moment can
25 depend on what happens in the course of the metabolism.

26 Q. Okay.

27 A. In the liver there are a number of enzymes
28 which will act on that agent. One of those enzymes will

1 oxidize acrylamide to glycidamide. Glycidamide is the epoxide
2 form of oxidation of acrylamide.

3 Q. Is that enzyme you're referring to that famous
4 one called cytochrome P-450 2E1? Is that it?

5 A. That is the common enzyme for low molecular
6 weight vinyl type of compounds, yes. There's a bunch of
7 cytochrome P-450s. 2E1 is the form which is the primary
8 metabolism on compounds like vinyl chloride, butadiene as well
9 as acrylamide.

10 Q. Okay.

11 A. So in the liver metabolism is occurring, and
12 I'm going to show in a little more detail in the next slide,
13 but what I'm representing here is that this is how glycidamide
14 can get into our bloodstream.

15 Q. Wait a second. It was acrylamide. How did we
16 get to glycidamide?

17 A. By that cytochrome P-450 2E1 metabolism
18 oxidized acrylamide to glycidamide.

19 Q. So it converts or changes the acrylamide into
20 the genotoxic glycidamide?

21 A. This is extra additionally called an activation
22 step because the glycidamide is the activated form of major
23 concern for acrylamide exposure.

24 Q. All right. So now we have glycidamide in a
25 vein, right?

26 A. Right. And as a consequence, so you can see
27 within here how materials get distributed in the venous blood,
28 which is shown as blue, where it's passing into the heart and

1 the lungs and get distributed. Eventually, it comes back to
2 the heart and then passes into the arterial blood, and you can
3 see even on the right side there at AA. That's acrylamide
4 which hasn't been metabolized, which also exited the liver
5 unmetabolized, can also get distributed to other organs within
6 the body. And some of it will go back to the liver. Some
7 will go on to other organs.

8 So what this diagram is intended to do is just to
9 show how chemicals which are ingested can be distributed
10 throughout the body and a role for liver in the metabolism of
11 that particular agent.

12 Q. All right. I believe you're going to tell us
13 now about specifically metabolism of acrylamide in the liver.

14 A. Okay. So this is now the liver where we're
15 just talking about the metabolism of acrylamide. So you can
16 see in the upper left, that's acrylamide. Acrylamide can
17 undergo two different pathways of metabolism. One is the
18 cytochrome P-450. And that we would call an activation step
19 forming glycidamide, or the acrylamide may be conjugated with
20 glutathione. You may remember this morning when I mentioned
21 cysteine binding to acrylamide. Glutathione is the three
22 amino acid molecule which can bind to acrylamide.

23 And in the liver this is catalyzed by an enzyme
24 called glutathione S-transferase. Once that happens, like I
25 mentioned with cysteine, that metabolite is no longer able to
26 be oxidized to glycidamide. So that's a detox pathway.

27 Glycidamide itself can also be conjugated with
28 glutathione by glutathione S-transferase, forming conjugates,

1 glutathione conjugates of glycidamide, or it can undergo
2 hydrolysis to glyceramide.

3 So you have competing pathways and the direction of
4 that pathway depends in essence on the affinity of the enzymes
5 for acrylamide.

6 So the P-451 typically has a stronger affinity than
7 the glutathione transferases. But one thing I also want to
8 point out is that these enzymes, the epoxide hydrolase and the
9 glutathione S-transferase, are what we call polymorphic,
10 meaning that there are different forms of that enzyme in
11 different people within the population. Polymorphism would
12 represent at least 1 percent of a population having an altered
13 form of that. And some of these polymorphisms result in
14 lacking the activity of certain of these enzymes.

15 So, for example, there are a number of glutathione
16 transferases. But there are polymorphisms that some people
17 lack an enzyme which is capable of causing that detoxification
18 pathway as efficiently as another individual.

19 So to me, polymorphism is an important issue because
20 not everybody is the same in terms of how they will activate
21 and detoxify the enzyme.

22 And one other thing on cytochrome P-450 2E1, it's
23 also an inducible enzyme.

24 Q. Meaning what?

25 A. Meaning there are certain agents which will
26 increase the level of cytochrome 450 in people exposed to
27 certain drugs. Alcohol, for example, is an inducer of
28 cytochrome P-450 2E1.

1 So the metabolism can vary substantially in
2 individuals because of the levels of activities of these
3 enzymes which are activating and detoxifying acrylamide.

4 Q. So why is this all important?

5 A. The importance is we're trying to characterize
6 what I mentioned earlier, the dosimetry of glycidamide.
7 Because the belief is that glycidamide is the primary
8 carcinogen of exposure to acrylamide. It doesn't mean
9 acrylamide doesn't do anything. It's just that glycidamide is
10 the stronger genotoxic agent that binds to the DNA.

11 So in order to understand the risk associated with
12 exposure to acrylamide, you want to understand what is the
13 dosimetry, which I mentioned before is the concentration in a
14 tissue over the time that that compound is in there.

15 So like in the liver, you can see acrylamide enters.
16 As soon as you finish your coffee, the acrylamide is being
17 metabolized. Some is being distributed. Some is
18 disappearing. Glycidamide is formed. It's also being
19 metabolized away, or it may bind to certain structures.

20 So to understand the risk of exposure to an agent
21 such as acrylamide, there are a number of ways to calculate
22 exposure or dose. One is just what are you exposed to.
23 Milligrams per kilogram.

24 Another is what is the internal dose of acrylamide.

25 Q. In a particular tissue?

26 A. Right. In particular tissues. And taking it
27 further, what is the tissue dose over time for glycidamide.

28 And that's what physiologically based

1 pharmacokinetic models are attempting to characterize so that
2 they could be used in a risk assessment as opposed to simply
3 saying what is the exposure that the individual received.

4 Q. All right. So are there various factors that
5 affect glycidamide in tissues?

6 A. Yes. This is the kind of information. And
7 this isn't all of it, but it's as many as I could fit on the
8 slide, that are involved in affecting the blood levels of
9 glycidamide exposure to acrylamide. And these are the types
10 of parameter values that would be included in a
11 physiologically based pharmacokinetic model. So when I say
12 physiologically based, this is not just two compartments of
13 something moving. This is taking into account breathing
14 rates, cardiac output, movement of materials in the blood.

15 So it accounts for the full physiological basis of
16 the organism, human or rodent, and it's pharmacokinetic, make
17 it changes its action that's happening. It's changing levels.
18 So this is what would lead into the formation of a
19 physiologically based pharmacokinetic model.

20 Q. If a physiologically based pharmacokinetic
21 model is well developed and supported, what goal is
22 accomplished? What do you do with that?

23 A. Well, you can, as I mentioned, there's a lot of
24 variability among humans. We can include different parameter
25 values into the model to see how individuals may respond
26 differently. We can identify the tissue level in humans
27 compared to rodents to see how well they compare. If we have
28 a good physiologically based pharmacokinetic model, then that

1 information could be used in the risk assessment as opposed to
2 body weight scaling for the pharmacokinetic portion of the
3 risk assessment.

4 Q. So if a physiologically based pharmacokinetic
5 model is validated and is well done and documented, does
6 that -- is the concept that this helps improve the risk
7 assessment?

8 A. Yes, definitely. This is the kind of work that
9 we've done with the 13 butadiene, for example. To
10 characterize the epoxide -- there's two epoxides with
11 butadiene concentrations in rodents and humans.

12 Q. When you say this is what we have done, is that
13 the national toxicology program? Who is the "we"?

14 A. The we is Michael Cohen, who is a mathematical
15 modeler, and myself, and we've published numerous papers on
16 this.

17 Q. And those are listed in your CV?

18 A. Yes.

19 Q. All right.

20 A. So I just want to finish on this.

21 Q. Yes, please.

22 A. So some of the types of information that you
23 want are, for example, how does it get absorbed from the
24 GI tract? What is the rate? Remember, this is kinetic
25 modeling. So we're interested in rates. What are the
26 parameters physiological, the heart in terms of how much blood
27 goes to various organs. What is the organ volume.

28 A partition code is a value which relates to the

1 distribution between the blood and the tissue itself. So
2 there would be a partition coefficient for a small crossing
3 from the blood into the liver or blood into the kidney.

4 Then we have the metabolic processes. What is the
5 rate of oxidation of acrylamide to glycidamide, to P-450 2E1.
6 The rate of glutathione conjugation, what I showed in the
7 liver. These are rates that you can input into a model, but
8 if you don't have them, you base it on the experimental data
9 that you have available, and you run the model to match the
10 experimental data such that the model will tell you this is
11 the best fitting parameter value that will match the
12 experimental data.

13 Q. Okay. And you have all of these other. Rates
14 of glutathione conjugation, hydrolysis of glycidamide,
15 transfer of glycidamide into blood. Binding of macro
16 molecules and excretion of glycidamide into urine. These are
17 a bunch of the things that you have --

18 A. You either have some of this information, for
19 example, binding to hemoglobin. You can do that externally in
20 vitro. In terms of setting up a model, if you have no idea
21 what the metabolic rate could be, you may have, for example,
22 in vitro measurements of the oxidation of a chemical like
23 acrylamide to glycidamide, and you can plug in that kind of
24 information into the model.

25 Now, the model is going to run. These are runs of
26 iterations looking for the best parameter values. And it may
27 say well, it's a little bit off. But this is the best I can
28 do in terms of fitting the model to the data. You don't fit

1 data to a model. The data is sacred. The model is what's
2 being adjusted to fit the data.

3 Q. Got it.

4 All right. So your next graph is entitled
5 physiologically based pharmacokinetic model. Could you
6 explain what this is.

7 A. So this is now in a different diagram. The
8 person that I showed earlier of what a model might look like.

9 So next, with an oral dose, you characterize it
10 entering into the GI tract. Some of it may pass into the
11 feces. Or it may enter into the GI blood and pass by the
12 portal vein into the liver blood and eventually come into the
13 liver where it can undergo metabolism.

14 So the model is intended to mimic the human or
15 rodent, depending on the nature of your data, to the extent
16 possible.

17 I don't have a connection between the venous blood
18 and arterial blood, but that's basically the heart and lung,
19 where the heart is pumping, and the lung is oxidizing.

20 Q. Okay. So what did you consider next regarding
21 the pharmacokinetics?

22 A. So I just hope it's clear that the model is
23 producing parameter values that are uncertain or unknown or
24 not well characterized to fit available data.

25 Now, one type of information which is useful to have
26 is the formation of adducts.

27 Q. Which are?

28 A. Adducts are basically addition products that

1 are formed when a material binds to something else and forms a
2 new product.

3 Q. Dr. Rappaport testified all about that in 2014.
4 I remember it now.

5 All right. So what about DNA and hemoglobin adducts
6 for acrylamide or glycidamide?

7 A. So glycidamide is a relatively small molecule.
8 It's only a few carbons. Three carbons with the epoxide. And
9 it will find places on DNA because as I mentioned earlier,
10 acrylamide and glycidamide in particular is an electrophile.
11 It's looking for electrons that it can bind to. When it's in
12 the formation of an epoxide, it's less stable than the
13 acrylamide itself. It is looking for those electrons to allow
14 that strain on the epoxide to be relieved, and it can find
15 those electrons in DNA. It can bind to where there may be
16 certain free amines on the DNA basis that I mentioned earlier
17 briefly and form a DNA adduct.

18 Also, both acrylamide and glycidamide have been
19 shown to form adducts with hemoglobin. There's a particular
20 site, the terminal valine amino acid, where these tend to show
21 good binding, and this is another characteristic of epoxide
22 and other electrophilic compounds.

23 Q. And why are you looking at hemoglobin adducts
24 in particular?

25 A. In the next slide I want to try to explain the
26 concept of area under the curve.

27 Q. Okay.

28 A. Okay. Because I believe you've heard that

1 term. It may have been explained adequately. Maybe it
2 wasn't. But just to keep everybody in the same understanding.

3 So with what is plotted here is the blood
4 concentration over time. And if we gave a dose, as I show
5 there, of a compound such as acrylamide, there's going to be a
6 rise in the blood levels of acrylamide or glycidamide,
7 depending on what is measured because it may have come from
8 passing through the liver if it wasn't all metabolized as the
9 acrylamide. Some acrylamide will wind up in the blood. And
10 glycidamide will also wind up in the blood.

11 So you can see this is not an experimental data set.

12 Q. This is illustrative?

13 A. Illustrative, right. So because starting off
14 with essentially zero, you see an increase, and with time it's
15 going to decrease because it's being metabolized away and
16 eventually excreted. That's what the body wants to do. It
17 wants to get rid of it. But unfortunately, the body activated
18 it as well.

19 So this would represent the AUC for glycidamide or
20 acrylamide in the blood. And that then becomes a marker of
21 the internal dosimetry because we're looking at time and
22 concentration at the same -- on the same graph. So that area
23 under the blue curve is what is called the area under the
24 curve.

25 For hemoglobin it's a little bit different. You can
26 see it rises, and these values are not necessarily scaled
27 properly. But it rises, and it remains eventually flat. And
28 the reason for this is that once it binds to hemoglobin, it

1 forms a stable adduct, but it doesn't disappear until the red
2 blood cell undergoes degradation. And the red blood cell has
3 a half life somewhere around three, four months.

4 So it can remain in the blood for some time, and
5 this then becomes a valuable biomarker for exposure, but it's
6 also then used in trying to determine the relative hemoglobin
7 adduct levels for glycidamide across species.

8 So what I showed here, though, was a theoretical
9 curve. Now, the model -- this might be the output of a model.
10 But I didn't show data. And if I showed X's on that blue
11 line, that would have said wow, that model did a great job of
12 representing the experimental data. We've got some pretty
13 good confidence.

14 If I put those little dots of what the measurements
15 were, and they are all over the place, or maybe one of the
16 compounds increases whereas the model is showing a decrease
17 and say wait a second. That's not a very good fit of the
18 model to the data.

19 So what you need to do is if you think you have a
20 good fit, because you fit it to a particular data set, is to
21 try to validate that you got it right.

22 Q. How do you do that?

23 A. Validation would be to test your model with a
24 different set of data. So if you have blood time course data
25 in rodents, if you have it in humans and you try to fit a
26 model to that, you may look at an alternative exposure and see
27 whether the model still predicts the levels that are
28 determined experimentally.

1 So what we're looking at, does the model predict the
2 actual outcome, and the outcome is the data. So the data is
3 sacred. The model needs to fit the data.

4 Q. Okay. All right. So how does this concept
5 that you just described, explained, how does this now fit into
6 the risk assessment?

7 A. Okay. So the risk assessment, as I mentioned,
8 could be done based on the actual exposure, but if you have a
9 model and the model is valid and good, then maybe you can use
10 the model in replacement of the body weight scaling factor.

11 So a body weight scaling factor is to adjust the
12 animal cancer potency for differences in animals and humans
13 for pharmacokinetic and pharmacodynamic differences. There's
14 two aspects. The pharmacokinetics, characterizing the
15 internalized dosimetry. What is the dose that gets to the
16 tissue. And the pharmacodynamics is what is the change that
17 occurs in the tissue as a consequence of that dose of the
18 chemical.

19 So a pharmacodynamic property might be causing DNA
20 damage, as an example, or a mutation. What is that
21 relationship. Now, there's very little pharmacodynamic
22 information. So the focus has now been for acrylamide on the
23 pharmacokinetic factor.

24 And Prop 65 says you can make a pharmacokinetic
25 adjustment when the data can be taken into account with
26 confidence, and that's what I want to explore. Can we take it
27 into account with confidence.

28 So the PK factor, as I mentioned, can be the ratio

1 of the blood area under the curve of glycidamide. That would
2 be the carcinogen in exposed humans compared to the blood area
3 under the curve of glycidamide in the exposed animal.

4 So we're comparing a ratio. Is there greater, less,
5 or what is that value? Okay? And that's what has been
6 attempted in this particular case.

7 Alternatively, it is the ratio of the area under the
8 curve of the hemoglobin adducts in exposed humans compared to
9 exposed animals. So when I showed you the AUC graphs, we're
10 comparing those area under the curve for humans versus rodents
11 to see how do these stack up with respect to how the body is
12 absorbing, metabolizing, and eliminating glycidamide.

13 Q. Okay. So what's the next step?

14 A. I looked at what Dr. Rhomberg did. And in my
15 feeling the PK factors that he used didn't meet this level of
16 confidence, that they are not reliable.

17 And this is what I hope to explain over the next
18 series of slides. But for mice, they used a pharmacokinetic
19 model for the tumors induced in mice, and this was a model
20 that actually was not used by EPA. The model that was
21 available at that time was the model by Young. And it's been
22 referred to, I know, in this case from 2007. Young developed
23 a PBPK physiologically based pharmacokinetic model for rats,
24 mice, and humans. That's pretty much the title of their
25 publication.

26 Now, why wouldn't EPA use that model for rats since
27 in 2010 when they did their risk assessment, they were -- they
28 had rat tumor data. And here was the Young model which was

1 available. But they claimed you can't because --

2 Q. You can't what?

3 A. Use that model for risk assessment. So as I
4 mentioned, there are a number of parameter values which come
5 out of a model.

6 Now, when you have multiple data sets, so for
7 example, you may have one data set in which the animal was
8 exposed by what we call gavage, it's a bolus dose injected
9 into the animal's stomach. It's with a syringe with a bill
10 hard ball at the end so you don't scratch the esophagus. And
11 it places a bolus dose of that chemical right into the stomach
12 of the animal.

13 Alternatively, you may expose the animal in drinking
14 water, such as was done in the two-year study, or in the feed.
15 And in that case, rather than seeing it all come in at once,
16 it's coming in more slowly. And the data will be different,
17 but the parameter values, these are called rate constants.
18 They are expected to be constant by definition.

19 So unfortunately, within the Young model, they
20 needed different rate constants to fit different data sets.
21 And EPA said, which I agree, is that you need to find a single
22 set of data of parameters that will fit all of the data.

23 And another thing which I hadn't mentioned was you
24 also need to look at a sensitivity analysis of your parameter
25 values. Now, why do you do a sensitivity analysis? Because
26 there's uncertainty. When your model gives you a parameter,
27 say, a rate for oxidation of glycidamide, or for GST. If you
28 don't have that parameter value very carefully determined, if

1 this is coming out of your model and you have multiple values,
2 one thing is which one do you use?

3 Secondly, is how big of an impact is it on the
4 outcome of the model if that parameter value is off by a
5 little bit? And that's what you do with a sensitivity
6 analysis. You are trying to check up on your parameters to
7 see is a small error in that parameter going to have a big
8 impact or a little impact on the output of the model. Because
9 if it has a big impact, you've got to be careful that you have
10 the right parameter value because you're going to get answers
11 all over the place. If it's a small value, it won't matter so
12 much if that parameter is off by a little bit.

13 So you can test your model by varying parameter
14 value, maybe by 10 percent or so, and seeing how well did that
15 affect the fit of the model to the data.

16 And that's what a sensitivity analysis entails. So
17 EPA, and I agree, said that by having multiple parameters to
18 fit multiple data sets and no sensitivity analysis, the model
19 was not ready for use in risk assessment.

20 Q. Are you referring to the Young model?

21 A. Exactly. That's the Young paper in which the
22 model was produced.

23 Q. So in the EPA risk assessment for acrylamide,
24 the EPA rejected and did not use the Young pharmacokinetic
25 model?

26 A. That is correct. Now, remember, that was for
27 rats.

28 Q. Okay.

1 A. Because at that time EPA only had rat tumor
2 data. But the Young model was available in 2007. And it had
3 also a model for rats. But that rat model then was not
4 accepted for use by EPA in their risk assessment of
5 acrylamide.

6 Q. So what about mice?

7 A. Okay. So Dr. Rhomberg derived a PK factor for
8 mice. And his determination of that value, again, this would
9 be the area under the curve for mice, was based on the Young
10 model, the Young 2007 model, of which there was information in
11 terms of a prediction of that area under the curve, in the
12 blood of mice from the Young model.

13 However, the data that was used for that model was
14 by a co-author of the Young paper, Dan Doerge. This is from
15 the FDA laboratories outside of Little Rock, Arkansas, that
16 there is actual data, actual serum measurements. And rather
17 than using the serum measurements, which is data, they used --
18 he used --

19 Q. Who is the "they"?

20 A. I'm sorry. Dr. Rhomberg used, and he was
21 basing it somewhat on the EFSA document, but he used the
22 model-based estimate. And now, as I said a couple of times,
23 the data is sacred. The model is trying to mimic, to explain
24 the data.

25 So this is a criticism of the use of the mouse model
26 for the AUC. This is the blood concentration over time rather
27 than using actual data.

28 Q. So I'm not understanding. There was data for

1 mice, area under the curve. What did Dr. Rhomberg use?

2 A. He used the model prediction of the area under
3 the curve.

4 Q. Is there any precedent or authority for doing
5 that?

6 A. Well, in my view I don't know if there's
7 precedent or not, but data --

8 Q. You should use the data.

9 A. If I can use the word, trump's model
10 predictions -- one is a predicted value based on fitting model
11 parameters which have uncertainties in them compared to actual
12 data. If you have actual data, that is primary.

13 Q. Okay. And did you assess what the impact
14 Dr. Rhomberg's use of a prediction rather than the data that
15 was available, how that affected his calculated NSRL?

16 A. This causes a decrease right now in the PK
17 factor.

18 Q. Okay.

19 A. And it's -- if you use body weight scaling, the
20 PK factor for pharmacokinetics is approximately 1.9. I'm
21 sorry. We're dealing with mice. I don't know what the number
22 is offhand. But by using the model instead of the data, the
23 decrease is approximately 10 or 20 percent.

24 Q. The decrease is the PK factor?

25 A. Yes.

26 Q. And what effect does that have?

27 A. That's comparable in decrease in the potency
28 index for the chemical by that same proportion.

1 Q. Okay. And did Dr. Rhomberg, in doing this, use
2 data from gavage or from dietary administration?

3 A. Okay. In a paper by Doerge, again, this is
4 from the FDA laboratories outside of Little Rock. They
5 provided information on area under the curve AUC for mice for
6 both dietary as well as by gavage. And what they found was
7 that there's a difference. And as I mentioned, with gavage
8 it's a bolus dose which is good for characterizing a
9 parameter, but you can wind up with a difference if the
10 material is coming in more slowly, such as through drinking
11 water or consuming a diet.

12 The difference was by using the gavage
13 administration as opposed to the dietary, it decreases the PK
14 factor by 60 to 70 percent. And the consequence of that on
15 the NSRL is to increase the NSRL by 3.3 for male mice and 2.3
16 for female mice.

17 So which one is more appropriate? Well, most humans
18 don't just gulp through coffee like we do with the gavage
19 experiment in animals. And they may consume coffee over the
20 course of a day.

21 The NTP's carcinogenicity study was a drinking water
22 study. So it wasn't a situation in which the animals received
23 all of their dose was one bolus by gavage. So to me the more
24 appropriate value to use for the AUC would be the drinking
25 water or the dietary administration AUC that had available
26 data. It was there. But that wasn't used to calculate a PK
27 factor for mice. And as I say, this has a reasonably big
28 increase in the NSRL for male mice and for female mice by 2.3

1 and 3.3 fold.

2 Q. Okay. Well, what about the serum glycidamide
3 under the curve for humans?

4 A. Well, this one becomes a major problem because,
5 as I mentioned, to get a PK factor, you're comparing the area
6 under the curve in humans compared to rodents. Okay? So up
7 to here, we were discussing the issues and problems with how
8 the rodent AUC was determined.

9 But now we're looking at how do we get an AUC for
10 humans. As I mentioned, the Young model, it's multiple
11 models. They also developed a model for humans. However,
12 that model was never validated.

13 Q. What does that mean in this context?

14 A. Well, in this context there was no human blood
15 data in order to determine whether the predictions of the
16 blood levels were correct. Because the model is predicting
17 that AUC blood levels of glycidamide in human blood, and they
18 have no blood data to which they can parameterize their model
19 or validate it.

20 So you can make a prediction with a model. A model
21 is a hypothesis until it's demonstrated to be accurate. So
22 you have a hypothesis, but it's untested because you don't
23 have the blood data that enables you to say yes, the model
24 that we created actually does reflect the blood concentrations
25 in humans.

26 And if you had one set of good data and you created
27 a model, you can't use the same data set to validate the model
28 because if you use the same data set, you're going to be right

1 100 percent of the time. Because you create a model with the
2 data set, and then you can say well, let's see how well it did
3 against the data set. And, of course, you're going to get it
4 right. So you need an alternative data set to see whether you
5 can actually show that your model can predict other
6 circumstances.

7 Now, for the human glycidamide PBPK model, there was
8 some data available, but it wasn't blood data. It was urinary
9 metabolites that were determined from a paper by Fuhr taken
10 from six healthy individuals who consumed a meal containing
11 acrylamide. So what the model has for its data set are
12 concentrations of those glutathione conjugated metabolites
13 that I showed in the liver that eventually get excreted in the
14 urine.

15 So you have these metabolites in the urine. And
16 from that information, you're trying to predict the blood
17 concentration of glycidamide which led to those excretions in
18 the urine.

19 So to me this is not a very strong data set in which
20 to create a model because you're using urine measurements to
21 predict rates of metabolism in the liver and consequent
22 concentrations of glycidamide in the blood.

23 And as I mentioned, those enzymes are also
24 polymorphic, and there was a study done by Duale in which they
25 compared in humans the ratio of glycidamide to acrylamide
26 hemoglobin adducts because this gives a reflection whether
27 it's constant or variable. And they saw a ninefold
28 variability among 44 individuals in whom they measured this

1 adduct level. This is just the measurement in which it's
2 dietary exposure that happens naturally to humans.

3 So you got a variability effect, and unfortunately,
4 the agencies don't know how to deal with variability. And
5 they don't adjust for it. But if you had a good
6 physiologically based pharmacokinetic model and you knew a
7 distribution of these parameter values, you can plug that in
8 and come up with the determination of how human variability
9 impacts the risk.

10 Q. And what do you conclude regarding this?

11 A. Well, that the use of a human model has no
12 reliability for determining a pharmacokinetic factor. It's
13 totally unreliable. It's not based on sufficient data. And
14 in my view, you can't use the human proposal for the area
15 under the curve for glycidamide based on the model and the
16 limited data set that was available for creating the model.
17 So my view is that the pharmacokinetic adjustment factors that
18 were used have no scientific basis.

19 Q. All right. And I think you mentioned that for
20 Prop 65, you could use a pharmacokinetic factor where the data
21 was -- did you say with confidence, where you could -- what
22 was that?

23 A. I'll have to go back to see how Prop 65 words
24 it. You need to have good confidence in -- a pharmacokinetic
25 adjustment may be made when available data can be taken into
26 account with confidence.

27 Q. And in your opinion can the available data be
28 taken into account with confidence?

1 A. I have no confidence in the PK factor that is
2 used for the mouse tumor response.

3 Q. So what was the effect of Dr. Rhomberg's using
4 PK factors that he derived based upon the Young and the Doerge
5 or the Young model and the Doerge data instead of using the
6 body weight scaling?

7 A. I have a table coming up with two slides after
8 we do the rat on this.

9 Q. Oh, we still have the rat to do. Okay.

10 A. But as a hint to your question, it raises the
11 NSRL by about four- to fivefold.

12 Q. Okay. I didn't mean to cut you off. Can you
13 tell us what was the significance regarding the rat?

14 A. Okay. So the rat was based on hemoglobin
15 adducts. The rat was based on glycidamide-hemoglobin adducts
16 that were measured in rats and humans. There were six
17 individuals per dose group. And the hemoglobin adducts were
18 measured 24 hours after acrylamide dosing.

19 A couple of concerns that I have on that. One is
20 the recovery of urinary metabolites in this study was
21 34 percent for humans and 50 percent for rats. Now, I know
22 we're talking about hemoglobin adducts. But my concern is
23 that they may not have formed sufficient number of hemoglobin
24 adducts from glycidamide. And if we can go back one slide.
25 Let me explain.

26 This is the actual data from Fuhr that was used for
27 creating the human model. But I just want to point out the
28 different relationships that you can see here for the

1 glycidamide adduct, which is the bottom one versus the
2 acrylamide conjugates in the urine at 24 hours.

3 So what you can see is for the acrylamide, the top
4 two, this is acrylamide glutathione conjugates in the urine.
5 By 24 hours it's not changing in the top. It's almost
6 complete for the middle one, but if you look at the third one,
7 that's for glycidamide urinary adducts. They are still
8 increasing with time. And, in fact, in many cases it's only
9 50 percent recovery at 24 hours compared to 72 hours, which to
10 me implies that there's more glycidamide in the human which
11 hasn't been excreted totally.

12 And therefore, when we consider the use of the PK
13 factor for rats, it may have some uncertainties, inaccuracies.
14 The 1.2 has been used by -- OEHHA used it, but I don't think
15 anyone has looked at this kind of consideration. Are the
16 glycidamide concentrations fully accounted for in the
17 estimation of the glycidamide-hemoglobin adducts for the area
18 under the curve.

19 So if you go to the next slide, with 34 percent
20 recovery, I have some concern that we may not have a full
21 determination of the -- we're using the hemoglobin adducts as
22 a surrogate for glycidamide concentrations that we may not
23 have fully evaluated in this particular study for phenyls, the
24 phenyl paper may not have fully evaluated the glycidamide
25 concentration to hemoglobin by stopping their study at
26 24 hours.

27 THE COURT: At this time we'll take the afternoon
28 recess for 15 minutes.

1 You can step down, Dr. Melnick. And I'm going to
2 call another case.

3 (Recess taken.)

4 THE COURT: All right. Back on the record.

5 Counsel, you may proceed.

6 MR. METZGER: Thank you, your Honor.

7 Q. Dr. Melnick, thank you for the explanation
8 regarding the pharmacokinetic modeling.

9 Now what I'd like to ask you is if you've assessed
10 the effect from Dr. Rhomberg's use of pharmacokinetic factors
11 instead of body weight scaling on the derivation of the no
12 significant risk level.

13 A. Certainly. I hope it's in the next slide.
14 Yes, that looks like it.

15 Q. All right. So let me first ask you to address
16 how the use of the PK factors versus body weight scaling
17 affected cancer potency.

18 A. Okay. That is the second column, labeled
19 potency, with the cancer slope factors for animals compared
20 and converted to the cancer slope factor for human equivalent
21 dose.

22 So the values in that particular set there indicate
23 how the PK factor influences potency of comparing body weight
24 scaling versus PK factor.

25 And in each of these cases you can see there is a
26 decrease in cancer potency, for male rat from 3.6 to 2.3.

27 Female rat, 4.0 to 2.4.

28 Male mouse, 6.1 to 1.3.

1 And female mouse, 7.3 to 1.9.

2 So in each case potency is reduced by using a PK
3 factor instead of body weight scale.

4 Q. And how did the use by Dr. Rhomberg of the PK
5 factors that he selected affect the no significant risk level
6 compared to body weight scaling?

7 A. So in each case here, the reversal, with less
8 potency there's an increase in the NSRL. And it's showing
9 NSRLs at one times 10 to the minus 5. That there is an
10 increase with the body weight scaling compared -- with the PK
11 factor compared to body weight scaling. And that ratio is
12 shown in the fourth column, what is the effect on NSRL.

13 And this would be the ratio of that previous column
14 for the PK factor relative to the body weight scaling
15 adjustment. And you can see for the male rat, the PK factor
16 is increased 50 percent. Same with the female rat.

17 Q. The NSRL or the PK factor?

18 A. This is the NSRL. The effect of applying a PK
19 factor instead of body weight scaling on the NSRL. So there's
20 a 50 percent increase in the NSRL based on male rat and female
21 rat tumor responses. But with the mouse, it's more than a
22 fivefold increase for the male mouse and a three and a half
23 fold increase for the female mouse.

24 So these are substantial increases.

25 Q. On the NSRL?

26 A. On the NSRL, yes.

27 Q. Okay. And did you assess -- oh, by the way,
28 before we leave that, this is the NSRL which is one cancer per

1 1,000, correct?

2 A. That is correct.

3 Q. And Dr. Rhomberg calculated an ASRL by
4 multiplying the NSRL by 10; is that correct?

5 A. To make an adjustment of one per hundred
6 thousand or 10 to the minus 5 to one times 10 to the minus 4,
7 it is a multiple of 10, yes.

8 Q. All right. So for Dr. Rhomberg's ASRL, the
9 effect of the body of the pharmacokinetic factor instead of
10 body weight scaling, that would be a 15-fold increase for the
11 male rat and the female rat?

12 A. Right. So I showed this as based on one per
13 hundred thousand, if you multiply that by 10, that would be
14 the consequence at one times 10 to the minus 4.

15 Q. All right. And have you also assessed the
16 effect on the NSRL of using the tumor sites and body weight
17 scaling?

18 A. Yes. So this is a combination of both of these
19 factors which I've been discussing this afternoon.

20 Q. What two factors, please, for the record?

21 A. I'm sorry. Including all tumor sites as
22 opposed to excluding tumor sites and using body weight scaling
23 as opposed to a PK factor.

24 Q. Right. So if you include all tumor sites and
25 apply a body weight scaling from animal potency to human
26 potency, the NSRL would be derived would be 1.0 for male rat,
27 .8 for female rat, .3 for male mouse, and .4 for the female
28 mouse. This is at the one times 10 to the minus 5 cancer

1 risk.

2 Now, the next column is the NSRLs that Rhomberg --
3 Dr. Rhomberg has proposed for risk at one times 10 to the
4 minus 5, not his one times 10 to the minus 4. But in this
5 case it's based on the exclusion of sites.

6 So I just want to look at what is the effect if we
7 include all sites versus Rhomberg -- Dr. Rhomberg's exclusion
8 of sites, and use body weight scaling.

9 You can see the effects on the NSRL for the male rat
10 is approximately twofold higher at 10 to the minus 5 risk.

11 4.4 for the female rat.

12 25 for the male mouse?

13 25 fold?

14 A. 25 fold.

15 And 7.8 for the female mouse. The consequence of
16 this is that the male mouse or the female mouse are no longer
17 the most sensitive species for the risk assessment. The rat
18 has become, by Dr. Rhomberg's calculations, the sensitive
19 species for calculating risk.

20 Q. And what is the import of that?

21 A. Well, as I indicated, I don't see a basis for
22 excluding tumor sites. And I don't see a basis for applying a
23 pharmacokinetic factor; however, if you do that, you are
24 decreasing the potency of the response, but most important is
25 leading to an increase in the NSRL by quite a substantial
26 number, especially for male mice.

27 Q. Okay. All right. So let's talk now about the
28 quantitative risk assessment. And was there a particular part

1 of the final statement of reasons adopted by OEHHA regarding
2 quantitative risk assessment that you considered to be
3 important in your analysis?

4 A. Yes. This is in the addendum to the final
5 statement of reasons.

6 Q. And what is the risk?

7 A. That the necessity is to show that a beneficial
8 health effect outweighs the risks. That is the requirement as
9 stated within the final statement of reasons. If that cannot
10 be done, then the application of the one times 10 to the
11 minus -- something different than 10 to the minus 5 is not
12 available. That one times 10 to the minus 5 then becomes the
13 standard unless the health benefits can be demonstrated to
14 outweigh any health risks.

15 Q. Okay. And do you have opinions on health
16 benefits and health risks that we're going to talk about?

17 A. We can talk about that.

18 Q. Okay. All right. So first of all, is there a
19 methodology for quantitatively assessing health benefits and
20 health detriments of a food?

21 A. A methodology has been written into the
22 literature in 2012. It's called by the acronym BRAFO, or
23 benefit risk analysis for foods.

24 MR. KENNEDY: Object and move to strike. The
25 benefit analysis has already been done by the agency.

26 THE COURT: Objection overruled.

27 Q. BY MR. METZGER: All right. And who did this?

28 A. Who developed this methodology?

1 Q. Yes.

2 A. Okay. This was a project funded by the
3 European Commission coordinated by the International Life
4 Sciences Institute. I've served as a reviewer for some of the
5 European Commission projects. What they tried to do is
6 identify an important health issue and encourage investigators
7 from different countries within the European union to develop
8 an approach to answer that particular question. And that's
9 what was done. And it was titled then How to Perform a
10 Benefit Risk Analysis For Foods.

11 Q. And has this methodology been subjected to
12 publication and peer review?

13 A. Yes, this was published in the peer-reviewed
14 literature.

15 Q. All right. Could you explain to the Court what
16 this BRAFO technology or methodology is that quantitatively
17 assesses health benefits and detriments?

18 A. It's basically a comparison of health risks and
19 health benefits of a reference condition. And I provide this
20 as the reference scenario being coffee at the current
21 acrylamide levels.

22 And the alternative would be coffee at reduced
23 acrylamide levels.

24 So the comparison to look for this analysis is to
25 see how these match up. For example, it's a four-tier
26 process. If there's no benefits from the alternative, that
27 would be, for example, reducing acrylamide in coffee, then why
28 do it? The reference would be advised.

1 However, if there are only benefits with the
2 alternative, removing acrylamide from coffee, then that is the
3 preferred scenario.

4 So it's a qualitative determination. Are there
5 benefits from the alternative or not. And if there are
6 benefits, then we can -- and that's all, then we can stop at
7 Tier 1.

8 However, if risks dominate benefits from the
9 alternative, then the reference is advised. So when you have
10 benefits and risks, if the risks are greater from the
11 alternative, removing acrylamide from coffee, then you stay
12 with the current -- the reference.

13 However, if benefits of the alternative dominate the
14 risks, then the alternative is preferred. So it's comparing
15 benefits and risks for two different scenarios.

16 It then can get more complex in the assessment
17 because what if there's both risks and benefits. And this now
18 goes into quantitative analyses because now we need to find
19 some parameter values that allow a comparison of benefits and
20 risks.

21 So, for example, a willingness to pay to avoid an
22 adverse disease is a numerical value that might be obtainable
23 from this comparison or to avoid -- or a disability, how many
24 changes in the quality adjusted years or avoiding adverse
25 health disabilities.

26 So you start to look at what are you gaining and
27 what are you losing between the two with respect to quality
28 and disabilities and see if one dominates the other in a

1 quantitative way.

2 Q. Let me ask you, under Tiers 3 and 4, which
3 involve quantitative integration of risks and benefits, could
4 one do an analysis using the BRAFO methodology where you,
5 apart from just acrylamide, but where you would quantify
6 health benefits of coffee, if there are any, and health
7 detriments of coffee?

8 A. That could certainly be done.

9 Q. So this methodology could be used to do that.

10 A. Right, yes.

11 Q. Okay. And could you tell us -- give us some
12 examples of how this methodology has been used to quantify
13 health benefits and detriments of foods?

14 A. So in one of the publications from the BRAFO
15 work -- and there were probably about five publications that
16 came out. One of them conducted a benefit/risk analysis for
17 potatoes and cereal products for acrylamide mitigation, and
18 that they conclude is the reference versus the use of
19 asparaginase to reuse acrylamide levels.

20 So it's something similar to what we're talking
21 about with respect to coffee. How do the benefit risks
22 compare in potatoes and cereal products before removing the
23 acrylamide or after you remove it, reduce the asparaginase. I
24 believe the reductions that they were considering were only
25 about 30 percent.

26 And that group concluded that you can stop at Tier
27 1. You don't need to go to Tier 2, 3, or 4 because of the
28 beneficial effects of reducing acrylamide in processed foods.

1 And that was it.

2 So Tier 1, if you recall I mentioned, if there are
3 only held benefits with the alternative, then why go further.
4 And that's what they concluded, and I agree. For potatoes and
5 cereal products, there is a benefit.

6 But they conclude that reducing acrylamide reducing
7 actions should be applied as long as any adverse side effects
8 are recognized and minimized to the extent possible. And that
9 makes public health sense.

10 So the fact that that can be done in terms of making
11 this comparison with potato and cereal products, I conclude
12 that that same analysis is applicable to acrylamide in coffee.

13 Q. Okay.

14 A. And that hasn't been done. There has been no
15 BRAFO analysis conducted by the defendants for acrylamide in
16 coffee.

17 Q. Okay. All right. So now let's talk about
18 sound considerations of public health and the use of a 10 to
19 the minus 5 standard or a 10 to the minus 4 cancer risk
20 standard.

21 What have you taken into account in answering that
22 question?

23 A. Well, I don't think I need to state, but it's
24 on my slide that I prepared, is that obviously cancer is a
25 devastating disease. It's costly. We know from records that
26 the number of new cancer cases per year in the United States
27 is 1.7 million. 176,000 in California. And there's a big
28 cost for health care, lost wages, and caregiving. 230- to

1 \$300 billion per year. So cancer is a disease we would
2 attempt to reduce to the incident possible. And myself coming
3 from an environmental cancer program, this is one which I feel
4 very strongly about, is cancer prevention. The diet is linked
5 to about 30 to 35 percent of human cancers --

6 Q. Let me ask you, that's about a third of human
7 cancers, and I think 40 percent of humans or something get
8 cancer?

9 THE COURT: Did you attempt to limit that to those
10 areas of cancer that could increase risk? In other words,
11 some specific cancers that were associated according to what
12 you said with acrylamide. The statement about cancer. Was it
13 limited to that? Or just cancer generically.

14 THE WITNESS: This is a general survey of cancer
15 rates within the United States and separate for states.

16 Q. BY MR. METZGER: So you've indicated here that
17 the diet is linked to about a third of human cancer. Where
18 does that come from?

19 A. There are reports in the literature where
20 people have made these types of estimations. In terms of
21 whether it's genetic factors, lifestyle habits, obesity. But
22 in these types of estimates, the diet was linked with
23 approximately 30 to 35 percent of human cancers, that there
24 are dietary components which are linked to increased cancers.

25 Q. And what are these dietary components or
26 constituents that are linked to human cancer?

27 A. Well, it's probably pretty complex because it
28 might be carcinogens in food. It might be high lipid -- high

1 fat diets can contribute. There's just an array of factors,
2 but one of those factors would be environmental contaminants.

3 Q. All right. So tell us -- you had some articles
4 about primary prevention of cancer. We discussed that
5 earlier. How does that play into this puzzle here?

6 A. Well, as I mentioned, the National Toxicology
7 Program where I worked conducts studies to identify agents
8 that can cause cancer. And this information then is used by
9 regulatory agencies to set limits on exposure of the public.
10 And this is identified as primary prevention. Prevent the
11 cancer from developing. And one way of doing that is reducing
12 or eliminating exposure to those agents that cause cancer.
13 And by doing that, it's serving as a public health protective
14 approach.

15 Q. And in the human diet, what constituents or
16 what are the carcinogens that are prevalent in the human diet?

17 MR. KENNEDY: Foundation.

18 THE COURT: Overruled.

19 THE WITNESS: Okay. Well, there are those caused by
20 overcooking meats. Processed meats are contributors. There
21 could be acrylamide as a factor. I'm trying to think of some
22 of the others offhand.

23 Q. BY MR. METZGER: Is acrylamide the most
24 prevalent carcinogen in the human diet?

25 MR. KENNEDY: Lack of foundation.

26 THE COURT: Overruled.

27 THE WITNESS: It's very prevalent in the human diet.
28 And of which, I believe, 40 percent for adults of acrylamide

1 exposure comes from coffee.

2 Q. BY MR. METZGER: All right. So let's talk
3 briefly about the carcinogenicity of acrylamide. And is that
4 something that you considered in forming your opinion
5 regarding sound considerations of public health?

6 THE COURT: Before we go there, let me ask you this:
7 Did you attempt to eliminate all of those other cancers caused
8 by foods other than coffee from all these statistics?

9 THE WITNESS: No, I haven't. I don't think
10 anybody's done that.

11 THE COURT: Mr. Metzger.

12 Q. BY MR. METZGER: All right. So what is your
13 assessment of acrylamide as a carcinogen in the context of
14 sound considerations of public health?

15 A. Okay. Well, based on my experience and
16 knowledge with epoxide-forming chemicals, I consider it of
17 high concern for acrylamide-induced cancers. This was
18 evaluated by IARC the last time, I believe, in 1994 and termed
19 a probable, probably carcinogenic to humans. This was based
20 on sufficient evidence in animals and, as I mentioned, those
21 were the Johnson and Freedman studies prior to the NTP
22 publication of their studies.

23 And part of the reason for this was many times a
24 carcinogen is active at one site. For acrylamide it's
25 carcinogenic at multiple sites in both sexes of two species,
26 rats and mice.

27 When a compound does that, it's likely to be also
28 carcinogenic in humans. However, there is inadequate evidence

1 for the carcinogenicity of acrylamide in humans. The data
2 don't exist. And consequently, IARC classified this as
3 probably carcinogenic to humans.

4 And in the IARC review process, what they include,
5 when inviting participants, is there's four groups. One
6 related to exposure. One evaluates the epidemiological data.
7 One evaluates the animal cancer data. And the fourth one
8 makes considerations of mechanistic information.

9 Even at that time in 1994, it was known that
10 acrylamide and its metabolite, glycidamide, were both known
11 that they form covalent DNA adducts in mice and rats.
12 Acrylamide in glycidamidic form, covalent adducts with
13 hemoglobin in humans and in rats.

14 So this shows that glycidamide is distributed
15 systemically in exposed humans, and I believe even one of the
16 studies that looked at urinary metabolites, I believe it was
17 the phenyl study, found glycidamide excreted in the urine.

18 So this is a compound that I have large concerns for
19 because of what it can do, that it is being systemically
20 distributed in humans, in the body of humans. And it induces
21 gene mutations and chromosomal aberrations in germ cells as
22 well as somatic cells in mice or rats. So this is a bad
23 compound.

24 Q. Okay. Tell us, if you would, based on your
25 research and your publications regarding epoxide chemicals,
26 their effects in different tumors in animals.

27 A. Okay. Well, there are certain sites, as
28 mentioned in my 2002 paper, where epoxides tend to form tumors

1 in animal models, rats or mice. And this commonality also
2 shows up for acrylamide and glycidamide.

3 So the mammary gland in rats, this was the site that
4 was used in the FAO/WHO risk assessment, is a site which is
5 vinyl chloride in 1,3-butadiene induced tumors, and
6 1,3-butadiene are established human carcinogens.

7 The mammary gland in mice was a site of tumor
8 induction by acrylamide and glycidamide.

9 The NTP conducted a study of acrylamide but also
10 conducted a study at that same time of glycidamide. So when I
11 show glycidamide up here, that is based on a separate study of
12 glycidamide in rats and mice.

13 So the mammary gland was a target for both
14 acrylamide and glycidamide, but the mammary gland in mice is
15 also a target for vinyl chloride, 1,3-butadiene and ethylene
16 oxide. Ethylene oxide is a Group 1 known human carcinogen.

17 And as we discussed earlier on the harderian gland,
18 this was the site used by EFSA for their acrylamide risk
19 assessment. Tumors are induced again by butadiene, ethylene
20 oxide, glycidamide, acrylamide, as well as other
21 epoxide-forming chemicals.

22 And lastly, in the lung of mice. Both acrylamide
23 and glycidamide induced tumors in the mouse lung, but so does
24 vinyl chloride, butadiene, ethylene oxide. So the picture I'm
25 trying to demonstrate here is glycidamide or exposure to
26 acrylamide which produces glycidamide is causing tumors
27 similar to known human carcinogens that are either epoxides or
28 metabolites to epoxides.

1 So we're seeing a lot of similarity between the two,
2 which leads me to believe that this is a likely, very likely
3 human carcinogen.

4 Q. And based on this, is it your opinion that
5 tumors of the mammary gland, the rats, the mice, and the
6 harderian gland should be included in human cancer risk
7 assessments for epoxide chemicals?

8 A. Definitely. Because as I mentioned before, for
9 the harderian gland, I consider this to be the canary in the
10 coal mine for epoxide-forming chemicals. I assume everybody
11 knows what that means.

12 Q. Okay. Thank you, Dr. Melnick.

13 Let's change topics and talk about the FDA guidance
14 for industry acrylamide in foods. You've reviewed that,
15 correct?

16 A. Yes, I have.

17 Q. Okay. And what was your assessment of that
18 publication?

19 A. Well, first of all, there were a number of
20 statements that the FDA made that I think are relevant to this
21 case. So, for example, reducing acrylamide in foods may
22 mitigate potential human risks from exposure to acrylamide.

23 So the FDA is recognizing that there are potential
24 health risks, and reducing that would be a valuable
25 consideration.

26 However, they also indicate, and this has been cited
27 in this case a number of times. FDA is not aware of any
28 proven mitigation measures for acrylamide in food and that a

1 viable commercial process is not yet available.

2 Q. I think you said food instead of coffee.

3 A. Oh. I'm sorry. I meant coffee. I guess I
4 can't read that well from here. I meant coffee.

5 Q. Okay.

6 A. Okay. My criticism of this is that the
7 statements in that second bullet are based on outdated
8 sources. One was from an article by Seal in 2008. And the
9 other is the coffee industry's tool box or the tool box for
10 industry on acrylamide for the Food Drink Europe, what they
11 use as their source of information for making this kind of
12 statement.

13 I went through this morning a number of mitigation
14 approaches. And those don't seem to have made it into the
15 FDA's guidance for industry. And there may be an explanation
16 in part for this.

17 Q. What is that?

18 A. Well, I believe that the FDA concealed
19 information from the FDA in 2000 --

20 Q. The FDA? I'm sorry?

21 A. The Nestle Company concealed information from
22 FDA in a meeting which, from a document written by one of the
23 coffee producers, this was Mwangi, M-W-A-N-G-I, that the
24 purpose of the meeting was to persuade FDA to not set
25 regulatory limits for acrylamide in coffee and told their
26 managers that we would not divulge any data that would be
27 damaging to us.

28 So to me the suppression of information might have

1 had some bearing on FDA not being aware of mitigation
2 measures.

3 MR. KENNEDY: Object. Move to strike as sheer
4 speculation.

5 THE COURT: Motion granted. No foundation for the
6 witness's statements. The whole answer will be stricken.

7 MR. KENNEDY: Object. No foundation, ask that the
8 answer be stricken.

9 THE COURT: I just said that. The answer is
10 stricken.

11 MR. KENNEDY: Okay. I'm sorry. I thought you were
12 telling me to say the magic words.

13 THE COURT: I'm sorry?

14 MR. KENNEDY: I'm sorry. I thought you were telling
15 me to say the magic words. I thought I had.

16 THE COURT: No. I granted the motion to strike.

17 Q. BY MR. METZGER: Dr. Melnick, did you review
18 some confidential documents in this case that were produced
19 which indicated that there was a meeting between Nestle
20 managers and the FDA and that the Nestle folks decided that
21 they would not disclose information to the FDA at that
22 meeting?

23 A. Yes, that --

24 MR. KENNEDY: Object, your Honor. Lack of
25 foundation, multiple levels of hearsay --

26 THE COURT: Let me hear the answer.

27 THE WITNESS: That meeting was described in these
28 confidential documents that I received, that the meeting

1 occurred in 2010 with Stadler and Mwangi. The meeting had
2 representatives from the FDA. But they wrote their purpose,
3 which I've already stated, but it was divulged in their
4 documents where Mwangi was describing his accomplishments for
5 the year.

6 THE COURT: Dr. Melnick, were you at any of these
7 meetings?

8 THE WITNESS: No, I wasn't.

9 THE COURT: All right. The answer is stricken.

10 Q. BY MR. METZGER: So now let's talk about
11 another of the defense's favorite documents, the USDA
12 Scientific Committee report, or the Dietary Advisory
13 Committee.

14 Have you reviewed that, Dr. Melnick?

15 A. Yes, I have.

16 Q. And what have you considered in that report
17 with respect to sound considerations of public health for
18 coffee consumption?

19 A. Okay. That document writes that moderate
20 coffee consumption can be incorporated into a healthy dietary
21 pattern, along with other healthful behaviors.

22 That statement is based on observational studies in
23 healthy individuals. Observational studies have limitations
24 in terms of their adequacy for determining causation. So it's
25 simply a statement that this is what they believe. However,
26 they do raise concerns about caffeinated coffee consumption by
27 pregnant women, children, and adults and adolescents or other
28 vulnerable individuals. And they also recommend minimizing

1 cream and sugar consumption. And they even make the comment
2 that individuals who do not consume caffeinated coffee should
3 not start to consume it.

4 So to me, if there's a health benefit, why would
5 they recommend not consuming it for any type of health benefit
6 if it doesn't exist?

7 Q. Okay. Now, regarding this statement that
8 moderate coffee consumption can be incorporated into a healthy
9 dietary pattern, does the FDA also say that soft drinks,
10 sodas, sugar sweetened beverages can be -- in moderate
11 consumption can be incorporated into a healthy diet?

12 A. Yes, they do.

13 Q. Do they also say the same for alcohol?

14 A. Yes.

15 Q. So now let's talk a little about the FDA and
16 coffee. First of all, has the FDA ever authorized any health
17 claim for coffee?

18 A. I was not able to find any health claim. And
19 we searched for those, and, in fact, EFSA rejected health
20 claims for coffee. There's no evidence that any government
21 agency has concluded that drinking coffee prevents cancer or
22 any chronic disease. And in reading the testimonies of
23 Dr. Kessler and Dr. Alexander, they also concluded that coffee
24 does not prevent any disease.

25 So there's no evidence for supporting health claims
26 in any sources that I'm aware of.

27 But one thing that concerns me about this document
28 from the USDA scientific report, the Dietary Guideline

1 Advisory Committee, is that the issue of acrylamide in food,
2 as he mentions, has been known since 2002. There have been
3 hundreds of papers regarding health concerns for acrylamide in
4 food. And when I looked into this document and try to search
5 for acrylamide to see how this Dietary Guideline Advisory
6 Committee would react to the presence of acrylamide in foods,
7 I found that it wasn't there.

8 There's no comment in this report regarding
9 acrylamide in foods. And obviously, if there's no comment
10 about it, there's no recommendation on an acceptable risk
11 level for this carcinogen in coffee.

12 So this report is totally silent on issues related
13 to acrylamide in foods and human health.

14 Q. Okay. So let's talk about the FDA and its
15 regulation of carcinogens.

16 Have you reviewed over the years the Food, Drug, and
17 Cosmetic Act, how that addresses carcinogens in food?

18 A. I've seen it. I haven't gone thoroughly
19 through reviewing it. But I'm aware of it from just
20 experience because, as I mentioned, the NTP is made up of
21 several agencies. FDA is one of the agencies that's part of
22 the NTP. So I'm aware that the Delaney clause prohibits FDA
23 from adopting regulations that allow carcinogenic food
24 additives. And their policy for regulating carcinogens is one
25 per million. One times 10 to the minus 6.

26 However, I'm aware of a couple of rare exceptions
27 that FDA has regulated carcinogens to allow more than one
28 cancer per 10,000.

1 Q. Okay. And let's talk about those rare
2 circumstances. What are those?

3 A. Well, the circumstances, first, are that the
4 food has proven to have a health benefit. And there is no
5 practical way of reducing those carcinogens in the food. The
6 chemicals, and these were mentioned by Dr. Kessler, of what
7 FDA has done. They have adopted a level of seven times 10 to
8 the minus 5 for PCBs, polychlorinated biphenyls, in fish. And
9 that's because fish contains omega 3 fatty acids which have
10 been established as effective in reducing coronary heart
11 disease. However, PCBs have been banned since approximately
12 1980.

13 So they are not being produced into the environment
14 anymore. But PCBs are very stable. So they are in the
15 environment, but the PCBs become incorporated into the fat or
16 lipid components in tissue, and they can remain there and are
17 essentially impossible to get out unless you removed the
18 source of the fat within the fish.

19 So if you pick up a fish which has PCBs, you can't
20 set -- it can't be eliminated. It's an issue that is
21 unsolvable at this time.

22 Q. So what is your understanding as to why the FDA
23 allowed a higher carcinogenic risk for PCBs in fish?

24 A. They had --

25 MR. KENNEDY: Object. Lack of foundation.

26 THE COURT: Overruled. You may answer.

27 THE WITNESS: They had an identified health benefit
28 which was recognized. The reduction of coronary heart disease

1 and the condition in which it could not be removed.

2 So in wanting people not to avoid fish, they adopted
3 a level of higher risk. How they came up with 7.2 times 10 to
4 the minus 5 I really don't know.

5 Q. BY MR. METZGER: Okay. And the other example
6 that Dr. Kessler mentioned was arsenic in rice. And what is
7 your understanding of how that came about?

8 A. This was for whole grains, that they reduce
9 cancer and coronary disease. So there's an established health
10 benefit. However, arsenic is a naturally occurring element,
11 and it can't be removed from rice. And the FDA adopted a
12 level of 3.9 times 10 to the minus 5. But how they got to
13 that number I don't know.

14 I think this is something related to your question
15 earlier this morning. How do you select the number? I really
16 don't know how FDA selected 7.2 and 3.9. It might be that
17 that was a level that wasn't overly excessive and could be
18 accommodated. But I really don't know.

19 Q. Dr. Melnick, are you aware of any other food
20 that the FDA has allowed a cancer risk at 10 to the minus 4?

21 A. No, I'm not aware of any. I haven't seen
22 anything like that.

23 Q. So are these, PCBs in fish and arsenic in rice,
24 rare exceptions to the FDA's one in a million cancer risk
25 policy?

26 A. These are definitely exceptions, and these are
27 higher concentrations or risk levels than 10 to the minus 4,
28 even for the PCBs in fish and arsenic in rice.

1 Q. Okay. You've also indicated here the EPA, how
2 it has regulated acrylamide in water.

3 And what is the significance of that to you?

4 A. Well, the significance is that the regulation
5 is at a half part per billion, which is close to the level of
6 the NSRL for -- from consumption of coffee. This has a use
7 for clarifying potable water, for treatment in waste water.
8 But again, it was one in which it could not be practically
9 removed from drinking water.

10 So EPA for carcinogens identifies what they call a
11 maximum contaminant level goal and a maximum contaminant
12 level. The goal is zero. But if you can't achieve it and
13 they feel that it serves a purpose, they can establish a
14 maximum contaminant level, and this would be the standard for
15 acrylamide in water.

16 Q. All right. Thank you. Now, in assessing sound
17 considerations of public health, have you evaluated whether
18 the epidemiologic studies regarding coffee consumption and
19 cancer or chronic disease provide support for a health
20 benefit?

21 A. Well, there's no evidence right now available
22 demonstrating an actual health benefit from coffee
23 consumption. Now, there have been observational
24 epidemiological studies that have shown inverse relationships,
25 but the FDA has already noted that observational studies
26 cannot determine whether such an observed relationship is one
27 in which the substance caused that reduction in disease or
28 whether it's coincidence. There's a reduction, but the basis

1 for it cannot be determined.

2 In contrast, intervention studies cannot
3 establish -- in comparison to intervention studies, the
4 observational studies cannot establish cause and effect. This
5 is what FDA has addressed for a number of years.

6 Q. And are any of the epidemiologic studies
7 regarding coffee consumption and cancer or chronic disease,
8 are any of those intervention studies?

9 A. No. I don't think they can actually be done.

10 Q. Okay. All right. So in assessing sound
11 considerations of public health, in your opinion is it
12 important to consider both health benefits and health
13 detriments?

14 A. Yes. That's similar to what I was talking
15 about earlier with BRAFO. You consider both the benefits and
16 the detriments in making a consideration for public health.

17 Q. Okay. And what have you concluded regarding
18 any health benefit from coffee consumption?

19 A. There's no agency or expert that can conclude
20 that coffee prevents any disease. The prevention of a disease
21 would be a reflection of the health benefit. But there's no
22 statements within the government or even in the defendants in
23 this case demonstrating causation for reduction of disease.

24 Q. In the absence of any health benefit of coffee
25 consumption, in your opinion do sound considerations of public
26 health justify allowing acrylamide exposure in excess of the
27 NSRL?

28 A. Well, I think that's the whole basis of this

1 consideration is that to consider it, it needs to demonstrate
2 that there's a benefit. Without the benefit, in my view this
3 does not justify allowing a level higher than the NSRL.

4 THE COURT: When you say allowing, are you talking
5 about without a warning? You're not talking about
6 prohibiting.

7 THE WITNESS: No.

8 MR. METZGER: Correct, your Honor.

9 Q. Right. Proposition 65 doesn't say you can't
10 expose people to carcinogens even at high levels, right?

11 A. Right. It's a labeling act. It's not a
12 banning act.

13 Q. Right. All right. So now let's talk about
14 acrylamide in coffee. What is your assessment regarding
15 acrylamide in coffee regarding sound considerations of public
16 health?

17 A. As a strong proponent of primary prevention,
18 reducing exposures to carcinogens can reduce what would be
19 preventable cancers among the exposed population. I think you
20 want to go forward a slide for the reading audience.

21 Q. Sure.

22 A. So in my view a sound policy, public health
23 policy, this is what public health is all about, from the view
24 of primary prevention, is to reduce the risk of diseases,
25 cancers among the exposed population.

26 And my concern, which I think I've expressed enough
27 today, is that acrylamide is not a good chemical. It is a
28 genotoxic carcinogen. There's no doubt about that. And

1 earlier, when we're talking about the margin of exposure,
2 again, this is -- I think I mentioned the dose associated with
3 a 150 percent excess cancer risk compared to human exposure
4 levels has been determined by both FAO/WHO, as well as EFSA,
5 in saying that margin of exposure is too low. It signifies a
6 high human health concern. And I share that concern that
7 these agencies have expressed.

8 Q. Is there any health benefit to acrylamide in
9 coffee?

10 A. No -- for acrylamide?

11 Q. Acrylamide.

12 A. No, there's no health benefit for acrylamide.

13 This is -- you know, back in the 60's, when people were
14 treating individuals with -- who had cancer, they were using
15 these kinds of compounds to destroy cancer cells. But what
16 they found on a number of cases was that they got an increase
17 in another type of cancer. Particularly non-Hodgkin's
18 lymphoma.

19 So a number of the chemotherapeutic drugs that were
20 used back in the 50's and 60's were these same type of
21 electrophilic compounds. The mustards, et cetera. But I
22 would not recommend using acrylamide as a health benefit, as a
23 chemotherapeutic drug. There's better ones out there.

24 Q. Is acrylamide an essential constituent of
25 coffee in your opinion?

26 A. No. It doesn't provide any value in coffee.
27 It doesn't provide flavor. There's no nutritive value from
28 acrylamide. That's for sure.

1 Q. All right. And in assessing sound
2 considerations of public health, what significance do you
3 attribute to the fact that, as you have testified, acrylamide
4 concentrations in coffee can be reduced by about 90 percent
5 without negatively affecting palatability?

6 A. Well, therefore, the approach that I would
7 recommend very strongly is because it can be selectively
8 reduced, and it can be reduced without affecting significantly
9 palatability, there's no reason why that approach should not
10 be taken because it can be done. It's doable.

11 So if you can remove the acrylamide, which I believe
12 can be done, I would prefer that coffee had lower levels of
13 acrylamide rather than having a label.

14 Q. A cancer warning label, you mean.

15 A. Yeah. You know, I'm thinking from the public
16 health perspective. You know, I would prefer that people
17 don't get exposure to acrylamide as opposed to reading the
18 label and in some cases ignoring it because this is a compound
19 which we want to reduce human exposure to.

20 Q. And have you considered that for some people,
21 even if they read the label, if they are dependent on caffeine
22 in coffee, that they are going to drink it anyway because they
23 feel compelled to?

24 A. People will do that, yes.

25 Q. So in your opinion, getting the acrylamide out
26 is the best solution?

27 A. That would be my preference. Very strongly.

28 Q. Just like the potato chip manufacturers got it

1 out of potato chips?

2 A. It can be done. So if it can be done, I would
3 prefer to see it done.

4 Q. In any event, do you see any justification for
5 allowing, devising a 10 to the minus 4 risk, allowing that
6 much more cancer risk for acrylamide in coffee?

7 A. I see no justification for an alternative
8 cancer risk for acrylamide in coffee. As I just stated, it
9 can be removed. The potato industry was successful in
10 reducing its levels. I think it can be reduced substantially
11 without having large impact on palatability. And therefore,
12 to me, saying the risk level could be one times 10 to the
13 minus 4 seems to be an arbitrary value with no supportive
14 rationale. There's no health benefit that can be identified
15 by allowing a one times 10 to the minus 4 risk level.

16 Q. What is your ultimate conclusion? Is that it?

17 A. Well, no. I have one more what I consider a
18 sound consideration for public health.

19 Q. What is that?

20 A. And that is the people of California expressed
21 that in passing Prop 65. That was they want to find what are
22 the hazardous chemicals that are posing threats to their
23 health and well-being. And they were dissatisfied that the
24 government agencies failed to provide them with adequate
25 protection. They were asking for sound considerations of
26 public health. That is why they declared their rights to be
27 informed about exposures to chemicals that cause cancer, birth
28 defects, or other reproductive harm. And they wanted to see

1 enforcement of those laws controlling the hazardous chemicals
2 that threaten public health.

3 And to me, that is a strong expression of sound
4 consideration for health that was expressed by the citizens of
5 California.

6 MR. METZGER: All right. Thank you very much,
7 Dr. Melnick.

8 THE WITNESS: Well, I have my conclusions.

9 Q. BY MR. METZGER: Oh. More conclusions?

10 A. No. Just my overall conclusions.

11 Q. Okay. What are your overall --

12 THE COURT: Do you have a question, Mr. Metzger,
13 that you'd like to ask the witness?

14 MR. METZGER: Yes, I do.

15 Q. What are your overall conclusions, Dr. Melnick?

16 A. If you remember, I indicated at the beginning
17 that the topics to be covered would include my overall
18 conclusions, and these are them posted on the screen over
19 there. That there's no health benefit from acrylamide in
20 coffee and that the concentrations can be selectively reduced
21 by significantly affecting the sensorial properties of coffee.

22 Because of the beneficial effect of reducing
23 acrylamide in foods, similar to the BRAFO statement on
24 potatoes, I believe an acrylamide reducing action should be
25 applied to coffee as long as there's no further demonstration
26 of adverse effects identified.

27 With respect to that pharmacokinetic adjustment,
28 which I hope people were able to grasp, I find that

1 pharmacokinetic adjustments cannot be taken into account with
2 confidence, and the exclusion of cancer sites produces
3 significant increases in the NSRL for acrylamide in coffee.

4 I see no justification for supporting an alternative
5 cancer risk level for this genotoxic carcinogen in coffee.

6 MR. METZGER: Thank you very much, Dr. Melnick.

7 THE COURT: Mr. Kennedy, are you going to have any
8 questions? You don't have to do it today.

9 MR. KENNEDY: Okay.

10 THE COURT: I just want to make sure you had
11 questions.

12 MR. KENNEDY: We're not going to pass.

13 THE COURT: Okay. We're going to resume the trial
14 tomorrow morning at 9:00 o'clock.

15 MR. METZGER: Your Honor, could we just chat with
16 you briefly about the remainder of the week?

17 THE COURT: Sure.

18 MR. METZGER: What your plans are.

19 THE COURT: Yes.

20 MR. METZGER: So I expect that Dr. Melnick will
21 be -- his testimony will conclude tomorrow, on Tuesday.

22 And that leaves in question what is to be done for
23 the remainder of the week. I don't know if your Honor has
24 seen it. I have a new witness, a percipient witness that I
25 just discovered, and I notified counsel and the Court about
26 this witness. I'd like to have that witness testify on
27 Wednesday. And that witness is willing to give a deposition
28 before testifying, if your Honor feels that that's necessary.

1 THE COURT: Well, where did this witness come from?
2 How come after seven and a half years you discovered a new
3 percipient witness?

4 MR. METZGER: I put this all in my declaration.
5 Your Honor probably hasn't seen it. Do you want to take a
6 moment to read it, or should I give you a narration?

7 THE COURT: Why don't you give me a quick summary.

8 MR. METZGER: Okay. So on Friday I was contacted by
9 a gentleman by the name of Harvey Durand, who is the president
10 of Healthy Cafe, LLC, which actually is the assignee for a
11 patent for reducing acrylamide in coffee. And he has informed
12 me that he has some very significant information regarding
13 this case.

14 That was just on Friday. And I immediately notified
15 counsel this morning, the first court day after I discovered
16 this.

17 I believe he has relevant information as a
18 percipient witness to give, especially regarding the coffee
19 industry's unwillingness to adopt or implement this technology
20 even though it improved the flavor of coffee and specifically
21 because it incidentally reduced the concentration of
22 acrylamide.

23 So he has some percipient knowledge about this. I
24 don't think his testimony will be very long. But he first
25 came to my attention when he called me on Friday.

26 THE COURT: All right. And defendants?

27 MR. KENNEDY: If he's been able to keep this secret
28 this long, I don't see how he thinks testimony is going to

1 bear on what the industry should have known since he probably
2 hasn't come out of the woodwork until Friday. So we would
3 object. If the Court is inclined to let him testify, we would
4 request a deposition.

5 THE COURT: Well, I have concern at this late stage.
6 Supposing next week the defendants discover a new witness. Do
7 you think we ought to let this trail along like this? Each
8 party coming up with new witnesses?

9 MR. METZGER: Well, your Honor, the only reason I
10 learned about him --

11 THE COURT: I'm not blaming you. A guy comes out of
12 the woodwork --

13 MR. METZGER: -- was because of the publicity from
14 the case, that he contacted me. And I'll tell you, there's
15 probably 50 people that contacted me. But this is the only
16 one that I thought, oh, this gentleman actually has some
17 relevant information because he's had conversations with
18 executives of the coffee industry. And these are party
19 opponent admissions that they don't want to do it because of
20 the litigation.

21 THE COURT: He's just had conversations, and he's
22 been around for a while. So all of a sudden, he wants to
23 interject himself in this case. At any rate, I'll give
24 counsel for the defendant an opportunity to file some papers
25 tomorrow morning. But we'll discuss it tomorrow.

26 I'm a little concerned about having a new witness
27 come forward, especially a witness who is introducing himself
28 to the proceedings.

1 We'll be in recess until tomorrow morning at 9:00
2 o'clock.

3 MR. METZGER: Thank you, your Honor.
4

5 (Proceedings concluded at 4:25 P.M.)
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SUPERIOR COURT OF THE STATE OF CALIFORNIA
FOR THE COUNTY OF LOS ANGELES

DEPARTMENT 323 HON. ELIHU M. BERLE, JUDGE

CERT,)
))
PLAINTIFF,)
))
VS.) CASE NO. BC 435759
))
STARBUCKS CORP, ET AL.,) BC 461182
))
DEFENDANTS.)
_____)

I, MARK SCHWEITZER, OFFICIAL COURT REPORTER PRO TEM
OF THE SUPERIOR COURT OF THE STATE OF CALIFORNIA, COUNTY OF
LOS ANGELES, DO HEREBY CERTIFY THAT THE FOREGOING TRANSCRIPT,
DATED OCTOBER 2, 2017, P.M. SESSION, COMPRISES A FULL, TRUE,
AND CORRECT TRANSCRIPT OF THE PROCEEDINGS HELD IN THE
ABOVE-ENTITLED CAUSE.

DATED THIS 2ND DAY OF OCTOBER, 2017.

/S/ MARK SCHWEITZER
MARK SCHWEITZER, RPR, CRR, CSR NO. 10514

EXHIBIT “F”

1
1 SUPERIOR COURT OF THE STATE OF CALIFORNIA

2 FOR THE COUNTY OF LOS ANGELES

3 DEPARTMENT 323

HON. ELIHU M. BERLE, JUDGE

4
5 CERT,)
6)
7) Plaintiff,)
8) vs.) SUPERIOR COURT
9) CASE NO. BC 435759
10) BC 461182
11) STARBUCKS CORP, ET AL.,)
12)
13) Defendants.)
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11 REPORTER'S TRANSCRIPT OF PROCEEDINGS

12 Tuesday, October 3, 2017

13 (A.M. Session)

14 APPEARANCES OF COUNSEL:

15 FOR THE PLAINTIFFS: METZGER LAW GROUP
16 BY: RAPHAEL METZGER, ESQ.
17 ABRAHAM I. PARISER, ESQ.
18 401 East Ocean Boulevard
19 Suite 800
20 Long Beach, California 90802
(562) 437-4499
sbrust@toxictorts.com
rmetzger@toxictorts.com
apariser@toxictorts.com

21 FOR THE ROASTER AND DOE DEFENDANTS:
22 MORRISON/FOERSTER
23 BY: JAMES M. SCHURZ, ESQ.
24 425 Market Street
25 San Francisco, California 94105-2482
(415) 268-7124
jschurz@mofo.com

26 (Appearances continued on next page.)

27
28 DAVID A. SALYER, CSR, RMR, CRR
Official Pro Tem Court Reporter
License No. 4410

1 APPEARANCES OF COUNSEL: (CONTINUED)

2 FOR KEURIG: SKADDEN, ARPS, SLATE, MEAGHER
& FLOM, LLP
3 BY: RAOUL D. KENNEDY, ESQ.
4 525 University Avenue
Palo Alto, California 94301
5 (650)470-4550
rkennedy@skadden.com

6 FOR HN FERNANDEZ, ET AL.:

7 NORTON ROSE FULBRIGHT, LLP
8 BY: JEFFREY B. MARGULIES, ESQ.
555 South Flower Street
9 41st Floor
Los Angeles, California 90071
10 (213)892-9286
jmargulies@nortonrosefulbright.com

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1 CASE NUMBER: BC 411192/BC435759
2 CASE NAME: CERT CASES
3 LOS ANGELES, CALIFORNIA TUESDAY, OCTOBER 3, 2017
4 DEPARTMENT 323 ELIHU M. BERLE, JUDGE
5 REPORTER: DAVID A. SALYER, CSR 4410
6 TIME: 9:00 A.M.

7 -o0o-

8 THE COURT: Calling the trial, CERT versus Starbucks.
9 All counsel are present and Dr. Melnick is on the
10 stand.

11 RONALD MELNICK,
12 witness, resumed the stand and testified further as follows:

13
14 THE COURT: Good morning, Dr. Melnick.
15 You understand you're still under oath?

16 THE WITNESS: I understand that.

17 THE COURT: And Mr. Kennedy is going to proceed with
18 cross-examination.

19 MR. KENNEDY: Your Honor, two housekeeping matters.

20 One, we've prepared binders with some -- I can't say
21 all, but some of the documents that we're going to be using
22 this morning.

23 I tried to put them in more or less the same order.

24 Secondly, I'm on some medication that may require me to
25 ask the Court's indulgence for a bathroom break.

26 THE COURT: Any time you need a break, just give me a
27 signal and we'll take a recess.

28 MR. KENNEDY: I appreciate that, your Honor. You get

1 old, these things happen.

2 THE COURT: That goes for any counsel and the witnesses
3 and even the court reporter.

4 Counsel, you may proceed.

5

6

CROSS-EXAMINATION

7

BY MR. KENNEDY:

8

Q. Good morning, Dr. Melnick.

9

10 As you told us in your statement of opinions -- you
11 told us in your statement of opinions while roasting coffee
12 beans is necessary to make coffee products and to reduce
13 microbial contaminants to some extent, the presence of
14 acrylamide in coffee provides no health benefits.

14

15 THE COURT: Mr. Kennedy, could you just hold on one
16 second.

16

I just want to open up the LiveNote on my computer.

17

MR. KENNEDY: Plaintiff's Exhibit 600 --

18

THE COURT: Mr. Kennedy, wait just one second.

19

All right. Thank you, Mr. Kennedy. You may proceed.

20

MR. KENNEDY: Yes, your Honor.

21

22 Q. Dr. Melnick, directing your attention to the
23 screen and to Exhibit 60077, that's part of the opinions of
24 Ronald Melnick that you submitted in this case; is that
25 correct?

25

A. That's correct.

26

27 Q. Going to page 3 of Exhibit 60077, you say, in
28 part, "While roasting coffee beans is necessary to make coffee
products and to reduce microbial contaminants to some extent,

1 the presence of acrylamide in coffee provides no health
2 benefits."

3 Correct?

4 A. That's correct.

5 Q. And you do agree that roasting coffee beans is
6 necessary to make coffee products, correct?

7 A. That's correct.

8 Q. And going to page 8 of Exhibit 60077, you also
9 say, "While acrylamide is formed as product of the Maillard
10 reaction which produces many aromatic and flavorful chemicals,
11 acrylamide itself is not an essential component of coffee."

12 Correct?

13 A. Yes, that's correct.

14 Q. So you agree that acrylamide is formed in the
15 product from the Maillard reaction. No disagreement on that?

16 A. No disagreement on that.

17 Q. Then directing your attention to the
18 demonstrative slides that you used yesterday, Exhibit 71356,
19 slide four, and that's on the screen now, the "No Significant
20 Risk Level" slide, correct?

21 A. That is correct.

22 Q. And directing your attention to the third bullet
23 point that talks about "an alternative level must be supported
24 by sound considerations of public health."

25 Then you give, "For example, where chemicals in food
26 are produced by cooking necessary to render the food palatable
27 or to avoid microbial contamination."

28 Do you see that?

1 A. Yes, I do.

2 Q. And then in the fourth bullet point you say, "If
3 beneficial effects do not outweigh the risks, then the 10 to
4 the minus 5 standard applies." And you cite addendum FSOR.

5 What are you referring to there?

6 A. The final statement of reasons.

7 Q. The addendum to the final statement?

8 A. The addendum, yes.

9 Q. And that's the final statement for 75203?

10 A. Yes.

11 Q. And then Exhibit 71356, the demonstratives, you
12 also quote from the final statement at slide 43, do you not,
13 where you say that, "The person responsible for the exposure
14 must be able to show that the beneficial health effects of the
15 additive outweigh the risks."

16 Correct?

17 A. Correct.

18 Q. And directing your attention next to
19 Exhibit 71356, which was the more complete statement from the
20 addendum.

21 And what they're talking about there is they explain
22 the commentor who this is all pertaining to talks about
23 chemicals that are intentionally added to a food product,
24 correct?

25 A. Yes.

26 Q. And acrylamide is not something which is
27 intentionally added to a food product, is it?

28 MR. METZGER: Objection. That's actually a legal

1 conclusion.

2 THE COURT: Overruled.

3 You may answer.

4 THE WITNESS: It's not intentionally added, correct.

5 Q. BY MR. KENNEDY: If you go into a roasting
6 plant, there isn't a station that says here's where we
7 intentionally add the acrylamide, is there?

8 A. No, there isn't.

9 Q. Okay. So the addendum is talking about the
10 effect of intentionally added substances, which acrylamide
11 isn't, correct?

12 MR. METZGER: Objection, legal conclusion.

13 THE COURT: Overruled.

14 You may answer.

15 THE WITNESS: But it is a chemical which has been
16 included in the final product. But it is a consequence of
17 roasting.

18 Q. BY MR. KENNEDY: No, no.

19 We're talking about, it is not something that's
20 intentionally added?

21 A. That is correct.

22 Q. And the addendum has nothing to do with
23 acrylamide, does it?

24 MR. METZGER: Objection, legal conclusion.

25 THE COURT: It's argumentative.

26 I think we've already established that there's not some
27 product of acrylamide that's being added, that it happens in
28 the process of roasting coffee.

1 MR. METZGER: And they intentionally roast coffee.

2 THE COURT: Let's move on.

3 Q. BY MR. KENNEDY: Sticking with the
4 demonstratives from yesterday, Exhibit 61950, let's go, for
5 example, to slide 14.

6 This talks about the effect of steaming and pressure on
7 acrylamide levels, correct?

8 A. Yes, that's correct.

9 Q. A different way of preparing the beans?

10 A. Right.

11 Q. And similarly, slide 15 talks about the effect
12 if you did vacuum roasting, correct?

13 A. Yes.

14 Q. And slide 16 talks about if you used heat
15 curing, correct?

16 A. Correct.

17 Q. And 17 talks about supercritical extraction?

18 A. Correct.

19 Q. And 18 talks about cysteine addition?

20 A. Cysteine.

21 Q. Cysteine.

22 And at the time -- and you prepared these slides,
23 didn't you?

24 A. Yes, I did.

25 Q. And at the time you prepared them, were you
26 familiar with the final statement of reasons that we talked
27 about here this morning already, correct?

28 A. Some of that was discussed over the weekend.

1 Q. Well, you've told us about the addendum to the
2 final statement?

3 A. Oh, the statement of reasons? Yes.

4 Q. You read it. You're familiar with the
5 statement?

6 A. Yes, sure.

7 Q. Going to Exhibit 71356, the May 1990 final
8 statement of reasons, as you read that over and became
9 familiar with it, you learned that the word "necessary" in the
10 necessary cooking exception is not intended to favor one
11 cooking practice over another.

12 If a food could be boiled or broiled to avoid
13 contamination or render the food palatable but broiling
14 produces more chemical byproducts than boiling, broiling does
15 not become necessary --

16 MR. METZGER: Unnecessary.

17 MR. KENNEDY: Unnecessary, thank you.

18 "The agency's intention is that whatever method of
19 cooking is chosen, the amount of cooking which is necessary to
20 avoid bacterial contamination or to render the food palatable
21 should provide a basis for the application of a risk level
22 other than a risk of 1 times 10 to the minus 5."

23 Q. You saw that language, didn't you?

24 A. Yes, I have.

25 Q. And from that you concluded, did you not, that
26 the particular method of cooking was really irrelevant to
27 whether an ASRL would apply, didn't you?

28 MR. METZGER: Objection, legal conclusion,

1 argumentative. It's all roasting. So it's one method of
2 cooking.

3 THE COURT: Objection overruled.

4 The witness may answer.

5 THE WITNESS: I concur that roasting is the method for
6 preparing coffee.

7 Q. BY MR. KENNEDY: And if there's some other
8 variation on how to render coffee beans palatable, that
9 doesn't make any difference under the language we've just
10 talked about, does it?

11 MR. METZGER: Objection, legal conclusion,
12 argumentative.

13 THE COURT: Overruled.

14 The witness may answer.

15 THE WITNESS: I think some of the slides I presented
16 and that you showed were variations on roasting or methods
17 that could be used during roasting to remove acrylamide.

18 So they're not changing from roasting to boiling or
19 broiling. I don't think that ever came up.

20 Q. You don't think the language we have up there
21 says that the ASRL exception applies regardless of whether
22 there are other methods that might produce less of the
23 carcinogen? You don't think that's what it means?

24 MR. METZGER: Objection, argumentative, legal
25 conclusion.

26 THE COURT: Overruled.

27 THE WITNESS: I think the variation in roasting is
28 still a roasting process.

1 I think we're comparing roasting to boiling. I don't
2 think anyone would, at this point, claim that boiling is an
3 alternative. But roasting and applying supercritical CO2
4 extraction is still roasting.

5 So I don't think the supercritical CO2 extraction
6 deviates from these particular statements.

7 Q. BY MR. KENNEDY: And you'll agree it's his
8 Honor's prerogative to decide what these words mean.

9 A. You asked me.

10 Q. And you're trying to do your best to help him
11 reach the right answer; is that correct?

12 A. Certainly.

13 Q. Now, you spent a lot of time yesterday talking
14 about various ways of mitigating acrylamide in coffee.

15 You recall that discussion, don't you?

16 A. Sure.

17 Q. And in the course of reading over the section
18 75203 and the statement of reasons, you didn't find the word
19 "mitigation" anywhere, did you?

20 A. I would have to look again to recall.

21 Q. You're assuming that there's a mitigation
22 requirement, correct?

23 A. Oh, no, no. I believe mitigation is not a
24 requirement.

25 Q. Okay.

26 A. It's a labeling act.

27 I think mitigation is an option that might be
28 considered by the industry or facilities which are involved in

1 a Prop 65 case in terms of how to avoid labeling, but the act
2 is a labeling act.

3 It doesn't indicate that the judge would necessarily
4 say you must mitigate.

5 Q. Or say unless you mitigate you must put a
6 warning label on it, right?

7 MR. METZGER: Objection, argumentative, legal
8 conclusion.

9 THE COURT: Overruled.

10 THE WITNESS: No. I think the decision would be the
11 level is above the NSRL. Under that condition a labeling
12 would be required.

13 And I would imagine -- I would prefer to see acrylamide
14 removed from coffee as opposed to labeling. And hopefully an
15 interaction could occur such that the labeling could be
16 avoided if there were attempts to remove or reduce
17 substantially the acrylamide from coffee.

18 That would be my preferred finality to the situation.

19 THE COURT: Why do you think that's not happening?

20 THE WITNESS: You want my honest answer?

21 THE COURT: I hope your answer is honest.

22 THE WITNESS: My honest answer is it appears to me that
23 the coffee company thinks that they can win on litigation and
24 don't need mitigation.

25 THE COURT: Do you think there would be some
26 competitive advantage for some innovator to come into the
27 market with a coffee that has had acrylamide eliminated?

28 THE WITNESS: I think it would be a huge advantage.

1 THE COURT: So do you have any opinions as to why no
2 one has done that?

3 You testified yesterday about this German company. Do
4 you know of any information why the German company has not
5 entered the American market?

6 THE WITNESS: I don't know why that hasn't happened.
7 But I would imagine if there were two products side by side on
8 a shelf, one had a label saying that this is known to the
9 State of California to have a carcinogen, acrylamide, and side
10 by side was another product that didn't have that label, I
11 would imagine very strongly people would opt for the one that
12 doesn't have that label.

13 Why that hasn't developed further, I don't know the
14 reason, but I know the industry is quite united among most of
15 the coffee roasters.

16 THE COURT: All right. Thank you.

17 Mr. Kennedy?

18 Q. BY MR. KENNEDY: Now, in terms of mitigation of
19 acrylamide in coffee, you yourself have never devised a method
20 for doing that, have you?

21 A. No, I haven't.

22 Q. You've never worked for a company that was doing
23 that or trying to do it, have you?

24 A. No, I haven't.

25 Q. And outside of this case, you've never written
26 or lectured on the reduction of acrylamide in coffee?

27 A. That's correct.

28 Q. And you've never visited a company that was

1 involved with trying to reduce acrylamide in coffee?

2 A. I didn't know of any companies that were trying
3 to reduce acrylamide in coffee. I only know about it largely
4 from the confidential papers that I received.

5 Q. And you learned about Novozymes from
6 confidential sources?

7 A. You asked me in coffee. I did not know of
8 coffee companies that were working on mitigating acrylamide.

9 Q. I'll try again.

10 You've never visited any company that you understood
11 was working on reduction of acrylamide in coffee?

12 A. That is correct.

13 Q. Okay. And you've never drunk a cup of coffee
14 that reflected anybody's attempted mitigation method, have
15 you?

16 A. No, I haven't.

17 Q. So what you know about reduction of acrylamide
18 in coffee is what you've learned working on this case,
19 correct?

20 A. That is correct.

21 Q. And you've learned in the course of working on
22 this case that the FDA doesn't think there's a commercially
23 viable process for reducing acrylamide in coffee?

24 MR. METZGER: Objection. Vague as to time.

25 THE COURT: Objection sustained.

26 Can you pinpoint -- if there is a differentiation in
27 time, then pin it down?

28 If not, at any time.

1 MR. KENNEDY: Sure, your Honor.

2 THE COURT: Fine tune that, please.

3 MR. KENNEDY: Sure.

4 Why don't we put up Defendants' Exhibit 71830, the
5 guidance for industry document we talked about yesterday.

6 Q. You're familiar with that, aren't you?

7 A. Yes, I am.

8 Q. That's a March 2016 publication, correct?

9 A. That is correct.

10 Q. And that's a joint effort of the U.S. Department
11 of Health and Human Services, correct?

12 A. Correct.

13 Q. And of the Food and Drug Administration?

14 A. Yes.

15 Q. And of the Center for Food Safety and Applied
16 Nutrition, correct?

17 A. Yes.

18 Q. Let's go over to page 23.

19 As of March, 2016 they told us they did not -- I'm
20 sorry.

21 If we went to page 27, it might be much better. My
22 apologies.

23 Coming to the end of the second full paragraph, right
24 before the, E, Properties and Cooking Interaction., the last
25 sentence.

26 "A viable commercial process is not yet available,
27 Reference 30."

28 That's what those three agencies had to say as of

1 March, 2016, correct?

2 A. That's what's written here.

3 Q. And let's go over to page 35 of that same
4 document, 71830.

5 Let's go to reference 84.

6 And the reference is comments submitted by Novozymes.
7 So apparently these three agencies were aware of something
8 about Novozymes, correct?

9 A. I haven't seen those comments, so I don't know
10 what they contain.

11 Q. Okay. In any event, you disagree with those
12 three agencies, correct?

13 A. Yes, I do.

14 Q. You think there are at least two commercially
15 viable ways of reducing acrylamide in coffee, correct?

16 A. I think there's more than two.

17 Q. Well, you told us about long-term storage and
18 you've told us about Novozymes.

19 Are there more than that?

20 A. Curing.

21 There was another depending on the nature of the coffee
22 product, cysteine.

23 I would have to look at my full list, but it's more
24 than two.

25 Q. Okay. Let's go back to page 3 of the guidance
26 exhibit.

27 And going to the black bordered box at the top.

28 Can we enlarge that, Tom.

1 This explains that the guidance represents the current
2 thinking of the FDA, but you can use an alternative approach
3 if it satisfies the requirements. And to discuss an
4 alternative approach, contact the FDA staff responsible for
5 this guidance.

6 Do you see that?

7 A. Yes, I do.

8 Q. You told us yesterday cancer is an absolutely
9 horrible disease, right?

10 A. Yes.

11 Q. And you consider that acrylamide is a risk
12 factor in causing cancer, right?

13 A. Correct.

14 Q. And you believe that with the adoption of the
15 mitigation methods you've proposed here, that risk factor
16 could be reduced, correct?

17 A. That is correct.

18 Q. Could save lives, correct?

19 A. Correct.

20 Q. And so you seem to have knowledge that the FDA
21 doesn't have, correct?

22 A. I don't know what knowledge the FDA has. All I
23 know is that the sentence that you read to me was based on, as
24 you read it, reference 30 which was a document from
25 EuropeFoodDrink, which was prepared by the coffee companies.

26 So they have the information that the coffee companies
27 provided to them.

28 Q. Correct.

1 You came to the conclusion that the FDA was dealing
2 with incomplete information, right?

3 A. That is correct.

4 Q. And that people were potentially dying because
5 they didn't have complete information, correct?

6 A. Potentially dying, yes.

7 Q. Okay. And when did you first learn about this
8 March, 2016 document?

9 A. In the course of this case.

10 Q. Six months ago, a year ago?

11 A. Probably within the past six months to a year --
12 eight months, somewhere in that range.

13 Q. And tell us everything you've done during those
14 intervening six to eight months to try to call the FDA's
15 attention to the fact that there are potentially lifesaving
16 methodologies out there that for some reason they don't know
17 about.

18 Do you find that funny, doctor?

19 MR. METZGER: Objection, argumentative.

20 He's under a protective order that he cannot disclose
21 the confidential documents to the FDA.

22 THE COURT: Well, the question as phrased is
23 argumentative.

24 But the witness can answer the question as to whether
25 he's had any communications with the FDA about any new
26 processes.

27 MR. KENNEDY: Do you want me to rephrase, your Honor?

28 THE COURT: Yes.

1 Q. BY MR. KENNEDY: Tell us, first, have you had --
2 made any attempt whatsoever to contact the FDA to try to share
3 the information that you have about potential reduction of
4 acrylamide in coffee?

5 A. No, I haven't.

6 Q. And the information that you have includes
7 publicly available information such as things on the
8 Novozymes' website, correct?

9 A. Much of what I saw came from the documents under
10 the confidential documents that I was under the court order
11 not to discuss.

12 Q. So it's your testimony that the reason you
13 haven't made any attempt to contact the FDA is you feel it
14 might potentially be violating the protective order in this
15 case?

16 A. That's one reason.

17 Q. What are the others?

18 A. Sometimes -- I've worked in the federal
19 government for nearly 30 years. Sometimes policy decisions
20 take a long time.

21 Perhaps through a court case there could be a faster
22 means of reducing acrylamide from coffee.

23 Q. So rather than telling the FDA about it, you
24 thought it would be quicker to come tell about it in a trial
25 in a courtroom in L.A.?

26 A. I find that within the federal government one
27 person's comment does not necessarily move a bureaucracy that
28 fast.

1 Q. You didn't think you had a duty to at least try,
2 given what's at stake here?

3 MR. METZGER: Objection, argumentative.

4 THE WITNESS: Again, these were confidential documents
5 that I was aware of in the past six months.

6 If you relieve the court order, I would be happy to
7 do it.

8 Q. BY MR. KENNEDY: During those six months, have
9 you ever had a conversation with Mr. Metzger along the lines
10 of is there something we can do to get an exception to this
11 protective order so that we can at least share this with the
12 FDA? Any conversations along those lines?

13 A. I don't recall any.

14 Q. Now, you talked quite a bit yesterday about the
15 200-ton production example from Novozymes and the German
16 company, correct?

17 A. I don't know if I spent a lot of time on it.

18 Q. It was discussed?

19 A. Yes.

20 Q. And that's the only example you have of any kind
21 of wide-scale commercial production of at least an enzyme
22 attempt to reduce acrylamide in coffee, correct?

23 A. That is correct.

24 Q. And turning, if we could, to your declaration,
25 which was referred to yesterday, Exhibit 59957, this is your
26 most recent declaration you talked about yesterday, correct?

27 A. Is there a date stamp on this one? I'm looking
28 for it.

1 Q. This is the one that's unsigned.

2 Do you want us to go to the signature page to confirm
3 there?

4 A. That's okay. It's probably the --

5 Q. Why don't we turn to paragraph 63 of
6 Exhibit 59957.

7 And what you explain there is in September of 2011
8 Helmut Guenther, a food scientist at Kraft Foods, prepared an
9 update on acrylamide and using asparaginase to reduce levels
10 in coffee in which you say he updated the European coffee
11 industry regarding the collaborative effort between Novozymes
12 and Hermanson. That's the German company we talked about,
13 right?

14 A. Correct.

15 Q. And then you go on to say that, "Novozymes is
16 aware of the current coffee industry," and skipping down over
17 to the --

18 MR. METZGER: Objection to skipping.

19 MR. KENNEDY: All right. We will not skip.

20 THE COURT: All right. Read the whole thing.

21 MR. KENNEDY: (Reading:)

22 "Novozymes is aware of the current
23 coffee industry position that using enzymes
24 is not seen as an option to reduce for
25 efficiency, quality and cost and food
26 safety reasons (as detailed in the Food
27 Drink Europe Acrylamide Toolbox) and is
28 addressing this by showing data which

1 achieved reductions of up to 70 percent
2 instead of our industry findings of a 10
3 max 45 percent reduction.

4 "This is together with mentioning that
5 coffee has been processed at industrial
6 scale already.

7 "According to the presentations of
8 Sara Lee, more than 200 tons of coffee have
9 been processed on industrial scale and sold
10 in the market" --

11 MR. METZGER: To the market.

12 MR. KENNEDY: (Reading:)

13 -- "to the market.

14 "Additionally they are referring to the
15 opportunity to combine the enzyme process
16 with other green coffee treatments,
17 (steaming), stating that under the current
18 green price environment they believe coffee
19 roasters are interested in the possibility
20 of modifying blends to lower costs without
21 impacting quality and without increasing
22 level of acrylamide."

23 That's what it says, correct?

24 A. Yes, that's from the --

25 Q. Were you present at the presentation to Sara
26 Lee?

27 A. No, I wasn't.

28 This is a quote that I obtained from the confidential

1 documents.

2 Q. And you've never talked to anybody that has told
3 you for sure they were present at the presentation to Sara
4 Lee, have you?

5 A. No, I haven't.

6 Q. And you don't know one way or another whether
7 Mr. Guenther was present at the presentation to Sara Lee,
8 do you?

9 A. You would have to go back to see how he worded
10 it since that's where the page split is.

11 Q. Well, you certainly never talked to him to find
12 out whether he was there or not, have you?

13 A. No, I haven't spoken to Guenther.

14 Q. Or made any effort to find out whether
15 Mr. Guenther was present at the Sara Lee presentation?
16 You haven't done that either, have you?

17 A. Under the assumption that he was there in order
18 to have acquired that information as opposed to simply just
19 making it up?

20 Q. You don't know whether Mr. Guenther talked to
21 someone who was at Sara Lee, whether he talked to someone who
22 talked to someone at Sara Lee? You don't know how he came to
23 have this information, do you?

24 A. Could we go back to page 21 again?

25 Q. Sure.

26 THE COURT: I'm sorry. Could you speak in the
27 microphone. I can't hear.

28 THE WITNESS: I just asked to move the page.

1 THE COURT: But in general, please speak closer to the
2 microphone.

3 Q. BY MR. KENNEDY: Let's go back to the beginning
4 of paragraph 63.

5 A. I'm under the assumption that he heard directly
6 in terms of making a presentation, but I wasn't there and I
7 haven't spoken with him so I can't confirm that assumption.

8 But I would see no reason why he would make such a
9 statement to the European coffee industry if he who works for
10 the Kraft Foods would be misleading.

11 It seems to me he's writing this in an encouraging way.

12 Q. You assumed, correct?

13 MR. METZGER: Assumed what?

14 Q. BY MR. KENNEDY: You assumed that Mr. Guenther's
15 comments were accurate?

16 A. I assumed they were accurate because he's
17 representing a coffee company indicating that there is
18 information that is relevant to producing a product that would
19 be -- have reduced levels of acrylamide.

20 Q. Again, I don't mean to be argumentative, but you
21 don't believe everything you're told by a coffee company, do
22 you?

23 MR. METZGER: Objection, argumentative.

24 THE COURT: Objection sustained.

25 Q. BY MR. KENNEDY: Now, going to the 200 tons of
26 coffee referenced there, you don't know anything about that
27 other than what's on this piece of paper, do you?

28 A. I learned about that this year when I received

1 these documents.

2 Q. Okay. You don't know whether anybody actually
3 drank any of that coffee, do you?

4 A. Again, I would assume it's more likely that the
5 coffee was drank rather than poured into the Boston Harbor.

6 Q. How about into coffee ice cream.
7 You don't know whether it went there or not?

8 A. The 200 tons?

9 Q. Yeah.

10 A. I don't know if the 200 tons went into coffee
11 ice cream.

12 Q. Or coffee candy?

13 MR. METZGER: I thought coffee ice cream and coffee
14 candy were not a part of the case.

15 THE COURT: Objection sustained.

16 The witness doesn't know. He's just speculating.
17 Let's move on to something the witness knows about.

18 Q. BY MR. KENNEDY: And you haven't talked to
19 anybody who could tell you anything about the success or lack
20 of success of that market, can you?

21 MR. METZGER: Objection, 352, your Honor.

22 THE COURT: Overruled.

23 THE WITNESS: No, I haven't.

24 Q. BY MR. KENNEDY: And have you seen anywhere that
25 after that 200-ton production they ever sold any more of it?

26 A. I haven't seen any additional information on
27 that.

28 Q. The world coffee market is tens of millions of

1 metric tons, correct?

2 A. Correct.

3 Q. Okay. So if somebody has a successful like
4 product, you would expect them to sell more than 200 tons,
5 wouldn't you?

6 MR. METZGER: Objection, calling for speculation.

7 The coffee industry has boycotted it.

8 THE COURT: The objection is sustained.

9 Let's go on to another question.

10 Q. BY MR. KENNEDY: Has the Novozyme process for
11 coffee been approved by the FDA?

12 MR. METZGER: Objection, vague.

13 THE WITNESS: The enzyme has been --

14 THE COURT: Overruled.

15 You may answer. Go ahead.

16 THE WITNESS: I don't know if the Novozymes process,
17 but I know the enzyme has been approved by FDA, the use of
18 that enzyme in foods.

19 Q. BY MR. KENNEDY: Okay. And the product has not
20 been what you would consider thoroughly safety tested, has it?

21 A. I haven't seen information on safety testing of
22 asparaginase-treated coffee.

23 Q. And you would certainly want to see further
24 analysis done before, for example, a pregnant woman started
25 drinking coffee that had been treated with the Novozymes
26 process, correct?

27 MR. METZGER: Objection. That's argumentative as
28 phrased and compound.

1 THE COURT: Overruled.

2 You may answer.

3 THE WITNESS: Although I don't expect this to create a
4 problem, I would still feel comfortable -- more comfortable if
5 the product was tested for safety.

6 But by selectively removing this amino acid, there
7 would not be any reason to believe that a highly toxic
8 material would arise.

9 Q. BY MR. KENNEDY: But you would like to see more
10 testing as a cautious scientist, correct?

11 A. That would be correct.

12 Q. And you're familiar with a researcher named Fei,
13 F-E-I, Xu, X-U, at the University of Redding.

14 In fact, you cited some of his articles in this case,
15 correct?

16 A. I'm familiar with the college and the Xu papers,
17 yes.

18 Q. And going to Plaintiff's Exhibit 57084,
19 plaintiff's exhibit, it talks about the effect of asparaginase
20 on flavor formation in roasted coffee.

21 You've seen that, haven't you?

22 A. Yes, I have.

23 Q. And going over to the third page of that
24 document, if we could, under figure 2, we've highlighted
25 there:

26 "Two-way ANOVA," A-N-O-V-A, of groups three
27 and four showed that furfural and 5 methyl
28 furfural increased as a result of steaming,

1 while furfuryl alcohol increased with
2 increasing asparaginase dose with levels in
3 treatment being significantly higher."

4 You see that, don't you?

5 A. Yes, I do.

6 Q. And furfuryl is a carcinogen, isn't it?

7 A. Yes.

8 Q. In fact, it's on the Prop 65 --

9 MR. METZGER: Hold it. Let him answer.

10 THE COURT: Let the witness complete his answer.

11 THE WITNESS: Yes. It's shown to induce tumors in
12 rodents.

13 In fact, that was one of the chemicals that was
14 discussed at the IARC meeting last June when I was there.

15 Q. BY MR. KENNEDY: And it's on the Prop 65 list,
16 isn't it?

17 A. I believe it was recently added to the list.
18 But I also believe there's no NSRL established yet or cancer
19 potency value established for furfuryl by OEHHA.

20 Q. You agree with me it is a good step?

21 A. I believe acrylamide is worse than furfuryl
22 alcohol.

23 Q. Do you have any published research to that
24 effect?

25 A. Acrylamide is a probable human carcinogen from
26 IARC evaluation based on its multi-site carcinogenicity in
27 rodents as well as the types of chromosomal damage,
28 mutagenesis.

1 Furfuryl does not have the same extent of information
2 as acrylamide, and for a number of reasons like that the IARC
3 panel voted unanimously that furfuryl alcohol should be listed
4 as a possible human carcinogen.

5 Q. Let's go back to Exhibit 61950, the
6 demonstratives from yesterday and going to your slide 44.

7 Do you remember this is where you talked about a
8 benefit-risk analysis and discussed the BRAFO proposal?

9 A. Yes.

10 Q. Now let's go back once again to Exhibit 71536,
11 the final statement of reasons for section 25703.

12 Slide 11, please.

13 And in the course of reading the final statement, you
14 saw that among others things they agreed with you that:

15 "On the other hand, there's extensive
16 information in the scientific literature
17 that indicates that chemicals having
18 mutagenic or carcinogenic properties are
19 formed as a result of cooking food.

20 "The chemicals formed and their
21 amounts vary with such factors as the
22 method of cooking (e.g., boiling, pan
23 frying, grilling, et cetera,) the
24 temperature and duration of cooking and the
25 type of food.

26 "Chemicals that have been found in
27 cooked food include benzoapyrene and other
28 polycyclic aromatic hydrocarbons" -- how do

1 you pronounce that?

2 A. Tryptophan.

3 Q. (Reading:)

4 -- tryptophan 1 and other amino acids
5 pyrolusites, nitrosamines and aldehydes. A
6 number of these chemicals have been listed
7 as known to the state to cause cancer."

8 Going to slide 12:

9 "In light of the offsetting public
10 health benefit that the cooking of food
11 provides, the agency takes the position
12 that businesses which utilize cooking
13 necessary for the processing or preparation
14 of food should not be strictly held to the
15 10 to the minus 5 standard."

16 You see that, don't you?

17 A. Yes, I do.

18 Q. Wouldn't you agree the State has already made
19 the risk-benefit analysis?

20 A. For acrylamide in coffee?

21 Q. For cooking exception.

22 For carcinogens formed as a result of necessary
23 cooking, hasn't the state said we find the benefits and
24 palatability outweigh the risks of carcinogen --

25 MR. METZGER: Objection, legal conclusion,
26 argumentative.

27 THE COURT: Overruled.

28 THE WITNESS: I'm not sure if that necessarily means

1 when there is a condition in which a chemical carcinogen can
2 be easily removed.

3 I don't think that exception would hold under that kind
4 of a scenario.

5 Q. BY MR. KENNEDY: As we've already established,
6 even if broiling causes more carcinogens than boiling, that
7 doesn't make a difference, but you think it does here?

8 MR. METZGER: Objection, argumentative, compound.

9 THE WITNESS: Yes, I do.

10 THE COURT: Overruled.

11 Q. BY MR. KENNEDY: Now, let's turn next to a
12 document you discussed yesterday, the Dietary Guidelines
13 Advisory Committee.

14 Going to Exhibit 61950, the demonstratives, slide 51.

15 There you summarize some of your thoughts about the
16 USDA scientific report of the 2015 Dietary Guidelines Advisory
17 Committee.

18 Do you recall that?

19 A. Yes, I do.

20 Q. Okay. Have you read Dr. Kessler's testimony in
21 this case?

22 A. Yes, I have.

23 Q. And you recall he described this advisory
24 committee as being about as good as science gets?

25 You recall that, don't you?

26 A. That is what he said.

27 Q. Do you agree?

28 A. No.

1 Q. Well, tell us, what's your opinion of the
2 advisory committee?

3 A. Well, I'm referring to a particular situation
4 because I haven't reviewed all aspects of the advisory
5 committee as well as the members. But I noted yesterday in
6 looking at the Dietary Guidelines, that it does not mention
7 acrylamide.

8 The issue of acrylamide in foods has been known since
9 2002. It has been raised as a health concern for more than
10 10, 12 years. Going back to the WHO/FAO risk assessment on
11 acrylamide in foods.

12 I think the Dietary Guideline Advisory Committee was
13 deficient in addressing, to me, what is an important health
14 concern.

15 Q. Okay. And you then had four bullet points on
16 this slide. You felt those were the most significant
17 takeaways from what you got out of the report?

18 A. The most significant takeaway for me was what
19 wasn't in the report, and that was acrylamide.

20 Q. You found that -- how would you describe in your
21 own words -- disappointing, surprising, incomplete?

22 A. Deficient.

23 Q. Outdated?

24 A. Deficient.

25 Q. Okay. So we can add the advisory committee to
26 the list of entities that you feel are dealing with either
27 outdated or deficient information, correct?

28 MR. METZGER: Objection, argumentative, cumulative.

1 THE COURT: Objection sustained.

2 Q. BY MR. KENNEDY: Now, going to your fourth
3 bullet point, "Recommends that individuals who do not consume
4 caffeinated coffee should not start to consume it."

5 It's not quite a complete thought, is it?

6 Let's go to the report itself, Exhibit 71322.73.

7 Sorry, 71073.

8 My mistake, your Honor.

9 71073.023, Kessler 58.

10 And can you scroll down to the bottom of the page, last
11 sentence beginning with "furthermore."

12 The sentence actually read, didn't it, "Furthermore,
13 individuals who do not consume caffeinated coffee should not
14 start to consume it for health benefits alone."

15 You cut that off, didn't you?

16 A. I have no problem with that phrase --

17 Q. Why didn't you --

18 A. -- for health benefits.

19 Q. Why didn't you include it on your slide?

20 A. That's the rationale that -- I have no -- those
21 words are correct.

22 Q. But yours weren't, were they?

23 MR. METZGER: Objection, argumentative.

24 THE COURT: Overruled.

25 THE WITNESS: It was simply that the committee did not
26 recommend the consumption of caffeinated coffee for people who
27 were non-coffee drinkers to start if it's for health benefits.

28 I recall Dr. Kessler said in his testimony he's not a

1 coffee drinker. He said also, after seeing this information,
2 maybe I should consume it.

3 So maybe this is a statement written for Dr. Kessler,
4 since he's not a coffee consumer and he believes that there
5 are potential health benefits.

6 Q. Okay. And if you can go just above where you
7 quoted the -- can you go back to slide 51 for a minute.

8 The first bullet is "Moderate Coffee Consumption."

9 Now, let's go back to the report itself, .023.

10 And right above moderate coffee, if we go up just two
11 paragraphs, Tom, we get to "Conclusion."

12 We have two conclusions.

13 You'll notice the first conclusion is:

14 "Strong and consistent evidence shows that
15 consumption of coffee within the moderate
16 range, three to five cups or up to
17 400 milligrams a day of caffeine, is not
18 associated with increased risk of major
19 chronic diseases such as cardiovascular
20 disease, CVD, and cancer and premature
21 death in healthy adults. Grade: Strong."

22 You didn't include that in your summary of what the
23 advisory committee found, did you?

24 A. No, I didn't.

25 Q. Is that because you disagree with that?

26 A. Well, I think it's an complete consideration.

27 Q. You didn't think it was worth putting on a slide
28 when you were talking about considerations of health benefits,

1 correct?

2 MR. METZGER: Objection, argumentative.

3 THE COURT: Sustained.

4 THE WITNESS: For example --

5 THE COURT: No.

6 Next question.

7 Q. BY MR. KENNEDY: And going to the next paragraph
8 on your conclusions, it states, does it not:

9 "Consistent observational evidence
10 indicates that moderate coffee consumption
11 is associated with reduced risk of type 2
12 diabetes and cardiovascular disease in
13 healthy adults. In addition, consistent
14 observational evidence indicates that
15 regular consumption of coffee is associated
16 with reduced risk of cancer of the liver
17 and endometrium and slightly inverse or
18 null associations are observed for other
19 cancer sites."

20 You didn't include that in any of your demonstratives,
21 did you?

22 A. No.

23 Since the evidence was moderate and it was based on
24 observational evidence, I didn't think it was necessary.

25 Q. Okay. Other than you yourself, are you aware of
26 anybody who's criticized the 2015 advisory committee findings?

27 A. For being deficient in addressing acrylamide?

28 Q. Better question, yes.

1 A. I --

2 Q. Start there.

3 A. I haven't read the comments that have been
4 forwarded to the advisory committee, but to me it's an obvious
5 deficiency within that committee's report.

6 Q. But as you sit here now, you can't think of
7 anybody else who shares your criticisms of them?

8 A. Again, I haven't seen any comments that were
9 made to this report, so I can't say anybody who shares.

10 But I would be sure that anybody who's worked in
11 toxicology and knows the issues related to acrylamide as a
12 carcinogen, a genotoxic carcinogen, a germ cell mutagen and
13 that it's present in food would feel it should be included in
14 any type of dietary guidelines.

15 But I can't name people because I haven't seen any
16 comments that were written to this report.

17 Q. Okay. Let's go back to the demonstratives
18 61950, slide 58.

19 That was "Sound Considerations of Public Health" and
20 you identified four or five factors, correct?

21 A. Correct.

22 Q. And those are based on criteria that are in your
23 reports for applying an ASRL, correct?

24 A. I would prefer if you would call it an ARL as
25 opposed to an ASRL, because I think the definition of
26 "significant" under Prop 65 is 1 per 100,000.

27 So this is actually just an alternative risk level, not
28 an alternative significant risk level.

1 So in answering a question, I would be answering it
2 under the condition that I hear an ASRL to really mean an ARL.

3 Q. You have trouble with the term ASRL?

4 A. The S in that acronym, yes.

5 Q. Okay. In any event, on slide 58, you don't
6 identify any source for these criteria, do you?

7 MR. METZGER: Objection. Vague. What criteria? What
8 are the criteria he's talking about?

9 THE WITNESS: These are --

10 THE COURT: Objection overruled. You may answer.

11 THE WITNESS: These are my take-home messages from work
12 in the field and primary prevention.

13 I've written in papers with Dr. Lorenzo Tomatis, who
14 was the director of the International Agency for Research on
15 Cancer in terms of stating that certain environmental
16 carcinogens provide no health benefit. This is something I've
17 written about more than ten years ago.

18 The mitigation aspects of my report indicate that the
19 level can be significantly reduced, so that's basically just a
20 take-home from sound considerations of public health and that
21 it can be substantially reduced without negatively affecting
22 palatability.

23 It's not a necessary constituent in coffee, because it
24 has no flavor or nutritive value.

25 So these are just conclusions that are very easily
26 reached from anyone in the public health environment.

27 Q. And did you attempt to compare those conclusions
28 with the final statement of reasons for section 25703?

1 MR. METZGER: Objection, lacking foundation.

2 Those were written before it was even known that
3 acrylamide was in food.

4 THE COURT: Objection overruled.

5 THE WITNESS: No, I haven't compared them.

6 Q. BY MR. KENNEDY: Going back to the final
7 statement, 71 -- Exhibit 71356, slide nine, again, in the
8 course of reading the final statement you saw, didn't you,
9 that:

10 "The agency made an exception where
11 sound considerations of public health
12 support an alternative level of risk.

13 "To illustrate what constitutes a
14 sound consideration of public health, the
15 existing regulation provides a single
16 example.

17 "The agency believes that additional
18 examples will better serve to illustrate
19 what kinds of public health considerations
20 warrant special treatment.

21 "The public health exception is
22 justified because the act was intended by
23 the voters as a measure to protect the
24 public health and well-being, ballot
25 pamphlet, Safe Drinking Water and Toxic
26 Enforcement Act of 1986, Section 1.

27 "It might contravene this intent if
28 the act were construed to prohibit

1 activities which protect the public health.

2 "It would be ironic and
3 counterproductive if, as a result of
4 warnings, the public avoided practices
5 which protect the public health."

6 Did you have that in mind when you were preparing your
7 list of considerations of public health?

8 A. Probably I didn't have it in mind, but I can see
9 what it says at this point.

10 Q. And then going to slide ten from Exhibit 71356,
11 the final statement goes on to explain:

12 "This regulatory action amends
13 subsection B of section 12703 to add two
14 additional examples of public health
15 considerations: Where chemicals in food
16 are provided by cooking necessary to render
17 the food palatable or to avoid
18 microbiological contamination and two,
19 where chlorine disinfection, in compliance
20 with all applicable state and federal
21 safety -- where chemicals in food are
22 produced by cooking necessary to render the
23 food palatable or to avoid microbiological
24 contamination and, two, where chlorine
25 disinfection in compliance with all
26 applicable state and federal safety
27 standards is necessary to comply with
28 sanitation requirements."

1 Did you have that language in mind when you were coming
2 up with your considerations of public health?

3 A. No. I was aware of these, but I don't see any
4 inconsistency.

5 Q. You don't feel that your list is adding
6 additional requirements beyond what the section already
7 provides?

8 A. No.

9 I view it as a situation for sound considerations of
10 public health, that the removal of a carcinogen is a public
11 health consideration.

12 So in my view removal of a carcinogen is an important
13 goal for an industry which provides a product that has a
14 carcinogen in it at levels greater than the NSRL.

15 Q. You would agree with me, however, the State of
16 California has already concluded that the benefits of
17 palatable food outweigh the carcinogenic risk?

18 We can agree on that?

19 MR. METZGER: Objection, argumentative, legal
20 conclusion.

21 THE WITNESS: But I think we can also agree --

22 THE COURT: Hold on one second.

23 THE WITNESS: Pardon?

24 THE COURT: The objection is overruled.

25 The witness can comment on his understanding as to what
26 the State of California has concluded.

27 With that caveat, you can answer the question.

28 THE WITNESS: Okay. I think we can also agree that

1 removal of acrylamide does not prevent the roasting of coffee
2 to make it palatable and remove microbiological contaminants.

3 So I think there is a consistency in terms of the view
4 from a public health consideration.

5 Q. BY MR. KENNEDY: Now, you talked yesterday about
6 acrylamide being responsible for, what, up to 40 percent of
7 the -- excuse me, for coffee being responsible for up to
8 40 percent of the acrylamide in the adult diet, correct?

9 A. Yes.

10 Q. Okay. And you base that 40 percent statement on
11 a paper by a gentleman named Mucci, correct?

12 A. I would have to go through my documents again.
13 I think it was made by -- it could be Mucci. It might be
14 Friedman as well.

15 I would have to look at a variety of sources. I didn't
16 scan the full literature to see any other -- the total
17 evaluations of acrylamide from dietary sources.

18 But I've seen 40 percent as a numerical value that has
19 been attributed to coffee in adults.

20 Q. And in your deposition you told us that you had
21 relied on Mucci and Friedman, as you recalled here, correct?

22 A. At that point, I believe so.

23 But, again, I would have to re-look at the references
24 in total.

25 Q. And let's go to defendants' exhibit 69866.

26 Let us know if that is the Mucci article, "Prospective
27 Study of Dietary Acrylamide and Risk of Colorectal Cancer
28 Among Women."

1 A. I really don't recall if this was the article
2 from which I got that value.

3 Q. If there is any doubt about it, let me move on
4 to Friedman.

5 Let's take a look at Exhibit 68647.

6 THE COURT: Before we go there, let me ask a general
7 question.

8 To your knowledge, is there any other food product that
9 when processed in cooking or otherwise, it creates acrylamide
10 or releases acrylamide?

11 THE WITNESS: Potatoes.

12 Potatoes actually have higher --

13 THE COURT: Potatoes and potato chips. Any others?

14 THE WITNESS: Breads, baking breads.

15 That's in many products from baking at high
16 temperatures.

17 THE COURT: And to your knowledge in terms of your
18 experience, has there been any concern about the risks of
19 cancer, other than the coffee and potato chips or french
20 fries?

21 THE WITNESS: I would have to, again, look at the full
22 literature on that.

23 It is in a number of products. It might be in some of
24 the baby foods as well.

25 THE COURT: In processing baby foods?

26 You're talking about baby foods that include some kind
27 of a grain or is it just any baby food, the processing, or
28 vegetables?

1 THE WITNESS: I'm not sure if it's just grain. I think
2 it's in vegetables, as well.

3 But, again, it's the condition in which you have free
4 asparagine in reducing sugars that are heated to sufficiently
5 high temperature.

6 THE COURT: To your knowledge, has anyone raised a
7 concern of the risk of cancer from any of those other
8 products?

9 THE WITNESS: I'm not sure how concerns are raised,
10 whether they're --

11 The totality of acrylamide in foods has been raised as
12 a concern. That was done by the WHO/FAO who considered the
13 total acrylamide in human diets, as well as EFSA in their
14 documents raised a concern of total acrylamide.

15 THE COURT: We've seen these articles about the concern
16 for dietary content and toxicity of acrylamide but mainly
17 discussing the product of coffee and the potatoes you
18 mentioned.

19 Any other particular foodstuffs?

20 THE WITNESS: Those are the ones that are highlighted
21 because potatoes had the highest levels. But coffee has the
22 highest consumption levels on a daily basis.

23 So coffee becomes more of a target of concern because
24 in the adults the level -- the acrylamide source can approach
25 40 percent in adults, though it is present in other foods.

26 THE COURT: Any acrylamide released in the processing
27 of tea leaves?

28 THE WITNESS: I would have to look at the tables. I

1 don't know foods, in general, that have been shown to contain
2 acrylamide, but I know the list the fairly large.

3 THE COURT: Thank you.

4 Mr. Kennedy?

5 MR. KENNEDY: I think the next exhibit may be of
6 interest to your Honor.

7 THE COURT: Yes. Go ahead.

8 Q. BY MR. KENNEDY: Going to Exhibit 68647, that's
9 Friedman and Levin, "Review of Methods for the Reduction of
10 Dietary Content and Toxicity of Acrylamide," correct?

11 A. Yes.

12 Q. And let's go to page 4.

13 And they have a number of pie charts, don't they, here,
14 breaking down important sources of acrylamide in various
15 populations.

16 And in Sweden it's up at 39 or 40 percent as coffee,
17 correct?

18 A. Yes.

19 Q. Okay. And if we use the United States -- again,
20 other things, your Honor, would be -- let's stay with Sweden.

21 Coffees, 39 percent, bread is 11 percent, fried potato
22 products and chips are 36 percent, crackers, cookies, et
23 cetera, 11 percent, cereal products 2 percent.

24 Other, 1 percent.

25 Now, let's take a look at the pie chart for the United
26 States.

27 Coffee, 8 percent.

28 You didn't mention that when you talked about this

1 article, did you?

2 MR. METZGER: Objection, argumentative.

3 THE COURT: Sustained.

4 Q. BY MR. KENNEDY: You'll agree with me the
5 article you relied upon shows that in the United States coffee
6 is responsible for 8 percent of acrylamide intake?

7 A. I would have to look to see if this is for
8 adults or the total population.

9 So if it's including children, you have a large
10 population which is diluting out the effect -- the acrylamide
11 source of coffee in adults.

12 So it depends on how you present data in terms of how
13 you can make a conclusion. But if this is total population,
14 that includes children, probably includes non-coffee drinkers
15 as well.

16 So I think the issue here is really the acrylamide
17 exposure among coffee drinkers and that percentage of
18 acrylamide that comes from the diet, not from non-coffee
19 drinkers.

20 So you have a dilution factor in here which needs to be
21 accounted for.

22 Q. They have children in Sweden, don't they?

23 A. I think so.

24 MR. METZGER: Objection, argumentative.

25 THE COURT: Sustained.

26 Q. BY MR. KENNEDY: Do you have any reason to think
27 that they would have different populations for different pie
28 charts here and not say something about it?

1 MR. METZGER: Objection, argumentative.

2 THE COURT: Sustained.

3 Q. BY MR. KENNEDY: In any event the Levin article
4 doesn't support a 40 percent coffee acrylamide factor for the
5 United States, does it?

6 A. Not for the total population, including children
7 and non-coffee consumers.

8 But that number will grow substantially if you take out
9 the non-coffee consumers. And whether it reaches 39 percent
10 or even goes higher, I can't tell you.

11 But I would imagine in Sweden, if we take out the
12 children from that population, it would probably go higher as
13 well.

14 But when you look at data, you have to understand the
15 full conditions under which these data are being presented.

16 We're sort of cherry-picking numbers to make a point.

17 MR. METZGER: It says Swedish adults. The other is
18 children.

19 Q. BY MR. KENNEDY: Going back to the Mucci article
20 again, Exhibit 69866, that was a study just of Swedish women,
21 wasn't it?

22 A. That's what it says.

23 Q. There were no Americans at all in that article,
24 as far as you know?

25 A. No.

26 I believe, though, when I referred to these articles, I
27 said it had been estimated from 8 to 40 percent among adults,
28 citing Mucci, the Friedman and Levin, as well as EFSA.

1 Q. Changing topics.

2 Your Ph.D. is in food science?

3 A. That is correct.

4 Q. And since getting your Ph.D. in 1970, you've
5 never actually worked anyplace where your title is food
6 scientist, correct?

7 A. No.

8 After receiving my Ph.D., I did post-doctoral research
9 at the University of California and Berkeley in which I became
10 more involved in cell biology, cell physiology.

11 I sought an academic position from there. And after my
12 academic career, I went and joined the U.S. government in the
13 National Toxicology Program.

14 So I did not work for a food company, although I did
15 summer work at a food company when I was in college.

16 Q. But the answer is since 1970 you've never worked
17 anyplace where your title was food scientist, correct?

18 A. That's correct.

19 Q. And what's organoleptic testing?

20 A. It's sensory testing. Tasting is an example.

21 Q. And you don't have any expertise or training in
22 that, do you?

23 A. I've done taste testing. In coursework, it
24 included taste testing. But I don't have any experience after
25 my Ph.D. with taste testing.

26 Q. And you're not here expressing any opinions on
27 whether there is or is not an effect on the taste and aroma of
28 coffee with the various acrylamide reduction methods you've

1 talked about, correct?

2 MR. METZGER: Objection.

3 THE WITNESS: No.

4 I think I indicated that there have been demonstrations
5 of acceptable quality of coffee which has been treated to
6 reduce acrylamide levels.

7 Q. BY MR. KENNEDY: And we talked yesterday about
8 FDA tolerances for PCB's in fish.

9 Do you remember that?

10 A. Yes, I do.

11 Q. And you pointed out that the FDA has found that
12 fish have a positive health benefit?

13 A. Correct.

14 Q. Okay. And they found that in about 2004,
15 correct?

16 A. I don't recall the year.

17 Q. And do you recall that they gave the fish the
18 deviation level in 1984, approximately 20 years before the
19 health claim was made.

20 Do you remember that?

21 A. I don't know the dates.

22 Q. Now, one of the critiques you had of
23 Dr. Rhomberg was his use of a PK factor, correct?

24 A. Yes, that is correct.

25 Q. And OEHHA in some of its work has used PK
26 factors, correct?

27 A. I know it was used in the 2005 assessment for
28 acrylamide, if that's what you're referring to.

1 I don't know if it's been used in other documents. I
2 assume it might have been, but I haven't read all of their
3 risk assessment documents.

4 Q. And you're critical of OEHHA for doing that, for
5 the same reasons that you're critical of Dr. Rhomberg,
6 correct?

7 A. Well, there's multiple aspects which I thought I
8 presented hopefully clearly yesterday in terms of the use of a
9 PK factor for mouse tumor responses versus rat tumor
10 responses.

11 OEHHA used a PK factor for the rat tumor response
12 because when they did their risk assessment, the mouse tumor
13 data were not available.

14 The mouse tumor response, to me, was massively
15 incorrect.

16 The rat, I have less of a problem with what they did.
17 But I pointed out certain aspects which lead to uncertainties
18 in the 1.2 numerical value that was used. And I think I
19 mentioned those yesterday, but I can mention them again if you
20 would like.

21 Q. This 1.2 is a value that was used by
22 Dr. Rhomberg, correct?

23 A. For rats but not for mice.

24 Q. And OEHHA used it, correct?

25 A. In the document that never was finalized, yes.

26 Q. And Dr. Bayard used it, correct?

27 A. That is correct.

28 Q. And if you had been doing it, you wouldn't have

1 done it, used a PK factor, correct?

2 A. If I was involved in the risk assessment, I
3 would have looked carefully at the data and pointed it out to
4 a group that was conducting the risk assessment to be sure
5 before applying it whether we had high confidence in that
6 value or not.

7 And I expressed areas in which my confidence was not
8 total on the use of that 1.2 value.

9 I'm not saying that there's not a PK factor that might
10 be usable, but the data upon which that PK factor is based, to
11 me, has much uncertainty.

12 Using an uncertain PK factor is a concern, because it
13 might be underestimating the numerical value that is used in
14 the estimation of risk.

15 MR. KENNEDY: Your Honor, I have a hypothetical
16 question for the doctor that I've written out.

17 With the Court's permission, may I --

18 THE COURT: Can you show it to Mr. Metzger?

19 MR. KENNEDY: Sure.

20 I predict an objection.

21 THE COURT: Since it's one page, I hesitate to see how
22 many subordinate clauses there are.

23 MR. METZGER: There are several.

24 THE COURT: All right. Present it to me.

25 MR. METZGER: So I do have several objections.

26 THE COURT: Mr. Metzger?

27 MR. METZGER: Should I state my objections now?

28 THE COURT: Go ahead.

1 MR. METZGER: So the hypothetical --

2 THE COURT: For a complete record, Mr. Kennedy, why
3 don't you ask the question first and then Mr. Metzger can
4 assert his objections.

5 MR. KENNEDY: Would it help if I approach and give the
6 witness a copy or just read it?

7 THE COURT: You can give a copy to the witness, please.
8 Before the witness says anything, Mr. Metzger, we
9 should have it on the record so we all know what we're talking
10 about.

11 You may read the question.

12 Q. BY MR. KENNEDY: Dr. Melnick, I want you to
13 assume the following.

14 First, that cooking necessary to achieve palatability
15 is, by itself, a sound consideration of public health which
16 supports an alternative significant risk level or ARL, if you
17 prefer, of more than one excess case of cancer in an exposed
18 population of 100,000.

19 Second, that the ASRL or ARL cannot impede the cooking
20 necessary to achieve palatability.

21 Third, that there is no duty to mitigate or reduce the
22 amount of acrylamide created by the cooking necessary to
23 achieve palatability.

24 Under those assumed circumstances, what would be the
25 proper ASRL or ARL?

26 MR. METZGER: Objection. This is going to be lengthy.

27 The hypothetical is grossly compound, argumentative,
28 ambiguous, assumes erroneous facts, assumes erroneous law.

1 I am now going to address the particulars of it.

2 The phrase that says that "cooking necessary to achieve
3 palatability is by itself a sound consideration of public
4 health which supports an alternative significant risk level or
5 alternative risk level," that is argumentative legally and
6 factually.

7 It assumes that -- just a moment. It assumes that a
8 particular level has been calculated pursuant to a
9 quantitative risk assessment as required in the regulation
10 which has not been done.

11 It assumes that palatability cannot be achieved without
12 acrylamide present or without reducing acrylamide.

13 The second part, that the ASRL cannot impede the
14 cooking necessary to achieve palatability, that is
15 argumentative legally. That's not in any regulation.

16 Mr. Kennedy is making up regulation and law.

17 It assumes that an alternative level cannot be achieved
18 without palatability.

19 It assumes that acrylamide cannot be reduced without
20 negatively affecting palatability.

21 The third part that there is no duty to mitigate or
22 reduce the amount of acrylamide is purely a legal question.
23 It's a question of duty.

24 It's also irrelevant because Proposition 65 does not
25 require any company to reduce the amount of any carcinogen.

26 Companies are free to expose Californians to
27 100 percent carcinogens as long as they give a warning.

28 So this is all grossly argumentative legally and

1 factually.

2 I think I've covered enough of it.

3 I object to the entire hypothetical question.

4 THE COURT: All right.

5 MR. KENNEDY: Yes, your Honor.

6 Mr. Metzger has just given us his view of the case.

7 With one exception, I believe the hypothetical not only
8 sets forth our view of the case but is supported by quotations
9 that have already come in.

10 If I might, Tom, can we put up Exhibit 71341, slide 2.

11 Your Honor, the source of the word "impede" I got from
12 the June, 1989 cleanup example. You will recall, that was --
13 the cleanup of toxic tort sites was the first of the three
14 examples that the agency adopted.

15 At that time they said,

16 "The agency was informed that
17 in most cleanups water is taken up, treated
18 and returned to the same source of ground
19 or surface water.

20 "The proposed regulation would
21 prevent liability for chemicals received in
22 the water.

23 "It's the intention of the agency
24 that ground and surface water cleanups not
25 be impeded."

26 As your Honor knows, they thereafter decided one
27 example wasn't enough. They really needed two more. And the
28 cooking and chlorine examples came along. Nothing to suggest

1 the same desire to prevent liability.

2 And we're talking about a statute which, as Mr. Metzger
3 has pointed out, deals with a duty to warn. The liability is
4 whether you have to warn or not and the exemplar conduct not
5 be impeded.

6 So it's our position that the ASRL, to the extent a
7 numerical one is required -- and obviously we're not conceding
8 that -- it has to be done in a way that will not impede the
9 roasting of coffee through any mechanism or means it's
10 entitled to.

11 Clearly, this is not the only argument that could be
12 made. We, however, feel it would be a benefit to your Honor
13 to know if you should accept our position supported by the
14 language we have as to what this esteemed toxicologist
15 believes on the subject.

16 MR. METZGER: All right. Now I have a further
17 objection.

18 THE COURT: Yes.

19 MR. METZGER: That with this clarification, this is
20 irrelevant because it is concerning toxic waste or water
21 cleanup.

22 There is no claim being made in this case that roasting
23 need be impeded. Everything that Dr. Melnick has testified to
24 regarding reduction of acrylamide fully allows roasting of the
25 coffee. It's not in any way being impeded.

26 He's not proposing that coffee be -- that coffee beans
27 be boiled or fried or grilled or anything like that. This is
28 purely a roasting process.

1 Proposition 65 and these things, these regulations, do
2 not in any way say that it cannot be optimized to reduce
3 levels of carcinogens.

4 This is all just argument. It's their position of the
5 case. I consider it wrong.

6 But to include basically their whole legal argument,
7 including all this stuff from 1989 before acrylamide was known
8 to be present in food is compound, argumentative. It's
9 nonsensical.

10 THE COURT: All right. Well, as we all know, expert
11 witnesses are entitled to be asked hypothetical questions.

12 The witness is being asked to assume certain facts. It
13 will be up to counsel to argue whether the facts that are
14 being asked to be assumed have been established.

15 The witness is called upon to assume certain legal
16 positions that counsel is arguing about, and that will
17 necessitate further argument of counsel after the conclusion
18 of the testimony.

19 So I recognize that a number of the clauses and
20 assumptions have not been established in this case yet.

21 Nevertheless the witness may be asked the question with
22 these assumptions. And we'll discuss it with counsel later
23 on, if any of the assumptions are appropriate from either a
24 factual or a legal position.

25 MR. METZGER: So you're allowing the witness to answer
26 subject to a motion to strike, your Honor?

27 THE COURT: Yes.

28 MR. METZGER: All right.

1 THE COURT: Mr. Kennedy, do you want to rephrase the
2 question to refresh the witness's recollection of the
3 question.

4 MR. KENNEDY: Certainly, your Honor.

5 Q. Dr. Melnick, I want to ask you to assume the
6 following.

7 That cooking is necessary to achieve palatability is by
8 itself a sound consideration of public health which supports
9 an alternative significant risk level, whether you call it
10 ASRL or ARL, of more than one excess case of cancer in an
11 exposed population of 100,000.

12 Second, that the ASRL/ARL cannot impede the cooking
13 necessary to achieve palatability.

14 And, third, that there is no duty to mitigate or reduce
15 the amount of acrylamide created by the cooking necessary to
16 achieve palatability.

17 Under those assumed circumstances, what is the proper
18 ASRL or ARL, if you prefer to call it that?

19 MR. METZGER: May I just confirm my objections are
20 preserved?

21 THE COURT: Yes.

22 MR. METZGER: Thank you.

23 THE WITNESS: I believe that the citizens of California
24 wanted to be notified --

25 THE COURT: No, we're not going there. We're not going
26 there. We're not going to discuss political process of
27 approving propositions.

28 Please focus on the question.

1 THE WITNESS: You're asking me to provide an arbitrary
2 number, as I see it, a number that is different than 1 per
3 100,000, if I accept these assumptions. That's the way I'm
4 reading your question and hypothetical situation.

5 Q. BY MR. KENNEDY: If you believe it has to be
6 arbitrary, that's your prerogative. I'm asking you if you can
7 answer the question as phrased.

8 I'm asking you to assume the correctness of all three
9 of those assumptions.

10 MR. METZGER: Objection. Now it's argumentative. The
11 witness has answered. He doesn't like the answer.

12 THE COURT: I haven't heard an answer yet.

13 There was a question about the question.

14 Let's focus on the question. If the witness doesn't
15 have an answer to the question, it's appropriate to say I
16 don't have an answer or I don't know. Those are acceptable
17 responses.

18 THE WITNESS: I don't have the arbitrary value that
19 would be appropriate.

20 It would not be one that is necessarily the level of
21 that agent, acrylamide, in coffee, such that we simply accept
22 what's there. So I cannot give you my arbitrary value.

23 But I don't think that arbitrary value should be just
24 selected by anybody without quantifying the benefits and risks
25 associated with these conditions.

26 Q. Does that complete your answer?

27 A. Yes.

28 I cannot give you a numerical value.

1 MR. KENNEDY: I have no further questions.

2 Thank you, Dr. Melnick.

3 THE COURT: Mr. Metzger, any redirect?

4 MR. METZGER: Yes, your Honor.

5 THE COURT: How long is it going to take?

6 MR. METZGER: I would -- I haven't timed it, but I
7 would say probably a half hour.

8 Should we take a break?

9 THE COURT: At this time we'll take a recess at this
10 time. We'll be in recess for 15 minutes.

11 (Recess.)

12 THE COURT: Mr. Metzger, are you ready to proceed?

13 MR. METZGER: Yes, your Honor.

14 THE COURT: Back on the record.

15 All counsel are present and Dr. Melnick is on the and
16 stand.

17

18

REDIRECT EXAMINATION

19 BY MR. METZGER:

20 Q. Dr. Melnick, are you in any way suggesting that
21 the coffee industry should not roast coffee?

22 A. No, I've never made that statement.

23 Q. Are you in any way suggesting that the coffee
24 industry should not roast coffee sufficiently to reduce
25 microbial contamination to the levels that they currently are?

26 A. No.

27 Q. Are you in any way suggesting that the coffee
28 industry should fry, pan fry, broil, boil or prepare coffee or

1 process coffee in any manner other than roasting?

2 A. No, I'm not.

3 Q. So one of the documents that you were shown was
4 the FDA guidance regarding acrylamide.

5 There was a statement in there that the FDA is
6 unaware -- presently unaware of a viable option for reducing
7 acrylamide in coffee.

8 You mentioned that there was a reference for that,
9 reference number 30.

10 What was that reference?

11 A. Yes. That was the FoodDrinkEurope document that
12 was prepared in 2013.

13 Q. Okay. And that was actually drafted by one of
14 the defendants in this case.

15 Are you aware of that?

16 A. I didn't know that.

17 MR. KENNEDY: Objection, assuming facts not in
18 evidence.

19 Move to strike.

20 THE COURT: The objection is sustained to the question.

21 The answer will be stricken.

22 Q. BY MR. METZGER: You are aware that
23 FoodDrinkEurope is the food and beverage industry of Europe,
24 correct?

25 A. Yes, it is.

26 Q. Okay. And do you recall reading among the
27 confidential industry documents that you were provided that
28 that statement in FoodDrinkEurope was actually prepared by

1 Nestle?

2 MR. KENNEDY: Objection, assuming facts not in
3 evidence.

4 THE COURT: Overruled.

5 THE WITNESS: I believe Nestle was involved in it. I
6 don't know if it was totally Nestle or not.

7 Q. BY MR. METZGER: All right. Now, have you
8 reviewed a subsequent publication by Food Drink Europe from
9 May of 2016?

10 MR. KENNEDY: Object. Beyond the scope of cross.

11 THE COURT: Overruled.

12 THE WITNESS: I'm aware that there has been an update
13 on the FoodDrinkEurope.

14 Q. BY MR. METZGER: And in that updated
15 FoodDrinkEurope document, the industry has now taken the
16 position that the asparaginase treatment of Novozymes does
17 have applications in certain contexts in reducing acrylamide
18 in coffee; isn't that true?

19 MR. KENNEDY: Object. Best evidence, your Honor.

20 THE WITNESS: Yes. I've seen that statement.

21 THE COURT: The objection is overruled.

22 The answer will stand.

23 Q. BY MR. METZGER: All right. Do we have that
24 article that was posted up there, the Mucci -- the Friedman?

25 Perhaps the defense could put it up since they had
26 it up.

27 THE COURT: All right. Please put that up.

28 MR. METZGER: It was the one with the pie charts on it.

1 MR. KENNEDY: If I might, your Honor, I think it's
2 69866.

3 MR. PARISER: That's Mucci.

4 MR. METZGER: The one that had the pie charts,
5 whichever it was.

6 There we go. That's it.

7 Q. So we're looking at the document Bates numbered
8 Smucker. 19474 is the page.

9 The title here is "Important Sources of Acrylamide in
10 Various Populations," with a subheading "(Percentage of Total
11 Acrylamide in the Diet.)"

12 May I approach that, your Honor, so I can actually
13 read it?

14 THE COURT: Yes.

15 Q. BY MR. METZGER: I don't know if you can see it,
16 Dr. Melnick.

17 A. I see it on my screen.

18 Q. You were shown this pie chart for Sweden. It
19 had coffee at 39 percent.

20 But the heading above that is actually "Sweden,
21 adults," parentheses -- it looks like 18 through 74 years of
22 age?

23 A. Yes, I see that.

24 Q. So that is an adult population. That is coffee
25 consumption for an adult population, correct?

26 A. That's what it is, Sweden adults.

27 Q. And then when you were shown for the United
28 States, you were indicating that, well, there might be

1 children included in there.

2 In fact, it says United States and in parentheses
3 "2 plus populations."

4 So that's including children age two and more, correct?

5 A. Correct.

6 Q. So are these comparable pie charts?

7 A. Definitely not.

8 That's what I was trying to address, but I hadn't
9 noticed it at that very moment because it was sprung on me.

10 But, yes, my concern was that the population value for
11 the United States of 8 percent may have included children and
12 non-coffee consumers, and therefore this would be a total
13 underestimate for adults.

14 Q. Right. And Dr. Scrafford included children in
15 her exposure assessment, likewise, correct?

16 A. I believe so, yes.

17 Q. Yeah.

18 A. And Dr. Rhomberg excluded in his risk assessment
19 the age up to 16.

20 Q. Right. Because he agreed with Dr. Bayard that
21 it was improper to include children who were not consumers,
22 correct?

23 A. Correct.

24 Q. All right. Now, is acrylamide as the defense
25 has used the phrase, "an inevitable byproduct"? I want to ask
26 the question using that phrase.

27 Is acrylamide an inevitable byproduct of roasting
28 coffee?

1 A. Most of the acrylamide is not an inevitable
2 byproduct of roasting coffee to provide a palatable product.

3 Q. Why is that?

4 A. Because if you remove asparagine from the
5 coffee, you will reduce most of the acrylamide that is formed.
6 Therefore, most of it is not an inevitable byproduct.

7 Q. And how do you remove the asparagine from the
8 coffee?

9 A. You can treat it with asparaginase.

10 Q. Okay. And that's one of the -- is one of the
11 companies that has developed that technique or methodology the
12 Novozymes?

13 A. Yes. Novozymes has developed the enzyme, yes.

14 Q. Right. And is that the specific technique that
15 the 2016 FoodDrinkEurope recognizes as a viable option for
16 reducing acrylamide in certain coffees?

17 A. Yes, it is.

18 Q. Now, do you believe that there should be an
19 alternative risk level for coffee?

20 A. No, I don't.

21 Q. Why not?

22 A. Because coffee can be prepared by roasting,
23 producing a palatable product in which the acrylamide levels
24 could be achieved at levels below the current NSRL.

25 Q. So why do you believe there shouldn't be an
26 alternative risk level?

27 Can you explain that further?

28 A. It's unnecessary.

1 THE COURT: Is there any, any alternative risk level
2 that you would think would be appropriate?

3 THE WITNESS: Not if you can achieve the current NSRL,
4 then no alternative risk level would be appropriate, in my
5 view.

6 Q. BY MR. METZGER: And why is that?

7 A. Why can't --

8 Q. Why would no alternative risk level be
9 appropriate if, as you have indicated, coffee can be produced
10 with acrylamide levels below the NSRL that's still palatable?

11 A. That's basically the reason, is that you have a
12 product in which acrylamide is below the NSRL, so there's no
13 reason to require or need an alternative risk level.

14 Q. And what would devising or allowing an
15 alternative risk level do in that circumstance?

16 A. An alternative risk level would allow higher
17 concentrations of acrylamide in the coffee products.

18 Q. And why is that -- why should that not be done?

19 A. Because acrylamide is a potent carcinogen which
20 is, for public health considerations one in which you want to
21 reduce human exposure not allow it.

22 Q. Not increase it?

23 A. Not increase it.

24 Q. Okay.

25 A. Sure.

26 THE COURT: So aside from what may happen in future
27 innovation in the wonderful world of chemistry, living today
28 in terms of what should be provided today, do you find that no

1 alternative risk level would be acceptable?

2 THE WITNESS: Because it hasn't been adequately
3 scaled up.

4 But there are methodologies available that can reduce
5 the acrylamide to levels of 90 percent or more reduction that
6 in a very short interval, or what could have been done years
7 ago was to have produced a product that would have met the
8 NSRL.

9 THE COURT: Well, while we're waiting for that
10 development, what should be done now?

11 THE WITNESS: The coffee industry should pursue --
12 well, there are a number of steps that can be done.

13 One is they can start packaging appropriately so that
14 coffee can be stored for a certain amount of time to start to
15 reduce the level of acrylamide to a reasonably high extent.

16 I'm not sure if it was in the range of 30, 40 percent.

17 They can apply methods that are available.

18 For example, the supercritical CO2 method, which is
19 available at most facilities, might require a little bit of
20 work.

21 But there are methods available that can, right now,
22 reduce acrylamide to levels probably below the NSRL.

23 And I would also suggest that they make better use of
24 the asparaginase treatment since it's already been implemented
25 in the German roaster. Why it hasn't pursued -- there may be
26 a number of reasons beyond what I can imagine, but it exists
27 and should be done.

28 Q. And can it be done? That is, can the industry

1 reduce acrylamide in instant coffee?

2 A. Oh, yes.

3 Q. And in decaffeinated coffee?

4 A. Certainly. This works for all coffee products.

5 Q. And when you say "this," what are you referring
6 to?

7 A. The treatments to reduce acrylamide. There are
8 methods to reduce it in all coffee products.

9 Q. And does the asparaginase treatment, would that
10 reduce it in all types of coffee?

11 A. Yes. Because this occurs prior to roasting. So
12 therefore all acrylamide which forms subsequent to roasting
13 will be at a lower level. So all coffee products will contain
14 less acrylamide with asparaginase treatment.

15 Q. And would simply storing roasted coffee in
16 sealed containers at room temperature or at 37 degrees, would
17 that likewise reduce acrylamide in all types of coffee that
18 are roasted?

19 A. It would be -- not in the drink because it's
20 binding to the matrix.

21 When the matrix is present, it can be reduced, if you
22 use 37 degrees, up to nearly 50 percent.

23 So as long as the matrix material is there, as I tried
24 to mention yesterday, the acrylamide will bind with those free
25 sulphidal groups similar to the way it is detoxified in the
26 human body.

27 Q. You're losing me, doctor.

28 What I'm trying to understand is can the industry

1 simply by roasting coffee using -- I'm so sorry.

2 Can the industry simply by using the Novozyme
3 asparaginase treatment reduce acrylamide in all different
4 types of roasted coffee?

5 A. Yes.

6 Q. And by storing coffee that has been roasted,
7 whether in whole bean or ground form, storing it in sealed
8 foil bags or containers, the cans, simply storing it for
9 several months, is that something that the coffee industry
10 could do right now to substantially reduce acrylamide in
11 coffee?

12 A. Yes. Under an inert gas or nitrogen environment
13 in the can, yes.

14 Q. And are there some coffee companies that
15 actually store their coffee that way or produce their coffee
16 that way right now?

17 A. Oh, yes.

18 Q. Okay. And all that they would need to do is to
19 hold that for a certain period of time to reduce the
20 acrylamide concentrations; is that correct?

21 A. That is correct.

22 Q. And then there are all these other technologies
23 that you mentioned which are a little more complicated than
24 that; is that correct?

25 A. The asparaginase and storage is the easiest.

26 Q. Okay?

27 A. Asparaginase is already developed.

28 Q. Okay. And is it your understanding that, in

1 fact, the reason that although there are 200 tons of coffee
2 produced and sold to market in Europe using the Novozymes
3 asparaginase treatment, that the reason there has not been a
4 market for that is because the coffee industry has boycotted
5 any reduction in acrylamide treatment?

6 MR. KENNEDY: Assuming facts not in evidence.

7 THE COURT: Objection sustained.

8 Q. BY MR. METZGER: Did you review any documents
9 that indicated that?

10 A. Some of the documents that were confidential
11 indicated that, yes.

12 Q. Okay.

13 MR. METZGER: Just one moment, your Honor.

14 I have no further questions.

15 Thank you very much, Dr. Melnick.

16 THE COURT: Any recross?

17 MR. KENNEDY: Very short, your Honor.

18
19 RE CROSS EXAMINATION

20 BY MR. KENNEDY:

21 Q. As I understand it, to correctly decide this
22 case, your opinion is that his Honor should reject the FDA
23 statement that there is no commercially viable means, correct?

24 MR. METZGER: Objection, argumentative.

25 THE COURT: Overruled.

26 THE WITNESS: He should recognize that that statement
27 is not true.

28 Q. BY MR. KENNEDY: And instead of accepting that,

1 he should accept your proposals for how acrylamide should be
2 reduced, correct?

3 A. These are not my proposals. These are evidence
4 based on data.

5 Q. The proposals that you've told us about, he
6 should accept those, correct?

7 A. To accept the proposal that acrylamide could be
8 reduced?

9 Q. Yes.

10 A. Yes, I think he should accept the idea that
11 acrylamide can be reduced in coffee.

12 Q. And these are all proposals that you know about
13 but have never shared with the FDA, correct?

14 MR. METZGER: Objection. It's cumulative,
15 argumentative.

16 THE COURT: It's been asked and answered.

17 MR. KENNEDY: Thank you very much.

18 I have no further questions, your Honor.

19 Thank you.

20 THE COURT: Anything further?

21 MR. METZGER: I do have one final follow-up on that.

22 THE COURT: One final follow-up. Go ahead.

23 MR. MARGULIES: I have a question, if I may. I'll just
24 do it from here, your Honor.

25

26 **CROSS-EXAMINATION**

27 BY MR. MARGULIES:

28 Q. Dr. Melnick, with regard to the storage of

1 coffee, you'd be concerned if storage would create other toxic
2 byproducts, right?

3 A. Would I be concerned?

4 I've never seen evidence to that effect.

5 Q. So you were relying on the Baum study, right,
6 the radioactive label to acrylamide that they looked at and
7 then collected on the filter paper?

8 A. Well, that's the demonstration of why it
9 decreases.

10 I'm relying on products that are available on the
11 market, such as Illy coffee and Starbucks coffee, in which
12 coffee does not have to be consumed within one week or two
13 weeks of which the proposal had been made that staling occurs
14 within two weeks.

15 Q. Simple question, doctor.

16 You relied on the Baum study, correct?

17 A. As I mentioned, to demonstrate how it occurs.

18 Q. All right. And Baum said that the mechanisms
19 underlying the loss of acrylamide during storage are as yet
20 unknown, correct?

21 A. No.

22 They demonstrated that it's binding to the matrix.

23 Q. Okay. And what was the metabolite of acrylamide
24 that you believed was the carcinogenic compound that was
25 causing cancer in lab animals?

26 A. Glycidamide would be the primary. But there may
27 also be some effects associated with acrylamide itself but
28 primarily associated with glycidamide.

1 Q. Did Baum discuss whether the acrylamide in the
2 stored coffee might, in fact, be oxidized into glycidamide?

3 A. No, that wouldn't happen. That's an enzymatic
4 reaction.

5 Q. You don't recall them saying, "Further, since
6 coffee has been reported to contain hydrogen peroxide, it is
7 not unlikely that oxidation into the acrylamide-derived
8 epoxide glycidamide might potentially also contribute to some
9 extent to acrylamide loss"?

10 A. But that was a hypothesis. That's a
11 speculation.

12 If they demonstrated it --

13 Q. But you would be concerned. You wouldn't want
14 that to happen in a method that you are suggesting should
15 reduce acrylamide, right?

16 MR. METZGER: Objection. As to what. What is "that to
17 happen"?

18 THE COURT: Overruled.

19 THE WITNESS: I would not want to see that happen, but
20 if you don't remove the acrylamide, it's going to form
21 glycidamide in the consumer.

22 Q. BY MR. MARGULIES: But if at the end of the day
23 it's simply forming glycidamide in the can, you haven't really
24 achieved anything by storing it, correct?

25 A. It's a complex question because you're dealing,
26 then, with distribution of glycidamide in the body from the
27 coffee itself.

28 I don't know what would happen once you start to boil

1 coffee to make it a consumable product, what would happen to
2 the glycidamide.

3 So it's not a simple question. It sounds simple, but
4 it's not really a simple question to answer.

5 You need to look at a cup of coffee to see if there is
6 any glycidamide in it, but I haven't seen any data to indicate
7 that.

8 Q. So you've offered a simple solution, but there
9 is a lot of complexity to it that would need to be resolved
10 before the coffee company would adopt it to reduce acrylamide,
11 right?

12 MR. METZGER: Objection, argumentative.

13 THE COURT: Overruled.

14 THE WITNESS: That would be easy to be done.

15 The analysis of stored coffee for glycidamide? That
16 could be done in a week.

17 Q. BY MR. MARGULIES: Has it ever been done?

18 A. I don't work for the coffee companies. Maybe
19 they have. I don't know.

20 Q. But you're here offering an opinion that this is
21 a safe way to reduce acrylamide exposure, which really means
22 glycidamide exposure, correct?

23 A. I would assume that Starbucks and Illy would not
24 say you could store your coffee for 60 weeks or up to two
25 years knowing that glycidamide is being formed.

26 MR. MARGULIES: Move to strike as non-responsive.

27 THE COURT: The motion is granted.

28 The last answer will be stricken.

1 MR. MARGULIES: No further questions. Thank you.

2 THE COURT: Anything further, Mr. Metzger? Last
3 question.

4

5 **FURTHER REDIRECT EXAMINATION**

6 BY MR. METZGER:

7 Q. Dr. Melnick, have you seen any data whatsoever
8 that glycidamide is formed in stored coffee?

9 A. No.

10 But let me address one thing, because it relates to the
11 point you just made, that it might occur through hydrogen
12 peroxides.

13 Those are products of lipid oxidation and when storing
14 the coffee under a nitrogen atmosphere, those peroxide
15 products don't form. You don't get the lipid oxidation.

16 So therefore it's not going to happen.

17 Q. Oh, I'll just end there.

18 MR. METZGER: Thank you, your Honor.

19 THE COURT: Thank you.

20 May Dr. Melnick be excused?

21 MR. MARGULIES: Yes, your Honor.

22 THE COURT: You may step down, Dr. Melnick.

23 THE WITNESS: Thank you.

24 THE COURT: Plaintiff have any further witnesses?

25 MR. METZGER: Not live witnesses.

26 Well, actually, we do.

27 THE COURT: Not the deposition testimony?

28 MR. METZGER: There is this additional witness who I

1 mentioned yesterday who we would like to call tomorrow. He's
2 currently having -- undergoing a surgical procedure today so
3 he's not available today. But he's available --

4 THE COURT: This is a newly discovered witness?

5 MR. METZGER: It's a newly discovered witness.

6 THE COURT: And defendants have not known about this
7 witness either?

8 MR. KENNEDY: No. We've not known about him
9 previously.

10 THE COURT: Is this a self-identified individual who
11 has volunteered to become a part of this case?

12 MR. METZGER: He did contact me upon reading media
13 reports of the case.

14 He is the assignee -- well, his company is the assignee
15 of an acrylamide reduction technology which, as he described
16 it to me, uses herbs to -- the initial goal was to make a more
17 flavorful coffee, which was achieved.

18 And then, in doing further studies to see what
19 resulted, there was the incidental finding of a substantial
20 reduction of acrylamide.

21 THE COURT: And did you check out all this information
22 that he gave you?

23 MR. METZGER: Well, I do have the patent application.
24 Yes.

25 THE COURT: Okay. And has defendant had an opportunity
26 to take his deposition?

27 MR. METZGER: No.

28 One thing that puzzled me is that the defendants'

1 production of documents did not include anything about this,
2 although he had communications, written communications, with
3 several of the defendants regarding this technique.

4 So had they produced that, I would have discovered him
5 much earlier, but they did not.

6 THE COURT: And they have not taken his deposition?

7 MR. METZGER: No.

8 THE COURT: And supposing they take his deposition and
9 then they decide, well, they need three experts to respond to
10 him. Then what do we do?

11 This is a slippery slope we go to.

12 MR. METZGER: I do not intend to have him offer any
13 expert testimony. I'm merely going to have -- largely have
14 him offer party opponent admissions of certain defendants in
15 this case.

16 THE COURT: Mr. Kennedy?

17 MR. KENNEDY: We filed a short brief on this this
18 morning, your Honor.

19 Our principal concern is it's our understanding he will
20 be trying to introduce hearsay conversations with some small
21 number of the defendants, none of which, as far as I know, I
22 represent, but I wouldn't be surprised that those people are
23 then going to want the opportunity to respond to what he
24 claims they said or didn't say.

25 Beyond that, we will withdraw our request for his
26 deposition. We have no desire to delay the proceedings.

27 So at least remove that obstacle.

28 I think your Honor is in the best position to know what

1 would be helpful to you at this point.

2 THE COURT: The Court is going to exclude this witness.

3 The witness has not been previously identified, not
4 been made available for deposition.

5 There is a concern that it is somebody who apparently
6 has some other motivation, some other interest, an economic
7 interest in some patent or some process that may or may not be
8 relevant, and he's self-identified.

9 He's interested in volunteering to become a witness. I
10 don't think at this stage of the proceedings it's appropriate.

11 The Court will exclude that witness.

12 All right. Mr. Metzger, any other witnesses besides
13 those witnesses that are going to have their testimony
14 reviewed through depositions?

15 MR. METZGER: Plaintiff has no other live witnesses.
16 It's just the deposition excerpts of the defendants' PMKs.

17 Then there is also the discovery responses, likewise,
18 to be reviewed by your Honor, but no one live. This is our
19 last live witness now that you've excluded, Mr. Durand.

20 THE COURT: The defendants, any further witnesses?

21 MR. KENNEDY: Yes, your Honor. As we mentioned
22 previously, we have a rebuttal witness from Covance who is
23 here in the courtroom.

24 In addition, in light of Dr. Spingarn's testimony that
25 even the FDA data is unreliable, we also served an offer of
26 proof this morning offering Dr. Troxell, which would be a
27 very, very short -- both of these would be very short true
28 rebuttal responses to factual inaccuracies.

1 I think Mr. Metzger is going to hurt himself if I don't
2 let him stand up, but those are our next two live witnesses.

3 THE COURT: All right. Are you ready to call your next
4 witness?

5 MR. METZGER: Excuse me, your Honor.

6 They want to call this Dr. Mastovska as an undesignated
7 expert.

8 THE COURT: Besides that. We'll get to that.

9 What about the witness in the courtroom?

10 MR. KENNEDY: That is the doctor.

11 THE COURT: Oh, I thought that was the second one.

12 MR. KENNEDY: Dr. Mastovska. And Dr. Troxell is in
13 town. He's available. It will be very, very brief. It will
14 be rebuttal to some errors of fact by Dr. Spingarn.

15 MR. METZGER: This is the first I'm hearing about
16 Dr. Troxell.

17 Dr. Troxell is an expert who the defense previously
18 submitted a declaration to the Court.

19 They chose not to designate him, and now they want to
20 bring him in as a witness even though -- after concealing him
21 and choosing not to designate him.

22 As a matter of fact, I filed a motion in limine to
23 preclude all of the defendants' designated experts from
24 relying on Dr. Troxell's opinions set forth in his report.

25 THE COURT: All right. Briefly with Dr. Troxell, I
26 understand he's not being called to venture any opinions
27 whatsoever.

28 The doctor is going to be called to impeach some

1 factual statements made by some witness?

2 MR. KENNEDY: Yes, it will be very brief.

3 If we go beyond true rebuttal, I'm sure your Honor will
4 shut us down.

5 Frankly, we can hear it in less time.

6 THE COURT: Let's go back to the other witness.

7 MR. KENNEDY: Mr. Schurz is probably in the best
8 position to answer questions about her.

9 THE COURT: Okay. Any problem with the other witness,
10 that's Dr. -- what is the name again?

11 MR. SCHURZ: Mastovska, M-A-S-T-O-V-S-K-A.

12 MR. METZGER: Yes, there is a problem, your Honor.

13 As you recall, you directed Mr. Schurz to send me a
14 communication, a letter, an email advising specifically what
15 foundational facts that the defense claims are either false or
16 non-existent Dr. Mastovska would testify to; that is, what
17 facts relied upon by another expert who testified in this
18 trial --

19 THE COURT: Yes.

20 MR. METZGER: -- are false or non-existent.

21 THE COURT: Just a second.

22 I just want to confirm that Dr. Mastovska is not going
23 to render any new opinions, contrary opinions?

24 She's going to testify only as to factual issues
25 concerning Covance?

26 MR. SCHURZ: Correct.

27 MR. METZGER: So Mr. Schurz sent me nine topics.

28 The first one was validation of the Covance method.

1 All of these are topics that Mr. Sullivan testified
2 about and that also Dr. Spingarn testified about.

3 None of them are in the nature of -- he did not
4 identify a single fact that Dr. Spingarn or any other expert
5 testified about that is false or non-existent.

6 These are entirely opinions that contradict opinions.

7 In fact, most of her opinions that they are proposing
8 to offer contradict sworn testimony of their designated
9 expert, Mr. Sullivan.

10 I have prepared and submitted an in limine motion which
11 lays all of this out. Every one of the nine topics are not in
12 the nature of a false or non-existent predicate fact.

13 Every one of them is a contradict -- is an opinion that
14 contradicts testimony offered by Mr. Sullivan and/or
15 Dr. Spingarn.

16 THE COURT: That may be, but that's defendants'
17 problem.

18 So Dr. Mastovska is going to offer impeachment
19 testimony about what, specifically?

20 MR. SCHURZ: She will address eight specifics areas,
21 your Honor.

22 She will testify that Dr. Spingarn told the incorrect
23 formula to this Court when calculating the concentration of
24 acrylamide.

25 You will recall, your Honor, he got up --

26 THE COURT: You don't have to go into more detail.

27 So the formula.

28 Next?

1 MR. SCHURZ: Dr. Spingarn provided and displayed a
2 table, Exhibit 61939, that is factually incorrect with respect
3 to the material that was provided there. He's just got it
4 wrong.

5 It's pretty straightforward.

6 THE COURT: And how much time will be consumed by
7 Dr. Mastovska's testimony?

8 MR. SCHURZ: Less than an hour.

9 THE COURT: The Court will allow the defendant to call
10 Dr. Mastovska, again, not to provide any opinions. Just for
11 the purpose of impeachment of any factual testimony.

12 MR. METZGER: Your Honor, while you're doing this, may
13 I provide you with a copy of our in limine motion? Because
14 I'm going to be referring to testimony that she's
15 contradicting opinions.

16 THE COURT: Well, if she contradicts defendants'
17 testimony, that's defendants' problem.

18 MR. METZGER: You don't want this?

19 THE COURT: Yes, you can present it.

20 I know you're thinking you were concerned about
21 defendant impeaching themselves, but that's okay.

22 All right. Dr. Melnick, please step down from the
23 stand.

24 Mr. Schurz.

25 MR. SCHURZ: Thank you, your Honor.

26 MR. METZGER: Your Honor, do I get to depose this
27 witness?

28 THE COURT: It is just for impeachment of the

1 plaintiff's witnesses, not impeachment of defendants'
2 witnesses.

3 MR. METZGER: Foundational facts.

4 THE COURT: Right.

5 MR. SCHURZ: Your Honor, at this time we would call
6 Katerina Mastovska.

7 THE CLERK: Please raise your right hand.

8
9 KATERINA MASTOVSKA,
10 having been called as a witness and sworn testified as
11 follows:

12 THE WITNESS: Yes, I do.

13 THE CLERK: And can you please state and spell your
14 name for the record.

15 THE WITNESS: My first name is Katerina,
16 K-A-T-E-R-I-N-A. And my last name is Mastovska,
17 M-A-S-T-O-V-S-K-A.

18 THE CLERK: Thank you.

19 THE COURT: Good morning, Dr. Mastovska.
20 And, Mr. Schurz, you may proceed.

21 MR. SCHURZ: Thank you, your Honor.

22

23 **DIRECT EXAMINATION**

24 BY MR. SCHURZ:

25 Q. Good morning, Dr. Mastovska.

26 A. Good morning.

27 Q. And let me ask you, if you would, to lean into
28 the microphone that's there in front of you so we can all hear

1 you.

2 Dr. Mastovska, I've provided you with a binder, and to
3 opposing counsel as well as the Court, with a set of exhibits
4 that we may be referring to over the course of our brief
5 discussion. And you should feel free to refer to those as we
6 discuss them.

7 But with that as an orientation, can I ask you to
8 describe for the Court your current position at Covance?

9 MR. METZGER: Objection. She doesn't need to be
10 qualified as an expert. She's not testifying as an expert.

11 THE COURT: Well, let's hear about what she does for a
12 living.

13 Go ahead, Mr. Schurz.

14 THE WITNESS: I'm associated at Covance Solutions, and
15 I lead the global chemistry research development and
16 innovation group.

17 Q. BY MR. SCHURZ: Now, let's turn specifically to
18 the work that you've done with respect to the analysis of the
19 defendants' coffee products by Covance.

20 Can you tell this Court when you became involved in
21 Covance's work relating to the acrylamide testing in
22 defendants' brewed coffee products?

23 MR. METZGER: Objection, CCP 2034.310(b). This is not
24 going to a foundational fact.

25 THE COURT: This is just merely background. We'll get
26 to the testimony as to this case in a moment.

27 THE WITNESS: Should I answer?

28 THE COURT: You may answer the question.

1 THE WITNESS: Okay. I got first involved on July 19th
2 of this year.

3 Q. BY MR. SCHURZ: And how did you become involved
4 in the work that Covance performed relating to defendants'
5 brewed coffee products?

6 A. I was contacted by Julie Lowe who is the
7 technical leader and by Ben Abel who is the supervisor in the
8 group who performed the testing.

9 And they asked me to review calculations performed in
10 this case.

11 Q. And did you, in fact, review the calculations of
12 the acrylamide concentrations for the defendants' coffee
13 products in this matter?

14 A. Yes, I did.

15 Q. And as a result of that review, what did you do?

16 MR. METZGER: Objection. This is not going to --

17 THE COURT: Overruled.

18 THE WITNESS: I confirmed that there was a calculation
19 issue, and I also was involved in the generation of the CAPA,
20 C-A-P-A. It's the corrective action/preventative action.

21 Q. And directing your attention in the binder to
22 Exhibit DX 72470, can you identify this document for us.

23 A. Yes, I can. That is the corrective
24 action/preventative action document.

25 Q. Now, as part of your review of the calculations,
26 did you check on how the calculation concentration value set
27 out in the Covance data sheets was developed?

28 A. Yes, I did.

1 Q. All right. And we'll come back to that in a
2 moment.

3 In addition to your work on the corrective
4 action/preventative action plan, did you have any other
5 involvement with respect to the coffee products in this case
6 following your involvement in July of 2017?

7 A. Yes. I also reviewed a revised supplemental
8 validation report.

9 Q. And directing your attention to, in the binder,
10 72484, can you identify this document for us?

11 A. Yes. That's the document which I reviewed and
12 revised, and my revisions were implemented.

13 I also reviewed the data tables provided in this
14 report.

15 Q. All right. Thank you.

16 With that context, then, I would like to turn now
17 specifically to certain statements that were made by Dr. Neil
18 Spingarn in his testimony.

19 Showing you first Dr. Spingarn's testimony at 164,
20 lines 16 to 24.

21 And did you review the testimony of Dr. Neil Spingarn
22 in your preparation for your testimony today?

23 A. Yes, I did review it.

24 Q. Directing your attention to the specific
25 statement made at page 164, line 16 through 24, it reads as
26 follows:

27 "Q. All right. And did you review a
28 series of these?

1 "A. Yes.

2 "Q. And what did you find?

3 "A. I found that they had corrected the
4 unit issue so that the units in the lower
5 left box are now micrograms per
6 milliliter, as they should have been in
7 the first set. But I also noticed what
8 appears to be a calculation error in
9 these sheets."

10 Did you review that testimony?

11 A. Yes, I did.

12 Q. As a factual matter, did Covance make a
13 calculation error?

14 MR. METZGER: Objection. This is a contrary opinion.
15 It's not a factual foundation.

16 THE COURT: Overruled.

17 THE WITNESS: No, we did not.

18 Q. BY MR. SCHURZ: Showing you the exhibit that
19 Dr. Spingarn was relying on, which is Exhibit 61941 -- do you
20 have that in front of you?

21 A. Yes, I have.

22 Q. Now, Dr. Spingarn started with the premise that
23 calculating the concentration is a fairly simple calculation
24 and that everything you need to perform that calculation is
25 present on this sheet, referencing 61941.

26 MR. METZGER: Objection. I object to Mr. Schurz's
27 characterization Dr. Spingarn's testimony.

28 He's mischaracterizing it and including it in the

1 question to the witness.

2 THE COURT: Yes. Please avoid doing that.

3 You can ask the witness. And if the witness has
4 different information about Dr. Spingarn, she can so state.

5 Q. BY MR. SCHURZ: As a factual matter, is
6 Dr. Spingarn correct that everything he needed to arrive
7 at --

8 MR. METZGER: Objection.

9 THE COURT: Objection sustained.

10 Please phrase the questions where you do not have the
11 witness commenting on some other witness's testimony.

12 Q. BY MR. SCHURZ: Did Dr. Spingarn --

13 THE COURT: Again, go to facts, not whether they agree
14 or disagree with some other witness.

15 MR. SCHURZ: I understand.

16 Q. Did Dr. Spingarn use the correct formula?

17 A. No, he did not.

18 MR. METZGER: Objection. This is contradicting his
19 opinion.

20 THE COURT: Again, just -- you can ask the witness as
21 to some specific factual statement that you believe is
22 inconsistent with the previous testimony but not to argue
23 about whether the witness agrees or disagrees or whether the
24 witness is right or wrong.

25 Q. BY MR. SCHURZ: Is all the information necessary
26 to calculate the acrylamide concentration available on 61941?

27 MR. METZGER: Objection. This is contradicting an
28 opinion.

1 THE COURT: Overruled.

2 You may answer the question.

3 THE WITNESS: No, it's not.

4 Q. BY MR. SCHURZ: What is missing?

5 A. What's missing is the calculation equation which
6 is needed to calculate the concentration of acrylamide in the
7 extracts.

8 Q. Showing you 73517.

9 Can you tell us what this document is?

10 A. This is the calibration which relates to that
11 batch for the sample which was shown on the previous screen.

12 Q. And where is the relevant formula required for
13 calculating the acrylamide concentration necessary for the
14 data sheet 61941?

15 MR. METZGER: Your Honor, this is all beyond the scope
16 of the --

17 THE COURT: Overruled.

18 THE WITNESS: The formula is in the upper left corner.

19 If you could zoom on it. So you can see it here.

20 That's an integration equation which I won't read, but
21 this is the equation that is used for calculation in this case
22 and in this matter.

23 Q. BY MR. SCHURZ: Did Dr. Spingarn use this
24 formula in calculating the acrylamide concentration values?

25 A. No, he did not.

26 Q. All right. So did Dr. Spingarn use the correct
27 formula for calculating the concentration values in these data
28 sheets?

1 MR. METZGER: Objection. He's seeking a contrary
2 opinion.

3 THE COURT: Overruled.

4 THE WITNESS: No, he did not.

5 Q. BY MR. SCHURZ: All right. Let me turn to the
6 second issue relating to Dr. Spingarn's testimony.

7 I would show you Exhibit 61939, the Covance modified
8 protocol demonstrative that Dr. Spingarn provided to this
9 Court.

10 Have you reviewed this document?

11 A. Yes, I have.

12 Q. Directing your attention to the lower right-hand
13 corner in which 61939 states with respect to validation as
14 with respect to the column "Will Be Washed," Dr. Spingarn
15 states, "None. Ineffective. Retention at start of June 21st
16 data equals 4.0 minutes. Retention at start of June 22nd data
17 equals 5.3 minutes."

18 Do you have that in mind?

19 A. Yes, I can see it. I have it in mind.

20 Q. Let's start with the retention times from the
21 June 22nd that are referenced here.

22 Did you try to look up to determine whether the data
23 and retention times that are reflected in Dr. Spingarn's
24 exhibit are accurate with respect to June 22nd?

25 MR. METZGER: Objection. It's a contrary opinion.

26 THE COURT: Overruled.

27 THE WITNESS: Yes, I tried.

28 Q. BY MR. SCHURZ: And what did you find?

1 A. I couldn't find his data.

2 Q. Did you find a retention time of 5.3 minutes, as
3 stated by Dr. Spingarn in Exhibit 61939?

4 A. No, I did not.

5 Q. Why not?

6 MR. METZGER: Well, objection. Now she's offering an
7 opinion.

8 THE WITNESS: No, it's not an opinion.

9 THE COURT: Hey, wait. Your job is to answer
10 questions, not to argue with the lawyer.

11 The objection is overruled.

12 Next question.

13 Q. BY MR. SCHURZ: How is it that you did not find
14 the 5.3-minute retention times at the start of the June 22nd
15 data?

16 A. Because no data were required on June 22nd in
17 this case.

18 Q. How do you know that?

19 A. I reviewed all data. I put it all together and
20 was trying to find acquisition date on June 22nd.

21 I also confirmed with Mr. Ladd, with Julie Lowe and Ben
22 Abel.

23 MR. METZGER: Objection. It's hearsay.

24 THE WITNESS: It's not hearsay.

25 THE COURT: Dr. Mastovska, your job is to answer
26 questions, not to argue.

27 THE WITNESS: I'm sorry.

28 THE COURT: Do you understand that?

1 THE WITNESS: Yes.

2 I apologize.

3 THE COURT: Please repeat the question.

4 Q. BY MR. SCHURZ: Dr. Mastovska, how did you
5 confirm that there was no testing performed on June 22nd?

6 A. I reviewed the data myself.

7 Q. Thank you.

8 Now, let's turn to Dr. Spingarn's statement with
9 respect to June 21.

10 He states, "The retention at start of June 21 data
11 equals 4.0 minutes."

12 Do you see that?

13 A. Yes, I can see that.

14 MR. METZGER: Objection, offering a contrary opinion.

15 THE COURT: Overruled.

16 THE WITNESS: Can you repeat the question, please?

17 Q. BY MR. SCHURZ: Is that a correct statement,
18 that the retention time at the start of the June 21 data is
19 4.0 minutes?

20 A. No, it's not a correct statement.

21 Q. And what was the retention time for the testing
22 that was performed on June 21?

23 A. The retention time for the first injection on
24 June 21st was 4.5 minutes.

25 Q. And directing your attention in the binder to
26 Exhibit 72344.065, can you identify this document for us?

27 A. Yes. That's the worksheet. That's the printout
28 for the -- for the first injection date on June 21st.

1 Q. And what is the retention time for the first
2 sample on 6/21/2017?

3 A. The retention time for acrylamide is
4 4.5 minutes.

5 Q. All right. So with respect to this value, if we
6 could go back Dr. Spingarn's table, 61939, so is it the case,
7 Dr. Mastovska, that Dr. Spingarn's statement that the
8 retention time at the start of June 21 data of four minutes is
9 incorrect?

10 MR. METZGER: Objection. He's expressly seeking a
11 contrary opinion.

12 THE COURT: Overruled.

13 THE WITNESS: Yes, that's incorrect.

14 Q. BY MR. SCHURZ: All right. Now, so having
15 determined what the retention time was for the first sample on
16 June 21st, when was the next testing performed with respect to
17 the defendants' coffee products at Covance?

18 A. The next testing was performed on June 27th.

19 Q. And what was the retention time for the first
20 sample tested on June 27th?

21 MR. METZGER: Objection. This is not addressing any
22 opinion rendered by an expert, any fact testified to by an
23 expert.

24 THE COURT: I don't know what that is addressing in
25 terms of any prior correction of somebody else or
26 contradiction.

27 Objection sustained.

28 Q. BY MR. SCHURZ: All right. So what we have here

1 is a statement in both respects as to the retention time that
2 are incorrect from Dr. Spingarn, correct?

3 MR. METZGER: Objection. Contrary opinion.

4 THE COURT: Overruled.

5 You may answer.

6 THE WITNESS: Can you repeat the question, please.

7 Q. BY MR. SCHURZ: Yes.

8 Both statements by Dr. Spingarn in Exhibit 61939 with
9 respect to the retention times are factually incorrect?

10 A. Yes, they are.

11 Q. All right. Now, what was the start time --
12 strike that.

13 What was the retention time for the next start of
14 testing following the June 21st data?

15 A. It was 4.38 minutes which was on June 27th.

16 Q. And what is the consequence or significance of
17 the retention times that you have now testified to with
18 respect to June 21 and June 27?

19 MR. METZGER: Objection. Now he's asking for an
20 opinion which has not anything to do with the factual
21 predicate.

22 THE COURT: The objection is sustained.

23 Q. BY MR. SCHURZ: Was Dr. Spingarn correct in his
24 statement that the retention times reflected that the
25 equipment was not operating correctly?

26 MR. METZGER: Objection, seeking a contrary opinion.

27 THE COURT: Sustained.

28 The way the question is phrased, it's sustained.

1 MR. SCHURZ: All right.

2 Q. Let me turn to the retention times and a third
3 area of Dr. Spingarn's testimony.

4 Here I would direct, Dr. Mastovska, your attention to
5 page 58, lines 1 through 13, of Dr. Spingarn's testimony.

6 "Q. You mean where temporally?

7 "A. In time.

8 "That is, you have a ten-minute run.
9 You start your injection. How long does
10 it take for the peak, the internal
11 standard, to come out the other end of
12 the machine. That has to be extremely
13 consistent also for the system to be in
14 control.

15 "In these two cases, the June 21st
16 and June 22nd, the June 21st peaks came
17 out at 5.3 minutes. The June 22nd came
18 out at 4.0 minutes.

19 "We have a tremendous change in the
20 retention time. That means the
21 chromatography isn't working. That's the
22 first half of the machine."

23 Do you have that testimony in mind?

24 A. Yes, I have.

25 Q. Did you examine any retention time data to
26 determine if the chromatography method was working during the
27 time period being referenced here by Dr. Spingarn?

28 MR. METZGER: Objection, contrary opinion.

1 THE COURT: Overruled.

2 THE WITNESS: Yes.

3 In addition to those you just mentioned, I also
4 reviewed the retention times for both the acrylamide peak and
5 the internal standard peak across all batches.

6 Q. BY MR. SCHURZ: And what did you find?

7 MR. METZGER: Objection. This is not a factual
8 predicate. She is now testifying as to what she found.

9 THE COURT: Objection sustained.

10 Q. BY MR. SCHURZ: And in looking in your analysis
11 with respect to the change that was purportedly found by
12 Dr. Spingarn, what did you find?

13 MR. METZGER: Same objection.

14 THE COURT: Objection sustained.

15 Q. BY MR. SCHURZ: Now, did you find that there was
16 a tremendous change in the retention time from the period of
17 June 21st to the next actual testing of samples in this case?

18 MR. METZGER: Objection.

19 THE COURT: Objection sustained.

20 MR. SCHURZ: All right.

21 Q. So let me turn to another area of testimony of
22 Dr. Spingarn.

23 Now I would like to show you the second of his two
24 demonstratives that he provided which you will find in your
25 binder at 16940. It's the second tab.

26 Do you have that in front of you?

27 A. Yes, I have.

28 Q. Is the factual foundation upon which this

1 demonstrative rests correct?

2 MR. METZGER: Objection. That's asking for an opinion.

3 THE COURT: Objection sustained.

4 Q. BY MR. SCHURZ: Are the facts upon which
5 Dr. Spingarn relies in depicting on Exhibit 61940 correct?

6 MR. METZGER: Objection, vague as to what facts.

7 THE COURT: Objection sustained.

8 Q. BY MR. SCHURZ: Let's try it this way.

9 Do you see the title "Internal Standard Response
10 Factors"?

11 A. Yes, I see it.

12 Q. Does this Exhibit 61940 accurately depict the
13 internal standard response factors?

14 MR. METZGER: Objection.

15 THE COURT: I think we'll take the recess, and I would
16 ask counsel to discuss this over lunch.

17 I think we have some miscommunication here. The Court
18 allowed the witness to testify for impeachment purposes only.

19 That is, if a witness came in and said that
20 January 15th, 1965, was a Thursday and gave some opinion based
21 on that, then a witness could come in and say, no,
22 January 15th is not a Thursday. It was a Wednesday.

23 That is an underlying foundational fact that is in
24 dispute but the purpose was not to call a witness to render a
25 whole bunch of additional opinions to bootstrap positions of
26 the parties.

27 So think about what a foundational fact is to support
28 some other witness as opposed to opinion.

1 We'll be in recess until 1:30.

2 (At 12:00 noon a recess was taken until.

3 1:30 p.m. of the same day.)

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EXHIBIT “G”

CURRICULUM VITAE – Ronald L. Melnick

Address: [REDACTED] [REDACTED]
[REDACTED], UT [REDACTED] [REDACTED], CT [REDACTED]

Phone: Home: 435-[REDACTED] 203-[REDACTED]
Mobile: 919-[REDACTED]

Email: ron.melnick@gmail.com

Date & Place of Birth: May 19, 1943, New York, NY

Citizenship: United States

Education:

- 1965 B.S. (Food Science) Rutgers University, New Brunswick, NJ
- 1967 M.S. (Food Science/Biochemistry) University of Massachusetts, Amherst, MA. Thesis: *A Study of Bound and Solubilized Lactate Dehydrogenase in Skeletal Muscle.*
- 1970 Ph.D. (Food Science/Biochemistry) University of Massachusetts, Amherst, MA. Thesis: *Cellular Organization. A Study of Glycolytic Enzymes in Skeletal Muscle.*

Chronology of Employment:

- 1970 - 1973 Postdoctoral fellow, Department of Physiology-Anatomy, University of California, Berkeley, CA.
- 1973 - 1980 Assistant Professor of Life Sciences, Polytechnic Institute of New York, Brooklyn, NY.
- 1980 – 1990 Toxicologist, National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC. Study scientist for NTP toxicology/carcinogenesis studies on 1,3-butadiene, bromoform, chloroacetophenone, chloroprene, chlorpheniramine, 2,4-dichlorophenol, diethanolamine, diphenhydramine, isoprene, melamine, phthalate esters, succinic anhydride.
- 1981 – 1990 Project Officer, National Toxicology Program, NIEHS:

- 1) Twelve toxicology/ carcinogenicity studies at Physiological Research Labs., Minneapolis, MN;
 2) Development and use of an in vitro system for the study of toxicity in renal tubules from several mammalian species, SRI International, Menlo Park, CA
- 1985 - 1989 Manager, Experimental Toxicology Unit, Carcinogenesis and Toxicology Evaluation Branch, NIEHS
- 1990 – 1993 Toxicologist, Division of Biometry and Risk Assessment, NIEHS
- 1993 – 1995 Toxicologist, Environmental Carcinogenesis Program, NIEHS,
- 1995 - 1996 Agency Representative in the White House Office of Science and Technology Policy (Environment Division), Washington, DC.
- 1995 – 2000 Group Leader, Toxicokinetics and Biochemical Modeling Group, Laboratory of Computational Biology and Risk Analysis, Environmental Toxicology Program, NIEHS
- 2001- 2008 Director of Special Programs, Environmental Toxicology Program, NIEHS. Identification and characterization of the potential health effects of cell phone radiofrequency radiation, perfluorinated chemicals, and drinking water disinfection byproducts.
- 2001-2008 Project Officer, NTP/NIEHS: 1) Interagency Agreement with the National Institute of Standards and Technology (Boulder, CO) on “Determining the potential hazards of exposures to radio frequencies generated during the use of cellular phones “
 2) IIT Research Institute (Chicago, IL) on “Studies to evaluate the toxic and carcinogenic potential of cell phone radio frequency radiation in laboratory animals for the National Toxicology Program”
- 2001-2002 Consultant to the Attorney General of the State of California, concerning cancer risk of di(2-ethylhexyl)phthalate.
- 2006-2009 Consultant to the Attorney General of the State of California on cancer risks associated with dietary exposure to acrylamide.
- 2009- Independent Consultant, Ron Melnick Consulting LLC

Awards and Honors:

Tuition Scholarship from the New York Division of the Institute of Food Technologists,

1964-1965

Sigma Xi, Phi Kappa Phi, Alpha Zeta, Phi Tau Sigma

NIEHS representative in the U.S.-Japan Non-Energy Research and Development Program, 1985

Cited in: American Men and Women of Science

Selected for a one-year appointment to work on risk assessment issues at the White House Office of Science and Technology Policy, 1995-1996

Elected to the Council of Fellows of the Collegium Ramazzini, 1996

Commendations for Sustained High Quality Work Performance, NIEHS, numerous dates

NIH Merit Award for outstanding accomplishments as a member of the NIEHS/NTP Review Committee for the Report on Carcinogens, 2000

Cited in: Who's Who in America, 58th Edition, 2003

NIH Plain Language Award 2005, for the NCI/NIEHS brochure "Cancer and the Environment: What You Need to Know, What You Can Do"

2007 David P. Rall Award for Advocacy in Public Health from the American Public Health Association

2008 NIH Merit Award

Professional Activities:

NIEHS Committees:

Toxicokinetics Faculty, Chairman 1996-2000

Review group for the NTP Report on Carcinogens, Chairman 2005-2008

Chemical Nominations Committee

Project Design and Evaluation teams for NTP chemicals or toxicological issues

NTP Project Review Committee

Committee on Promotions II

Committee for the Development of the NTP Vision

Journal Reviewer:

Cancer Research

Carcinogenesis

Critical Reviews in Toxicology

Environmental Health Perspectives (Editorial Board 1991-1997)

Environmental Health (Editorial Board)

Environmental and Molecular Mutagenesis
Fundamental and Applied Toxicology/Toxicological Sciences
International Journal of Occupational and Environmental Health (Editorial Board)
Journal of the National Cancer Institute
Toxicology
Toxicology and Applied Pharmacology
Toxicology and Industrial Health

Symposium/Workshop Organizer:

International Symposium on the "Toxicology, Carcinogenesis, and Human Health Aspects of 1,3 Butadiene," Research Triangle Park, NC, April 12-13, 1988. Editor of the symposium proceedings published in Environ. Health Perspect. 86: 1-171, 1990.

International Symposium on "Cell Proliferation and Chemical Carcinogenesis," Research Triangle Park, NC, January 14-16, 1992. Editor of the symposium proceedings published in Environ. Health Perspect. 101 (suppl. 5): 1-285, 1993.

Workshop on "Colorectal Cancer: Trihalomethanes and other Environmental Factors," Research Triangle Park, NC, September 14, 1993. Workshop report published in Environ. Health Perspect. 102: 586-588, 1994.

Workshop on "Characterizing the Effects of Endocrine Disruptors on Human Health at Environmental Exposure Levels," Raleigh, NC, May 11-13, 1998. Editor of the workshop proceedings published in Environ. Health Perspect. 107 (suppl. 4): 601-649, 1999.

Co-chair of session on Use of Mechanistic Data in Risk Assessment: Human Variability and Susceptibility in Risk Assessment, conference on "Toxicology and Risk Assessment Approaches in the 21st Century," King's Island, OH, April 10-13, 2000.

Organizing Committee for the international symposium: on "Evaluation of Butadiene, Isoprene and Chloroprene Health Risks," London, September 2000.

Organizing Committee (Chair) for the NTP/NIEHS Endocrine Disruptors Low-Dose Peer Review, Research Triangle Park, NC, October 2000.

Invited Member of Scientific Review/Advisory Panels:

Working group of the International Agency for Research on Cancer that prepared the "IARC Monograph on the Evaluation of Carcinogenic Risks to Humans: Volume 54: Strong Acid Mists and Some Other Industrial Exposures," Lyon, France, October 1991.

Working group of the International Program on Chemical Safety that prepared the IPCS Environmental Health Criteria document titled "Scientific Principles for Assessment of Human Health Risks Associated with Exposures to Chemicals," Surrey, England, March 1992.

Butadiene subgroup of the Health Effects Institute Workshop on Mobile Air Toxics that prepared the HEI Communications document "Research Priorities for Mobile Air Toxics," Monterey, CA, December 1992.

International Symposium on Health Hazards of Butadiene and Styrene, Espoo, Finland, April, 1993: Editorial Board for the Symposium Proceedings published in the IARC Scientific Publications Series, No. 127, 1993; Rapporteur for session on Dose Estimation

National Toxicology Program Workshop on Mechanism-Based Toxicology in Cancer Risk Assessment: Implications for Research, Regulation, and Legislation. Working group: Mechanism-based toxicology for species extrapolation, Chapel Hill, NC, January 1995.

Working group of the International Agency for Research on Cancer that prepared the "IARC Monograph on the Evaluation of Carcinogenic Risks to Humans, on Dry Cleaning, Some Chlorinated Solvents and Other Industrial Chemicals," Volume 63, Lyon, France, February 1995.

Risk Assessment Advisory Committee of the Office of Environmental Health Hazard Assessment's Science Advisory Board, California Environmental Protection Agency. The committee's report "A Review of the California Environmental Protection Agency's Risk Assessment Practices, Policies, and Guidelines" was completed in 1996.

Interagency Task Force for the Assessment of the Health Effects of Oxygenated Fuels for the White House Office of Science and Technology Policy and the preparation of the National Science and Technology Council's report "Interagency Assessment of Potential Health Risks Associated with Oxygenated Gasoline" 1996.

Endocrine Disruptor Working Group of the National Science and Technology Council's Committee on Environment and Natural Resources that prepared the documents "The Health and Ecological Effects of Endocrine Disrupting Chemicals: A Framework for Planning," "Endocrine Disruptors: Research Needs and Priorities, 1998" and that created the Federal Endocrine Disruptor Inventory.

Working group of the International Agency for Research on Cancer that prepared the Consensus Report "Species Differences in Thyroid, Kidney and Urinary Bladder Carcinogenesis," IARC Scientific Publication No. 147. Lyon, France, November 1997.

ILSI Expert Panel's Evaluation of EPA's Proposed Guidelines for Carcinogen Risk Assessment Using Chloroform and Dichloroacetate as Case Studies Canadian Environmental Health Assessment on 1,3-Butadiene, September 1997.

Consultant to the Science Advisory Board Environmental Health Committee's review of EPA's health risk assessment of 1,3-butadiene. Washington, DC, April 1998.

Member of the National Occupational Research Agenda (NORA) subgroup on Cancer Research Methods that is charged with identifying research needs that will address occupational cancer risks and lead to improved worker safety, 1998-2002.

Invited technical consultant to EPA's Federal Advisory Committee on Cancer Health Effects of Disinfection Byproducts (DBPs). Presented a "Perspective on Toxicology Data and DBP Cancer Health Risk." Washington, DC. May 1999.

Toxicology and Risk Assessment working group for the NIOSH workshop on Future Research for Improving Risk Assessment Methods. Aspen CO. August 16-18, 2000.

Member of the National Drinking Water Advisory Council Working Group on Drinking Water Research. This group will assist EPA in identifying and prioritizing drinking water research needs to support drinking water regulatory activities. 2000.

Member of the NCI and NIEHS group of scientists (2001-2003) that prepared the public information booklet "Cancer and the Environment: What you need to know and what you can do". US DHHS, NIH Publication No. 03-2039, 2003.

Reviewer for EPA's proposed research program on "Evaluation and prioritization of genetic and molecular events as biomarkers of carcinogenicity and comparison of the molecular biology of cancer in humans and laboratory animals." Cincinnati, OH, November 2001.

Member of EPA's Science Advisory Board to review the document "Trichloroethylene Health Risk Assessment: Synthesis and Characterization." Washington, DC, 2002

Member of the International Advisory Committee and the Research Coordination Committee of WHO's International Electromagnetic Fields Project. Geneva, SW, June 2003.

Participant in the WaterReuse Foundation's Water Reuse Research Needs Workshop. San Diego, CA, February 2004.

Participant/consultant for the UAW-Ford Peer Review of cohort mortality and leukemia case-control studies of workers in metal stamping and transmission plants. Detroit, MI, February 2004.

Member of the North Carolina Science Advisory Board on Toxic Air Pollutants. North Carolina Department of Environment and Natural Resources. 2004-2006.

External peer reviewer of EPA's Revised Technical Review of Diisononyl Phthalate. 2004.

External peer reviewer of grant proposals on non-ionizing radiation submitted to the Danish Research Agency, Copenhagen, Denmark. 2004 and 2005.

Member of EPA's Science Advisory Board for review of "Draft Risk Assessment of the Potential Human Health Effects Associated with Exposure to Perfluorooctanoic Acid and its Salts." Washington, DC, 2005.

Member of Planning Committee and Participant in ILSI-Health and Environmental Sciences Institute Workshop on "Improving the use of quantitative pharmacokinetic methods to determine dosimetry for evaluating human health risks." Research Triangle Park, NC, 2005.

Member of the Federal Interagency Working Group on "Pharmaceuticals in the Environment." Lead for the chapter on potential human health effects, 2005 – 2007.

Working group member (chair of the section on mechanistic considerations) of the International Agency for Research on Cancer expert panel that prepared the "IARC Monograph on the Evaluation of Carcinogenic Risks to Humans, on 1,3-Butadiene, Ethylene Oxide and Vinyl Halides (Vinyl Fluoride, Vinyl Chloride and Vinyl Bromide)" Volume 97, Lyon, France, June 2007.

Reviewer of the report Science and Decisions: Advancing Risk Assessment from the National Research Council's Board on Environmental Studies and Toxicology. The report was written by the Committee on Improving Risk Analysis Approaches Used by the US EPA. March 2008.

Member of the expert advisory panel for California Chemicals Policy and Breast Cancer Project. 2009. "Pathways to breast cancer: A case study for innovation in chemical safety evaluation."

Member of the expert review panel for the Health Risk Assessment of Methyl Iodide for the California Environmental Protection Agency, Department of Pesticide Regulation, 2009-2010.

Working group member (co-chair of the section on mechanistic considerations) of the International Agency for Research on Cancer for the preparation of volume 100 of the IARC Monograph on the Evaluation of Carcinogenic Risks to Humans on Chemical Agents and Related Occupations. Lyon, France, 2009.

Reviewer of the National Research Council's report Review of EPA's Draft IRIS Assessment on Tetrachloroethylene written by the NRC's Board on Environmental Studies and Toxicology, October 2009.

Member of the Integrated Risk Information System (IRIS) external peer review panel of US EPA's "Toxicological Review of Trichloroacetic Acid." Washington, DC, 2009.

Member of the IRIS external peer review panel of US EPA's "Toxicological Review of Chloroprene." Washington, DC, 2010.

Member of the External Advisory Board of the European Commission-supported project: Sound Exposure and Risk Assessment of Wireless Network Devices, 2009-2012.

Reviewer for the European Commission's Seventh Framework Programme: "Network for Environmental Chemical Toxicants Affecting Reproduction" 2010.

Working group member of the International Agency for Research on Cancer for the preparation of volume 101 of the IARC Monograph on the Evaluation of Carcinogenic Risks to Humans: Some Chemicals in Industrial and Consumer Products, Food Contaminants and Flavourings, and Water Chlorination By-Products. Lyon, France, 2011.

Working group member (chair of the section on exposure) of the International Agency for Research on Cancer for the preparation of volume 102 of the IARC Monograph on the Evaluation of Carcinogenic Risks to Humans: Non-Ionizing Radiation, Part II: Radiofrequency Electromagnetic Fields [includes mobile telephones]. Lyon, France, 2011.

Member of the IRIS external peer review panel of US EPA's "Toxicological Review of 1,4-Dioxane." 2011-12.

Invited participant to the International Agency for Research on Cancer workshops on "Tumor Concordance and Mechanisms of Carcinogenesis." Lyon, France, April and November, 2012.

Working group member (chair of the section on cancer studies in experimental animals) of the International Agency for Research on Cancer for the preparation of volume 106 of the IARC Monograph on the Evaluation of Carcinogenic Risks to Humans: Trichloroethylene and other chlorinated agents. Lyon, France, 2012.

Reviewer for the European Commission's Seventh Framework Programme: "Closing gaps of knowledge and reducing exposure to electromagnetic fields (EMF)". Brussels, Belgium, 2013.

Member of the external review panel of US EPA's "TSCA Workplan Chemical Risk Assessment for Trichloroethylene." 2013.

Consultant to the project "Protecting Human Health from Cumulative Effects of Exposure to Multiple Fumigant Pesticides." Funded by the Clarence E. Heller Charitable Foundation: Environmental and Health Program, 2015-2016.

Working group member of the International Agency for Research on Cancer for the preparation of volume 115 of the IARC Monograph on the Evaluation of Carcinogenic Risks to Humans: Some Industrial Chemicals. Lyon, France, 2016.

Invited lectures since joining NIEHS in 1980:

Melnick, R.L. (1981). Mitochondrial toxicity of phthalate esters. National Toxicology Program/Interagency Regulatory Liaison Group Conference on Phthalates. Washington, D.C.

Melnick, R.L. (1983). Toxicity of ethylene glycol and ethylene glycol monoethyl ether in F344 rats and B6C3F1 mice. NIOSH Symposium on Toxic Effects of Glycol Ethers. Cincinnati, OH.

Melnick, R.L. (1984). NTP toxicological and carcinogenic studies of 1,3-butadiene. 76th Meeting of the Interagency Collaborative Group on Environmental Carcinogenesis. Bethesda, MD.

Melnick, R.L. (1985). Toxicity and carcinogenicity of 1,3-butadiene. National Institute of Hygienic Sciences. Tokyo, Japan.

Melnick, R.L., Morrissey, R.E., and Tomaszewski, K.E. (1986). National Toxicology Program studies on di(2-ethylhexyl)phthalate (DEHP). CMA Symposium on Recent Advances in Phthalate Esters Research. Washington, DC.

Melnick, R., Roycroft, J., Chou, B., and Miller, R. (1988). Inhalation toxicology and carcinogenicity of 1,3-butadiene in B6C3F1 mice. International Symposium on the Toxicology, Carcinogenesis, and Human Health Aspects of 1,3-Butadiene. Research Triangle Park, NC.

Melnick, R., Roycroft, J., Chou, B., Ragan, H., and Miller, R. (1988). Inhalation toxicology of isoprene in F344 rats and B6C3F1 mice. International Symposium on the Toxicology, Carcinogenesis, and Human Health Aspects of 1,3-Butadiene. Research Triangle Park, NC.

Toxicology and carcinogenicity of 1,3-butadiene. International Life Sciences Institute (ILSI) Symposium on Assessment of Inhalation Hazards: Integration and Extrapolation Using Diverse Data. Hannover, Federal Republic of Germany, 1989.

Recent studies on 1,3-butadiene and other high volume chemicals used in the rubber industry. United Rubber Workers Joint Labor/ Management Health and Safety Symposium. Daytona Beach, FL, 1989.

Overview on the toxicity and carcinogenicity of 1,3-butadiene in mice. Testimony for the OSHA Hearing on the Proposed Occupational Standard for 1,3-Butadiene. Department of Labor, Washington, DC, 1991.

Is chemically induced hepatocyte proliferation a predictor of liver carcinogenesis? International Life Sciences Institute (ILSI) Workshop on Mouse Liver Tumors. Washington, DC, 1992.

Alternative hypothesis on the role of alpha₂-globulin in gasoline-caused kidney cancers. Collegium Ramazzini Symposium. Carpi, Italy, 1993.

Butadiene induced cancer in experimental animals. International Symposium on Health Hazards of Butadiene and Styrene. Espoo, Finland, 1993.

Carcinogenicity of 1,3-butadiene. International Conference on Motor Gasolines and Additives: Methyl-Tertiary Butyl Ether. Washington, DC, 1995.

Inhalation toxicity and carcinogenicity of isoprene in rats and mice: Comparisons with 1,3-butadiene. International Symposium: Evaluation of Butadiene & Isoprene Health Risks. Blaine, WA, 1995.

Role of the Office of Science and Technology Policy in federal risk assessment activities. US Department of Agriculture. Washington, DC, 1996.

CENR endocrine disruptor inventory: human health effects. Committee on Environment and Natural Resources (CENR) Meeting on Endocrine Disruptor Research. Washington, DC, 1996.

Carcinogenicity of trihalomethanes in female B6C3F₁ mice: Relationships among hepatotoxicity, regenerative hyperplasia and replicative DNA synthesis. Collegium Ramazzini Symposium. Carpi, Italy, 1997.

Possible mechanisms of induction of renal tubular cell neoplasms in rats associated with α_2 -globulin: role of protein accumulation versus ligand delivery to the kidney. IARC Meeting on "Mechanisms of Carcinogenesis thought to be Species-Specific." Lyon, France, 1997.

Endocrine disruptors. California's Emerging Environmental Challenges: A workshop to identify future issues for Cal/EPA. Sacramento, CA, 1998.

Dose-response analyses of experimental cancer data. Arkansas Toxicology Symposium Honoring David P. Rall. Little Rock, AR, 1998.

Perspective on chloroform cancer risk assessment. The Toxicology Forum. Washington, DC, 1999.

Chloroform cancer risk and dose-response relationships. University of Florida Symposium on Drinking Water and Health. Sarasota, Fla, 1999.

Melnick, R.L. Overview on the use of mechanistic data in risk assessment: Conference on Toxicology and Risk Assessment Approaches for the 21st Century. Kings Island, OH, 2000.

Melnick, R.L., Sills, R., Roycroft, J., Chou, and Miller, R.A. Comparative carcinogenicity of butadiene, isoprene, and chloroprene in rats and mice. International Symposium: Evaluation of Butadiene, Isoprene, and Chloroprene Health Risks. London, UK., 2000.

Role of the National Toxicology Program in drinking water research. EPA's Federal/State Toxicology and Risk Analysis Committee Biannual Meeting, Durham, NC, 2000.

Summary of the NTP/NIEHS endocrine disruptors low-dose peer review. International Symposium on Environmental Endocrine Disruptors 2000, Pacifico Yokohama, Japan, 2000.

NTP's Drinking Water Research Program. North Carolina Chapter of the Society of Toxicology, Chapel Hill, NC 2001.

Carcinogenicity of epoxides and epoxide-forming chemicals. New York Academy of Sciences Conference commemorating the Lifework of Cesare Maltoni. Chairman of Session On National Toxicology Program's Carcinogenesis Bioassays: Legacy of David P. Rall. New York, NY. 2002.

Studies on Drinking Water Disinfection Byproducts by The National Toxicology Program. ISEA/ISEE Conference, Vancouver, BC. 2002.

Carcinogenic responses in experimental animals after long-term inhalation exposures to dusts and particulates. Ramazzini International Conference on Carcinogenicity of Non-fibrous, Poorly Soluble Particulates, Carpi, Italy, 2002.

Endocrine disruption – what can work with laboratory animals tell us? 2nd Copenhagen Workshop on Endocrine Disruptors, Copenhagen, Denmark, 2002.

NTP research program on health effects of cell phone radio frequency radiation. The Toxicology Forum. Washington, DC, 2003.

Health effects of cell phone radiofrequency radiation: National Toxicology Program's carcinogenicity studies in rats and mice. Special symposium (Session Co-chair) of the Bioelectromagnetics Society 25th Annual Meeting. Maui, Hawaii, 2003.

Feasibility and design of rodent carcinogenicity studies on cell phone radio frequency radiation in reverberation chambers. Asia-Pacific EMF Conference on Electromagnetic Fields, Research, Health Effects, and Standard Harmonization. Bangkok, Thailand, 2004.

The hormesis thesis. Integrity in Science Conference sponsored by Center for Science in the Public Interest. Washington, DC, 2004.

Use and misuse of mechanistic data in risk assessment. Ramazzini International Conference: Framing the Future in Light of the Past: Living in a Chemical World. Bologna, Italy, 2005.

Induction of peroxisome proliferation by trichloroethylene and perchloroethylene: implications for risk assessment. Ramazzini International Conference: Framing the Future in Light of the Past: Living in a Chemical World. Bologna, Italy, 2005.

Determining disease causality from experimental toxicology studies. Science for Judges VII. Brooklyn Law School, Brooklyn, NY, 2006.

Experimental design and evaluation as sources of conflicting views in science. Project on Scientific Knowledge & Public Policy, Coronado Conference III: Truth and Advocacy: the Quality and Nature of Litigation and Regulatory Science. San Diego, CA, 2006.

Hormesis in public health decisions: Who benefits? EOHSI Days, Rutgers University, Piscataway, NJ, 2006.

National Toxicology Program's research on emerging and priority disinfection by-products. Gordon Research Conference on Drinking Water Disinfection By-products. Mount Holyoke College, South Hadley, MA, 2006.

Judicial Gatekeeping: Commentary by Scientists. Judicial Symposium on Scientific Evidence in the Courts. AEI-Brookings Joint Center for Regulatory Studies. Georgetown University Law Center, Washington, DC, 2007.

In vitro studies of PFAAs (perfluoroalkyl acids). PFAA Days Workshop, US EPA, Research Triangle Park, NC, 2008

Risk evaluations and governance. Health Risk from Exposure to Wireless Network Devices. EMF & Health Risk Research Workshop, Ascona, Switzerland, 2012.

A Framework for Considering the CYP2F2 MOA Hypothesis & Relevance of Mouse Lung Tumors to Humans. Co-chair of Session 3: Biological Mechanisms. US EPA Mouse Lung Tumor Workshop, Research Triangle Park, NC, 2014.

Radiofrequency radiation: A possible human carcinogen? Co-chair of Basic Science working group. IIAS/EHT Conference on Wireless Radiation and Health: Expert Forum on Environmental Health Research and Policy Priorities. Hebrew University, Jerusalem, Israel, 2017.

Publications

Scientific Journals

1. Melnick, R.L. and Hultin, H.O. Solubilization of bound lactate dehydrogenase by NADH in homogenates of trout skeletal muscle as a function of tissue concentration. *Biochem. Biophys. Res. Commun.* 33: 863-868, 1968.
2. Melnick, R.L. and Hultin, H.O. Factors affecting the distribution of lactate dehydrogenase between particulate and soluble phases of homogenized trout skeletal muscle. *J. Food Sci.* 35: 67-72, 1970.
3. Melnick, R.L. and Packer, L. Freeze fracture faces of inner and outer membranes of mitochondria. *Biochim. Biophys. Acta* 253: 503-508, 1971.
4. Hultin, H.O., Ehman, J.D., and Melnick, R.L. Modification of kinetic properties of muscle lactate dehydrogenase by subcellular associations and possible role in the control of glycolysis. *J. Food Sci.* 37: 269-273, 1972.
5. Melnick, R.L. and Hultin, H.O. Studies on the nature of the subcellular localization of lactate dehydrogenase and glyceraldehyde-3-phosphate dehydrogenase in chicken skeletal muscle. *J. Cell. Physiol.* 81: 139-148, 1973.
6. Melnick, R.L., Tinberg, H.M., Maguire, J., and Packer, L. Studies on mitochondrial proteins. I. Separation and characterization by polyacrylamide gel electrophoresis. *Biochim. Biophys. Acta* 311: 230-241, 1973.
7. Melnick, R.L. and Hultin, H.O. On the existence of a complex of glycolytic enzymes. *J. Bioenergetics* 5: 107-117, 1974.
8. Tinberg, H.M., Melnick, R.L., Maguire, J., and Packer, L. Studies on mitochondrial proteins. II. Localization of components in the inner membrane. Labeling with diazobenzenesulfonate, a non-penetrating probe. *Biochim. Biophys. Acta* 345: 118-128, 1974.
9. Tinberg, H.M., Melnick, R.L., Maguire, J., and Packer, L. Interaction of mitochondrial inner membranes with bifunctional alkylating agents. *BBA Library* 13: 539-541, 1974.
10. Melnick, R.L., Tavares de Sousa, J., Maguire, J., and Packer, L. Action of the adenosine triphosphate analog, adenylyl imidodiphosphate, in mitochondria. *Arch. Biochem. Biophys.* 166: 139-144, 1975.
11. Melnick, R.L. and Donohue, T. Use of an adenosine triphosphate analog, adenylyl imidodiphosphate, to evaluate adenosine triphosphate dependent reactions in mitochondria. *Arch. Biochem. Biophys.* 173: 231-236, 1976.

12. Melnick, R.L., Monti, L.G., and Motzkin, S.M. Uncoupling of mitochondrial oxidative phosphorylation by thallium. *Biochem. Biophys. Res. Commun.* 69: 68-73, 1976.
13. Melnick, R.L., Hanson, R.M., and Morris, H.P. Membranous effects on adenosine triphosphatase activities of mitochondria from rat liver and Morris Hepatoma 3924A. *Cancer Res.* 37: 4395-4399, 1977.
14. Melnick, R.L., Rubenstein, C.P., and Motzkin, S.M. Measurement of mitochondrial oxidative phosphorylation: Selective inhibition of adenylate kinase activity by P₁,P₅-(adenosine-5')-pentaphosphate. *Anal. Biochem.* 96: 7-11, 1979.
15. Melnick, R.L., Haspel, H.C., Goldenberg, M., Greenbaum, L.M., and Weinstein, S. Use of fluorescent probes that form intramolecular excimers to monitor structural changes in model and biological membranes. *Biophys. J.* 34: 499-515, 1981.
16. Melnick, R.L., Rubenstein, C.P., and Birenbaum, L. Effects of millimeter wave irradiation on ATP synthesis and calcium transport in mitochondria. *Radiat. Res.* 89: 348-360, 1981.
17. Melnick, R.L. and Schiller, C.M. Mitochondrial toxicity of phthalate esters. *Environ. Health Perspect.* 45: 51-56, 1982.
18. Melnick, R.L., Huff, J., Haseman, J.K., Dieter, M.P., Grieshaber, C.K., Wyand, D.S., Russfield, A.B., Murthy, A.S.K., Fleischman, R.M. and Lilja, H.S. Chronic effects of agar, guar gum, gum arabic, locust bean gum, or tara gum in F344 rats and B6C3F1 mice. *Food Chem. Toxicol.* 21: 305-311, 1983.
19. Melnick, R.L., Boorman, G.A., Haseman, J.K., Montali, R.J., and Huff, J. Urolithiasis and bladder carcinogenicity of melamine in rodents. *Toxicol. Appl. Pharmacol.* 72: 292-303, 1984.
20. Melnick, R.L. Toxicities of ethylene glycol and ethylene glycol monoethyl ether in Fischer 344/N rats and B6C3F1 mice. *Environ. Health Perspect.* 57: 147-155, 1984.
21. Melnick, R.L. and Schiller, C.M. Effect of phthalate esters on energy coupling and succinate oxidation in rat liver mitochondria. *Toxicology* 34: 13-27, 1985.
22. Huff, J.E., Melnick, R.L., Solleveld, H.A., Haseman, J.K., Powers, M. and Miller, R.A. Multiple organ carcinogenicity of 1,3-butadiene in B6C3F1 mice after 60 weeks of inhalation exposure. *Science* 227: 548-549, 1985.
23. Tomaszewski, K.E., Agarwal, D.K., and Melnick, R.L. In vitro steady-state levels of hydrogen peroxide after exposure of male F344 rats and female B6C3F1 mice to hepatic peroxisome proliferators. *Carcinogenesis* 7: 1871-1876, 1986.

24. Melnick, R.L., Jameson, C.W., Goehl, T.J., and Kuhn, G.O. Application of microencapsulation for toxicology studies. 1. Principles and stabilization of trichloroethylene in gelatin-sorbitol microcapsules. *Fundam. Appl. Toxicol.* 8: 425-431, 1987.
25. Melnick, R.L., Jameson, C.W., Goehl, T.J., Maronpot, R.R., Collins, B.J., Greenwell, A., Harrington, F.W., Wilson, R.E., Tomaszewski, K.E., and Agarwal, D.K. Application of microencapsulation for toxicology studies. 2. Toxicity of microencapsulated trichloroethylene in Fischer 344 rats. *Fundam. Appl. Toxicol.* 8: 432-442, 1987.
26. Melnick, R.L., Morrissey, R.E., and Tomaszewski, K.E. Studies by the National Toxicology Program on di(2-ethylhexyl)phthalate. *Toxicol. Indus. Health* 3: 99-116, 1987.
27. Tomaszewski, K.E., Derks, M.C., and Melnick, R.L. Acyl CoA oxidase is the most suitable marker for hepatic peroxisomal changes caused by treatment of F344 rats with di(2-ethylhexyl) phthalate. *Toxicol. Lett.* 37: 203-212, 1987.
28. Greenwell, A., Tomaszewski, K.E., and Melnick, R.L. A biochemical basis for 1,2-dibromo-3-chloropropane - induced male infertility: Inhibition of sperm mitochondrial electron transport activity. *Toxicol. Appl. Pharmacol.* 91: 274-280, 1987.
29. Melnick, R.L., Huff, J.E., Haseman, J.K., and McConnell, E.E. Chronic toxicity results and ongoing studies of 1,3-butadiene by the National Toxicology Program. *Ann. NY Acad. Sci.* 534: 648-662, 1988.
30. Tomaszewski, K.E., Montgomery, C., and Melnick, R.L. Modulation of 2,3,7,8-tetrachlorodibenzo-p-dioxin toxicity in F344 rats by di(2-ethylhexyl)phthalate. *Chem. Biol. Interactions* 65: 205-222, 1988.
31. Tice, R.R., Boucher, R., Luke, C.A., Paquette, D.E., Melnick, R.L., and Shelby, M.D. Chloroprene and isoprene: Cytogenetic studies in mice. *Mutagenesis* 3: 141-146, 1988.
32. Bond, J.A., Martin, O.S., Birnbaum, L.S., Dahl, A.R., Melnick, R.L., and Henderson, R.F. Metabolism of 1,3-butadiene by lung and liver microsomes of rats and mice repeatedly exposed by inhalation to 1,3-butadiene. *Toxicol. Lett.* 44: 143-151, 1988.
33. Kralovanszky, J., Jenkins, W.L., Greenwell, A., and Melnick, R.L. Metabolic processes in isolated rat small intestine villus cells: Effects of cis-diamminedichloro-platinum (II). *Res. Commun. Chem. Pathol. Pharmacol.* 64: 299-316, 1989.
34. Miller, R.A., Melnick, R.L., and Boorman, G.A. Neoplastic lesions induced by 1,3-butadiene in B6C3F1 mice. *Exptl. Pathol.* 37: 136-146, 1989.
35. Melnick, R.L., Huff, J.E., Bird, M.G., and Acquavella, J.F. Symposium overview: Toxicology, carcinogenesis, and human health aspects of 1,3-butadiene. *Environ. Health Perspect.* 86: 3-5, 1990.

36. Melnick, R.L., Huff, J.E., Roycroft, J.H., Chou, B.J., and Miller, R.A. Inhalation toxicology and carcinogenicity of 1,3-butadiene in B6C3F1 mice following 65 weeks exposure. *Environ. Health Perspect.* 86: 27-36, 1990.
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Book Chapters

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