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ORIGINAL SUBMISSION

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VERDAD GRAS Notification

Submitted By

PURAC

January 18, 2008

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BY FEDERAL EXPRESS

Office of Food Additive Safety (HFS-200)
Center for Food Safety and Applied Nutrition
Food And Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835

Dear Sirs

On behalf of our client, PURAC, we are hereby submitting the enclosed amended GRAS Notification for VERDAD for use as a flavoring agent and antimicrobial agent in meat and poultry products. In compliance with 21 C F R 170.36(b) (proposed), four copies of this Notification are enclosed.

Should you have any questions regarding this Notification, please do not hesitate to contact us

Sincerely,

Mark L. Itzkoff

MLI cr
Enclosures

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VERDAD GRAS NOTIFICATION

I GRAS Exemption Claim

A. Claim of Exemption From the Requirement for Premarket Approval Pursuant to Proposed 21 CFR §170.36(c)(1) [62 FR 18938 (17 April 1997)]

PURAC has determined that VERDAD, as defined in the report in Appendix I entitled, "EXPERT PANEL CONSENSUS STATEMENT CONCERNING THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS FOR THE PROPOSED FOOD USES OF VERDAD", dated December 7, 2007, is Generally Recognized As Safe (GRAS), consistent with Section 201(s) of the *Federal Food, Drug, and Cosmetic Act*. This determination is based on scientific procedures as described in the following sections, under the conditions of its intended use in food, among experts qualified by scientific training and expertise. Therefore, the use of VERDAD in food as described below is exempt from the requirement of premarket approval.

Signed,

Jeannette Verbart
PURAC
Arkelsedijk 46, P.O. Box 21
4200 AA Gorinchem, The Netherlands

10 January 2008
Date

B. Name and Address of Notifier

PURAC
Arkelsedijk 46, P.O. Box 21
4200 AA Gorinchem, The Netherlands

C. Common Name of the Notified Substance

Corn, cane, or beet sugar cultured with *Lactobacillus paracasei* subsp *paracasei*, *Bacillus coagulans* and *Propionibacterium freudenreichii* subsp *shermanii*.

D. Conditions of Intended Use in Food

PURAC intends to market VERDAD as a flavoring agent and antimicrobial agent in the United States at the same use-levels and in the same meat and poultry products as those already permitted in the U.S. for sodium lactate and potassium lactate, including fresh meats (beef, lamb and goat, organ meats, pork, veal), fresh poultry (chicken, duck, other poultry, turkey), meat products (bacon, frankfurters, ham, luncheon meats, processed meat products), and

VERDAD GRAS NOTIFICATION

poultry products (processed poultry products) [see Appendix I - **EXPERT PANEL CONSENSUS STATEMENT CONCERNING THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS FOR THE PROPOSED FOOD USES OF VERDAD**].

The consumption of VERDAD from all proposed food uses was estimated using the proposed food uses and use levels in conjunction with food consumption data included in the National Center for Health Statistics' (NCHS) 2003-2004 National Health and Nutrition Examination Surveys (NHANES) (CDC, 2006; USDA, 2006).

Approximately 93.7% of the total U.S. population was identified as consumers of VERDAD from the proposed food-uses (7,748 actual users identified). On an all-user basis, the mean intake of VERDAD by the total U.S. population from all proposed food-uses was estimated to be approximately 6.55 g/person/day or 108.00 mg/kg body weight/day. The heavy consumer (90th percentile) all-user intake of VERDAD by the total U.S. population from all proposed food-uses was estimated to be 12.31 g/person/day or 207.22 mg/kg body weight/day. Male adults were determined to have the highest mean all-user intake of VERDAD of 8.45 g/person/day (99.08 mg/kg body weight/day) and the highest 90th percentile all-user intake of VERDAD of 15.24 g/person/day (176.93 mg/kg body weight/day).

E. Basis for the GRAS Determination

Pursuant to 21 CFR § 170.30, PURAC has determined that the proposed use of VERDAD is Generally Recognized as Safe on the basis of scientific procedures (U.S. FDA, 2007a). This determination is based on the views of experts who are qualified by scientific training and experience to evaluate the safety of VERDAD as a component of food. VERDAD consists of a blend of organic acid salts (primarily lactate) and sugars. The safety of the components of VERDAD is supported by their regulatory status for use in food in the U.S., common consumption in the diet, endogenous presence in the human body, and published animal toxicology and clinical studies. [See Appendix I – **EXPERT PANEL CONSENSUS STATEMENT CONCERNING THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS FOR THE PROPOSED FOOD USES OF VERDAD**].

F. Availability of Information

The data and information that serve as the basis for this GRAS Notification will be sent to the U.S. Food and Drug Administration (FDA) upon request, or will be available for review and copying at reasonable times at the offices of

Mr. Mark L. Itzkoff
Olsson Frank Weeda Terman Bode Matz PC
1400 Sixteenth St., NW
Suite 400
Washington, DC 20036

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Should the FDA have any questions or additional information requests regarding this notification, PURAC will supply these data and information.

II. Detailed Information About the Identity of the Substance

A. Identity

VERDAD is a light to dark brown liquid with a sweet odor, containing a blend of either sodium or potassium organic salts, (primarily lactate, but also containing small amounts of acetate, succinate, formate, 2-hydroxybutyrate, and propionate) and sugars (glucose, fructose, and poly/oligosaccharides, consisting of glucose, galactose, rhamnose, glucosamine, mannose, and xylose).

Common or Usual Name: Corn, cane, or beet sugar cultured with *Lactobacillus paracasei* subsp *paracasei*, *Bacillus coagulans* and *Propionibacterium freudenreichii* subsp *shermanii*.

Chemical Name: A blend comprised primarily of either lactic acid (propanoic acid), 2-hydroxy-, monosodium salt or propanoic acid, 2-hydroxy-, monopotassium salt. The minor constituents of the blend include the sodium or potassium salt of acetic acid, succinic acid, formic acid, 2-hydroxybutyric acid, and propionic acid, as well as glucose, fructose and poly/oligosaccharides.

Chemical Abstracts Service (CAS) Number: Since VERDAD is a blend of chemical compounds, there is no Chemical Abstract Service (CAS) Number that corresponds to the food ingredient. Below are the CAS numbers of the components with a concentration >0.2% of the formulation of VERDAD.

Sodium lactate:	72-17-3
Potassium lactate:	996-31-6
L-Lactic acid:	79-33-4
Sodium acetate:	127-09-3
Potassium acetate:	127-08-2
Sodium succinate.	150-90-3
Potassium succinate:	676-47-1
Sodium formate:	141-53-7
Potassium formate:	590-29-4
Sodium 2-hydroxybutyrate:	No CAS number available
Potassium 2-hydroxybutyrate:	No CAS number available
2-Hydroxybutyrate:	565-70-8

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Sodium propionate:	137-40-6
Potassium propionate:	327-62-8
Glucose:	50-99-7
Fructose:	57-48-7

Empirical Formula: Not applicable

Molecular weight: Not applicable

Structural Formula: Not applicable

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B. Method of Manufacture

VERDAD is produced by the fermentation of sucrose, originating from sugar cane or beet, or dextrose, originating from corn. The substrate is fermented to organic acids, primarily lactic acid, by *Bacillus coagulans* (*B. coagulans*) LA-1, *Lactobacillus paracasei* (*L. paracasei*) subsp. *paracasei*, or *Propionibacterium freudenreichii* (*P. freudenreichii*) subsp. *shermanii*, or mixtures of these microorganisms. These are standard microorganisms commonly used in the food industry for the production of enzymes and cheese, and also are used as probiotics.

Prior to fermentation, the medium is pasteurized to eliminate any residual bacteria. During fermentation, a suitable base, such as calcium, sodium or potassium hydroxide is added to control the pH (pH 6 to 7). The fermentation end product is purified to remove biomass, ions, and other impurities, followed by mixing with water or more concentrated cultured sugar and pH adjustment to obtain the desired organic acid content as listed in the product specification. All microorganisms and any enzymes produced are removed in the solid-liquid separation step. In addition, the conditions in the subsequent processing steps ensure complete pasteurization (process temperatures up to 80°C)

The final products contain a blend of either sodium or potassium organic salts, (primarily lactate, but also containing small amounts of acetate, succinate, formate, 2-hydroxybutyrate, and propionate) and sugars (glucose, fructose, and poly/oligosaccharides, consisting of glucose, galactose, rhamnose, glucosamine, mannose, and xylose)

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C. Specifications for Food Grade Material

In order to ensure a consistent product, PURAC established numerous specification parameters of the final ingredient (see Tables 1 and 2), and representative lots of the manufactured product are routinely analyzed to verify that the manufacturing process produces a consistent product within final product physical, chemical, and microbiological parameters. VERDAD is produced in accordance with current Good Manufacturing Practices and meets appropriate food-grade specifications, and all raw materials and processing aids used in the manufacture of VERDAD are permitted for use in food in the U S. Furthermore, comprehensive analyses of potential residues from the manufacturing process have confirmed the purity of the final product.

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Specification Parameter	Specifications			Analysis Method
	From Cane Sugar	From Corn Sugar	From Beet Sugar	
Lactate	55 to 80%	55 to 80%	55 to 80%	AMSOL044 – Assay of Purasal S – titration with 1 N hydrochloric acid
Sodium	0 to 21%	0 to 21%	0 to 21%	AM12.3 45E – Metals in PURAC-PLN-G products by ICP
Potassium	0 to 31%	0 to 31%	0 to 31%	AM12 3 45E – Metals in PURAC-PLN-G products by ICP
Formate ^a	0 to 0.6%	0 to 0.6%	0 to 0.6%	RDT-A-0009 – Quantification of the total amount of organic acids and ethanol using a derivation and GLC1
Acetate ^a	0 to 6%	0 to 6%	0 to 6%	
2-Hydroxybutyrate ^a	0 to 0.25%	0 to 0.25%	0 to 0.25%	
Succinate ^a	0 to 1%	0 to 1%	0 to 1%	
Propionate ^a	0 to 7%	0 to 7%	0 to 7%	
Color (in solution)	Light brown to dark brown	Light brown to dark brown	Light brown to dark brown	Visual inspection
Sugars ^a	0 to 6.2%	0 to 6.2%	0 to 6.2%	RDT-A-0023 – Determination of total residual sugars using spectrophotometry
Glucose	0 to 2.5%	0 to 2.5%	0 to 2.5%	RDT-A-0029 – Quantification of sugars using anion exchange chromatography
Fructose	0 to 2.5%	0 to 2.5%	0 to 2.5%	
Poly/Oligosaccharides ^b	0 to 1.2%	0 to 1.2%	0 to 1.2%	Sugars minus glucose and fructose
Lead	<2 ppm	<2 ppm	<2 ppm	AM12 3 45E – Metals in PURAC-PLN-G products by ICP
pH (10%)	5 to 8	5 to 8	5 to 8	Metrohm 744 with combined glass electrode

^a The sum of non-lactate constituents is at least 1% on a dry weight basis

^b Poly/oligosaccharides are of varying length and composition, and consist on average of Glucose (52%), Galactose (20%), Rhamnose (9%), Glucosamine (8%), Mannose, and Xylose (together 7%) Other sugars are present at levels <0.1% of the total product
 Constituents not listed in the table occur at levels below 0.1%. Exposure to these constituents would be below the threshold of toxicological concern

Specification Parameter	Specification	Analysis Method
Mesophilic bacteria	<100 CFU/g	AMCAL004 – Yeasts, moulds, and aerobic mesophilic bacteria in PURAC
Moulds	<10 CFU/g	
Yeasts	<10 CFU/g	
Coliforms	absent in 10 g	ISO 21528-1:2004(E)
<i>E. coli</i>	absent in 10 g	ISO 16649-2
<i>Salmonella</i>	absent in 25 g	2000.07 AOAC
<i>Staphylococcus</i>	absent in 10 g	ISO 6888-2

CFU = colony forming units

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D. Safety of the Microorganisms

B. coagulans is listed in 21 CFR § 184.1372 as a non-pathogenic and non-toxicogenic microorganism that is permitted for use in the U.S. for food production (U.S. FDA, 2007b).

B. coagulans also is designated by the American Type Culture Collection (ATCC) as a Biosafety Level 1 microorganism, indicating that it is not known to cause disease in adult humans (ATCC, 2007). Although sporulation is a known trait for *B. coagulans*, sporulation has never been observed for the proprietary strain *B. coagulans* LA-1 throughout more than 70 years of safe use.

L. paracasei was not recovered in fecal samples of adults provided high doses (up to 10^{11} CFU/day) of *L. paracasei* subsp *paracasei* and *Bifidobacterium animalis* subsp *lactis* in combination suggesting that *L. paracasei* did not survive during passage through the gastrointestinal tract (Larsen *et al.*, 2006). Furthermore, none of the subjects reported any adverse effects associated with the probiotic supplementation.

The safety of *P. freudenreichii* subsp. *shermanii* is supported by FDA's response to a GRAS notice for skim milk or dextrose cultured with *P. freudenreichii* subsp. *shermanii* for use as an antimicrobial agent in various foods (GRN 000128), in which FDA had no questions (U.S. FDA, 2003).

Professor Eric Johnson (Food Research Institute, University of Wisconsin-Madison) reviewed the scientific and medical literature and concluded that *Lactobacillus paracasei* subsp *paracasei*, *Bacillus coagulans* and *Propionibacterium freudenreichii* subsp *shermanii* used in the production of VERDAD are not toxigenic or pathogenic.

III. Self-Limiting Levels of Use

The use of VERDAD in meat and poultry products is limited to the maximum use-levels already permitted for sodium lactate and potassium lactate for use as flavoring agents and antimicrobial agents (2% and 4.8%, respectively).

IV. Basis for GRAS Determination

The determination that VERDAD is GRAS is on the basis of scientific procedures. [See Appendix I – **EXPERT PANEL CONSENSUS STATEMENT CONCERNING THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS FOR THE PROPOSED FOOD USES OF VERDAD**].

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V. References

- ATCC. 2007. [Search for *Bacillus coagulans*, ATCC nos. 10545 ; 11369 ; 12245 ; 15949 ; 23498 ; 31284 , 35670 ; 8038 ; BAA-738 ; 53595 ; 11014 ; 7050]. In: ATCC. The Global Bioresource Center™; Manassas, Virginia. Available from: <http://www.atcc.org/common/catalog/numSearch/index.cfm> [Last accessed: July 19, 2007].
- CDC. 2006. Analytical and Reporting Guidelines: The National Health and Nutrition Examination Survey (NHANES). Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS); Hyattsville, Maryland. Available from: http://www.cdc.gov/nchs/data/nhanes/nhanes_03_04/nhanes_analytic_guidelines_dec_2005.pdf.
- Larsen, C.N.; Nielsen, S.; Kaestel, P ; Brockmann, E ; Bennedsen, M.; Chrstensen, H.R.; Eskesen, D.C.; Jacobsen, B.L.; Michaelsen, K.F. 2006. Dose-response study of probiotic bacteria *Bifidobacterium animalis* subsp *lactis* BB-12 and *Lactobacillus paracasei* subsp *paracasei* CRL-341 in healthy young adults. *Eur J Clin Nutr* 60(11):1284-1293.
- U.S. FDA. 2003. Agency Response Letter GRAS Notice No. GRN 000128 [Skim milk or dextrose cultured with *Propionibacterium freudenreichii* subsp. *shermanii*]. U.S. Federal Drug Association (FDA), Center for Food Safety and Applied Nutrition (CFSAN), College Park, Maryland. Available from: <http://www.cfsan.fda.gov/~rdb/opa-g128.html>.
- USDA. 2006. What We Eat In America: National Health and Nutrition Examination Survey (NHANES): 2003-2004. U.S. Department of Agriculture (USDA); Riverdale, Maryland Available from: <http://www.ars.usda.gov/Services/docs.htm?docid=13793#release>.
- U.S. FDA. 2007a. Part 170—Food additives. Section §170.30—Eligibility for classification as generally recognized as safe (GRAS). In: U.S. Code of Federal Regulations (CFR). Title 21: Food and Drugs (U.S. Food and Drug Administration). U.S. Food and Drug Administration (U.S. FDA). U.S. Government Printing Office (GPO), Washington, DC, pp. 13-15. Available from: http://a257.g.akamaitech.net/7/257/2422/26mar20071500/edocket.access.gpo.gov/cfr_2007/aprqr/pdf/21cfr170.30.pdf.
- U.S. FDA. 2007b. Part 184—Direct food substances affirmed as generally recognized as safe. Section §184.1372—Insoluble glucose isomerase enzyme preparations. In: U.S. Code of Federal Regulations (CFR) Title 21: Food and Drugs (U.S. Food and Drug Administration) U.S. Food and Drug Administration (U.S. FDA) U.S. Government Printing Office (GPO); Washington, DC, p. 531. Available from: http://a257.g.akamaitech.net/7/257/2422/26mar20071500/edocket.access.gpo.gov/cfr_2007/aprqr/pdf/21cfr184.1372.pdf.

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APPENDIX I

Expert Panel Consensus Statement

EXPERT PANEL CONSENSUS STATEMENT CONCERNING THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS FOR THE PROPOSED FOOD USES OF VERDAD

December 7, 2007

At the request of PURAC Biochem b v. (PURAC), an Expert Panel (the "Panel") of independent scientists, qualified by their relevant national and international experience and scientific training to evaluate the safety of food ingredients, was specially convened on 19 September 2007 to conduct a critical and comprehensive evaluation of the available pertinent data and information, and determine the Generally Recognized as Safe (GRAS) status of VERDAD for use as a flavoring agent and antimicrobial agent in meat and poultry products, based on scientific procedures. The Panel consisted of the below-signed qualified scientific experts Prof Eric A Johnson (University of Wisconsin-Madison), Prof John Doull (University of Kansas) and Dr. Ian Munro (Cantox Health Sciences International). *Curricula vitae* evidencing the Panel members' qualifications for evaluating the safety of food ingredients are provided in Attachment 1

The Panel, independently and collectively, critically examined a comprehensive package of data provided by PURAC. In addition, the Panel evaluated other information deemed appropriate or necessary, including scientific data compiled from the literature and other published sources through August 2007 by Cantox Health Sciences International. The information evaluated by the Panel included data pertaining to the method of manufacture and product specifications of VERDAD, supporting analytical data, the estimated consumption of the components of VERDAD based on the proposed uses, and a comprehensive assessment of the available scientific literature pertaining to the safety of VERDAD.

Following critical evaluation of such data and information, the Panel unanimously concluded that under the conditions of intended use in traditional foods described herein, VERDAD, meeting appropriate food-grade specifications, is GRAS based on scientific procedures. VERDAD consists of a blend of organic acid salts (primarily lactate) and sugars. These compounds are either approved for use in food in the U.S., are commonly consumed in the diet, or are endogenous to the body. The safety of the materials also is supported through published animal toxicological studies and clinical studies on the individual components of VERDAD. The GRAS status of VERDAD is based on this available published scientific information in relation to the intended conditions of use of the ingredient in foods. A summary of the basis for the Panel's conclusion, excluding confidential information, is provided below.

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MANUFACTURING, COMPOSITION, AND STABILITY

VERDAD is produced by the fermentation of sucrose, originating from sugar cane or beet, or dextrose, originating from corn. The substrate is fermented to organic acids, primarily lactic acid, by *Bacillus coagulans* (*B. coagulans*) LA-1, *Lactobacillus paracasei* (*L. paracasei*) subsp *paracasei*, or *Propionibacterium freudenreichii* (*P. freudenreichii*) subsp. *shermanii*, or mixtures of these microorganisms. These are standard microorganisms commonly used in the food industry for the production of enzymes and cheese, and also are used as probiotics.

B. coagulans is listed in 21 CFR 184.1372 as a non-pathogenic and non-toxicogenic microorganism that is permitted for use in the U S for food production (U S. FDA, 2007a). *B. coagulans* also is designated by the American Type Culture Collection (ATCC) as a Biosafety Level 1 microorganism, indicating that it is not known to cause disease in adult humans (ATCC, 2007) Although sporulation is a known trait for *B. coagulans*, sporulation has never been observed for the proprietary strain *B. coagulans* LA-1 throughout more than 70 years of safe use.

L. paracasei was not recovered in fecal samples of adults provided high doses (up to 10^{11} CFU/day) of *L. paracasei* subsp *paracasei* and *Bifidobacterium animalis* subsp *lactis* in combination suggesting that *L. paracasei* did not survive during passage through the gastrointestinal tract (Larsen *et al.*, 2006). Furthermore, none of the subjects reported any adverse effects associated with the probiotic supplementation

The safety of *P. freudenreichii* subsp *shermanii* is supported by FDA's response to a GRAS notice for skim milk or dextrose cultured with *P. freudenreichii* subsp. *shermanii* for use as an antimicrobial agent in various foods (GRN 000128), in which FDA had no questions (U.S. FDA, 2003)

Professor Eric Johnson (Food Research Institute, University of Wisconsin-Madison) reviewed the scientific and medical literature and concluded that *B. coagulans*, *L. paracasei*, and *P. freudenreichii* used in the production of VERDAD are non-pathogenic and non-toxicogenic

Prior to fermentation, the medium is pasteurized to eliminate any residual bacteria. During fermentation, a suitable base, such as calcium, sodium or potassium hydroxide is added to control the pH (pH 6 to 7). The fermentation end product is purified to remove biomass, ions, and other impurities, followed by mixing with water or more concentrated cultured sugar to obtain the desired organic acid content as listed in the product specification. All microorganisms and any enzymes produced are inactivated and removed in the solid-liquid separation step due to the pH shock and the high temperatures (65 to 90°C). In addition, the conditions in the subsequent processing steps ensure complete pasteurization (process temperatures up to 80°C)

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All materials used in the manufacturing process are permitted for use in food in the U.S. Fermentation media components and processing aids are removed through extensive purification processes.

The final products contain a blend of either sodium or potassium organic salts, (primarily lactate, but also containing small amounts of acetate, succinate, formate, 2-hydroxybutyrate, and propionate) and sugars (glucose, fructose, and poly/oligosaccharides, consisting of glucose, galactose, rhamnose, glucosamine, mannose, and xylose).

PURAC's VERDAD meets appropriate food-grade specifications. In order to ensure a consistent product, PURAC established specification parameters for the final ingredients (see Tables 1 and 2) Representative lots of the manufactured product, when analyzed, verify that the manufacturing process produces a consistent product within final product physical, chemical, and microbiological parameters.

Table 1 Chemical Specifications for VERDAD				
Specification Parameter	Specifications			Analysis Method
	From Cane Sugar	From Corn Sugar	From Beet Sugar	
Lactate	55 to 80%	55 to 80%	55 to 80%	AMSOL044 – Assay of Purasal S – titration with 1 N hydrochloric acid
Sodium	0 to 21%	0 to 21%	0 to 21%	AM12 3 45E – Metals in PURAC-PLN-G products by ICP
Potassium	0 to 31%	0 to 31%	0 to 31%	AM12 3 45E – Metals in PURAC-PLN-G products by ICP
Formate	0 to 0.6%	0 to 0.6%	0 to 0.6%	RDT-A-0009 – Quantification of the total amount of organic acids and ethanol using a derivation and GLC1
Acetate ^a	0 to 6%	0 to 6%	0 to 6%	
2-Hydroxybutyrate ^a	0 to 0.25%	0 to 0.25%	0 to 0.25%	
Succinate ^a	0 to 1%	0 to 1%	0 to 1%	
Propionate ^a	0 to 7%	0 to 7%	0 to 7%	
Color (in solution)	Light brown to dark brown	Light brown to dark brown	Light brown to dark brown	Visual inspection
Sugars ^a	0 to 6.2%	0 to 6.2%	0 to 6.2%	RDT-A-0023 – Determination of total residual sugars using spectrophotometry
Glucose	0 to 2.5%	0 to 2.5%	0 to 2.5%	RDT-A-0029 – Quantification of sugars using anion exchange chromatography
Fructose	0 to 2.5%	0 to 2.5%	0 to 2.5%	
Poly/Oligosaccharides ^b	0 to 1.2%	0 to 1.2%	0 to 1.2%	Sugars minus glucose and fructose
Lead	<2 ppm	<2 ppm	<2 ppm	AM12 3 45E – Metals in PURAC-PLN-G products by ICP
pH (10%)	5 to 8	5 to 8	5 to 8	Metrohm 744 with combined glass electrode

^a The sum of non-lactate constituents is at least 1% on a dry weight basis

^b Poly/oligosaccharides are of varying length and composition, and consist on average of Glucose (52%), Galactose (20%), Rhamnose (9%), Glucosamine (8%), Mannose, and Xylose (together 7%) Other sugars are present at levels <0.1% of the total product

Constituents not listed in the table occur at levels below 0.1% Exposure to these constituents would be below the threshold of toxicological concern

Table 2 Microbiological Specifications for VERDAD		
Specification Parameter	Specification	Analysis Method
Mesophilic bacteria	<100 CFU/g	AMCAL004 – Yeasts, moulds, and aerobic mesophilic bacteria in PURAC
Moulds	<10 CFU/g	
Yeasts	<10 CFU/g	
Coliforms	absent in 10 g	ISO 21528-1 2004(E)
<i>Escherichia coli</i>	absent in 10 g	ISO 16649-2
<i>Salmonella</i>	absent in 25 g	2000 07 AOAC
<i>Staphylococcus</i>	absent in 10 g	ISO 6888-2

Abbreviations: CFU = colony forming units

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VERDAD from cane sugar was tested in an accelerated shelf-life study in which samples were stored at 40°C with a relative humidity of 75%. Samples were stable for at least 174 days with respect to the following parameters: organic acid salts expressed as total lactates salts, color, pH, total residual sugars expressed as glucose, dry solids, and lead, indicating that VERDAD from cane sugar is stable for a period of at least 1 year at ambient temperature and normal humidity levels. As the composition of VERDAD from cane sugar is similar to VERDAD from corn sugar and beet sugar, the stability of the products is similar.

REGULATORY STATUS

The current regulatory status of the components of VERDAD in the U.S. is as follows:

Sodium Lactate and Potassium Lactate

Sodium lactate and potassium lactate are approved in the U.S. for use as an antimicrobial agent in various meat and meat food products, poultry and poultry food products, except infant formula and infant food, at levels not to exceed 4.8% of the total formulation (9 CFR 424) (U.S. FDA, 2007b). Sodium lactate and potassium lactate are also approved in the U.S. for use as a flavoring agent in various meat and meat food products, poultry and poultry food products, except infant formula and infant food, at levels not to exceed 2% of the total formulation (9 CFR 424) (U.S. FDA, 2007b). As flavoring agents, sodium lactate and potassium lactate are to be used in accordance with the regulations listed in 21 CFR 184.1768 and 21 CFR 184.1639, respectively (U.S. FDA, 2007a). Sodium lactate and potassium lactate also are affirmed to be GRAS as a direct food substance to be used in food as an emulsifier, a flavor enhancer, a flavoring agent or adjuvant, a humectant, and a pH control agent with no limitation other than current good manufacturing practices (cGMP) (21 CFR 184.1768 and 21 CFR 184.1639) (U.S. FDA, 2007a). Lactic acid is affirmed as GRAS as an antimicrobial agent, curing and pickling agent, flavor enhancer, flavoring agent and adjuvant, pH control agent, and as a solvent and vehicle, with no limitation other than cGMP (21 CFR 184.1061) (U.S. FDA, 2007a).

Organic Acids

Acetic acid is approved as a direct food substance affirmed as GRAS (21 CFR 184.1005) (U.S. FDA, 2007a), to be used at maximal levels of 0.6% in meat products. Furthermore, sodium diacetate, sodium acetate, and potassium acetate are approved in the U.S. for use as an antimicrobial or flavoring agent in various meat and poultry products at levels not exceeding 0.25% of the total formulation (U.S. FDA, 2007a,b; USDA, 2007). Although succinate does not have regulatory status for use in food in the U.S., dimethyl succinate and diethyl succinate are approved as synthetic flavorings and adjuvants permitted for direct addition to food for human consumption at levels in accordance with cGMP (21 CFR 172.515) (U.S. FDA, 2007a). Sodium formate and formic acid are approved as indirect food substances affirmed as GRAS and are to be used at levels not to exceed cGMP (21 CFR 186.1756 and 21 CFR 186.1316, respectively).

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(U S FDA, 2007a). 2-Hydroxybutyrate (also known as α -hydroxybutyrate) does not have regulatory status for use in food in the U S It is an endogenously-produced compound and is structurally related to a fatty acid present in fats and oils that is consumed regularly in the diet. Propionic acid is approved as a direct food substance affirmed as GRAS with no limitation of use other than cGMP (21 CFR 184.1081) (U S. FDA, 2007a)

Sugars

Glucose from corn is permitted as a direct food substance affirmed as GRAS with no limitations other than cGMP (21 CFR 184.1857) (U.S. FDA, 2007a). High fructose corn syrup, which is up to 55% fructose, is permitted as a direct food substance affirmed as GRAS with no limitations other than cGMP (21 CFR 184.1866) (U S FDA, 2007a). Galactose is one of the dominant monosaccharides present in arabinogalactan, furcelleran, and carrageenan, all of which are food additives permitted for direct addition to food for human consumption with no limitations other than cGMP (21 CFR 172.610, 172.655, 172.620, respectively) (U.S FDA, 2007a) respectively) Gellan gum, which primarily consists of rhamnose, is a food additive permitted for direct addition to food for human consumption with no limitations other than cGMP (21 CFR 172.665) (U S FDA, 2007a), as well as xanthan gum, which primarily contains mannose (21 CFR 172.695) (U.S. FDA, 2007a) Xylose and glucosamine do not have regulatory status for use in food within the U.S

INTENDED USE AND ESTIMATED EXPOSURE OF VERDAD

Intended Use and Use-Levels

VERDAD is intended for use at the same levels and in the same meat and poultry products as those already approved for sodium lactate and potassium lactate The proposed food uses and use-levels of VERDAD are provided in Table 3. Because it is intended for use as replacement for sodium lactate and potassium lactate as a flavor enhancer and preservative, the proposed use of VERDAD is not expected to affect the current dietary intakes of sodium, potassium, and lactate.

Table 3 Summary of the Individual Proposed Food-Uses and Maximum Use-Levels for VERDAD in the U.S.		
Food Category	Proposed Food-Uses	Maximum Use-Levels (%)
Fresh Meats	Beef	4.8
	Lamb and Goat	4.8
	Organ Meats	4.8
	Pork	4.8
	Veal	4.8
Fresh Poultry	Chicken	4.8
	Duck	4.8
	Other Poultry	4.8
	Turkey	4.8
Meat Products	Bacon	4.8
	Frankfurters	4.8
	Ham	4.8
	Luncheon Meats	4.8
	Processed Meat Products	4.8
Poultry Products	Processed Poultry Products	4.8

Natural Occurrence and Dietary Consumption

Sodium

The primary form of sodium in the diet is sodium chloride (NaCl), the majority of which is consumed as a result of food processing (IOM, 2004a). Other dietary forms of sodium include monosodium glutamate (MSG) and food additives such as sodium benzoate, sodium nitrite, sodium acid pyrophosphate, sodium bicarbonate, and sodium citrate.

The dietary intakes of sodium by men and women in the U.S., based on self-reported intake data, are 3.1 to 4.7 g/day (135 to 204 mmol/day) and 2.3 to 3.1 g/day (100 to 135 mmol/day), respectively (IOM, 2004a). These values may underestimate sodium intake as they do not include salt added at the table. Total sodium intake in the U.S. based on urinary sodium excretion measurements has been estimated to be 183 and 142 mmol (4.2 and 3.3 g)/day in men and women aged 40 to 59 years, respectively.

The tolerable upper limit (UL) for sodium, established by the Food and Nutrition Board of the Institute of Medicine (IOM), ranges from 1.5 to 2.2 g/day for children, and is 2.3 g/day for adolescents and adults (IOM, 2004a). These values are based on the effects of sodium on blood pressure.

Potassium

In unprocessed foods, potassium occurs mainly in association with bicarbonate-generating precursors like citrate, and to a lesser extent with phosphate. In foods to which potassium is added in processing and in supplements, the form of potassium is potassium chloride. In addition to dietary sources, potassium is also commonly found in over-the-counter supplements, where the maximum amount of potassium is 0.099 g (2.5 mmol) (PDRNS, 2001).

The dietary intakes of potassium by men and women in the U.S. are 1.9 to 3.2 g/day (74 to 82 mmol/day) and 2.1 to 2.3 g/day (54 to 58 mmol/day), respectively (IOM, 2004b).

A UL was not established for potassium since intake from foods poses no risk to healthy individuals with normal kidney function as excess potassium is readily excreted in the urine. The adequate intake (AI) values for potassium, established by the IOM, range from 0.4 to 0.7 g/day in infants, 3.0 to 4.7 g/day in children and teenagers, and 4.7 to 5.1 g/day in adults (IOM, 2004b).

Lactate

Lactate or lactic acid is a normal intermediary metabolite of mammalian metabolic processes formed primarily from muscular activity and is found in blood at concentrations of 80 to 170 mg/L. It has been estimated that the daily turnover of lactic acid is approximately 2 g/kg body weight (FASEB, 1978). Lactic acid has been identified in a variety of foodstuffs (dairy products, fruit, breads, tea, coffee) especially those products that are fermented (*i.e.*, cheese, yogurt, beer, and wine) (Maarse and Visscher, 1992). The *per capita* consumption of lactic acid from natural food sources was previously calculated in the GRAS notification for PURAC's potassium lactate products, and was estimated to be 603 mg/day (8.61 mg/kg body weight/day) by multiplying the estimated concentration in a specific food by the *per capita* disappearance of that food (USDA, 1992).

Organic Acids and Sugars

Acetic acid is the major component of naturally fermented vinegar. Formic acid is present in fruits (including apples, strawberries, and raspberries) and honey. Also, propionate is commonly found in cheese. Fructose is present in many commonly consumed foods, including fruits and vegetables.

Glucose, galactose, rhamnose, mannose, and xylose have been reported to be byproducts of carbohydrate fermentation in the large intestine in rats fed diets containing maize starch, wheat bran, guar gum, pectin, and beet fiber (Nyman and Asp, 1982). Xylose is a wood sugar that occurs in various fruits and vegetables, and may be fermented to the sugar alcohol xylitol, which is a sugar substitute. Glucosamine is found in a variety of foods (PDRHM, 2004).

Estimation of Dietary Intake from the Proposed Food Uses

Estimates for all-person and all-user intakes of VERDAD for specific demographic groups and for the total U.S. population were calculated based on the proposed food-uses and use-levels in conjunction with food consumption data included in the National Center for Health Statistics' (NCHS) 2003-2004 National Health and Nutrition Examination Surveys (NHANES) (CDC, 2006, USDA, 2006). Approximately 93.7% of the total U S population was identified as consumers of VERDAD from the proposed food-uses (7,748 actual users identified) On an all-user basis, the mean intake of VERDAD by the total U S. population from all proposed food-uses was estimated to be approximately 6.55 g/person/day or 108.00 mg/kg body weight/day (see Table 4) The heavy consumer (90th percentile) all-user intake of VERDAD by the total U.S population from all proposed food-uses was estimated to be 12 31 g/person/day or 207 22 mg/kg body weight/day (see Table 5). Male adults were determined to have the highest mean all-user intake of VERDAD of 8 45 g/person/day (99 08 mg/kg body weight/day) and the highest 90th percentile all-user intake of VERDAD of 15.24 g/person/ day (176.93 mg/kg body weight/day)

Population Group	Age Group (Years)	% Users	Actual # of Total Users	All-Person Consumption		All-User Consumption	
				Mean (g)	90 th Percentile (g)	Mean (g)	90 th Percentile (g)
Infants	0 to 2	64.4	599	2.15	5.45	2.98	6.19
Children	3 to 11	98.5	1,268	4.94	7.02	5.02	9.05
Female Teenagers	12 to 19	96.4	956	5.26	1.00	5.53	10.18
Male Teenagers	12 to 19	98.6	985	7.63	13.15	7.78	13.15
Female Adults	20 and Up	96.8	2,060	5.36	10.05	5.56	10.11
Male Adults	20 and Up	97.5	1,880	8.25	15.04	8.45	15.24
Total Population	All Ages	93.7	7,748	6.29	12.16	6.55	12.31

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Population Group	Age Group (Years)	% Users	Actual # of Total Users	All-Person Consumption		All-User Consumption	
				Mean (mg/kg)	90 th Percentile (mg/kg)	Mean (mg/kg)	90 th Percentile (mg/kg)
Infants	0 to 2	64.4	599	175.91	448.62	243.91	506.86
Children	3 to 11	98.5	1,268	184.11	346.30	187.02	348.52
Female Teenagers	12 to 19	96.4	956	92.99	186.20	97.72	187.56
Male Teenagers	12 to 19	98.6	985	118.05	219.19	120.30	220.73
Female Adults	20 and Up	96.8	2,060	74.20	140.17	76.95	141.50
Male Adults	20 and Up	97.5	1,880	96.71	175.87	99.08	176.93
Total Population	All Ages	93.7	7,748	103.73	204.81	108.00	207.22

Estimation of Consumption of Organic Acids and Sugars from VERDAD

Estimates of the mean and 90th percentile intakes of organic acids and sugars contained in VERDAD were based on the mean and 90th percentile intakes in male adults (all-users) as to represent an overestimate of consumption, as the highest intake values were calculated for this population group [*i.e.*, for lactate, 80% x 8.45 g/person/day (mean) and 80% x 15.24 g/person/day (90th percentile)]. These estimates are presented in Table 6

Table 6 Daily Consumption Estimates for the Components of VERDAD			
Component	Specification (maximum level)^a	Mean (g)	90th percentile (g)
Lactate	80%	6.76	12.19
Sodium	21%	1.69	3.20
Potassium	31%	2.62	4.72
Formate	0.6%	0.05	0.09
Acetate	6%	0.51	0.91
2-Hydroxybutyrate	0.25%	0.02	0.04
Succinate	1%	0.08	0.15
Propionate	7%	0.59	1.07
Sugars	6.2%	0.52	0.94
Glucose	2.5%	0.21	0.38
Fructose	2.5%	0.21	0.38
Poly/Oligosaccharides ^b	1.2%	0.10	0.18
Glucose	0.624%	0.05	0.10
Galactose	0.24%	0.02	0.04
Rhamnose	0.108%	0.01	0.02
Glucosamine	0.096%	0.01	0.01
Mannose and Xylose	0.084%	0.01	0.01

^a Expressed as percentage of the final product

^b Poly/oligosaccharides are of varying length and composition, and consist on average of glucose (52%), Galactose (20%), Rhamnose (9%), Glucosamine (8%), Mannose and Xylose (together 7%) Other sugars are present at levels <0.1% of the total product

Consumption data and information pertaining to the individual proposed food-uses of VERDAD were used to estimate the all-person and all-user intakes of VERDAD for specific demographic groups and for the total U.S. population. This type of intake methodology is generally considered to be 'worst case' as a result of several conservative assumptions made in the consumption estimates. For example, it is often assumed that all food products within a food category contain the ingredient at the maximum specified level of use. It is highly unlikely that all food products included in the intake calculations will contain VERDAD and that VERDAD will be used at the maximum permitted use-level in all of the listed products. In addition, it is well established that the length of a dietary survey affects the estimated consumption of individual users. Short-term surveys, such as the typical 2- or 3-day dietary surveys, overestimate the consumption of food products that are consumed relatively infrequently.

VERDAD is intended for use as a flavoring agent and anti-microbial agent for which sodium lactate and potassium lactate are already approved in the U.S. In these applications, VERDAD is intended for use as a replacement for sodium lactate and potassium lactate at levels that will not exceed the current maximum permitted concentration of sodium lactate or potassium lactate. Therefore, the proposed use of VERDAD will not increase the current dietary intakes of sodium, potassium, and lactate. The other components of VERDAD are permitted for use in

food at levels with no limits other than cGMP, with the exception of 2-hydroxybutyric acid, glucosamine, and xylose

DATA SUPPORTING THE SAFETY OF VERDAD

Because sodium lactate and potassium lactate are ionic and will dissociate *in vivo*, the safety of the ions may be considered separately. Thus, this report presents a brief overview of the safety data pertaining to sodium, potassium, and lactate. When available, data specific to sodium lactate and potassium lactate have also been provided. The safety of the other organic acid and sugar components of VERDAD also is discussed.

Effects of VERDAD on Shelf-Life and Color

VERDAD from cane sugar or PURASAL S (PURAC's sodium lactate product already permitted for use in the U.S.) was incubated with fresh pork loin or chicken breast at 4°C, over 35 and 10 days, respectively, to compare the effects of VERDAD and PURASAL S on shelf-life and color of the meat products. Aerobic bacterial counts were performed at various intervals, and spoilage was deemed to occur when the bacterial count was greater than log 6 colony forming units per gram of meat. The control sample of fresh pork loin was spoiled after 14 days, whereas the fresh pork loin samples incubated with VERDAD or PURASAL S were spoiled after 28 days. Among chicken breast samples, the control sample was spoiled after 2.5 days, whereas the samples incubated with VERDAD or PURASAL S were spoiled after 4.5 days. These results indicate that VERDAD has similar efficacy as sodium lactate in extending the shelf-life of fresh pork loin and chicken breasts. Therefore, replacement of sodium lactate with VERDAD in meat and poultry products will not affect the safety of the food consumed.

In addition to their effects on shelf-life, the ability of VERDAD and PURASAL S to alter the color of spoiling pork loin was evaluated. After 14 days of storage, the color of the control pork loin was no longer acceptable, which coincides with the time at which the product is considered spoiled (>log 6 CFU/g). The color of pork loin incubated with 4% VERDAD or 4% PURASAL S was no longer acceptable after 28 days, coinciding with the time at which the product was considered spoiled (>log 6 CFU/g). Therefore, the addition of VERDAD does not mask spoilage, similar to PURASAL S.

As the composition of VERDAD from cane sugar is similar to VERDAD from corn and beet sugar, the efficacy of these products is similar.

Metabolic Fate

Sodium and potassium both are absorbed in the small intestine. Absorbed sodium is present in the extracellular fluid, including plasma, intestinal fluid, and plasma water in concentrations of around the 100 mmol/L range. Systemic potassium levels are independent of intake due to the

renal regulation of potassium balance Sodium and potassium largely are excreted in the urine and the balance of their levels is dependent on various hormones and systems. For example, the renin-angiotensin-aldosterone axis is stimulated by reduced salt intake, blood volume, or blood pressure, and acts to promote sodium retention and reabsorption in the kidney Similarly, the sympathetic nervous system is also activated under conditions of sodium depletion and suppressed when excess sodium is present. In contrast, atrial natriuretic peptide is released in response to elevated blood volume and serves to counteract the renin-angiotensin-aldosterone system Sodium homeostasis is also maintained by the kallikrein-kinin system, several intrarenal mechanisms, and other factors regulating renal and medullary blood flow. Excess potassium is removed by increasing excretion into the urine, whereas, a potassium deficiency would result in decreased urinary excretion (Sheng, 2000). Rate of excretion *via* the kidneys is dependent on the secretion of K^+ by renal tubular cells of the cortical collecting tubules (Rodríguez-Soriano, 1995) and is regulated by the hormone aldosterone

Lactic acid is produced as an intermediate of anaerobic metabolism through the metabolism of pyruvate. Orally administered sodium lactate has been reported to achieve maximal absorption after 4 hours. Once absorbed, L-lactate may be converted to glycogen. Less than 1% of L-lactate is excreted in the urine in comparison to D-lactate, where up to 30% may be excreted in the urine

Toxicological Studies

Sodium

Results from several animal studies have demonstrated a strong positive association between salt intake and cardiovascular disease, particularly stroke (Coyle, 1988, Chen *et al.*, 1997) Animals fed diets high in sodium (787 to 3,148 mg/kg body weight/day) had significantly increased blood pressure, incidence of stroke, and susceptibility to infarctions compared to those given low-sodium diets (59 to 118 mg/kg body weight/day)

Animal studies using *Helicobacter pylori*- (*H. pylori*) infected animals have shown that high-salt diets, providing approximately 500 to 3,000 mg Na/kg body weight/day, enhance the gastric carcinogenetic effects of *H. pylori* (Fox *et al.*, 1999; Kato *et al.*, 2006) Fox *et al.* (1999) concluded that the high-salt diet worked synergistically with *H. pylori* to accelerate the progression of gastric carcinogenesis by creating a hospitable environment for the colonization of *H. pylori*

The doses used in the high-salt diets in these studies, ranging from 477 to 3,148 mg Na/kg body weight/day, would provide a sodium intake for an adult human (weighing 70 kg) of 33 to 220 g/day These intakes are 7 to 46 times higher than the average male intake of sodium within the U.S. population of 4.7 g/day, therefore, the effects observed in these studies are unlikely to occur in humans.

Potassium

Specific safety data on potassium lactate were limited to an ocular irritation study in which New Zealand White rabbits instilled into the conjunctival sac of the eye with 0.1 mL 60% aqueous solution of potassium lactate were observed up to 7 days (Guillot *et al.*, 1982). Potassium lactate was reported to be slightly irritating.

The benefits of a high-potassium diet (up to 2,110 mg/kg body weight/day for 6 weeks) against hypertension and ischemic stroke in rats have been investigated in several studies (Zhou *et al.*, 1999, 2000; Pamnani *et al.*, 2000; Dorrance *et al.*, 2007). No adverse effects associated with high potassium diets were reported by the study authors.

Lactate

Animal studies have demonstrated that various lactate salts or lactic acids are well tolerated. In short-term studies with lactic acid using rats (11 days) and dogs (2.5 months), no effects were reported at doses up to 2,000 (rats) or 1,600 (dogs) mg/kg body weight/day (Faust, 1910, Furth and Engel, 1930). Effects on adrenal cortical activity and organ weights observed in rabbits fed 120 to 200 mg lactic acid/kg body weight/day were not considered toxicologically significant as they were observed with other organic acids or were attributed to an acid-base imbalance (Jonek, 1961; Fazekas, 1949, 1954). The doses used in the Jonek and Fazekas studies would provide an average 70 kg human with 8.4 and 14 g of lactic acid/day, respectively. These doses are 14 and 23 times larger than the intake of lactic acid provided from background dietary intake of lactic acid; thus, these effects would not be expected to occur in humans.

In a carcinogenicity study, calcium lactate produced no increases in the incidence of lesions or tumors when fed at dietary concentrations of 0 (control), 2.5, or 5% (approximately 0, 2, or 3.9 g/kg body weight/day) to male and female F344 rats for a period of 2 years (Maekawa *et al.*, 1991). Absolute kidney and relative brain weights were increased in some groups of treated rats, however, there were no corresponding histopathological changes. A no-observed-adverse-effect level from this study was determined to be 3.9 g/kg body weight/day, the highest dose tested, providing 1.6 g lactate/kg body weight/day.

Sodium lactate solution was shown to be negative for mutagenic activity in various strains of *Salmonella typhimurium* (*S. typhimurium*), either in the presence or absence of metabolic activation, at doses up to 100 mg/plate and did not induce structural or numerical chromosomal aberrations in a Chinese hamster fibroblast cell line at doses up to 2.0 mg/mL (Ishidate *et al.*, 1984). Furthermore, lactic acid and calcium lactate have shown no mutagenic activity in *S. typhimurium* at concentrations up to 2.7% or in *Saccharomyces cerevisiae* at concentrations up to 5.0%, both with and without metabolic activation (Litton Bionetics, 1976). However, lactic acid induced chromosomal aberrations in isolated Chinese hamster ovary cells when tested at concentrations of 12 mM or greater and pH of 6 or lower, with or without metabolic activation. These concentrations were shown to produce cytotoxicity (Morita *et al.*, 1990).

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Summary

The data from the available preclinical studies demonstrate that high-salt diets increase the risk of cardiovascular disease and induced gastric cancer, however, the high-salt diets administered to the animals provided more than 6 times the average salt intake for humans. Potassium has been shown to have a beneficial effect in terms of reversing or preventing hypertension and ischemic stroke without any associated adverse effects. The safety of moderate intakes of sodium and potassium is further supported by clinical studies (please see below)

Lactate has been reported to have low oral toxicity with a lack of adverse effects in feeding studies in which up to 3,900 mg/kg body weight/day was administered to rats for 2 years. Likewise, lactate was proven to be non-genotoxic or mutagenic.

Clinical Studies

Sodium

The major adverse effect associated with increased sodium intake (as NaCl) is elevated blood pressure. Numerous clinical intervention trials have been conducted to evaluate the relationship between sodium intake and blood pressure. Overall, these indicate that decreased sodium intake lowers blood pressure levels, with a more pronounced reduction in hypertensive subjects compared to non-hypertensive subjects. In trials that included 3 or more levels of sodium intake, a direct, progressive, dose-response relationship was demonstrated in the majority of studies (Kirkendall *et al.*, 1976, Luft *et al.*, 1979; Sullivan *et al.*, 1980, Roos *et al.*, 1985; Fuchs *et al.*, 1987; MacGregor *et al.*, 1989; Bruun *et al.*, 1990; Ferri *et al.*, 1996; Johnson *et al.*, 2001; Sacks *et al.*, 2001). Results from the largest trial demonstrated a decrease in systolic blood pressure by 2.1 mmHg following a reduction in sodium intake from 3.3 g to 2.3 g/day (Sacks *et al.*, 2001). An additional decrease in sodium intake to 1.2 g/day resulted in further lowering of blood pressure.

Observational studies generally indicate that higher sodium intake levels may increase the risk of cardiovascular disease (CVD), especially stroke (Kagan *et al.*, 1985, Perry and Beevers, 1992; Yamori *et al.*, 1994, Sasaki *et al.*, 1995, Alderman *et al.*, 1997; Yang *et al.*, 1997). Sodium intake may contribute to increased stroke risk through its effects on blood pressure, but there also is evidence that sodium may have a direct effect on stroke risk independent of its effects on blood pressure (Brahimi *et al.*, 1995; Tobian and Hanlon, 1990, Perry and Beevers, 1992; Xie *et al.*, 1992).

Although the results of observational studies suggest that higher sodium intake levels increase the risk of CVD, there is a lack of well designed clinical trials that investigate the effects of dietary sodium reduction on clinical measures of CVD. The IOM stated that these types of studies are typically required to provide conclusive evidence of a causal relationship (IOM, 2004a)

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Findings from several studies demonstrate that there is a progressive relationship between sodium intake (typically measured by urinary sodium excretion) and left ventricular mass (Schmieder *et al.*, 1988, 1990, 1996; du Cailar *et al.*, 1989, 1992, 2002; Daniels *et al.*, 1990, Liebson *et al.*, 1993, Kupari *et al.*, 1994, Gerds *et al.*, 1996; Langenfeld *et al.*, 1998), which is a predictor of myocardial infarction, stroke, congestive heart failure, and sudden death. Sodium may affect left ventricular mass either directly or indirectly (through its effects on blood pressure)

Increased NaCl intake has been shown to result in elevated urinary calcium excretion in numerous intervention studies (Shortt *et al.*, 1988; Nordin *et al.*, 1993; Itoh and Suyama, 1996; Dawson-Hughes *et al.*, 1996). However, as elevated calcium excretion may be accompanied by increased intestinal calcium absorption (Breslau *et al.*, 1982), the influence of sodium intake on calcium balance is not clear. Studies investigating the effects of sodium intake on markers of bone resorption and formation have produced conflicting results (Greendale *et al.*, 1994, Matkovic *et al.*, 1995; Devine *et al.*, 1995, Jones *et al.*, 1997), as effects vary among age groups, diets, and form of dietary sodium consumed. Increased consumption of sodium may also result in the formation of renal stones (Burtis *et al.*, 1994; Curhan *et al.*, 1997, Stamler and Cirillo, 1997; Martini *et al.*, 2000), as hypercalciuria is a risk factor for renal stone formation (Strauss *et al.*, 1982).

Studies evaluating the relationship between sodium intake and pulmonary function have indicated that in most cases, increased sodium intake is related to bronchial reactivity, bronchitis, and asthma (Burney *et al.*, 1986; Schwartz and Weiss, 1990; Carey *et al.*, 1993; Medici *et al.*, 1993; Tribe *et al.*, 1994; Gotshall *et al.*, 2000;). However, no relationship between sodium intake and pulmonary function was reported in studies conducted by Britton *et al.* (1994) and Zoia *et al.* (1995)

In support of the hypothesis that high intake levels of salt leads to destruction of the stomach mucosa, rendering it susceptible to invasion by carcinogens (Correa *et al.*, 1975), a significant positive association between salt intake and gastric cancer incidence or mortality has been reported in numerous studies (Montes *et al.*, 1985; Bernstein and Henderson, 1985; Tsugane *et al.*, 1991; Kneller *et al.*, 1992; Lee *et al.*, 1995, Joossens *et al.*, 1996, La Vecchia *et al.*, 1997; Tsubono *et al.*, 1997; Palli *et al.*, 2001). However, no association between salt intake and gastric cancer was observed in two studies conducted by Ikeda *et al.* (1988) and Honjo *et al.* (1994). Due to these opposing results and because the majority of evidence is based on epidemiological studies rather than appropriately designed clinical trials, the IOM stated that the evidence of the effects on sodium and gastric cancer is unclear in humans (IOM, 2004a).

As epidemiological studies and clinical trials indicate that the major adverse effect associated with increased sodium intake is elevated blood pressure, which in turn, may be a risk factor for cardiovascular and renal diseases, an upper tolerable limit for sodium intake was established to be 2.3 g/day. Based on the proposed uses of VERDAD, the mean and 90th percentile intakes of

sodium were estimated to be 1.69 and 3.20 g/person/day, respectively, for male adults. The intake levels are based on several assumptions, such as VERDAD being used in 100% of the proposed meat and poultry products, VERDAD being used at maximum proposed use-levels in all products (4.8% on a dry weight basis), and adult male heavy-consumers being the most conservative endpoint, which result in an overestimate of the mean and 90th percentile estimated intakes for sodium. Furthermore, VERDAD is intended for use in the same foods and at the same use-levels as those already approved for sodium lactate and potassium lactate as an alternative antimicrobial or flavoring agent and will be used as a direct replacement. Therefore, resulting intakes of sodium will not be increased compared to current dietary intakes.

Potassium

Excess potassium ingestion rarely produces toxicity in healthy individuals with no renal impairment because of the kidney's high capacity to excrete K⁺ (Sheng, 2000). However, acute intoxication with potassium was estimated by NRC (1980) to occur at sudden increases in potassium intake levels of approximately 18 g/adult/day. In individuals with impaired renal function or problems with aldosterone activity, excess potassium ingestion may lead to hyperkalemia.

Hyperkalemia (>5.5 mmol K⁺/L plasma) causes depolarization of the membrane resulting in muscular weakness and cardiac arrhythmias (Rodríguez-Soriano, 1995). Higher plasma concentrations (8 mmol K⁺/L plasma) may result in cardiac arrest. In potassium-deficient individuals, hypokalemia may result. Hypokalemia (<3.5 mmol K⁺/L plasma) causes hyperpolarization of membranes, interfering with the normal function of nerves and muscles and results in decreased smooth muscle contractility, which under severe conditions can lead to cardiac arrhythmias, paralysis, metabolic alkalosis and eventual death (Rodríguez-Soriano, 1995).

The majority of the safety data on potassium is related to its beneficial effects on hypertension. In its review of potassium (NRC, 1989), the Committee on Diet and Health reviewed numerous epidemiological and animal studies investigating the effect of dietary potassium levels on hypertension and concluded that "an intake of ≥ 3.5 g/day of elemental potassium is associated with a beneficial effect, and no threshold for this effect is known."

Because increased potassium intakes are considered to have a positive effect on hypertension, and there are no reported adverse effects associated with the estimated potassium intakes from the proposed uses of VERDAD (4.72 g/day in male heavy-consumers), the consumption of potassium contained in VERDAD does not pose a safety concern.

Lactate

In humans, calcium lactate supplements of 1 to 5 g/day (approximately 14 to 68 mg lactate/kg body weight/day) have been used to supply the daily calcium requirement in adults without adverse effects (Lieberman, 1930; Osol and Pratt, 1973). At a single dose of 10 g (approximately 136 mg lactate/kg body weight/day), calcium lactate was reported to produce abdominal distress, vomiting, and diarrhea in healthy men (Lieberman, 1930). Newborn infants and 4-month-old infants administered 6 g of calcium lactate in a 10% aqueous solution by gavage (providing approximately 1,073 and 536.7 mg lactate/kg body weight/day, respectively) were reported to have significantly increased serum calcium and mild diarrhea. No other adverse effects were reported (Durlacher *et al.*, 1946).

FASEB (1978) reviewed a number of studies in which lactic acid had been used to acidify infant feeding formulas given to full and pre-term infants. These studies involved formulas made with either L(+) or DL-lactate, with dose levels ranging from 600 to 1,275 mg/kg body weight/day for periods of up to 36 days. Most of the studies lacked comparative control groups. In the studies involving DL-lactate, metabolic acidosis and reduced growth were reported, mostly in pre-term infants but also in some full-term infants. Reduced growth rate, however, did not occur in the absence of metabolic acidosis. The studies involving L(+)-lactate formulas did not report either metabolic acidosis or reduced growth rates.

In reviewing the safety of lactic acid and its sodium, potassium, and calcium salts, the Joint FAO/WHO Expert Committee on Food Additives (JECFA, 1974) concluded that it was "unnecessary to set ADI limits" for these additives since lactic acid is a normal constituent of food and a normal intermediary metabolite in humans. In another review of the safety of lactic acid and calcium lactate conducted by the Federation of American Societies for Experimental Biology (FASEB, 1978) for the FDA, similar conclusions were drawn by the Select Committee indicating that lactic acid and calcium lactate were safe for use by "individuals beyond infancy when they are used at levels that are now current or that might reasonably be expected in the future".

The evaluations of lactic acid (and its salts) by JECFA and FASEB indicate that consumption of lactate from the proposed uses of VERDAD is safe.

Other Organic Acids and Sugars

2-Hydroxybutyrate is produced in mammals by the degradation of the amino acids methionine, threonine, homoserine and 2-aminobutyric acid (Landaas, 1975). It has been detected in the urine of healthy individuals at levels ranging from 0.10 to 2.68 µg/mL (Shima *et al.*, 2005) and its production is enhanced in diabetics and during lactic acidosis (Shima *et al.*, 2005; Pettersen *et al.*, 1973). Its isomer, 3-hydroxybutyrate (also known as β-hydroxybutyrate), is a ketone body that is generated in the liver from acetyl coenzyme A (CoA) during fasting conditions or in

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diabetic patients and is used as an energy source by the brain and heart (Stryer, 1995). Moreover, butyric acid (a.k.a. butanoic acid) is a short-chain fatty acid that occurs as an ester in various fats and oils, including butter. It is expected that ingested 2-hydroxybutyrate would be cleaved to form butyric acid

Based on the estimated 90th percentile intake of 15.44 g VERDAD/person/day for adult male all-users, it was estimated that 40 mg 2-hydroxybutyrate/person/day would be consumed under the proposed conditions of use. Based on the 2006 per capita U.S. butter consumption, 180 mg butyric acid/person/day is consumed from butter alone¹. The consumption of 2-hydroxybutyric acid from VERDAD is more than 4 times lower than the dietary intake of butyric acid from butter (Gould, 2007). This indicates that the added 2-hydroxybutyric acid from VERDAD would not pose a safety concern.

Glucosamine is an endogenous aminomonosaccharide synthesized from glucose (PDRHM, 2004). It is commonly used as a supplement of up to 1,500 mg/day for people suffering from osteoarthritis with little to no adverse events reported, which is 100 times higher than the intake of glucosamine of 15 mg/day resulting from the proposed uses of VERDAD.

Acetate, succinate, formate, and propionate are permitted for use in food in the U.S. with no limitation other than cGMP (21 CFR 184.1005, 21 CFR 172.515, 21 CFR 186.1316, and 21 CFR 184.1081) (U.S. FDA, 2007a). Thus, consumption of these organic acids under the intended conditions of use is of no safety concern.

Glucose, fructose, galactose, rhamnose, and mannose are either permitted for use in food in the U.S. or are major components of foods that are permitted for use in food in the U.S. Xylose is a sugar that is present in a variety of fruits and vegetables and is consumed regularly in the diet. The estimated intakes of these sugars from the intended uses of VERDAD are well below dietary intake levels, therefore, there is no safety concern.

Summary

While the preclinical and clinical studies for sodium show that increased salt intake may cause cardiovascular disease such as hypertension and stroke, the proposed uses of VERDAD will not increase current dietary intakes of sodium, as well as potassium and lactate, because VERDAD is intended as a direct replacement for sodium lactate and potassium lactate in meat and poultry products. Also, preclinical and clinical studies show that consumption of potassium and lactate at the proposed levels of use present no safety concern.

³ *Per capita* butter consumption = 4.73 lb/year. On a gram per day basis, $(4.73 \text{ lbs/year} * 0.454 \text{ kg/lb})/365 = 5.88 \text{ g butter/day}$. Butter contains 3 to 4% butyric acid, therefore daily intake of butyric acid is $5.88 \text{ g/day} * 0.03$ or $5.88 \text{ g/day} * 0.04$, which is equal to 0.18 to 0.24 g butyric acid/day, respectively.

2-Hydroxybutyrate is produced in mammals from the degradation of several amino acids. Furthermore, the estimated intake of 2-hydroxybutyrate resulting from the proposed uses of VERDAD is 4.5 times lower than the intakes from butter. The other components of VERDAD, such as acetate, succinate, formate, glucose, fructose, galactose, rhamnose, mannose, xylose, and glucosamine, either have regulatory status within the U.S., are major components of foods that have regulatory status within the U.S., or are consumed regularly in the diet at higher levels than those estimated from the proposed uses of VERDAD. Thus, the consumption of the components of VERDAD is expected to be of no safety concern.

SUMMARY

VERDAD is produced from fermentation using non-genetically modified bacteria that have a long history of safe use in foods. Furthermore, Professor Eric Johnson has concluded that these microorganisms are non-toxicogenic and non-pathogenic. The final products (in solution) contain approximately 50 to 60% sodium lactate or potassium lactate, as well as small amounts (<5% each) of organic acids (acetate, succinate, formate, 2-hydroxybutyrate, and propionate) and sugars (glucose, fructose, and poly/oligosaccharides). These compounds are either approved for use in food in the U.S., are major components of foods with regulatory status in the U.S., are commonly consumed in the diet, or are endogenous to the body.

Sodium lactate and potassium lactate are expected to be hydrolyzed *in vivo* into their respective components, sodium, potassium, and lactate. These components are absorbed in the small intestine and excreted in the urine or utilized within the body for energy or cellular signaling.

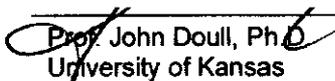
VERDAD is intended for use at the same levels and in the same meat and poultry products as those already approved for sodium lactate and potassium lactate for use as a flavoring or antimicrobial agent. Because VERDAD is intended as a direct replacement for sodium lactate and potassium lactate, the current intakes of sodium, potassium, and lactate will not be affected. The mean and 90th percentile all-user intakes of VERDAD in the total U.S. population were estimated to be 6.55 and 15.24 g/person/day, respectively. The estimated intakes of sodium, potassium, and lactate, based on adult male all-user heavy-consumer data (the population with the highest estimated intakes of VERDAD), were 3.20, 4.72, and 12.19 g/person/day, respectively. These values are an over-estimate of the actual levels that would be consumed from the use of VERDAD because of several conservative assumptions made in the intake estimates. These include assumptions that all of the meat and poultry products in which VERDAD is proposed for use will contain the ingredients, and that VERDAD will be used at the maximum level.

The safety of sodium, potassium, and lactate is further supported by the available toxicological and clinical studies, which indicate no adverse effects associated with moderate intakes of sodium, potassium, and lactate. Based on the entirety of the available scientific data, it is

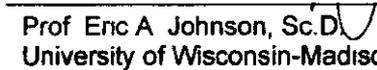
concluded that VERDAD is safe for their intended use in food. The data and information summarized in this dossier demonstrate that VERDAD, meeting appropriate food-grade specifications, would be GRAS based on scientific procedures under the conditions of intended use in foods, as described herein.

CONCLUSION

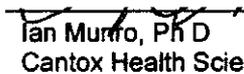
We, the Expert Panel, have independently and collectively critically evaluated the data and information summarized above and conclude that VERDAD, meeting appropriate food-grade specifications, is Generally Recognized as Safe (GRAS) under the conditions of intended use in foods specified herein, based on scientific procedures.


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REFERENCES

- Alderman, M , Sealey, J.; Cohen, H.; Madahavan, S ; Laragh, J. 1997 Urinary sodium excretion and myocardial infarction in hypertensive patients: a prospective cohort study *Am J Clin Nutr* 65(2, Suppl):682S-686S
- ATCC. 2007 [Search for *Bacillus coagulans*, ATCC nos. 10545 ; 11369 , 12245 ; 15949 , 23498 ; 31284 , 35670 , 8038 , BAA-738 , 53595 ; 11014 , 7050] In. ATCC. The Global Bioresource Center™, Manassas, Virginia. Available from: [http //www atcc org/common/catalog/numSearch/index.cfm](http://www.atcc.org/common/catalog/numSearch/index.cfm) [Last accessed July 19, 2007].
- Bernstein, L ; Henderson, B E. 1985 Studies comparing population differences in sodium intake and gastric cancer rates *J Cancer Res Clin Oncol* 110(2):184.
- Brahimi, M ; Kondon, R.T.; Tual, J.L , Diallo, A ; Safer, M 1995 Influence of sodium on arterial elasticity in essential hypertension. In: Working Group on Hypertension and the Heart of the European Society of Cardiology. Seventh European Meeting on Hypertension Abstracts, June 9-12, 1995, Milan, Italy. University of Milan, Milan, Italy, p. 26 [Abstract No. 103].
- Breslau, N A ; McGuire, J L ; Zerwekh, J.E.; Pak, C.Y C. 1982. The role of dietary sodium on renal excretion and intestinal absorption of calcium and on vitamin D metabolism *J Clin Endocrinol Metab* 55(2) 369-373.
- Britton, J , Pavord, I , Richards, K , Knox, A.; Wisniewski, A., Weiss, S.; Tattersfield, A. 1994 Dietary sodium intake and the risk of airway hyperreactivity in a random adult population *Thorax* 49(9):875-880.
- Bruun, N.E., Skott, P., Damkjaer Nielsen, M , Rasmussen, S., Schutten, H J , Leth, A ; Pedersen, E B ; Giese, J. 1990 Normal renal tubular response to changes of sodium intake in hypertensive man *J Hypertens* 8(3):219-227
- Burney, P G ; Britton, J R ; Chinn, S.; Tattersfield, A.E , Platt, H S ; Papacosta, A.O , Kelson, M C 1986. Response to inhaled histamine and 24 hour sodium excretion *Br Med J* 292(6534) 1483-1486
- Burtis, W J ; Gay, L ; Insogna, K L., Ellison, A.; Broadus, A E. 1994. Dietary hypercalcemia in patients with calcium oxalate kidney stones. *Am J Clin Nutr* 60(3):424-429.
- Carey, O J , Locke, C.; Cookson, J.B 1993. Effect of alterations of dietary sodium on the severity of asthma in men *Thorax* 48(7) 714-718.
- CDC. 2006 Analytical and Reporting Guidelines: The National Health and Nutrition Examination Survey (NHANES). Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS), Hyattsville, Maryland Available from [http //www cdc.gov/nchs/data/nhanes/nhanes_03_04/nhanes_analytic_guidelines_dec_2005.pdf](http://www.cdc.gov/nchs/data/nhanes/nhanes_03_04/nhanes_analytic_guidelines_dec_2005.pdf).

000036

- Chen, J ; Delaney, K.H., Kwiecien, J M., Lee, R M 1997. The effects of dietary sodium on hypertension and stroke development in female stroke-prone spontaneously hypertensive rats. *Exp Mol Pathol* 64(3) 173-183
- Correa, P.; Haenszel, W., Cuello, C., Tannenbaum, S.; Archer, M. 1975 A model for gastric cancer epidemiology. *Lancet* 306(7924) 58-59
- Coyle, P. 1988 High NaCl predisposes Dahl rats to cerebral infarction after middle cerebral artery occlusion. *Hypertension* 12(2) 96-101
- Curhan, G C., Willett, W C , Speizer, F.E.; Spiegelman, D ; Stampfer, M.J. 1997. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk of kidney stones in women. *Ann Intern Med* 126(7):497-504.
- Daniels, S.D., Meyer, R A ; Loggie, J M. 1990 Determinants of cardiac involvement in children and adolescents with essential hypertension. *Circulation* 82 (4):1243-1248.
- Dawson-Hughes, B., Fowler, S E ; Dalsky, G., Gallagher, C. 1996. Sodium excretion influences calcium homeostasis in elderly men and women *J Nutr* 126(9):2107-2112.
- Devine, A ; Criddle, R.A , Dick, I.M.; Kerr, D A ; Prince, R.L 1995. A longitudinal study of the effect of sodium and calcium intakes on regional bone density in postmenopausal women. *Am J Clin Nutr* 62(4) 740-745
- Dorrance, A.M., Pollock, D M ; Romanko, O P ; Stepp, D.W. 2007. A high-potassium diet reduces infarct size and improves vascular structure in hypertensive rats. *Am J Physiol Regul Integr Comp Physiol* 292(1):R415-R422.
- du Cailar, G., Ribstein, J.; Grolleau, R ; Mimran, A 1989. Influence of sodium intake on left ventricular structure in untreated essential hypertensives *J Hypertens* 7(6) S258-S289.
- du Cailar, G.D.; Ribstein, J ; Daures, J.P.; Mimran, A. 1992 Sodium and left ventricular mass in untreated hypertensive and normotensive subjects *Heart Circ Physiol* 32(1, Part 2):H177-H181
- du Cailar, G.; Ribstein, J , Mimran, A. 2002. Dietary sodium and target organ damage in essential hypertension. *Am J Hypertens* 15(3):222-229
- Durlacher, S.H ; Harrison, W. (Jr.), Darrow, D C 1946 The effects of calcium chloride and of calcium lactate administered by gavage. *Yale J Biol Med* 18 135-143.
- FASEB. 1978. Evaluation of the Health Aspects of Lactic Acid and Calcium Lactate as Food Ingredients Prepared by Federation of American Societies for Experimental Biology (FASEB), Life Sciences Research Office (LSOR), Bethesda, Maryland for U S. Food and Drug Administration (U.S. FDA), Bureau of Foods; Washington, DC, FDA/BF-78/108 [PB238-713 / SCOGS-11]
- Faust, E S. 1910. Cothener Chem Z 34.57. Cited In. JECFA, 1974; Anderson, 1998

000037

- Fazekas, I G. 1949 Kísérleti adatok a petefészekműködés befolyásolására egyszerű vegyületekkel = [Experimental data on influencing ovarian functions by simple compounds] Orv Hetil 90:777-781. (Translation supplied with Informatics, Inc 1975. Monograph on Lactic Acid Submitted under DHEW Contract No. FDA 72-104 Rockville, Maryland. 212 pp. Cited In: FASEB, 1978
- Fazekas, I G 1954 Beeinflussung der Nebenschilddrüsenfunktion (serum Ca und P) durch azidotische Verbindungen = [The influence of acidotic compounds on parathyroid function (serum Ca and P)] Endokrinologie 32:45-57. (Translation supplied with Informatics, Inc 1975. Monograph on Lactic Acid Submitted under DHEW Contract No. FDA 72-104 Rockville, Maryland. 212 pp.)
- Ferrì, C , Bellini, C.; Carlomagno, A , Desideri, G., Santucci, A. 1996. Active kallikrein response to changes in sodium-chloride intake in essential hypertensive patients. J Am Soc Nephrol 7(3):443-453.
- Fox, J G , Dangler, C.A.; Taylor, N S., Kng, A ; Koh, T.J.; Wang, T.C 1999 High-salt diet induces gastric epithelial hyperplasia and parietal cell loss, and enhances *Helicobacter pylori* colonization in C56BL/6 mice. Cancer Res 59(19):4823-4828.
- Fuchs, F D., Wannmacher, C.M ; Wannmacher, L.; Guimaraes, F S , Rosito, G.A , Gastaldo, G , Hoeffel, C.P ; Wagner, E M. 1987. Effect of sodium intake on blood pressure, serum levels and renal excretion of sodium and potassium in normotensives with and without familial predisposition to hypertension Braz J Med Biol Res 20(1):25-34.
- Fürth, O ; Engel, P. 1930. Über die Assimilierbarkeit und Toxizität racemischer Milchsäure Biochem Z 228(4-6) 381-396
- Gerds, E.; Myking, O.L , Omvik, P. 1996. Factors influencing left ventricular mass in hypertensive type-1 diabetic patients Am J Hypertens 9(4, Suppl. 1):65A [Abstract No 141]
- Gotshall, R W.; Mickleborough, T D ; Cordain, L. 2000 Dietary salt restriction improves pulmonary function in exercise-induced asthma Med Sci Sports Exerc 32(11):1815-1819
- Gould, B. 2007 Per Capita Butter Consumption. Agricultural and Applied Economics, UW Madison http://future.aae.wisc.edu/data/annual_values/by_area/2205?tab=sales
- Greendale, G.A.; Barrett-Connor, E.; Edelstein, S., Ingles, S ; Haile, R. 1994. Dietary sodium and bone mineral density results of a 16 year follow-up. J Am Geriatr Soc 42(10) 1050-1055.
- Guillot, J P., Gonnet, J.F.; Clement, C ; Caillard, L.; Truhaut, R. 1982 Evaluation of the ocular-irritation potential of 56 compounds. Food Cosmet Toxicol 20(5) 573-582
- Honjo, S , Kono, S.; Yamaguchi, M 1994 Salt and geographic variation in stomach cancer mortality in Japan Cancer Causes Control 5(3) 285-286.
- Ikeda, M., Nakatsuka, H , Watanabe, T 1988 The absence of correlation between Na in diet duplicates and stomach cancer mortality in Japan Tohoku J Exp Med 155(3):285-294

- IOM. 2004a. Sodium and chloride *In*. Dietary Reference Intake for Water, Potassium, Sodium, Chloride, and Sulfate National Academy of Sciences, Food and Nutrition Board, Institute of Medicine (IOM), National Academy Press (NAP); Washington, DC, pp 269-423. Available from [http //books.nap.edu/catalog.php?record_id=10925](http://books.nap.edu/catalog.php?record_id=10925)
- IOM 2004b. Potassium *In* Dietary Reference Intake for Water, Potassium, Sodium, Chloride, and Sulfate. National Academy of Sciences, Food and Nutrition Board, Institute of Medicine (IOM), National Academy Press (NAP); Washington, DC, pp. 186-268. Available from: [http //books.nap.edu/catalog.php?record_id=10925](http://books.nap.edu/catalog.php?record_id=10925).
- Ishidate, M. (Jr), Sofuni, T ; Yoshikawa, K., Hayashi, M ; Nohmi, T.; Sawada, M.; Matsuoka, A. 1984 Primary mutagenicity screening of food additives currently used in Japan *Food Chem Toxicol* 22(8) 623-636
- Itoh, R., Suyama, Y 1996 Sodium excretion in relation to calcium and hydroxyproline excretion in a healthy Japanese population *Am J Clin Nutr* 63(5):735-740
- JECFA. 1974 Lactic acid and its ammonium, calcium, potassium and sodium salts. *In*. Toxicological Evaluation of Some Food Additives Including Anticaking Agents, Antimicrobials, Antioxidants, Emulsifiers and Thickening Agents 17th Meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA), June 25-July 4, 1973, Geneva, Switz Food and Agriculture Organization of the United Nations (FAO); Rome. FAO Nutrition Meetings Report Series, No. 53A / WHO Technical Report Series, No. 539 / WHO Food Additives Series, No. 5, pp. 461-465. Available from: [http //www.inchem.org/documents/jecfa/jecmono/v05je86.htm](http://www.inchem.org/documents/jecfa/jecmono/v05je86.htm)
- Johnson, A G.; Nguyen, T V ; Davis, D 2001. Blood pressure is linked to salt intake and modulated by the angiotensinogen gene in normotensive and hypertensive elderly subjects. *J Hypertens* 19(3) 1053-1060
- Jonek, J. 1961. Wpływ kwasu glutaminowego i innych substancji zakwaszających na obraz histochemiczny gruczołów dokrewnych królic (nadnercza). *Endokrynol Pol* 12: 279-289. (Translation supplied with Informatics, Inc 1975 Monograph on Lactic Acid Submitted under DHEW Contract No FDA 72-104. Rockville, Maryland. 212 pp.). *Cited In*: FASEB, 1978.
- Jones, G.; Beard, T ; Parameswaran, V.; Greenaway, T., von Witt, R. 1997. A population-based study of the relationship between salt intake, bone resorption and bone mass *Eur J Clin Nutr* 51(8) 561-565.
- Joossens, J.V , Hill, M L , Elliott, P , Stamler, R ; Stamler, J ; Lesaffre, E.; Dyer, A.; Nichols, R.; Kesteloot, H 1996. Dietary salt, nitrate and stomach cancer mortality in 24 countries *Int J Epidemiol* 25(3) 494-504
- Kagan, A., Popper, J S ; Rhoads, G.G.; Yano, K 1985 Dietary and other risk factors for stroke in Hawaiian Japanese men. *Stroke* 16(3):390-396.

- Kato, S , Tsukamoto, T., Mizoshita, T., Tanaka, H ; Kumagai, T , Ota, H , Katsuyama, T , Asaka, M ; Tatematsu, M. 2006 High salt diets dose-dependently promote gastric chemical carcinogenesis in *Helicobacter pylori*-infected Mongolian gerbils associated with a shift in mucin production from glandular to surface mucous cells. *Int J Cancer* 119(7):1558-1566
- Kirkendall, W.M.; Conner, E.W.; Abboud, F.; Rastogi, S.P.; Anderson, T.A.; Fry, M. 1976. The effect of dietary sodium chloride on blood pressure, body fluids, electrolytes, renal function, and serum lipids of normotensive man. *J Lab Clin Med* 87(3):418-434
- Kneller, R.W.; Guo, W.D.; Hsing, A.W.; Chen, J.S.; Blot, W.J.; Li, J.Y.; Forman, D.; Fraumeni, J.F. 1992. Risk factors for stomach cancer in sixty-five Chinese counties. *Cancer Epidemiol Biomarkers Prev* 1(2) 113-118
- Kupari, M.; Koskinen, P.; Virolainen, J. 1994 Correlates of left ventricular mass in a population sample aged 36 to 37 years focus on lifestyle and salt intake *Circulation* 89(3):1041-1050
- La Vecchia, C ; Negri, E.; Franceschi, S., Decarli, A 1997 Case-control study on influence of methionine, nitrate, and salt on gastric carcinogenesis in Northern Italy. *Nutr Cancer* 27(1) 65-68.
- Landaas, S. 1975. The formation of 2-hydroxybutyric acid in experimental animals. *Clin Chim Acta* 58(1):23-32.
- Langenfeld, M.R.; Schobel, H.; Veelken, R., Weihprecht, H.; Schmieder, R.E. 1998. Impact of dietary sodium intake on left ventricular diastolic filling in early essential hypertension. *Eur Heart J* 19(6) 951-958
- Larsen, C.N.; Nielsen, S.; Kaestel, P., Brockmann, E.; Bennedsen, M.; Christensen, H.R ; Eskesen, D.C.; Jacobsen, B.L.; Michaelsen, K.F. 2006. Dose-response study of probiotic bacteria *Bifidobacterium animalis* subsp *lactis* BB-12 and *Lactobacillus paracasei* subsp *paracasei* CRL-341 in healthy young adults. *Eur J Clin Nutr* 60(11):1284-1293.
- Lee, J.K., Park, B.J., Yoo, K.Y., Ahn, Y.O. 1995 Dietary factors and stomach cancer: A case-control study in Korea *Int J Epidemiol* 24(1):33-41.
- Lieberman, A L 1930. Studies on calcium. II. Urinary output of calcium in normal individuals after peroral administration of calcium lactate and calcium gluconate *J Pharmacol Exp Ther* 40(1):71-76
- Liebson, P.R.; Grandits, G ; Prineas, R., Dianzumba, S., Flack, J.M.; Cutler, J.A.; Grimm, R., Stamler, J 1993 Echocardiographic correlates of left ventricular structure among 844 mildly hypertensive men and women in the Treatment of Mild Hypertension Study (TOMHS) *Circulation* 87(2):476-486
- Litton Bionetics, Inc. 1976. Mutagenic Evaluation of Compound FDA 75-19, Calcium Lactate, USP. Prepared by Litton Bionetics, Inc ; Kensington, Maryland for U S. Food and Drug Administration (U S. FDA) under contract no. 223-74-2104 [36 pp]

- Luft, F.C., Rankin, L.I., Bloch, R., Weyman, A.E., Willis, L.R., Murray, R.H.; Grim, C.E.; Weinberger, M.H. 1979. Cardiovascular and humoral responses to extremes of sodium intake in normal black and white men. *Circulation* 60(3):697-706.
- Maarse, H.; Visscher, C.A. (Eds.). 1992. Volatile Compounds in Food: Qualitative and Quantitative Data Supplement 3 and Cumulative Index Willemsens, L.C.; Boelens, M.H. (Co-Eds.). TNO Biotechnology and Chemistry Institute, Zeist, The Netherlands. Vol 1-3, pp 44, 331 & 425
- MacGregor, G.A.; Markandu, N.D.; Sagnella, G.A.; Singer, D.R.J.; Cappuccio, F.P. 1989. Double-blind study of three sodium intakes and long-term effects of sodium restriction in essential hypertension. *Lancet* 334(8674):1244-1247
- Maekawa, A., Matsushima, Y., Onodera, H., Shibutani, M.; Yoshida, J.; Kodama, Y.; Kurokawa, Y.; Hayashi, Y. 1991. Long-term toxicity/carcinogenicity study of calcium lactate in F344 rats. *Food Chem Toxicol* 29(9):589-594.
- Martini, L.A.; Cuppari, L.; Colugnati, F.A.B.; Sigulem, D.M.; Szejnfeld, V.L.; Schor, N.; Heilberg, I.P. 2000. High sodium chloride intake is associated with low density in calcium in stone-forming patients. *Clin Nephrol* 54(2):85-93.
- Matkovic, V.; Ilich, J.Z.; Andon, M.B.; Hsieh, L.C.; Tzagournis, M.A.; Lager, B.J.; Goel, P.K. 1995. Urinary calcium, sodium and bone mass of young females. *Am J Clin Nutr* 62(2):417-425
- Medici, T.C.; Schmid, A.Z.; Hacki, M.; Vetter, W. 1993. Are asthmatics salt-sensitive? A preliminary controlled study. *Chest* 104(4):1138-1143
- Montes, G.; Cuello, C.; Correa, P.; Zarama, G.; Liuzza, G.; Zavala, D.; de Marin, E.; Haenszel, W. 1985. Sodium intake and gastric cancer. *J Cancer Res Clin Oncol* 109(1):42-45.
- Morita, T.; Takeda, K.; Okumura, K. 1990. Evaluation of clastogenicity of formic acid, acetic acid, and lactic acid on cultured mammalian cells. *Mutat Res* 240(3):195-202
- Nordin, B.E.C.; Need, A.G.; Morris, H.A.; Horowitz, M. 1993. The nature and significance of the relationship between urinary sodium and urinary calcium in women. *J Nutr* 123(9):1615-1622.
- NRC. 1980. Potassium. In: Recommended Dietary Allowances (9th Rev. Ed.). National Academy of Sciences (NAS); Washington, DC, p 174
- NRC. 1989. Potassium. In: Recommended Dietary Allowances (10th Ed.). Food and Nutrition Board, Commission on the Life Sciences, National Research Council. National Academy Press, Washington, DC, pp 255-257
- Nyman, M.; Asp, N.-G. 1982. Fermentation of dietary fibre components in the rat intestinal tract. *Br J Nutr* 47(3):357-366.
- Osol, A.; Pratt, R. (Eds.). 1973. Calcium lactate and lactic acid. In: The United States Dispensatory (27th Ed.). J.B. Lippincott Company; Philadelphia, pp. 216-217 & 658
Cited In. FASEB, 1978

000041

- Palli, D.; Russo, A, Decarli, A 2001 Dietary patterns, nutrient intake and gastric cancer in a high-risk area of Italy. *Cancer Causes Control* 12 163-172
- Pamrani, M.B ; Chen, X ; Haddy, F J ; Schooley, J.F ; Mo, Z 2000 Mechanism of antihypertensive effect of dietary potassium in experimental volume expanded hypertension in rats. *Clin Exp Hypertens* 22(6):555-569.
- PDRHM 2004 Glucosamine *In* PDR® for Herbal Medicines (3rd Ed). Medical Economics Company, Montvale, New Jersey, pp. 942-944.
- PDRNS. 2001. Potassium. *In* Physicians' Desk Reference for Nutritional Supplements (1st Ed) Medical Economics, Montvale, New Jersey, pp. 371.
- Perry, I.J , Beevers, D.G. 1992. Salt intake and stroke A possible direct effect. *J Hum Hypertens* 6(1):23-25.
- Pettersen, J.E , Landaas, S ; Eldjarn, L 1973. The occurrence of 2-hydroxybutyric acid in urine from patients with lactic acidosis *Clin Chim Acta* 48(2) 213-219.
- Rodríguez-Soriano, J 1995. Potassium homeostasis and its disturbances in children. *Pediatr Nephrol* 9(3) 364-374
- Roos, J.C.; Koomans, H.A.; Dorhout-Mees, E J ; Delawi, I M K 1985 Renal sodium handling in normal humans subjected to low, normal, and extremely high sodium supplies. *Am J Physiol* 249(6, Part 2) F941-F947
- Sacks, F.M.; Svetkey, L.P.; Vollmer, W.M ; Appel, L.J , Bray, G.A , Harsha, D., Obarzanek, E., Conlin, P.R ; Miller, E R ; Simons-Morton, D.G ; Karanja, N., Lin, P H. 2001. Effects of blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. *N Engl J Med* 344(1):3-10
- Sasaki, S.; Zhang, X , Kesteloot, H 1995. Dietary sodium, potassium, saturated fat, alcohol, and stroke mortality *Stroke* 26(5) 783-789
- Schmieder, R.E.; Messerli, F.H.; Ruddle, H.; Garavaglia, G G.; Grube, E , Nunez, B.D.; Schulte, W. 1988. Sodium intake modulates left ventricular hypertrophy in essential hypertension. *J Hypertens* 6(4):S148-S150.
- Schmieder, R E ; Grube, E., Impelmann, V ; Ruddle, H ; Schulte, W 1990 Determinanten für die myokardiale Hypertrophie bei der milden essentiellen Hypertonie: Der Einfluß von Kochsalz auf die linksventrikuläre Hypertrophie = Determinants of myocardial hypertrophy in mild essential hypertension. Impact of dietary salt intake on left-ventricular hypertrophy. *Z Kardiol* 79(8):557-564
- Schmieder, R E ; Langenfeld, M R ; Friedrich, A., Schobel, H.P.; Gatzka, C D , Weihprecht, H. 1996. Angiotensin II Related to sodium excretion modulates left ventricular structure in human essential hypertension. *Circulation* 94(6).1304-1309.
- Schwartz, J.; Weiss, S T 1990 Dietary factors and their relation to respiratory symptoms. *Am J Epidemiol* 132(1):67-76.

000042

- Sheng, H P. 2000. Sodium, Chloride, and Potassium. *In* Stipanuk, M.H. (Ed.). *Biochemical and Physiological Aspects of Human Nutrition*. W B Saunders Company; Philadelphia, pp 686-710
- Shima, N.; Miki, A.; Kamata, T.; Katagi, M ; Tsuchihashi, H. 2005 Urinary endogenous concentrations of GHB and its isomers in healthy humans and diabetics *Forensic Sci Int* 149(2&3):171-179.
- Shortt, C ; Madden, A ; Flynn, A., Morrissey, P.A 1988 Influence of dietary sodium intake on urinary calcium excretion in selected Irish individuals. *Eur J Clin Nutr* 42(7):595-603
- Stamler, J , Cirillo, M. 1997 Dietary salt and renal stone disease. *Lancet* 349(9050):506-507.
- Strauss, A.L.; Coe, F L., Deutsch, L., Parks, J.H 1982. Factors that predict relapse of calcium nephrolithiasis during treatment *Am J Med* 72(1).17-24.
- Stryer, L 1995 Fatty acid metabolism. *In*: *Biochemistry* (4th Ed). W H. Freeman and Company; New York, pp. 603-628.
- Sullivan, J.M , Ratts, T.E ; Taylor, J C.; Kraus, D H., Barton, B R , Patrick, D R., Reed, S W 1980 Hemodynamic effects of dietary sodium in man *Hypertension* 2(4):506-514
- Tobian, L ; Hanlon, S. 1990 High sodium chloride diets injure arteries and raise mortality without changing blood pressure. *Hypertension* 15(6, Part 2).900-903
- Tribe, R.M.; Barton, J.R.; Poston, L ; Burney, P.G J 1994. Dietary sodium intake, airway responsiveness, and cellular sodium transport *Am J Respir Crit Care Med* 149(6)·1426-1433
- Tsubono, Y , Takahashi, T.; Iwase, Y.; Itoi, Y., Akabane, M., Tsugane, S. 1997. Nutrient consumption and gastric cancer mortality in five regions of Japan *Nutr Cancer* 27(3):310-315.
- Tsugane, S., Akabane, M.; Inami, T , Matsushima, S ; Ishibashi, T., Ichinowatari, Y.; Miyajima, Y., Watanabe, S. 1991 Urinary salt excretion and stomach cancer mortality among four Japanese populations. *Cancer Causes Control* 2(3) 165-168
- U S FDA. 2003 Agency Response Letter GRAS Notice No. GRN 000128 [Skim milk or dextrose cultured with *Propionibacterium freudenreichii* subsp. *shermanii*]. U.S. Federal Drug Association (FDA), Center for Food Safety and Applied Nutrition (CFSAN), College Park, Maryland. Available from: <http://www.cfsan.fda.gov/~rdb/opa-g128.html>.

000043

- U S FDA 2007a Various Parts [102, 133, 172, 173, 175, 177, 182, 184, 186—Sections §102.22, §133.195, §172.320, §172.515, §172.610, §172.620, §172.665, §172.695, §173.5, §173.25, §175.105, §177.2910, §182.1073, §182.8159, §184.1005, §184.1061, §184.1081, §184.1095, §184.1141, §184.1143, §184.1205, §184.1212, §184.1311, §184.1316, §184.1322, §184.1372, §184.1631, §184.1639, §184.1643, §184.17.21, §184.1763, §184.1768, §184.1854, §184.1857, §184.1866, §184.1878, §184.1983, §186.1316; §186.1756] In U S Code of Federal Regulations (CFR). Title 21 Food and Drugs (U.S. Food and Drug Administration). U S Food and Drug Administration (U.S. FDA) U.S. Government Printing Office (GPO), Washington, DC Available from: <http://www.access.gpo.gov/cgi-bin/cfrassemble.cgi?title=200721>.
- U S FDA 2007b. Part 424—Preparation and Processing Operations. Sections §424.1-§424.23. In U.S. Code of Federal Regulations (CFR) Title 9 Animals and Animal Products (U.S. Food and Drug Administration) U.S. Food and Drug Administration (U.S. FDA). U.S. Government Printing Office (GPO), Washington, DC, pp. 636-662. Available from http://www.access.gpo.gov/nara/cfr/waisidx_07/9cfr424_07.html.
- USDA. 1992. Food Consumption, Prices and Expenditures, 1970-90 U.S. Department of Agriculture (USDA), Economic Research Service; Washington, DC. Statistical Bulletin, No. 840, pp. 29-30 & 63
- USDA 2006 What We Eat In America: National Health and Nutrition Examination Survey (NHANES) 2003-2004. U.S. Department of Agriculture (USDA), Riverdale, Maryland. Available from: <http://www.ars.usda.gov/Services/docs.htm?docid=13793#release>.
- USDA 2007 Safe and Suitable Ingredients Used in the Production of Meat & Poultry Products. United States Department of Agriculture (USDA), Food Safety and Inspection Service (FSIS); Washington, DC, FSIS Directive No 7120.1 [Amendment 12]. Available from: <http://www.fsis.usda.gov/OPPDE/rdad/FSISDirectives/7120.1Amend12.pdf>
- Xie, J.X.; Sasaki, S.; Joossens, J V ; Kesteloot, H 1992 The relationship between urinary cations obtained from the INTERSALT study and cerebrovascular mortality. *J Hum Hypertens* 6(1) 17-21
- Yamori, Y., Nara, Y., Misushima, S ; Sawamura, M., Horie, R. 1994 Nutritional factors for stroke and major cardiovascular diseases international epidemiological comparison of dietary prevention *Health Prev* 6(1) 22-27
- Yang, J., Zhang, H., Zhao, L , Zhou, B.; Wu, Y.; Zhang, X 1997 Protein, salt and stroke mortality. *Can J Cardiol* 13(Suppl. B).44B [Abstract No 0074].
- Zhou, M.S , Nishida, Y , Yoneyama, H., Chen, Q H ; Kosaka, H. 1999. Potassium supplementation increases sodium excretion and nitric oxide production in hypertensive Dahl rats *Clin Exp Hypertens* 21(8) 1397-1411
- Zhou, M.S.; Kosaka, H.; Yoneyama, H 2000. Potassium augments vascular relaxation mediated by nitric oxide in the carotid arteries of hypertensive Dahl rats. *Am J Hypertens* 13(6, Part 1).666-672.

00C044

Zoia, M.C ; Fanfulla, F ; Bruschi, C , Basso, O.; De Marco, R.; Casali, L.; Cerveri, I. 1995
Chronic respiratory symptoms, bronchial responsiveness and dietary sodium and
potassium: a population based study *Monaldi Arch Chest Dis* 50(2) 104-108

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Attachment 1

Curriculum Vitae of Expert Panel Members

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CURRICULUM VITAE

IAN CRAIG MUNRO

EDUCATION

ACCREDITATION

1999 Fellow of The Academy of Toxicological Sciences
1988 Fellow of Royal College of Pathologists, London, England

EMPLOYMENT HISTORY

COMMITTEE MEMBERSHIPS

2006-Present Chair, Faculty of Agriculture and Environmental Sciences Advisory Board, McGill University

2005-Present Member at Large, Executive Committee, Toxicology and Safety Evaluation Division, Institute of Food Technologists

2004 Chairman, Panel Member, The Tooth Whitening Products Task Force of COLIPA, The European Cosmetics Industry Association

2002-2006 Technical Advisory Committee, World Food Program (WFP), The Food Aid Organization of the United Nations

2001 Chairman, Safety Assessment of Foods Derived from Genetically Modified Microorganisms World Health Organization, Headquarters, Geneva, Switzerland – September 2001

2000-Present Member, Georgetown Dialogue Science Council, Georgetown University Center for Food and Nutrition Policy (CFNP)

2000-Present Consultant, FEMA Expert Panel

1999 Center for Food Safety and Applied Nutrition (CFSAN) Research Program Committee, Food and Drug Administration

1998-2001 Member, Minister's Advisory Board, Canadian Food Inspection Agency

1996-2002 Chairman, Institute of Medicine, Subcommittee on Upper Safe Reference Levels of Nutrients

1996 Member, Ad Hoc Expert Panel, Life Sciences Research Office, Federation of American Societies for Experimental Biology (FASEB)

1993-Present Member FAO/WHO Expert Committee on Food Additives

1989 Chairman, Expert Group to Develop a Threshold of Regulation for Indirect Food Additives

1989-1991 Member, Scientific Committee, International Food Biotechnology Council

1985-2000 Member, FEMA Expert Panel

1985 Member ILSI-NF, Nutrition and Safety Committee (FNCS)

1985 Member, NAS, Committee on Carcinogenicity of Cyclamates.

1984 Member, Committee on Food Chemicals Codex.

1983-1984 Member, Panel of Chemical Carcinogenesis Testing and Evaluation (National Toxicology Program)

1983 Member, The Nutrition Foundation Project on the Use of Mouse Hepatoma Data

1981-1983 Expert Committee on the Relevance of Mouse Liver as a Model for Assessing Carcinogenic Risk, The Nutrition Foundation, Inc

1981-1982 Expert Advisory Committee to The Nutrition Foundation, Inc., on the Assessment of the Safety of Lead and Lead Salts in Foods

1981 Chairman, International Committee on Hazards Associated with Dioxin in the Great Lakes.

1981 Chairman, WHO Ad Hoc Meeting on the Future of Joint Expert Committees in the Context of the International Program on Chemical Safety, Geneva

1980-1983 Chairman, Health Protection Branch/Food Industry Liaison Committee

1980-1983 Chairman, Interdepartmental Committee on Canning Regulations

1980 Member, Federal Interdepartmental Salmonella Committee

1980 Member, Senior Level Committee (U S , U K , Canada).

1980 Member, International Life Sciences Institute Experts in Pathology and Toxicology

1980 Member, Technical Committee WHO International Program on Chemical Safety

1978-1980 Expert Committee on Food Safety - Agriculture Canada

1978-1980 Food Safety Council, Social and Economic Committee

1978-1979 U S National Academy of Sciences, Subcommittee on Risk Assessment - Safe Drinking Water Committee.

1978 Chairman, Tripartite Toxicology Committee (U S , U K , Canada)

1977-1981 International Commission for Protection Against Environmental Mutagens and Carcinogens (ICPEMC), subcommittee 3

1977-1979 U S National Cancer Institute, Cause and Prevention Scientific Review Committee

1976-1984 WHO/FAO Joint Expert Committee on Food Additives

1976-1980 Food Safety Council, Toxicology Committee.
1976-1979 Canadian Council on Animal Care
1976-1979 Interdepartmental Committee on Toxicology Needs in Canada
1976-1978 National Research Council Task Force on Mercury and Captan
1975-1976 U.S National Academy of Sciences Committee on Toxicology
1975-1976 WHO/FAO Committee on Criterion Documents on the Toxicology of Environmental Chemicals

EDITORIAL RESPONSIBILITIES

1982-1996 Editorial Board *Journal of the American College of Toxicology*
1979-1991 Advisory Board *Neurotoxicology*
1978-1989 Editorial Board *Journal of Environmental Pathology and Toxicology*

PROFESSIONAL AFFILIATIONS

Professional Society Memberships:

Member, Society of Toxicology
 Member, Toxicology Forum
 Member, Society of Toxicology of Canada
 Member, American College of Toxicology
 Member, Institute for Risk Research
 Member, International Society of Regulatory Toxicology and Pharmacology
 Member, Institute of Food Technologists

Contributions to Professional Societies:

2004-2007 The Academy of Toxicological Sciences, Board of Directors
1981 Professional Standards Evaluation Board in General Toxicology, Academy of Toxicological Sciences
1978-1979 Society of Toxicology, Nominating Committee
1978-1979 Society of Toxicology, Finance Committee
1976-2006 Toxicology Forum, Inc., Board of Directors

AWARDS

2006 Joint FAO/ WHO Committee on Food Additives (JECFA) – on the 50th Anniversary of the Committee for his long service as an Expert Advisor to the Secretariat
2005 Institute of Food Technologists "Bernard L. Oser Food Ingredient Safety Award" for his contributions to the scientific knowledge of food ingredient safety or leadership in establishing principles for food ingredient safety evaluation or regulation.
1998 International Society of Regulatory Toxicology and Pharmacology "International Achievement Award" for his guiding role as Chairman of the Expert Panel of Members – "Interpretive Review of the Effects of Chlorinated Organic Chemicals".
1975 Society of Toxicology "Achievement Award" for outstanding contributions to the science of toxicology by an individual 35 years of age or younger.

SCIENTIFIC PUBLICATIONS AND MONOGRAPHS

Munro, I.C., Taylor, S.L., Veldkamp, P., and van Dissel, J.T. 2007. The Safety of Whey Protein Concentrate Derived from the Milk of Cows Immunized Against *Clostridium difficile*. Accepted for publication in Reg Toxicol Pharmacol.

Young, K.W.H., Danielewska-Nikiel, B., and Munro, I.C. 2006. An Evaluation of the Maximized Survey-Derived Intake (MSDI) as a Practical Method to Estimate Intake of Flavouring Substances. Food Chem Toxicol 44(2006):1849-1867

Munro, I.C., and Renwick, A.G. 2006. The Fifth Workshop on the Assessment of Adequate Intake of Dietary Amino Acids General Discussion. J Nutr 136(6 Suppl) 1755S-1757S.

Munro, I.C., Williams, G.M., Heymann, H.O., and Kroes, R. 2006. Use of Hydrogen Peroxide-Based Tooth Whitening Products and its Relationship to Oral Cancer J Esthet Restor Dent 18:119-125.

Munro, I.C. 2006. Setting Tolerable Upper Intake Levels for Nutrients. J Nutr 136(2) 490S-492S.

Munro, I.C., and Danielewska-Nikiel, B. 2006. Comparison of Estimated Daily Intakes of Flavouring Substances with No-Observed-Adverse-Effect Levels. Food Chem Toxicol 44(2006):758-809

Munro, I.C., Williams, G.M., Heymann, H.O., and Kroes, R. 2006. Tooth Whitening Products and the Risk of Oral Cancer. Food Chem Toxicol 44 301-315

Dwyer, J., Berner, L.A., and Munro, I.C. (Eds.) 2006. Understanding Tolerable Upper Intake Levels American Society for Nutrition; Bethesda, Maryland, Journal of Nutrition, Vol 136, No. 6, Suppl., pp 487S-521S

Munro, I.C., Newberne, P.M., Young, V.R., and Bär, A. 2004. Safety Assessment of γ -Cyclodextrin. Reg Toxicol Pharmacol 39:S3-S13.

Adams, T.B., Cohen, S.M., Doull, J., Feron, V.J., Goodman, J.I., Marnett, L.J., Munro, I.C., Portoghese, P.S., Smith, R.L., Waddell, W.J., and Wagner, B.M. 2004. The FEMA GRAS Assessment of Cinnamyl Derivatives Used as Flavor Ingredients. Food Chem Toxicol 42:157-185

Feron, V.J., Adams, T.B., Doull, J., Goodman, J.I., Hall, R.L., Marnett, L.J., Munro, I.C., Portoghese, P.S., Smith, R.L., Waddell, W.J., and Wagner, B.M. 2004. Safety Evaluation of Natural Flavour Complexes Toxicol Lett 144(Suppl. 1) S16

Munro, I.C. et al. 2003. Guidance for the Safety Assessment of Botanicals and Botanical Preparations for Use in Food Supplements. Expert Group Report reviewed at a Workshop held in May 2002, Marseille, France. Organized by the International Life Science Institute (ILSI) Europe Natural Toxin Task Force. Food Chem Toxicol 41:1625-1649

Hlywka, J.J., Reid, J.E., and Munro, I.C. 2003. Review: The Use of Consumption Data to Assess Exposure to Biotechnology-Derived Foods and the Feasibility of Identifying Effects on Human Health Through Post-Marketing Monitoring. Food Chem Toxicol 41 1273-1282

Munro, I.C., Haighton, L.A., Lynch, B.S., Hlywka, J.J., Doull, J., and Kroes, R. 2003. Letter to the Editor – Response to "Does Exposure to Bisphenol A Represent a Human Health Risk?" Reg Toxicol Pharmacol 37:409-410

Munro, I.C., Harwood, M., Hlywka, J.J., Stephen, A.M., Doull, J., Flamm, W.G., and Adlercreutz, H. 2003. Soy Isoflavones: A Safety Review. Nutr Rev 61(1) 1-33

Munro, I.C., Haighton, L.A., Hlywka, J.J., Lynch, B.S., Doull, J., and Kroes, R. 2002. Reply to Letter to the Editor – Carcinogenicity Bioassay of Bisphenol A *Toxicol Sci* 70, pp. 283-284

Munro, I.C. 2002. The Precautionary Principle and the Scientific Risk Assessment Process Submitted to Regul Toxicol Pharmacol July 31, 2002

Munro, I.C. et al. 2002. Exposure From Food Contact Materials Summary Report of a Workshop Held in October 2001 in Ispra, Italy. ILSI Europe Packaging Material Task Force in Collaboration with the European Commission's Joint Research Centre (JRC). International Life Science Institute (ILSI) Press; Washington, DC

Butchko, H.H., Stargel, W.W., Comer, C.P., Mayhew, D.A., Benninger, C., Blackburn, G.L., de Sonneville, L.M.J. Geha, R.S., Hertelendy, Z., Koestner, A., Leon, A.S., Liepa, G.U., McMartin, K.E., Mendenhall, C.L., Munro, I.C., Novotny, E.J., Renwick, A.G., Schiffman, S.S., Schomer, D.L., Shaywitz, B.A., Splers, P.A., Tephly, T.R., Thomas, J.A., and Trefz, F.K. 2002. Aspartame Review of Safety. *Reg Toxicol Pharmacol* 35(No 2) Part 2 of 2

Adams, T.B., Doull, J., Feron, V.J., Goodman, J.I., Marnett, L.J., Munro, I.C., Newberne, P.M., Portoghese, P.S., Smith, R.L., Waddell, W.J., and Wagner, B.M. 2002. The FEMA GRAS Assessment of Pyrazine Derivatives Used as Flavor Ingredients. *Food Chem Toxicol* 40 429-451

Munro, I.C., Hlywka, J.J., and Kennepohl, E.M. 2002. Risk Assessment of Packaging Materials. *Food Addit Contam* 19(Suppl 3-12) 3-12

Munro, I.C., Haighton, L.A., Hlywka, J.J., Lynch, B.S., Doull, J., and Kroes, R. 2002. Letter to the Editor – Carcinogenicity Bioassay of Bisphenol A *Toxicol Sci* 66(2) p 356

Stephen, A.M., Liston, A.J., Anthony, S.P., Munro, I.C., and Anderson, G.H. 2002. Regulation of Foods with Health Claims. A Proposal *Can J Public Health* 93(5) 328-331

Haighton, L.A., Hlywka, J.J., Doull, J., Kroes, R., Lynch, B.S., and Munro, I.C. 2002. An Evaluation of the Possible Carcinogenicity of Bisphenol A to Humans *Reg Toxicol Pharmacol* 35(2, Part 1) pp. 238-254

Kennepohl, E., and Munro, I.C. 2001. Phenoxy Herbicides (2,4-D) Volume 2 Handbook of Pesticide Toxicology Academic Press, pp. 1623-1638

Chassy, B.M., Abramson, S.H., Bridges, A., Dyer, W.E., Faust, M.A., Harlander, S.K., Hefle, S.L., Munro, I.C., Rice, M.E. 2001. Evaluation of the U.S. Regulatory Process for Crops Developed Through Biotechnology *CAST* 19 September

Chassy, B., and Munro, I.C. 2001. Evolution d'un Principe Fondateur. *La Recherche* (February) 339 70-72

Munro, I.C., and Kennepohl, E. 2001. Comparison of Estimated Daily *Per Capita* Intakes of Flavouring Substances with No-Observed-Effect Levels from Animal Studies *Food Chem Toxicol* 39(4) 47-70

Hoover, D., Chassy, B.M., Hall, R.L., Klee, H.J., Luchansky, J.B., Miller, H. I., Munro, I.C., Weiss, R., Hefle, S.L., and Quaiset, C.O. 2000. Human Food Safety Evaluation of rDNA Biotechnology-Derived Foods Institute of Food Technologists Expert Report on Biotechnology and Foods Reprinted from *Food Technol* 54(9) September

Kroes, R., Galli, C., Munro, I., Schilter, B., Tran, L.-A., Walker, R., and Würtzen. 2000. Threshold of Toxicological Concern for Chemical Substances Present in the Diet A Practical Tool for Assessing the Need for Toxicity Testing Reprinted from *Food Technol* 38(2-3) 255-312.

Munro, I.C. et al. 2000. Safety Aspects of Genetically Modified Foods of Plant Origin Report of a Joint FAO/WHO Expert Consultation on Foods Derived from Biotechnology. WHO Headquarters, Geneva, Switzerland, May 29-June 2, 2000.

Wilson, R.M., Sigal, E.A., Bacigalupo, C.M., Willes, R.F., and Munro, I.C. 2000. Derivation of Risk Management Criteria for Chemicals of Unknown Toxic Potency at Contaminated Sites. *Hum Ecol Risk Assessment* 6(1):131-139

Newberne, P., Smith, R.L., Doull, J., Feron, V.J., Goodman, J.I., Munro, I.C., Portoghese, P.S., Waddell, W.J., Wagner, B.M., Weil, C.S., Adams, T.B., and Hallagan, J.B. 2000. GRAS Flavoring Substances 19 *Food Technol* 54(6) 66-84

Williams, G.M., Kroes, R., and Munro, I.C. 2000. Safety Evaluation and Risk Assessment of the Herbicide Roundup and Its Active Ingredient, Glyphosate, for Humans. *Regul Toxicol Pharmacol* 31:117-165

Davies, T.S., Lynch, B.S., Monro, A.M., Munro, I.C., and Nestmann, E.R. 2000. Rodent Carcinogenicity Tests Need to Be No Longer Than 18 Months: An Analysis Based on 210 Chemicals in the IARC Monographs. *Food Chem Toxicol* 38(2-3) 219-235.

Newberne, P., Smith, R.L., Doull, J., Goodman, J.I., Munro, I.C., Portoghese, P.S., Wagner, B.M., Weil, C.S., Woods, L.A., Adams, T.B., Lucas, C.D., and Ford, R.A. 1999. The FEMA GRAS Assessment of *trans*-Anethole Used as a Flavouring Substance. *Food Chem Toxicol* 37 789-811

Munro, I.C., Delzell, E.S., Nestmann, E.R., and Lynch, B.S. 1999. Viadent Usage and Oral Leukoplakia: A Spurious Association *Regul Toxicol Pharmacol* 30 182-196.

Institute of Medicine*. 1999. Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. National Academy Press, Washington, D C *(Dr. Ian Munro, Chair, Subcommittee on Upper Reference Levels of Nutrients)

Bechtel, D.H. (Introduction by Munro, I.C.) 1999. Carcinogenicity Assessment of Allyl Isothiocyanate with Regard to IARC Classification Criteria (Abstract) *Intl J Toxicol* 18(1) 84

Munro, I.C., Kennepohl, E., and Kroes, R. 1999. A Procedure for the Safety Evaluation of Flavouring Substances *Food Chem Toxicol* 37(2/3) 207-232

Munro, I.C., Bernt, W.O., Borzelleca, J.F., Flamm, G., Lynch, B.S., Kennepohl, E., Bär, E.A., and Modderman, J. 1998. Erythritol. An Interpretive Summary of Biochemical, Metabolic, Toxicological and Clinical Data *Food Chem Toxicol* 36:1139-1174

Newberne, P., Smith, R.L., Doull, J., Goodman, J.I., Munro, I.C., Portoghese, P.S., Wagner, B.M., Weil, C.S., Woods, L.A., Adams, T.B., Hallagan, J.B., and Ford, R.A. 1998. GRAS Flavoring Substances 18 *Food Technol* 52(9):65-92

Munro, I.C., Shubik, P., and Hall, R. 1998. Principles for the Safety Evaluation of Flavoring Substances *Food Chem Toxicol* 36(1998) 529-540.

Adams, T.B., Greer, D.B., Doull, J., Munro, I.C., Newberne, P., Portoghese, P.S., Smith, R.L., Wagner, B.M., Weil, C.S., Woods, L.A., and Ford, R.A. 1998. The FEMA GRAS Assessment of Lactones Used as Flavour Ingredients *Food Chem Toxicol* 36(4):249-278

Lynch, B.L., Bryant, D.W., Hook, H.J., Nestmann, E.R., and Munro, I.C. 1998. Carcinogenicity of Monochloro-1,2-Propanediol (α -Chlorohydrin, 3, MCPD) *Int J Toxicol* 17(1):47-76.

Munro, I.C., and Kennepohl, E. 1997. A Procedure for the Safety Evaluation of Flavoring Substances. In: Colombo, E (Ed.), *Proceedings from the International Symposium on Flavours and Sensory Related Aspects - March 6 & 7, 1997, Cernobbio (Como), Italy.* Rivista Italiana EPPOS, pp 81-85

Adams, T.B., Doull, J., Goodman, J.I., Munro, I.C., Newberne, P., Portoghese, P.S., Smith, R.L., Wagner, B.M., Weil, C.S., Woods, L.A., and Ford, R.A. 1997. The FEMA GRAS Assessment of Furfural Used as a Flavour Ingredient *Food Chem Toxicol* 35(8):739-751

Miller, S.A., and Munro, I.C. 1997. Upper Safe Reference Levels for Nutrients. *Proceedings of the 16th International Congress of Nutrition, Montreal, Quebec, July 28-August 31, 1997*

Munro, I.C. and Kroes, R. 1997. Application of a Threshold Of Regulation Concept in the Safety Evaluation of Certain Flavoring Substances. Prepared for the Forty-ninth Joint FAO/WHO Expert Committee on Food Additives.

Adams, T.B., Hallagan, J.B., Putman, J.M., Gierke, T.L., Doull, J., Munro, I.C., Newberne, P., Portoghese, P.S., Smith, R.L., Wagner, B.M., Weil, C.S., Woods, L.A., and Ford, R.A. 1996. The FEMA GRAS Assessment of Alicyclic Substances Used as Flavour Ingredients *Food Chem Toxicol* 34(9):763-828.

Bernt, W.O., Borzelleca, J.F., Flamm, G., and Munro, I.C. 1996. Erythritol A Review of Biological and Toxicological Studies. *Regul Toxicol Pharmacol* 24(2)Part 2:S191-S197.

Lynch, B.S., Tischler, A.S., Capen, C., Munro, I.C., McGirr, L.G., McClain, R.M. 1996. Low Digestible Carbohydrates (Polyols and Lactose): Significance of Adrenal Medullary Proliferative Lesions in the Rat. *Regul Toxicol Pharmacol* 23:256-297

Munro, I.C., Ford, R.A., Kennepohl, E., and Sprenger, J.G. 1996. Correlation of Structural Class With No-Observed Effect Levels: A Proposal for Establishing a Threshold of Concern. *Food Chem Toxicol* 34(9) 829-867

Munro, I.C., McGirr, L.G., Nestmann, E.R., and Killie, J.W. 1996. Alternative Approaches to the Safety Assessment of Macronutrient Substitutes *Regul Toxicol Pharmacol* 23(1)Part 2 S6-S14.

Munro, I.C. 1996. A Procedure For the Safety Evaluation of Flavoring Substances. Toxicological Evaluation of Certain Food Additives and Contaminants. Prepared for the Joint FAO/WHO Expert Committee on Food Additives, WHO Technical Report Series #35, Annex 5

Munro, I.C., Ford, R.A., Kennepohl, E., and Sprenger, J.G. 1996. Thresholds of Toxicological Concern Based on Structure-Activity Relationships *Drug Metab Rev* 28(1&2):209-217.

Kraus, A.L., Munro, I.C., Orr, J.C., Binder, R.L., LeBeouf, R.A., and Williams, G.M. 1995. Benzoyl Peroxide An Integrated Human Safety Assessment for Carcinogenicity *Regul Toxicol Pharmacol* 21:87-107

Munro, I.C., Lynch, B.S., Kittur, A., and Nestmann, E.R. 1995. Modulators of Carcinogenesis *Regul Toxicol Pharmacol* 21 60-70.

Kroes, R., Munro, I., and Poulsen, E. 1993. Workshop on the Scientific Evaluation of the Safety Factor for the Acceptable Daily Intake (ADI) Editorial Summary *Food Addit Contam* 10(3):269-273.

Wiles, R.F., Nestmann, E.R., Miller, P.A., Orr, J.C., and Munro, I.C. 1993 Scientific Principles for Evaluating the Potential for Adverse Effects from Chlorinated Organic Chemicals in the Environment *Regul Toxicol Pharmacol* 18:313-356

Munro, I.C., Kennepohl, E., Erickson, R.E., Portoghese, P.S., Wagner, B.M., Easterday, O.D., and Manley, C.H. 1993 Safety Assessment of Ingested Heterocyclic Amines: Initial Report. *Regul Toxicol Pharmacol* 17(2) S1-S109

Munro, I.C., Carlo, G.L., Orr, J.C., Sund, K.G., Wilson, R.M., Kennepohl, E., Lynch, B.S., Jablinske, M., and Lee, N.L. 1992. A Comprehensive, Integrated Review and Evaluation of the Scientific Evidence Relating to the Safety of the Herbicide 2,4-D *J Amer Coll Toxicol* 11(5)

Munro, I.C. 1992 Ecological Risk Estimation *In* Bartell, S, Gardner, R, and O'Neill, R. (Eds.) *Toxicology and Environmental Health Series*. Editorial Board. Lewis Publishers, Chelsea, Maine

Carlo, G.L., Cole, P., Miller, A.B., Munro, I.C., Solomon, K.R., and Squire, R.A. 1992. Review of a Study Reporting an Association Between 2,4-Dichlorophenoxyacetic Acid and Canine Malignant Lymphoma Report of an Expert Panel. *Regul Toxicol Pharmacol* 16:245-252.

Nestmann, E.R., Munro, I.C., Willes, R.F., and Orr, J. 1992. Risk Assessment. An Overview. *In* *Canadian Environmental Directory* Second Edition. Canadian Almanac and Directory Publishing Company Ltd pp 13-16

Munro, I.C., Pariza, M.W., and Stewart, K.K. 1991. Scientific Information and Methodologies for Assessing the Safety of Genetically Engineered Foods and Feeds Prepared for the assessment "A New Technological Era for American Agriculture Issues and Choices for the 1990s", Office of Technology Assessment, U S Congress

Burdock, G.A., Wagner, B.M., Smith, R.L., Munro, I.C., and Newberne, P.M. 1990. 15 GRAS Substances: A List of Flavoring Ingredient Substances Considered Generally Recognized as Safe by the Flavor & Extract Manufacturers' Association Expert Panel Recent Progress in the Consideration of Flavoring Ingredients Under the Food Additives Amendment Reprinted from *Food Technology* 44 (2) 78, 80, 82, 84, & 86

Munro, I.C. 1990 Safety Assessment Procedures for Indirect Food Additives: An Overview. *Regul Toxicol Pharmacol* 12(1) 2-13.

Munro, I.C., et al. 1990. Biotechnologies and food. Assuring the safety of foods produced by genetic modification. *International Food Biotechnology Council*. Washington, D C *Regul Toxicol Pharmacol* 12(3)Part 2:S1-S190.

Munro, I.C. 1990 Natural Versus Man-made *In* *Pest Control Canada, A Reference Manual*. Burlington, Ontario, PACS.

Clayson, D.B., Munro, I.C., Shubik, P., and Swenberg, J.A. (Eds) 1990 Progress in Predictive Toxicology Elsevier Science Publishers

Zimmerman, R. Borzelleca, J., Crump, K., Doull, J., Gardner, D., Gardner, H., Hughes, D., Munro, I.C., Parke, D.M., Rodericks, J., Tardiff, R.G., and Travis, C. (Eds) 1990 Governmental Management of Chemical Risk. Lewis Publishers, Inc

Munro, I.C. 1990 Sweeteners: Health Effects-Neoplasm Promotion *In*: Williams, G M. (Ed) *Sweeteners Health Effects*

Munro, I.C. 1988 General Principles of Regulation of Nutrients *In* Middlekauf, R, and Shubik, P. (Eds) *Food Regulations: An International Handbook*

Munro, I.C. 1988 Risk Assessment of Carcinogens Current Status and Future Prospects *Biomedical and Environmental Sciences*

- Munro, I.C., Morrison, A.B. 1988.** Pesticides Nut Pharm Toxicol pp 187-196
- Munro, I.C. 1988** Qualitative Factors in Carcinogen Classification. *In*: Carcinogen Risk Assessment New Directions in the Qualitative and Quantitative Aspects. Cold Spring Harbor Laboratory, Banbury Report 31.
- Munro, I.C. 1987.** Expert Panel Report on Carcinogenicity of 2,4-D. Canadian Centre for Toxicology, Guelph, Ontario, Canada
- Munro, I.C. 1987.** International Perspectives on Animal Selection and Extrapolation *In* Roloff, M.V. (Ed.) Human Risk Assessment - The Role of Animal Section and Extrapolation
- Munro, I.C. 1986** The ingredients of foods How they are tested and why they are selected J Allerg Clin Immunol 78(1) 133-139
- Munro, I.C. 1986.** Overview of Recent Problems in Chemical Carcinogenesis *In*: Chambers, P.L., Gehring, P., and Sakai, F. (Eds.) New Concepts and Developments in Toxicology Elsevier Science Publishers, Amsterdam
- Clayson, D., Krewski, D., and Munro, I.C. (Eds.) 1985.** Toxicological Risk Assessment. Volume I CRC Press, Boca Raton, Florida
- Clayson, D., Krewski, D., and Munro, I.C. (Eds.) 1985** Toxicological Risk Assessment. Volume II CRC Press, Boca Raton, Florida
- Arnold, D.L., Moodie, C.A., Charbonneau, S.M., Grice, H.C., McGuire, P.F., Bryce, F.R., Collins, B.T., Zawadzka, Z.Z., Krewski, D.R., Nera, E.A., and Munro, I.C. 1985** Long-term toxicity of hexachlorobenzene in the rat and the effect of dietary Vitamin A Food and Chem Toxicol, 9:779-793
- Munro, I.C., Goldberg, L., and Farber, E. 1985.** Formaldehyde Risk Assessment Report to Ontario Ministry of Labour
- Tryphonas, H., and Munro, I.C. 1984.** Risk-Benefit Assessment in Immunotoxicology. *In*: Mullen, P.W. (Ed) NATO ASI Series, Vol G2 Immunotoxicology
- Clayson, D., Krewski, D., and Munro, I.C. 1984** The power and interpretation of the carcinogenicity bioassay Regul Toxicol Pharmacol 3 329-348
- Munro, I.C. 1984.** Risk Assessment and Environmental Regulation. Prepared for the ILSI Symposium on Safety Assessment, Tokyo.
- Munro, I.C. 1984.** Report to the Royal Commission to Inquire into the Use and Effects of Chemical Agents on Australian Personnel in Vietnam.
- Arnold, D.L., Krewski, D.R., and Munro, I.C. 1983** Saccharin A toxicologically and historically interesting sweetener. Toxicology 27 179-256.
- Munro, I.C., Miller, C.T., Krewski, D. 1983.** Regulatory control of environmental chemicals. A Canadian viewpoint. J Amer Coll Toxicol 2(1)
- Miller, C.T., Krewski, D., and Munro, I.C. 1983.** Conventional Approaches to Safety Evaluation. *In* Homburger, F. (Ed), Proceedings of First International Conference on Safety Evaluation and Regulation of Chemicals Publisher Krager, S., Basel
- Arnold, D.L., Krewski, D.R., Junkins, D.B., McGuire, P.F., Moodie, C.A., and Munro, I.C. 1983** Reversibility of ethylenethiourea-induced thyroid lesions Toxicol Appl Pharmacol 67 264-273.

- Arnold, D.L., Bickis, M.G., Nera, E.A., McGuire, P.F., and Munro, I.C. 1982** Assessing the reversibility of thyroid lesions that result from feeding ETU. (Abstract) *The Toxicologist*, 2(1).
- Miller, C.T., Krewski, D., and Munro, I.C. 1982.** Conventional Approaches to Safety Evaluation. Proceedings of the International Conference on Safety Evaluation and Regulation of Chemicals, February 24-26, Boston, Mass , sponsored by the American College of Toxicology
- Munro, I.C., and Krewski, D. 1982.** Regulatory Consideration in Risk Management *In*: Stich, H. (Ed.) Carcinogens and Mutagens in the Environment. Volume II Naturally Occurring Compounds CRC Press, Boca Raton, Florida.
- Krewski, D., Clayson, D., Collins, B., and Munro, I.C. 1982.** Toxicological Procedures for Assessing the Carcinogenic Potential of Agricultural Chemicals. *In*: Fleck, R (Ed) Genetic Toxicology: An Agricultural Perspective. Plenum Publishing, New York, New York
- Munro, I.C., and Krewski. 1981.** The Role of Risk Assessment in Regulatory Decision Making. *In* Walsh, P J , Richmond, C R , and Copenhaver, E D (Eds.) Health Risk Analysis Franklin Institute Press, Philadelphia.
- Munro, I.C., and Krewski, D.R. 1981** Risk assessment and regulatory decision making *Food and Cosmetics Toxicology*, 19 5:549-560
- Grice, H.C., Munro, I.C., Krewski, D.R., and Blumenthal, H. 1981.** *In utero* exposure in chronic toxicity/carcinogenicity studies *Food and Cosmetics Toxicology*, 19 373-379.
- Munro, I.C. 1980.** Environmental Contaminants. *In*: Santes, W , Lopres, N , Barbosa, J.J , and Chaves, D (Eds) Nutrition and Food Science Volume 2 Plenum Publishing Corporation.
- Arnold, D.L., Moodie, C.A., Grice, H.C., Charbonneau, S.M., Stavric, B., Collins, B.T., McGuire, P.F., Zawadzka, Z.Z., and Munro, I.C. 1980.** Long-term toxicity of ortho-toluenesulfonamide and sodium saccharin in the rat. *Toxicol Appl Pharmacol* 52:113-153
- Arnold, D.L., Moodie, C.A., Grice, H.C., Charbonneau, S.M., Stavric, B., Collins, B.T., McGuire, P.F., Zawadzka, Z.Z., and Munro, I.C. 1980** Long term toxicity of ortho-toluenesulphonamide and sodium saccharin in the rat. *Tox Appl Pharmacol* 52 113-152
- Munro, I.C., Nera, E.A., Charbonneau, S.M., Junkins, B., and Zawizka, Z. 1980** Chronic toxicity of methylmercury in the rat *J Environ Pathol Toxicol* 3 437-447.
- Munro, I.C. 1979** Assessment of Food Safety Testing. *Food Technology*, November, pp 43-60.
- Arnold, D.L., Munro, I.C., and Grice, H.C. 1979** A look at saccharin *IRPTC*, 2(1) January
- Arnold, D.L., Moodie, C.A., McGuire, P.F., Collins, B.T., Charbonneau, S.M., and Munro, I.C. 1979** The effect of orthotoluenesulphonamide and sodium saccharin on the urinary tract of neonatal rats *Toxicol Appl Pharmacol* 51 455-463.
- Khera, K.S., and Munro, I.C. 1979.** A review of the specifications and toxicity of synthetic food colors permitted in Canada *Cnt Rev Toxicol* 6(2).
- Stoltz, D.R., Bendall, R., Stavric, B., and Munro, I.C. 1978** Selection of species for cancer bioassay of naphthylamine-containing food colours on the basis of tissue-mediated mutagenicity (Abstract) *Mutat Res* 53(2) 267-268.

- Munro, I.C. 1978.** Proposed system for food safety assessment Scientific Committee, Food Safety Council Food Cosmet Toxicol 16(2).
- Munro, I.C. 1978** Introductory Remarks Proceedings of the First International Congress on Toxicology Academic Press, Inc., pp 165-167.
- Munro, I.C. WHO Working Group. 1978** Nitrates, Nitrites and N-nitroso Compounds Environmental Health Criteria 5.
- Munro, I.C., Charbonneau, S.M., and Zawidzka, Z.Z. 1978** Acute, Subacute and Chronic Toxicity Tests. Environmental Health Criteria 5
- Munro, I.C., and Arnold, D.L. 1978.** Chronic Bioassay Review International Symposium on Health and Sugar Substitutes Karger, S pp 76-81, Editor Guggenheim.
- Munro, I.C., and Willes, R.F. 1978** Reproductive Toxicity and the Problems of *In Utero* Exposure. In: Galli, G.L., Paoletti, R., and Vettorazzi, G. (Eds) International Symposium on Chemical Toxicology of Food. Elsevier/North-Holland, pp 133-145
- Munro, I.C., and Charbonneau, S.M. 1978** Environmental contaminants Federation Proceedings, 37:2582-2586
- Phillips, W.E., Mills, J.H.L., Charbonneau, S.M., Tryphonas, L., Hatina, G.V., Zawidzka, Z.Z., Bryce, F.R., and Munro, I.C. 1978** Sub-acute toxicity of pyridoxine hydrochlorine in the beagle dog Toxicol Appl Pharmacol 44:323-333
- Munro, I.C., Charbonneau, S.M., and Zawidzka, Z.Z. 1978.** Acute, Subacute and Chronic Toxicity Tests World Health Organization Environmental Health Criteria 6, pp 95-115
- Munro, I.C., and Willes, R.F. 1978.** Reproductive Toxicity and the Problems of *In Utero* Exposure. In: Galli, C.L., Paoletti, R., and Vettorazzi, G. (Eds) International Symposium on Chemical Toxicology of Food Elsevier/North-Holland, pp 133-145.
- Munro, I.C. 1977** Considerations in chronic toxicity testing: The dose, the design J Environ Pathol Toxicol 1:183-197
- Kulper-Goodman, T., Grant, D.L., Moodie, C.A., Korsrud, G.O., and Munro, I.C. 1977** Sub-acute toxicity of hexachlorobenzene in the rat. Tox Appl Pharmacol 40 529-549
- Munro, I.C. 1976.** Naturally occurring toxicants in foods and their significance Clinical Toxicology, 9(5) 647-663.
- Charbonneau, S.M., Munro, I.C., Nera, E.A., Armstrong, F.A.J., Willes, R.F., Bryce, F., and Nelson, F.R. 1976** Chronic toxicity of methylmercury in the adult cat Toxicology, 5:337-349.
- Munro, I.C. 1976.** Chronic Toxicity Testing Methods Contribution to Publication No. 1138, NAS, Washington.
- Munro, I.C. 1975.** Frequently Used Toxicity Tests Prepared for the World Health Organization Monograph entitled Principles and methods for Evaluating the Toxicity of Chemicals, Part 1.
- Munro, I.C., Stavric, B., and Lacombe, R. 1975** The Current Status of Saccharin Toxicology Annual, p 71

Charbonneau, S.M., Munro, I.C., Mera, E.A., Willes, R.F., Kuiper-Goodman, T., Iverson, F., Moodie, C.A., Stoltz, D.R., Armstrong, F.A.J., and Grice, H.C. 1974. Sub-acute toxicity of methylmercury in the adult cat *Toxicol Appl Pharmacol* 27:569

Harwig, J., and Munro, I.C. 1975 Mycotoxins of possible importance in diseases of Canadian farm animals *Can Vet Journal* 16:125-141

Munro, I.C., Moodie, C.A., and Grice, H.C. 1975 A carcinogenicity study of commercial saccharin in the rat *Toxicol Appl Pharmacol* 32 513-526

Hollins, J.G., Willes, R.F., Bryce, F.R., Charbonneau, S.M., and Munro, I.C. 1975 The whole body retention and tissue distribution of [²⁰³Hg] methylmercury in the adult cat. *Toxicol Appl Pharmacol* 33 438-449.

Stavric, B., Lacombe, R., Watson, J.R., and Munro, I.C. 1974. Isolation, identification and quantitation of 0-toluenesulfonamide, a major impurity in commercial saccharins *J AOAC*, 57:678.

Munro, I.C., Middleton, E.J., Kemeny, T., Scott, P.M., Charbonneau, S.M., Moodie, C.A., and Grice, H.C. 1974 Toxicological changes in rats fed graded dietary levels of Ochratoxin A. *Toxicol Appl Pharmacol* 28 180

Munro, I.C., Scott, P.M., Moodie, C.A., and Willes, R.F. 1973 Ochratoxin A - Occurrence and toxicity *Am Vet Med Assoc* 163 1269

Munro, I.C., Charbonneau, S.M., and Willes, R.F. 1972 An automated data acquisition and computer-based computation system for application to toxicological studies in laboratory animals *Lab Anim Sci* 22:753

Munro, I.C., Salem, F.A., Heggveit, H.A., and Goodman, T. 1972. Cardiotoxicity of Brominated Vegetable Oils. *Myocardiology*, Volume 1 Recent advances in studies on cardiac structure and function, p 588

Munro, I.C., Hand, B., Middleton, E.J., Heggveit, H.A., and Grice, H.C. 1972 Toxic effects of brominated vegetable oils in rats *Toxicol Appl Pharmacol* 22 432.

Munro, I.C., Hand, B., Middleton, E.J., Heggveit, H.A., and Grice, H.C. 1971 Biochemical and pathological changes in rats fed low dietary levels of brominated cottonseed oil *Food Cosmet Toxicol* 9 631

Munro, I.C., Salem, F.A., Goodman, T., and Hasnain, S.H. 1971 Biochemical and pathological changes in the heart and liver of rats given brominated cottonseed oil *Toxicol Appl Pharmacol* 19 62.

Munro, I.C., and Morrison, A.B. 1970 Anelgue problems récents reliés à la sécurité des additifs alimentaires *Annals de l'ACFAS*, 37 42.

Munro, I.C., and Morrison, A.B. 1970 Drug residues in foods of animal origin: Their significance to man. *Assoc Offic Anal Chem* 53:211

Munro, I.C., Middleton, E.J., and Grice, H.C. 1969 Biochemical and pathological changes in rats fed brominated cottonseed oil for 80 days *Food Cosmetics Tox.*, 7 25

Munro, I.C., Morrison, A.B., and Meyer, M. 1969 Fish protein concentrate as a supplement to cereal diets. *J Am Dietetic Assoc* 54 398

Morrison, A.M., and Munro, I.C. 1969 Appraisal of the significance to man of drug residues in edible animal products. *Nat Acad Sci Pub No* 1679

Grice, H.C., Heggveit, H.A., Munro, I.C., and Wiberg, G.S. 1969. *The pathology of experimentally induced cobalt cardiomyopathies A comparison with beer drinkers cardiomyopathy.* Clin Toxicol 2:278

Wiberg, G.S., Munro, I.C., Meranger, J.C., Morrison, A.B., Heggveit, H.A., and Grice, H.C. 1969 Factors affecting the cardiotoxic potential of cobalt. Clin Toxicol 2:257

Grice, H.C., Goodman, T., Munro, I.C., Wiberg, G.S., and Morrison, A.B. 1969 Myocardial toxicity of cobalt in the rat Ann NY Acad Sci 156-189

Wiberg, G.S., Munro, I.C., Meranger, J.C., and Grice, H.C. 1968 Factors affecting the cardiotoxicity of cobalt Proc Can Fed Biol Sci 11:134.

Wiberg, G.S., Munro, I.C., and Morrison, A.B. 1967 Effects of cobalt ions on myocardial metabolism Can J Biochem 45:1219.

Munro, I.C., and Morrison, A.B. 1967 Toxicity of 1,2 dichloroethane-extracted fish protein concentrate Can J Biochem 45:1779

Munro, I.C., and Morrison, A.B. 1967 Factors influencing the nutritional value of fish flour V Chlorocholine chloride, a toxic material in samples extracted with 1,2 dichloroethane Can J Biochem 45:1049

Munro, I.C., and Morrison, A.B. 1965 Effects of salting and smoking on the protein quality of cod J Fish Res Bd Can 22:1.

Morrison, A.B., and Munro, I.C. 1964. Factors influencing the nutritional value of fish flour. IV Reaction between 1,2-dichloroethane and protein Can J Biochem 43:33.

PRESENTATIONS

Munro, I.C. 2007. Conceptual Framework for a Tiered Approach to Risk Ranking and Prioritization. Presented at the Joint Institute for Food Safety and Applied Nutrition workshop – "Tools for Prioritizing Food Safety Concerns", Greenbelt, MD, June 4-6

Munro, I.C. and Roberts, A.S. 2006. How to Market Your Functional Foods and Nutraceuticals in the US, Canada, Europe and Japan. CANTOX Seminar co-sponsored by the Canadian Embassy, November 29, held at the Canadian Embassy in Tokyo, Japan

Munro, I.C. 2006. Historical Perspective of Post-Market Monitoring. Presented at ILSI Europe – Workshop on The Application of Post-Market Monitoring to Novel Foods, Barcelona, Spain, November 15-17

Munro, I.C. 2006. Talk 1: Regulation of Food Ingredients in Canada, Talk 2: The Approval Process of the Joint FAO/WHO Expert Committee on Food Additives (JECFA), Talk 3: Regulatory Challenges for Food Ingredients in Asia; Talk 4: Key Elements In Developing a Global Regulatory Strategy. Presented in Cooperation with the Institute of Food Technologists (IFT) Continuing Education Program, Fall 2006 Short Courses, Scottsdale, Arizona, October 5-6

Munro, I.C. 2006. Thresholds of Toxicological Concern. Presented at the 3rd International Fresenius Conference on Functional Food, Darmstadt, Germany, September 20-21

Munro, I.C. 2006. The Maximized Survey-Derived Daily Intake (MSDI) as a Practical and Conservative Method to Estimate Intake of Flavouring Substances Presented at the FEMA Expert Panel Meeting, Sorrento, Italy, September 16-18.

Munro, I.C. 2006. Thresholds for Food Flavorings Used by JECFA Presented at FDA Grand Rounds on Thresholds: Crossing the Thresholds of Tomorrow, College Park, Maryland, June 8

Munro, I.C. 2006. New Developments in Flavor Science Flavor and Extract Manufacturers Association, 97th Annual Convention, Sunny Isles Beach, Florida, May 9

Munro, I.C. 2006. The Canadian Food Regulatory System – It's Strengths and Limitations Presented at Smarter Regulations of Foods in Canada Conference, Ottawa, Ontario, March 21-22.

Munro, I.C. 2006. Talk 1 - Can the Concept of Thresholds Help? Promises and Problems Talk 2 - Regulatory Differences in Risk Assessment Requirements For Food Products From Biotech And Conventionally Bred Crops The ILSI/ILSI North America Annual Meeting, San Juan, Puerto Rico, January 16-18.

Munro, I.C. 2005. Assessing the Safety of Biotechnology-Derived Foods Korean Food and Drug Administration, Seoul, Korea, December 2

Munro, I.C. 2005. Assessing the Safety of Biotechnology-Derived Foods Food Industry Research and Development Institute Hsinchu, Taiwan, November 29

Munro, I.C. 2005. Talk 1 - Thresholds of Toxicological Concern and Safety Evaluation of Food Ingredients Talk 2 - The Threshold of Toxicological Concern Concept ECB Workshop on Chemical Similarity and TTC Approaches, Ispra, November 7-8

Munro, I.C. 2005. Safety Evaluation of Ferric Sodium Ethylenediaminetetraacetate (NaFeEDTA) For Use as a Source of Iron in Foods Symposium on the Role of NaFeEDTA in Iron Deficiency Control, Beijing, China, November 3

Munro, I.C. 2005. Talk 1 - Nutritional Assessment of GM Foods Talk 2: Assessing the Safety of Nutritionally Enhanced GM Foods. Presented at Foods Derived from GM Crops: Issues for Consumers, Regulators and Scientists, New Delhi, India, September 26-27

Munro, I.C. 2005. The Feasibility of Postmarket Monitoring of Foods Derived Through Biotechnology to Identify Effects on Human Health Presented at EUROTOX 2005, Cracow, Poland, September 12-13.

Munro, I.C. 2005. The Threshold of Toxicological Concern Concept. Presented at the National Food Safety & Toxicology Centre, Michigan State University, East Lansing, Michigan, April 18.

Munro, I.C. 2004. An Overview of the Safety Evaluation of Essential Oils by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Presented at the FEMA Expert Panel Meeting, Lisbon, Portugal, October 27-29

Munro, I.C. 2004. Safety Assessment of Nutritionally Improved Foods and Feeds Developed Through the Application of Modern Biotechnology Hlywka, J., and Munro, I.C. The Feasibility of Postmarket Monitoring of Foods Derived Through Biotechnology to Identify Effects on Human Health Presented at the ILSI Workshop on Nutritional and Safety Assessments of Foods and Feeds Nutritionally Improved through Biotechnology, Buenos Aires, Argentina, October 7-8.

Munro, I.C. 2004. Threshold of Toxicological Concern and Safety Evaluation of Food Ingredients Presented at the 31st Annual Meeting of the Japanese Society of Toxicology, Osaka, Japan, July 6-8, 2004

Munro, I.C. 2004. Biomarkers and Standards of Evidence Requirements for a Health Claim on Foods. Presented at the Canadian Society for Clinical Nutrition (CSCN) 3rd Annual Scientific Meeting, "Nutrition and Cardiovascular Disease in Cancer", Toronto, Ontario, April 23, 2004.

Munro, I.C. 2003. Safety Assessment of Nutritionally Improved Foods and Feeds Developed through the Application of Modern Biotechnology **Hlywka, J., and Munro, I.C.** The Feasibility of Postmarket Monitoring of Foods Derived Through Biotechnology to Identify Effects on Human Health. Presented at the Workshop on Nutritional and Safety Assessments of Foods and Feeds Nutritionally Improved Through Biotechnology. Organized by the ILSI International Food Biotechnology Committee (IFBIC), Paris France, December 18

Munro, I.C. 2003. The JECFA Procedure for the Safety Evaluation of Flavoring Substances Presented at the 3rd ASEAN Food Safety Standards Harmonization Workshop, Jakarta, Indonesia, December 10-11

Munro, I.C. 2003. 1. The JECFA Procedure for the Safety Evaluation of Flavoring Substances 2 The FEMA GRAS Program for Flavors. Presented at the Safety Assessment of Flavors – Indonesia Roundtable, Jakarta, Indonesia, December 9

Munro, I.C. 2003. Setting Tolerable Upper Intake Levels for Nutrients Presented at The Annual European Meeting of The Toxicology Forum, Brussels, Belgium, October 28-30

Munro, I.C. and Roberts, A.S. 2003. The Regulatory Evaluation of Functional Foods and Nutraceuticals – CANTOX Seminar co-sponsored by the Canadian Embassy, September 4, Tokyo, Japan

Munro, I.C. 2003. Key Elements in Developing a Global Regulatory Strategy Presented at the International Food Technologists' Pre-Annual Meeting Program "International Regulatory Approval of Food Ingredients and Dietary Supplements", July 11-12, Chicago, IL

Munro, I.C. 2003. Managing and Interpreting Vitamin and Mineral Science. Presented at the EANS one-day workshop on "Risk Assessment and Beyond Vitamins and Minerals", April 30, Brussels, Belgium

Munro, I.C. 2003. Setting Tolerable Upper Intake Levels for Nutrients Presented at the National Institute of Nutrition (NIN) – Annual Meeting, April 28, Toronto, ON

Munro, I.C. 2003. Setting Tolerable Upper Intake Levels for Nutrients Presented at ILSI North America – Understanding Tolerable Upper Levels Workshop, April 23-24, Washington, DC

Munro, I.C. 2003. Managing and Interpreting Vitamin and Mineral Science Presented at the European Academy of Nutritional Sciences (EANS) one-day workshop - Risk Assessment and Beyond Vitamins and Minerals, April 20, Brussels, Belgium

Munro, I.C. 2003. The Threshold of Toxicological Concern Concept. Presented at the ILSI Europe Workshop on Structure-based Thresholds of Toxicological Concern: Guidance for Application to Substances Present at Low Levels in the Diet, March 20-21, Vienna, Austria

Munro, I.C. 2003. Current Dietary Supplement Safety Issues. Presented at the Food and Drug Law Institute's Conference: Dietary Supplements At a Crossroads, January 16-17, Washington, D C

Munro, I.C., Hlywka, J., and Reid, J. 2003. Determining Unintended Health Effects of Biotechnology Derived Foods Presented at the Workshop of the Committee on Identifying and Assessing the Unintended Effects of Genetically Engineered Foods on Human Health, The National Academies, January 7, Washington, D C

Munro, I.C., and Roberts, A.S. 2002. Functional Foods and Nutraceuticals -- How to Launch Nutraceuticals on the U.S. Market. A workshop conducted by Dr. Ian Munro and Dr. Ashley Roberts in association with Archimex, November 26, Paris, France.

Munro, I.C. 2002. Setting Tolerable Upper Intake Levels for Nutrients. Presented at the workshop on "Dietary Reference Intakes and Discretionary Fortification". Sponsored by the Committee on Use of Dietary Reference Intakes in Nutrition Labelling of the Food and Nutrition Board, Institute of Medicine, November 21, Washington, DC

Munro, I.C. 2002. Setting Tolerable Upper Intake Levels for Nutrients. Presented at the American Dietetic Association, Food & Nutrition Conference & Exhibition 2002, October 21, Philadelphia, PA

Munro, I.C. 2002. Regulatory and Safety Requirements for Obtaining GRAS Status. Presented at the American College of Nutrition's 43rd Annual Meeting, October 3, San Antonio, TX

Munro, I.C. 2002. The JECFA Procedure for the Safety Evaluation of Flavoring Substances. Presented at the JECFA Symposium organized by the Japanese Flavor & Fragrance Material's Association (JFFMA), September 26, Tokyo, Japan.

Munro, I.C. 2002. Risks From Acrylamide in Food Presented at the Ceres Roundtable Acrylamide: Lessons Learned, Plans Ahead, September 9, VirginiaTech, Alexandria, VA

Munro, I.C. 2002. The Precautionary Principle and the Scientific Risk Assessment Process Presented at the International Society of Regulatory Toxicology and Pharmacology Meeting, June 21-22, Arlington, VA.

Munro, I.C. 2002. OECD/FAO Substantial Equivalence Framework for Whole Food Safety Assessment. Presented at the 41st Annual Meeting & ToxExpo, March 17-21, Nashville, TN

Munro, I.C. 2001. Dietary Exposure from Migration of Packaging Materials Presentation at the Joint JRC/ILSI Europe Workshop on Exposure from Food Contact Materials, October 15-16, Ispra, Italy

Munro, I.C. 2001. Safety Evaluation of Foods Derived from Genetically Modified Crops. Presented at the 222nd American Chemical Society Meeting, August 29, Chicago, IL

Munro, I.C. 2001 Appropriate Use of Preclinical Data in Drug Development Presented at the joint meeting of the Michigan Chapter of the Society of Toxicology (MISOT) and the Michigan Society for Medical Research (MISMR), May 18, Ann Arbor, Michigan.

Munro, I.C. 2001 Risk Analysis of Food Derived from Genetically Modified Plants Presented at the Food and Agriculture Organization of the United Nations' (FAO) "Seminar on Risk Analysis for Food Control. A Practical Approach Through Case Studies" organized jointly with ILSI and the University of Brasilia, May 9-11, Brasilia, Brazil

Munro, I.C. 2000. Safety Evaluation of Foods Derived from Genetically Modified Crops Presented at the Brazilian Association of Food Industries' "Safety Assessment of Biotechnology Derived Foods" seminar, December 5, 6 & 7, São Paulo, Brazil.

Munro, I.C. 2000. Risk Assessment of Packaging Materials Presented at the 2nd International Symposium on Food Packaging Ensuring Safety and Quality of Foods, November 8-10, Vienna, Austria

Munro, I.C. 2000. EUROTOX/SOT Debate An evaluation demonstrating that foods derived from GM crops are as safe as their traditional counterparts is an appropriate paradigm for assessing the safety of genetically modified foods For the motion: Ian C. Munro (SOT). EUROTOX 2000, XXXVIII European Congress of Toxicology, September 17-20, London, England

Munro, I.C. 2000. Safety of Foods Produced by rDNA Technology Presented at the Institute of Medicine/Food and Nutrition Board Meeting, July 20, Woods Hole, MA.

Munro, I.C. 2000. Society of Toxicology/EUROTOX Debate Presentation 2000 Society of Toxicology Annual Meeting, March 21, Philadelphia, PA.

Munro, I.C. 2000. Developing Integrated Scientific & Regulatory Strategies, Resolving Complex Scientific Issues, and Facilitating Timely Regulatory Approvals TNO Nutrition and Food Research Institute, February 29, Zeist, The Netherlands.

Munro, I.C. 2000. Applying a Threshold of Regulation Concept to the Safety Evaluation of Packaging Materials Nutripack Food & Beverage Packaging Congress, January 26-27, Paris, France.

Munro, I.C. 1999. Key Safety Issues in Bringing a Functional Food or Nutraceutical to Market Nutraceutical Opportunities Summit, December 8-9, Toronto, Ontario.

Munro, I.C. 1999. The Concept of Thresholds in Safety Assessment ILSI Europe Workshop on Threshold of Toxicological Concern for Chemical Substances Present in the Diet, October 5-6, Paris, France

Munro, I.C., Bechtel, D., Schinkel, H., and McColl, D. 1999. Functional Foods International Comparisons of the Scientific and Regulatory Attributes Affecting Product Development and Market Access

Munro, I.C., McColl, D., Bailey, R., Coutrelis, N., and Schinkel, H. 1999. Special Forum. International Regulatory Issues in Marketing Functional Foods Barriers and Opportunities Institute of Food Technologist's Annual Meeting, July 24-28, Chicago, IL

Munro, I.C. 1999. 1) Safety Assessment of Process Flavors 2) Perspective of the Food and Nutrition Board's Subcommittee on Upper Reference Levels of Nutrients. 1999 Annual Summer Meeting of The Toxicology Forum, July 12 - 16, Aspen, Colorado

Munro, I.C. 1999. The Crucial Role of Safety and Efficacy Principles for Nutraceuticals, Functional and Medical Foods - Nutraceutical, Functional & Medical Foods Conference, May 6-7, Toronto, Ontario.

Munro, I.C. 1999. Assessing the Safety of Flavoring Substances Flavor and Extract Manufacturers' Association of the United States - 90th Annual Convention, May 2-5, Palm Beach, Florida.

Munro, I.C. 1999. Concepts in Safety Evaluation of HPV Food Substances. Vision 20/20 Workshop - TestSmart - A Humane and Efficient Approach to SIDS Data, April 26-27, Fairfax, Virginia.

Munro, I.C. 1999. Effect of Intake Level on the Safety Evaluation of Flavoring Substances Scientific Committee on Food - DGIII - DGXXIV Joint Workshop on Chemically Defined Flavouring Substances, March 25, Brussels, Belgium

Munro, I.C., Berndt, W., Borzelleca, J., Flamm, G., Lynch, B., Kennepohl, E., Bär, A., and Modderman, J. 1999. Erythritol An Interpretive Summary of the Biochemical, Metabolic, Toxicological and Clinical Data Poster presentation at the Society of Toxicology Annual Meeting, March 14-18, New Orleans, Louisiana

Munro, I.C. 1998. 1) A Global Perspective on Regulatory Approval for Food Ingredients, Nutraceuticals, and Dietary Supplements. 2) Gaining Product Approval in Canada 3) Key Elements in Formulating a Global Regulatory Plan International Food Technologist's 1998 Pre-Annual Meeting Continuing Education Program #5, June 19 & 20, Atlanta, GA

Munro, I.C. 1998. FNB Model for Development of Tolerable Upper Intake Levels Presented at the European Toxicology Forum Meeting, May 13, Brussels, Belgium.

- Munro, I.C. 1998.** International Perspectives for Ensuring Safe Food Presented at the Institute of Medicine, April 29, Washington, D.C
- Munro, I.C. 1997.** *The Development of Tolerable Upper Intake Levels for Nutrients* Presented at the Insight Information Inc. Conference - New Nutrition Recommendations - Capitalizing on New Opportunities, December 11, Toronto, Ontario.
- Munro, I.C. 1997.** *A Model for the Development of Upper Levels* Presented at the Dietary Reference Intakes Conference - New Vision, New Challenges, Ontario Institute for Studies in Education, November 24, Toronto, Ontario
- Munro, I.C. 1997.** *A Model for the Development of Tolerable Upper Intake Levels for Nutrients* Presented at the Calcium Workshop, Program in Food Safety, University of Toronto, October 30, Toronto, Ontario
- Munro, I.C. 1997.** *A Model for the Development of Tolerable Upper Intake Levels for Nutrients* Presented at Dietary Reference Intakes: Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride Workshop, Institute of Medicine, September 23, Washington, D.C.
- Munro, I.C., Daniels, J.M., and Lynch, B.S. 1997.** *A Review of the Safety of Vitamin B6 (Pyridoxine): Implications for Determining the Safe Upper Intake from Dietary Supplements.* Presented at Vitamin B6. New Data, New Perspectives, Council for Responsible Nutrition, September 8, London, England.
- Munro, I.C., and Kroes, R. 1997.** Application of a Threshold of Regulation Concept in the Safety Evaluation of Certain Flavoring Substances Presented at the Forty-ninth Meeting of the Joint FAO/WHO Expert Committee on Food Additives, June 17-26, Rome, Italy
- Bechtel, D., Locke, L., and Munro, I.C. 1997.** Need for Scientific Substantiation for Functionality of Food Components for Health Promotion Presented at the ILSI N.A Workshop - The Future of Functional Foods for Health Promotion A Public Health Opportunity? June 4-5, Washington, D C
- Munro, I.C. 1997.** 2,4-D - Safety and Exposure Presented to Poisons Centre staff, academic pharmacology staff and postgraduate students at the University of Dunedin, March 13, Dunedin, New Zealand
- Munro, I.C. 1997.** 2,4-D - Safety and Exposure Presented to toxicologists and occupational health specialists from the New Zealand Ministry of Agriculture and Ministry of Environment, March 12, Wellington, New Zealand
- Munro, I.C. 1997.** Development of a Procedure for the Safety Evaluation of Flavouring Substances Presented at the International Symposium on Flavours and Sensory Related Aspects, March 6-7, Cernobbio (Como), Italy.
- Munro, I.C. 1996.** 1) Current Issues in the Evaluation of the Safety of Food and Food Ingredients 2) Issues in the Safety Assessment of Carbohydrate/Fat Substitutes Presented at the ASCEPT Toxicology Workshop, June 17-18, Canberra, Australia
- Munro, I.C. 1995.** Interpretive Review of the Potential Adverse Effects of Chlorinated Organic Chemicals on Human Health and the Environment Report of an Expert Panel Presented at Dioxin 95, 15th International Symposium on Chlorinated Dioxins and Related Compounds, August 21-25, Edmonton, Alberta
- Munro, I.C. 1995.** The Safety Evaluation of Flavoring Substances The GRAS Process. Presented at the Second Workshop - Harmonization and Food Safety, April 20-21, Hong Kong

Munro, I.C., McGirr, L.G., Nestmann, E.R., and Kille, J.W. 1994. Macronutrient Substitutes. Safety Factor Alternatives And Human Mimetic Models. Thirty-third Annual Meeting of Society of Toxicology, Dallas, Texas.

Munro, I.C., McGirr, L.G., Nestmann, E.R., and Kille, J.W. 1994. Macronutrient Substitutes: Alternatives To Traditional Safety Testing. Annual Meeting of Institute of Food Technologists, Atlanta, Georgia

Munro, I.C. 1993. Harmonization of Conventional Toxicology Studies - A Commentary Presented at ILSI Conference on RedBook II, December 16, Washington, DC.

Munro, I.C. 1993. The Exposure and Toxicity of 2,4-D. Presented at The Toxicology Forum, Aspen, CO (July)

Munro, I.C. 1992 Novel Foods, Workshop on Novel Foods and Novel Food Processes. Presented at the Program in Food Safety, Nutrition and Regulatory Affairs, Department of Nutritional Sciences, Faculty of Medicine, University of Toronto Toronto, Ontario (November)

Munro, I.C. 1992 Toxicology and Drug Development: Managing the Issues Presented to Ciba-Geigy Canada Ltd , Mississauga, Ontario (October)

Munro, I.C. 1992 Adverse Effects and Indoor Air Pollution Presented at the Thirteenth Annual Meeting of the American College of Toxicology, San Francisco, CA. (October).

Munro, I.C. 1992. Toxicology of Benzoyl Peroxide Presented at The Toxicology Forum, Aspen, CO. (July)

Munro, I.C., Borzelleca, J.F., and Squire, R.A. 1991. The Safety of Xylitol for Use in Food. Report of an Expert Panel

Munro, I.C. 1991. Food Safety Presented at a Food Safety Seminar Embassy of the United States, Ottawa, Ontario, Canada

Munro, I.C., and Orr, J. 1991 Dioxins in Paper Products Canadian Paediatric Society Workshop on Infant Diapers

Munro, I.C., and Orr, J. 1991. The Sacchann Lesson Presented at the Symposium on Chemical Carcinogenesis: The Relevance of Mechanistic Understanding in Toxicological Evaluation Berlin, Germany.

Munro, I.C. 1991 Impact of Agricultural Activities on Health Risks From Drinking Water Presented at the *Interdisciplinary Symposium on Agriculture and Water Quality* Centre for Soil and Water Conservation University of Guelph, Ontario

Munro, I.C. 1990 Scientific Aspects of the IFBC Report. Presented to the Toxicology Forum Washington, DC.

Munro, I.C., and Hall, R.L. 1990 Food Safety and Quality - Impact of Biotechnology Presented at the Agricultural Biotechnology, Food, Safety and Nutritional Quality for the Consumer Second Annual Meeting. Ithaca, New York.

Munro, I.C. 1990 Food Safety and Environmental Issues in the year 2010. Presented to the Western Canadian Wheat Growers' Association, Regina, Saskatchewan, Canada

Munro, I.C. 1990 & 1989 Issues in Food Safety, "Later in Life Learning Series", Toronto Ontario and The Environmental Forum, Belleville, Ontario.

Munro, I.C. 1989. Issues to be Considered in the Safety Evaluation of Fat Substitutes Presented at the Workshop on Re-evaluation of Toxicity Methodology including Gross Nutrients. Limelette, Belgium

Munro, I.C. 1989. Natural Versus Man-Made Presented to the Ontario Institute of Agrologists, Toronto, Ontario

Munro, I.C. Neoplasm Promotion. Prepared for Environmental Health and Safety Council of The American Health Foundation

Munro, I.C. 1986 Governmental Approach to Regulatory Priorities and Risk Management of Flavors and Fragrances. Presented at The Tenth International Congress of Essential Oils, Fragrances and Flavors Washington, DC

Munro, I.C. 1985 The Role of Toxicology in Strategies for Cancer Prevention. Presented at the American Society of Preventive oncology Eighth Annual Meeting, Toronto, Canada

Munro, I.C. 1985 The Ingredients of Foods: How They are Tested and Why They are Selected Presented at the ILSI Workshop on Adverse Reactions to Foods and Food Additives, Orlando, Florida

Munro, I.C., Goldberg, L., and Farber, E. 1985 Formaldehyde Risk Assessment Report to Ontario Ministry of Labour

Munro, I.C. 1984 Risk Assessment and Environmental Regulation Prepared for the ILSI Symposium on Safety Assessment. Tokyo, Japan

Munro, I.C. 1984. Report to the Royal Commission to Inquire into the Use and Effects of Chemical Agents on Australian Personnel in Vietnam

Munro, I.C. 1983. Artificial Sweeteners (Sacchann) - General Review of Carcinogenicity Data Presented at the Third European Toxicology Forum Geneva, Switzerland

Clayson, D.B., and Munro, I.C. 1983. Safety Evaluation of Low Levels of Toxic Agents in Food with Emphasis on Carcinogenesis and Mutagenesis Presented at the International Symposium on the Safety Evaluation of Animal Drug Residues. Berlin, Germany

Munro, I.C., and Bradshaw, L.R.A. 1983. Government Decision-Making with Incomplete Epidemiologic Evidence Presented at the Canadian Society for Clinical Investigations Symposium in Clinical Epidemiology Calgary, Alberta.

Munro, I.C. 1983 Overview of Factors that Influence Food Safety Decisions Presented at the international Life Sciences Institute Symposium, Safety Assessment: Interface Between Science, Law and Regulation. Washington, DC

1983. The Relevance of Mouse Liver Hepatoma to Human Carcinogenic Risk. Report of a Panel to the International Expert Advisory Committee to the Nutrition Foundation.

Munro, I.C. 1983 Introductory Remarks Presented at the Toxicology Forum Meeting Arlington, Virginia

Charbonneau, S.M., and Munro, I.C. 1982. Dietary Factors Affecting Pesticide and Xenobiotic Toxicity. Presented as a Poster at the Fifth International Congress on Pesticide Chemistry Kyoto, Japan

Tryphonas, H., and Munro, I.C. 1982 Risk-Benefit Assessment in Immunotoxicology. Presented by Mrs. Tryphonas at NATO Advanced Study Institute on Immunotoxicology. Acadia University, Wolfville, Nova Scotia

- Munro, I.C., Miller, C.T., and Krewski, D. 1982.** Regulatory Control of Environmental Chemicals A Canadian Viewpoint Presented at the First World Congress on Toxicology and Environmental Health Washington, DC
- Munro, I.C. 1982** The Necessity for Compatible Standards Presented at the 1982 Annual Winter Toxicology Forum Meeting, February 15-17, Arlington, Virginia.
- Munro, I.C. 1981.** Regulatory Concerns - Overview. Presented at the Fourteenth Annual Symposium of the Society of Toxicology of Canada Montreal, Quebec.
- Munro, I.C., and Krewski. 1981.** Risk Assessment and Regulatory Decision Making Presented at the Toxicology Forum Meeting, August 9-13, Vancouver, British Columbia
- Munro, I.C. 1981.** Risk Assessment and Regulatory Decision Making. Presented at the 64th Chemical Conference and Exhibition, Chemical Institute of Canada, May 31-June 3, Halifax, Nova Scotia
- Munro, I.C. 1981** Science and Issues of Food Additive Use Presented at Food Additives Symposium. University of Toronto, Faculty of Medicine and Program in Human Nutrition
- Munro, I.C., and Krewski, D.R. 1980** The Role of Risk Assessment in Regulatory Decision Making Presented at the Thirteenth Annual Symposium of the Society of Toxicology of Canada, December 2-3, Montreal, Quebec
- Munro, I.C., and Krewski, D. 1980** The Role of Risk Assessment in Regulatory Decision Making. Presented at Symposium on Health Risk Analysis, October 27-30, Gatlinburg, Tennessee
- Munro, I.C. 1980.** Scientific Evaluation of Benefit Risk Assessments in Food Safety. Presented at the Gordon Research Conference on the Microbiological Safety of Foods, June 16-20, Plymouth, New Hampshire
- Munro, I.C. 1980.** Regulatory Control of Carcinogens Presented at the Toxicology Forum Meeting, February 28-March 1, Arlington, Virginia
- Munro, I.C. 1979.** Reproductive Toxicity Presented at the International Course on the Principles and Methods in Modern Toxicology, October 22-24, Belgrate, Italy.
- Munro, I.C. 1979** Scientific Evaluation of Benefit/Risk Assessments in Food Safety. Presented at the 29th Annual Meeting of the Institute of Food Technologists, June 10-13, St. Louis, Missouri
- Munro, I.C. 1978** Compilation of United States and Canadian Legislation Pertaining to Environmental Safety Prepared for the International Commission for Protection Against Environmental Mutagens and Carcinogens.
- Munro, I.C. 1978** Chapter on ADI Concept Prepared for the Safe Drinking Water Committee, National Academy of Sciences
- Munro, I.C. 1978** Detecting and Measuring Carcinogens Presented at the Law and Public Affairs Seminar on Government Regulation of Cancer-Causing Chemicals, December, Washington, DC
- Munro, I.C. 1978.** Environmental Contaminants and Food Safety Presented at the XI International Congress of Nutrition Conference, September, Rio de Janeiro, Brazil
- Munro, I.C. 1978.** Reproductive Toxicity and the Problems of *In Utero* Exposure. Presented at the International Symposium on Chemical Toxicology of Food, June, Milan, Italy

Munro, I.C. 1978. Environmental Contaminants Presented at the Symposium on Principal Hazards in Food Safety and Their Assessment, FASEB Annual Meeting, April, Atlantic City, New Jersey.

Munro, I.C. 1977. Regulatory Applications of Short-Term Tests for Carcinogenicity Presented at the Gordon Research Conference, August, Meriden, New Hampshire

Munro, I.C. 1977 Overview - Dose Selection. Presented at the Toxicology Forum Meeting, July, Aspen, Colorado.

Munro, I.C. 1977 The Importance of Specifications for Substances in Their Safety Evaluation in Foods Prepared for the Scientific Committee of the Food Safety Council

Munro, I.C. 1977 Working Papers for 34 Food Colors. Prepared for Joint FAO/WHO Expert Committee, Geneva

Charbonneau, S.M., Munro, I.C., and Nera, E. 1977. Chronic Toxicity of Methylmercury in the Adult Cat Proc. X Symposium on Trace Substances in Environmental Health, Columbia, Missouri

Munro, I.C. 1976. Considerations in Chronic Toxicity Testing: The Chemical, The Dose, The Design Presented at the Status of Predictive Tools in Application to Safety Evaluation Conference, November, Little Rock, Arkansas.

Munro, I.C. 1975. Working Paper on Nitrates, Nitrites and Nitrosamines. Prepared for the World Health Organization

Grice, H.C., DaSilva, Stoltz, D.R., Munro, I.C., Clegg, D.J., and Abbatt, J.D. Testing of Chemicals for Carcinogenicity, Mutagenicity, Teratogenicity

Munro, I.C. 1974. Chemicals that Cause Food Poisoning Proc. of Symposium on Food Poisoning and its Significance in the Food Service Industry. Department of National Health and Welfare

Stavric, B, Lacombe, R., Munro, I.C., and Grice, H.C. 1973. Studies on Chemical Impurities in Commercial Saccharin (Interim Report). Submitted to NRC Committee on Artificial Sweeteners of the National Academy of Sciences of the United States

Munro, I.C., Moodie, C.A., and Grice, H.C. 1973. An Evaluation of the Carcinogenicity of Commercial Saccharin. Submitted to NRC Committee on Artificial Sweeteners of the national Academy of Sciences of the United States

Munro, I.C., Charbonneau, S.M., and McKinley, W.P. 1973 Studies on the Toxicity of Methylmercury Commission of the European Communities, Luxembourg

Grice, H.C., DaSilva, T., Stoltz, D.R., Munro, I.C., Clegg, D.J., and Abatt, J.D. 1973 Testing of Chemicals, Mutagenicity and Teratogenicity Department of National Health and Welfare

Munro, I.C., Hasnain, S., Salem, F.A., Goodman, T., Grice, H.C., and Heggveit, H.A. 1972 Cardiotoxicity of Brominated Vegetable Oils. Myocardiology Volume I Recent Advances in Studies on Cardiac Structure and Function. p 588.

Jun-07

CURRICULUM VITAE

John Doull, Ph.D., M.D

1/30/2004

OFFICE:

HOME:

EDUCATION:

PROFESSIONAL EXPERIENCE:

University of Chicago Medical School

Research Assistant, Univ. of Chicago Toxicity Laboratory, 1946-1950

**Research Associate, US Air Force Radiation Laboratory and Univ. of
Chicago Toxicity Laboratory, 1951-1953**

**Assistant Director, US Air Force Radiation Laboratory & Univ. of
Chicago Toxicity Laboratory, 1954-1967**

Assistant Professor, Department of Pharmacology, 1956-1957

Associate Professor, Department of Pharmacology, 1957-1967

University of Kansas Medical Center

**Professor of Pharmacology and Toxicology, Department of Pharmacology,
Toxicology and Therapeutics, 1967-1994**

Co-Director Clinical Pharmacology Toxicology Center, 1967-1978
Director, Univ. of Kansas Medical Center Safety Office, 1978-1985
Director, Center for Environmental and Occupational Health, 1986-1989
Professor Emeritus of Pharmacology and Toxicology, Department of
Pharmacology, Toxicology and Therapeutics 1995-

PROFESSIONAL SOCIETY MEMBERSHIPS:

American Chemical Society, 1949-1996
Kansas City Regional Chapter, 1967-1996
American Industrial Hygiene Association, 1950-1996
Radiation Research Society, 1953-1980
American Society for Pharmacology & Experimental Therapeutics, 1953-1996
Environmental Pharmacology Committee, 1975-1978
Society for Experimental Biology and Medicine, 1954-1995
New York Academy of Sciences, 1954-1975
American Ass. for the Advancement of Science, 1954- (Fellow, 1958-)
Society of Toxicology (Charter Member), 1961-
Technical Committee, 1967-1968
Education Committee, 1974-1976
Membership Requirement Revision Committee, 1975-1976
Biomed Research Oversight Committee, 1977-1978
Central States Regional Chapter, 1986-
Program Committee (Chairman), 1985-1986
Finance Committee, 1986-1987
Awards Committee (Chairman), 1987-1988
Nominating Committee (Chairman), 1988-1989
Council Member, 1981-1988
Vice President Elect, 1984-1985
Vice President, 1985-1986
President, 1986-1987
Past-President, 1987-1988
Toxicology Education Foundation (Trustee, President) 1997-1999
American Academy of Clinical Toxicology, 1970-1996
Board of Trustees, 1972-1977
Canadian Academy of Clinical Toxicology, 1976-1989
Program Committee, 1976-1977
The Toxicology Forum, 1979-1998
Board of Directors, 1981-1982

American Board of Toxicology, 1979-1983
Chairman Examination Committee, 1979-1982
Vice President, 1981-1982
President, 1982-1983
American Water Works Association, 1983-1995
Kansas Regional Section, 1983-1995
American Conference of Governmental Industrial Hygienists, 1989-
Chairman, TLV Committee, 1989-1997
The Academy of Toxicological Sciences (Fellow), 1999

EDITORIAL BOARDS:

Toxicology and Applied Pharmacology, 1970-1982
Forum for the Advancement of Toxicology, 1973-1983
AACTION (American Academy of Clinical Toxicology), 1974-1977
Environmental Health Sciences, 1976-1989
Archives Internationales de Pharmacodynamie et de Therapie, 1976-1989
Journal of Environmental Pathology and Toxicology, 1977-1989
Health & Environment Digest, 1987-1997
Toxicological Reviews 2003-
Therapeutics and Clinical Risk Management 2004-

CONSULTANTSHIPS

Walter Reed Army Institute for Research, 1960-1963
Radiation Protection Panel, 1962-1963
Atomic Defense Support Agency, Group N-3, 1961-1962
White House Evaluation Study (Woolridge Report), 1962-1963
NIH Special Grants Program Advisory Panel, 1962
NIH Toxicology Study Section, 1965-1970
HEW Secretary's Commission on Pesticides (Mrak Report), 1968-1969
Subcommittee on Interactions, 1968-1969
Midwest Research Institute, 1969-1990
Institute for Clinical Toxicology, Houston, Texas, 1969-1973
National Academy of Sciences, National Research Council
Toxicology Information Program (Chairman), 1970-1975
Food Protection Committee, 1974-1979
Committee on Non-nutritive Sweeteners, 1974-1975
Safe Drinking Water Committee, 1975-1978 (Chairman, 1976-1978)
Pesticides Subcommittee (Chairman), 1975-1977

Committee to Revise Publication 1138, 1976-1977
 Chronic Toxicity Subcommittee (Chairman), 1976-1977
 Board on Toxicology and Environmental Health Hazards, 1978-1986
 Board on Environmental Sciences and Toxicology, 1986-1989
 IOM Food Safety Policy Subcommittee, 1978-1979
 Committee to study Saccharin and Food Safety Policy, 1978-1979
 IOM Advisory Committee on CDC's Study of Vietnam Veteran Health,
 1985-1988
 Committee on Toxicity Testing Strategies (Chairman), 1982-1984
 Committee on Mixtures (Chairman), 1986-1988
 Committee on Toxicology (Chairman), 1987-1993
 Committee on Risk Assessment of Hazardous Air Pollutants, 1990-1993
 Committee to Study the Interactions of Drugs, Biologics and Chemicals
 in Deployed U. S. Military Forces, 1995-1996
 Subcommittee on Acute Exposure Guideline Levels, 1997-2003
 Board on on Environmental Studies and Toxicology (Vice Chair)1999-2003
 Committee on the Use of Third Party Toxicity Research with Human
 Participants, Science Technology and Law Program, 2002-2004
 Subcommittee on Fluoride in Drinking Water (chair) 2003-
 Environmental Protection Agency, Washington, D.C., 1976-1995
 FIFRA Science Advisory Panel, 1976-1980
 Worker Re-entry Protocol Group, 1977-1978
 Committee on Tolerances, 1978-1979
 Science Advisory Board, Environmental Health Committee, 1980-1989
 Organics Subcommittee (Chairman), 1986-1989
 Estimating Risks from Dioxins/Dibenzofurans, 1986-1987
 Severity of Effects Ranking Schemes, 1985-1986
 Acute Toxics Committee, 1986-1987
 Hazard Ranking System Committee, 1987-1988
 Dioxin Reassessment Review Committee 1995
 Science Advisory Board, Environmental Health Committee, 1997-2001
 National Institute of Environmental Health Sciences, 1975-1978
 NIEHS Advisory Council, 1975-1978
 University-Based Centers Subcommittee (Chairman), 1975-1978
 Second Task Force on Human Health and the Environment, 1976-1977
 Biologic Mechanisms and Toxicity Subcommittee, 1976-1977
 F.E.M.A., Washington, D.C., Expert Panel Member, 1977-2003
 National Advisory Committee, California Primate Center, Davis, 1977-1980

OTA, Wash., Panel on Assessment of Environmental Contaminants, 1978
 National Toxicology Program, Board of Scientific Counselors Ad Hoc
 Panel on Chemical Carcinogenesis Testing & Evaluation, 1982-1984
 DHHS Advisory Committee on Long-term Health Effects of Phenoxy
 Herbicides and Contaminants, 1982-1985
 UAREP Panel on Health Aspects of Waste Chemical Disposal, 1983-1984
 Nutrition Foundation, Washington Committee, 1982-1983, DC
 Predictive Role of Mouse Liver Tumors
 National Sanitation Foundation, Ann Arbor, 1983-1989
 Council of Public Health Consultants, 1983-1989
 Health Advisory Board, 1983-1989
 Drinking Water Additives Peer Review Group, 1987-1989
 Kansas Dept. Health and Environment, Topeka, 1983-1987
 Toxicology Advisory Committee, 1983-1987
 Governors Advisory Committee on Radon (Chairman), 1987-1988
 Governors Surface Water Quality Commission 1997-1999
 National Institute of Occupational Safety and Health, 1984-1987
 Board of Scientific Counselors, 1984-1987
 White House Advisory Panel on Ranchhand Veterans, 1984-1986
 Clean Sites Inc., Alexandria, Technical Advisory Panel, 1984-1993
 Naylor Dana Institute, Advisory Panel on Acetaminophen, 1986-1987
 Denver Water Dept. Reuse Demo. Project Advisory Committee, 1986-1992
 Scientific Advisory Panel on Ground Water Recharge (California), 1987
 Water Resource Recovery Pilot Plant Project (Tampa, FL), 1987-1992
 Health Effects Group (Chairman), 1987-1992
 International Life Sciences Institute, Risk Science Institute, 1988-
 Armed Forces Epidemiological Board, 1988-1991
 Lovelace Biomedical & Environmental Res. Inst. Board of Directors, 1988
 Presidential Risk Assessment & Management Commission, 1990-1998
 Food and Drug Administration, CFSAN Review Panel 1999
 Food and Drug Administration, OPS Advisory Committee, 1999-2002
 FDA, OPS Adv Com: Non-clinical studies subcommittee (chair), 1999-2003

LOCAL COMMITTEES:

Poison Control Center Committee (Chairman), 1968-1980
 Pharmacy and Therapy Committee (Chairman), 1969-1984
 Basic Science Lectureship Committee, 1970-1972
 Health Care Delivery Systems Committee, 1971-1972

Research Committee, 1971-1973
Animal Care Committee, 1972-1974
Computer Committee (Chairman), 1972-1974
Search Committee for Chair of Biochemistry, 1975
Search Committee for Dean of School of Nursing (Chairman), 1975
Education Committee, 1976-1977
Faculty Promotion and Tenure Committee, 1976-1977
Curriculum Implementation Committee, 1976
Ad Hoc Ethics Committee, 1976
Long Range Planning Committee, 1976
Information Systems Advisory Committee, 1977
Medical Center Safety Committee (Chairman), 1978-1983
 Radiation Safety Committee, 1978-1983
 Biohazards Committee, 1978-1983
 Engineering Safety Committee, 1978-1983
Committee for Intercampus Liaison (Chairman), 1978-1980
Search Committee for Director of Biomed. Engineering (Chairman), 1980
Search Committee for Graduate School Dean (Chairman), 1980
Task Force on Need for School of Public Health, 1980
Education and Curriculum Committee, 1984-1987
Center for Environmental and Occupational Health (Director 1986-1989)
 Executive Advisory Committee, 1986-1989
 External Advisory Committee, 1986-1989

HONORS/AWARDS:

Sigma Xi (Univ. of Chicago), 1960
Alpha Omega Alpha (Univ. of Kansas), 1973
The Kenneth P. DuBois Award (Midwest Chapter SOT), 1985
Samuel Kuna Award (Rutgers Univ.), 1989
Commander's Award for Public Service (Armed Forces Epidemiological Board), 1990
International Achievement Award (International Society of Regulatory Toxicology), 1990
Ambassador of Toxicology Award (Mid-Atlantic Chapter Society of Toxicology), 1991
Distinguished Medical Alumnus Award (Univ. of Chicago), 1991
Stokinger Award (Amer. Cont. Governmental Industrial Hygienists), 1992
John Doull Award (Mid-America Chapter Society of Toxicology), 1992

Special Recognition Award (University of Kansas Medical Center), 1992
Merit Award (Society of Toxicology), 1993
Snider Award (University of Arkansas Toxicology Symposium Series), 1994
Founders Award (Chemical Industry Institute of Toxicology), 1996
Distinguished Service Award, (American College of Toxicology), 1996
The Meritorious Service Award (Amer. Conf. Gov. Ind. Hygienists), 1996
Honorary Doctor of Pharmacy (The University of Kuopio, Finland), 1996

BOOKS/BOOK CHAPTERS:

Essays in Toxicology (F. Blood, ed.), Academic Press, New York, Effect of Physical Environmental Factors on Drug Response, 1972.
Casarett and Doull's Toxicology: The Basic Science of Poisons, Macmillan Publishing Co., Inc., New York.
First Edition (L. J. Casarett and J. Doull, eds.), 1975
Second Edition (C. D. Klaassen, M. O. Amdur and J. Doull, eds.), 1980
Third Edition (C. D. Klaassen, M. O. Amdur and J. Doull, eds.), 1986
Fourth Edition (M. O. Amdur, J. Doull and C. D. Klaassen, eds.), 1991
Fifth Edition (C. D. Klaassen ed., M. O. Amdur and J. Doull, emeritus eds.) 1995
Insecticide Biochemistry and Physiology (C. Wilkinson, ed.), Plenum Press, NY, The Treatment of Insecticide Poisoning, 1976.
Information Technology in Health Science Education (E. Deland, ed.), Plenum Pub. Co., Use of CATS in Pharmacology, 1978.
Food Safety (H. Roberts, ed.), Wiley & Sons, New York, Chapter 7, Food Safety and Toxicology, 1981.
Complex Mixtures, National Academy Press, Washington, D.C., 1988.
Methods to Assess Adverse Effects of Pesticides on Non-target Organism (R. G. Tardiff, ed.), John Wiley & Sons Ltd., Chapter 10, Assessment of Acute Toxicity of Pesticides on Humans and Domestic Animals, 1992.
Science and Judgement in Risk Assessment, Ed. Kurt Isselbacher, National Academy Press, Washington D. C. 1995
Environmental Toxicology, Current Developments (J. Rose Ed.), Chapter 1, General Principles of Toxicology, Gordon and Breach, Amsterdam, 1998
Acute Exposure Guideline Levels for Selected Airborne Chemicals, National Academy Press, Washington, D.C., 2000, 2001, 2002, 2003
Handbook of Pesticide Toxicology, Associate Editor, R. Krieger Ed., Vol 1. Principles, Vol 2. Agents, Academic Press, San Diego, 2000
Vol 1, Chapter 1, Dose Time and Other Factors Influencing Toxicity.

BIBLIOGRAPHY

1. DuBois, K. P., Doull, J., and Coon, J. M., Toxicity and Mechanism of Action of p-Nitro-phenyl-diethyl-thionophosphate (E605), *Fed. Proc.* 7: 216 (1948).
2. Dubois, K. P., Doull, J., Salerno, P. R., and Coon, J. M. Studies on the toxicity and mechanism of action of p-nitrophenyl diethyl thionophosphate (Parathion). *J. Pharmacol. Exp. Ther.* 95: 79 (1949).
3. Doull, J., DuBois, K. P., and Geiling, E. M. K., Biosynthesis of radioactive Bufagin containing C¹⁴. *Fed. Proc.* 8: 287 (1949).
4. DuBois, K. P., Doull, J., and Geiling, E. M. K., Inhibitory action of Bufagin on carbohydrate metabolism. *Fed. Proc.* 8: 288 (1949)
5. DuBois, K. P., Doull, J., and Cochran, K. W. Effects of acute beryllium poisoning on carbohydrate metabolism. *Proc. 116th Meeting Amer. Chem. Soc.*, p. 57 (1949).
6. DuBois, K. P., Doull, J., and Coon, J. M. The cholinergic action of alkyl pyrophosphoramides. *J. Pharmacol. Exp. Ther.* 98: 6 (1950).
7. Cochran, K. W., Doull, J., and DuBois, K. P., Toxicity and anticholinesterase activity of an alkyl coumarin thiophosphate (E838). *Fed. Proc.* 10: 287 (1950).
8. Cochran, K. W., Doull, J., Mazur, M., and DuBois, K. P. Acute toxicity of zirconium, columbium, strontium,, lanthanum, cesium, tantalum and yttrium. *J. Ind. Hyg. Occup. Med.* 1: 637 (1950).
9. DuBois, K. P., Doull, J., and Coon, J. M. Studies on the toxicity and pharmacological actions of octamethyl pyrophosphoramide (OMPA, Pestox III). *J. Pharmacol. Exp. Ther.* 99: 376 (1950).
10. DuBois, K. P., Cochran, K. W., and Doull, J. Inhibition of citric acid synthesis in vitro by x-irradiation. *Proc. Soc. Exp. Biol. Med.* 76: 422 (1951).
11. Doull, J., DuBois, K. P., and Geiling, E. M. K. The biosynthesis of radioactive bufagin. *Arch. Int. Pharmacodyn.* 86: 454 (1951).

12. Doull, J., Hermann, R. G., Geiling, E. M. K., and DuBois, K. P. Effects of bufagin on the respiration of cardiac muscle and other tissues. *Arch. Int. Pharmacodyn.* 86: 487 (1951).
13. Doull, J., and DuBois, K. P. Toxicity and anticholinesterase action of tetra-n-propyl dithionopyrophosphate. *J. Pharmacol. Exp. Ther.* 106: 382 (1952).
14. Doull, J., Petersen, D. F., and DuBois, K. P., Effects of x-irradiation on *Citellus tridecemlineatus*. *Fed. Proc.* 11: 340 (1952).
15. DuBois, K. P., Doull, J., Deroin, J., and Cummings, O. K. Studies on the toxicity and mechanism of action of some new insecticidal thionophosphates. *Arch. Ind. Hyg. Occup. Med.* 8: 350 (1953).
16. DuBois, K. P., Doull, J., Okinaka, A. J., and Coon, J. M. Studies on the toxicity and pharmacological actions of symmetrical and unsymmetrical diethyl bis(dimethylamido) pyrophosphate. *J. Pharmacol. Exp. Ther.* 107: 464 (1953).
17. Doull, J., and DuBois, K. P. Influence of hibernation on survival time and weight loss of x-irradiated ground squirrels. *Proc. Soc. Exp. Biol. Med.* 84: 367 (1953).
18. Doull, J., and DuBois, K. P., Effect of central nervous system stimulants on x-ray lethality. *Fed. Proc.* 12: 316 (1953)
19. Doull, J. Studies on the cholinesterase activity of tissues of irradiated animals. *J. Pharmacol. Exp. Ther.* 110: 14 (1954).
20. Okinaka, A. J., Doull, J., Coon, J. M., and DuBois, K. P. Studies on the toxicity and pharmacological actions of bis(dimethylamido) fluorophosphate (BFP). *J. Pharmacol. Exp. Ther.* 112: 231 (1954).
21. Fitch, F. W., Doull, J., and Wissler, R. W. Histopathology of the irradiated hibernating ground squirrel (*Citellus tridecemlineatus*). *A.M.A. Arch. Path.* 60: 644 (1955).

22. Doull, J., and Hasagewa, A. T., Effect of increased environmental temperature on radiation lethality in rats. *Fed. Proc.*, 14: 333 (1955).
23. Doull, J., Hasegawa, A. T., and DuBois, K. P., Effect of decreased barometric pressure on radiation lethality in rats. *Fed. Proc.* 15: 418 (1956)
24. Hallesy, D. W., and Doull, J. Acute and chronic toxicity of orange B and orange 1 in rats. *J. Pharmacol. Exp. Ther.* 116: 26 (1956).
25. Hallesy, D. W., and Doull, J., Effect of whole body x-irradiation on the free amino acid content of rat plasma. *Fed. Proc.* 15: 433 (1956).
26. Doull, J. Irradiation and survival in hibernating animals. *Med. Sci.* 1: 27 (1956).
27. Landahl, H. D., Hasegawa, A. T., and Doull, J. Effect of whole body x-irradiation on the heat production and temperature regulation of rats and mice. *Radiat. Res.* 5: 488 (1956).
28. Noble, J. F., Plzak, V., Dowben, R. M., and Doull, J., The influence of several thiol compounds on the mortality and survival time of x-irradiated mice. *Fed. Proc.* 16: 326 (1957).
29. Noble, J. F., Hasegawa, A. T., and Doull, J., Lens opacities in mice exposed to chronic gamma and fast neutron irradiation. *Fed. Proc.* 17: 399 (1958).
30. Burger, A., Beasley, J. G., Margerison, R. B., Doull, J., Plzak, V., and Noble, J. F. Synthesis and radioprotective properties of chlorinated O-dialkyl aminopropionamideo- and O-dialkylaminopropylaminodiphenyl sulfide derivatives. *J. Med. Pharm. Chem.* 1: 171 (1959).
31. Doull, J., Plzak, V., and Brois, S. J. Protective effects of various phenone derivatives against radiation lethality in x-irradiated mice. *Radiat. Res.* 11: 439 (1959).
32. Noble, J. F., Hasewaga, A. T., and Doull, J., Life span mice exposed to chronic gamma and fast neutron irradiation. *Fed. Proc.*, 18: 427 (1959).

33. Noble, J. F., Hasegawa, A. T., Landahl, H. D., and Doull, J. Effect of fractionation on survival of mice following chronic exposure to x-irradiation. *Radiat. Res.* 11: 457 (1959).
34. Doull, J., and Tricou, B. J., Studies on the radioprotective effect of serotonin in mice. *Fed. Proc.*, 20: 400 (1961).
35. Doull, J. Chemical antidotes for radiation injury. *Arch. Environ. Health* 2: 284 (1961).
36. Plzak, V., and Doull, J., Radioprotective effects of dithiooxamide derivatives against x-ray exposure in mice. *Fed. Proc.*, 20: 400 (1961).
37. Vesselinovitch, D., DuBois, K. P., Fitch, F. W., and Doull, J. Mammalian toxicity and histopathologic effects of 2,6-dibutyl-4-nitrophenol. *Toxicol. Appl. Pharmacol.* 3: 713 (1961).
38. Doull, J., Plzak, V., and Root, M. Protection against chronic radiation lethality in mice. *Radiat. Res.* 16: 578 (1962).
39. Doull, J., Plzak, V., and Brois, S. J. A survey of compounds for radiation protection. USAF School of Aerospace Med. Report, No. 62-29: 1 (1962).
40. Doull, J., Plzak, V., and Root, M. Toxicity and radioprotective activity of p-aminopropiophenone in mice. *Radiat. Res.* 16: 588 (1962).
41. Plzak, V., and Doull, J. Toxicity and radioprotective effects of acetyl p-aminopropiophenone in mice. *Radiat. Res.* 19: 228 (1963).
42. Oldfield, D. G., Doull, J., Plzak, V., Hasegawa, A., and Sandberg, A. Protection of proton-irradiated mice with p-aminopropiophenone (PAPP) and 2-mercaptoethylamine (MEA). *Radiat. Res.* 19: 229 (1963).
43. Vesselinovitch, D., Wissler, R. W., and Doull, J., Vascular lesions produced by the combined effects of diet and x-irradiation. *Fed. Proc.*, 22: 6 (1963).
44. Plzak, V., Hasegawa, A. T., and Doull, J. Radioprotective effects of cyclobutane derivatives in mice. *Radiat. Res.* 22: 224 (1964).

45. Dilley, J., Vesselinovitch, D., and Doull, J., Therapeutic effect of a thiazolidine derivative against x-ray exposure in mice. *Fed. Proc.* 23: 570 (1964)
46. Vesselinovitch, D., and Doull, J. Effect of adding Co-ral to the diet of rats and mice. *Lab. Anim. Care* 14: 325 (1964).
47. Doull, J., Oldfield, D. G., and Plzak, V. Chemical protection against high energy proton radiation in mice. *Blood, The Journal of Hematology* 24: 638 (1964).
48. Oldfield, D. G., Doull, J., and Plzak, V. Chemical protection against 440 Mev protons in mice treated with mercaptoethylamine (MEA) or p-aminopropiophenone (PAPP). *Radiat. Res.* 26: 12 (1965).
49. Oldfield, D. G., Doull, J., and Plzak, V. Chemical protection against absorber moderated protons. *Radiat. Res.* 26: 25 (1965).
50. Plzak, V., and Doull, J. Dose reduction factors (DRF) for various radioprotective agents in mice. *Radiat. Res.* 25: 228 (1965).
51. Plzak, V., and Doull, J. Comparative subacute oral toxicity of some organic phosphates in rats and dogs. *Toxicol. Appl. Pharmacol.* 8: 350 (1966).
52. Goepf, R. A., Fitch, F. W., and Doull, J. The use of parenteral chemicals for protection against oral radiation death in mice. *Radiat. Res.* 31: 149 (1967).
53. Doull, J. Pharmacologic responses in irradiated animals. *Radiat. Res.* 30: 333 (1967).
54. Vesselinovitch, D., Wissler, R.W. and Doull, J., Experimental production of atherosclerosis in mice. 1. Effect of various synthetic diets and radiation on survival time, *J. Atherosclerosis Res.*, 8(3), (1968).
55. Durie, R. H., and Doull, J., Factors influencing the toxicity of p-aminopropiophenone. *Pharmacologist* 10: 212 (1969).
56. Plzak, V., and Doull, J. A further survey of compounds for radiation protection. USAF School of Aerospace Med. Report, #SAM TR 69-1: 1 (1969).

57. Doull, J., et. al., Guidelines for estimating toxicologically insignificant levels of chemicals in food, Report of the Food Protection Committee, Food Nutrition Board, Nat. Res. Council/National Acad. Sci., Nat Acad. Press, Washington, D. C., (1969).
58. Doull, J., Use of case histories, video tapes and computer teaching, *Pharm.* 11: 212 (1969).
59. Goldstein, G. M., and Doull, J., Effect of hyperbaric oxygen on p-aminopropiophenone and sodium nitrite induced methemoglobinemia. *Pharm.* 12: 242 (1970).
60. Goldstein, G. M., and Doull, J. Treatment of nitrite-induced methemoglobinemia with hyperbaric oxygen. *Proc. Soc. Exp. Biol. Med.*, 138: 137 (1971).
61. Hunter, A., Klaassen, C.D., and Doull, J., Species differences in the plasma disappearance and biliary excretion of procain amide ethobromide, *Proc. Soc. Exp. Biol. Med.*: 139, 137-139 (1972).
62. DeFeo, F. G., Fitzgerald, T. J., and Doull, J., Synthesis and biologic activity of para-hydroxyamino propiophenone. *Tox. Appl. Pharm.*, 22: 301 (1972).
63. Doull, J. The effect of physical environmental factors on drug response. In *Essays in Tox.* (W. J. Hayes, ed.), Chapter 2, Academic Press, New York, N.Y. (1972).
64. Azarnoff, D., Doull, J., Hurwitz, A., Walaszek, E. J. and Rising, J. D., Effective drug utilization by the practicing physician, *J. Kansas Medical Society*: 73, 105-107 (1972).
65. Goldstein, G. M., and Doull, J., The use of hyperbaric oxygen in the treatment of p-aminopropiophenone-induced methemoglobinemia. *Tox. Appl. Pharm.*, 26: 247 (1973).
66. Fitzgerald, T. J., Doull, J., and DeFeo, F.G., Radioprotective activity of p-aminopropiophenone. *Rad. Res.*, 55: 547 (1973).

67. Pazdernik, T. L., Uyeki, E. M., and Doull, J., Carrier and hapten antibody producing cells in vitro. 1. Cytokinetics, Proc. Soc. Exp. Med.: 144, 232-237 (1973).
68. DeFeo, F. G., Fitzgerald, T. J., and Doull, J., Toxicity, methemoglobin-producing activity and partition coefficients of para substituted aniline derivatives. Pharm., 15: (1973).
69. Hurwitz, A., and Doull, J. Effect of irradiation on gastrointestinal drug absorption. Radiat. Res. 59: 606 (1974).
70. Doull, J. Factors influencing toxicity. In Casarett and Doull's Toxicology: The Basic Science of Poisons (J. Doull and L. J. Casarett, eds.), Chapter 5, Macmillan Publishing Co., Inc., N.Y. (1975).
71. Doull, J., and Casarett, L. J. (eds.). Casarett and Doull's Toxicology: The Basic Science of Poisons, Macmillan Publishing Co., Inc., N.Y. (1975).
72. Doull, J. Evaluation of the toxicity of food additives. Proc. Sixth Internat. Congress of Pharmacol. 6: 115 (1975).
73. Doull, J. Pesticide-induced delayed neurotoxicity. In Pesticide Induced Delayed Neurotoxicity (R. L. Baron, ed.), EPA 600/1-76-025, Chapter 8, Washington, D.C. (1976).
74. Doull, J. The treatment of insecticide poisoning. In Insecticide Biochemistry and Physiology (C. A. Wilkerson, ed.), Chapter 16, Plenum Press, New York, N.Y. (1976).
75. Doull, J., and Walaszek, E. J. The use of Computer Assisted Teaching Systems in Pharmacology. In Computers in Medical Education (E. DeLand, ed.), Chapter 12, Plenum Pub. Co., New York, N.Y. (1977).
76. Doull, J., Clinical toxicology aspects of controlled release pesticide formulations. ACS Symposia Series, Herbert Scher Ed., 53: 54 (1977).
77. Doull, J., Assessment of Food Safety. Fed. Proc.,: 37, 2594-2597 (1978).

78. Nelson, S. R., Doull, J., Tockman, B. A., Cristiano, P.J., and Samson, F. E., Regional brain metabolism changes induced by acetylcholinesterase inhibitors, *Brain Research*, 157: 186 (1978).
79. Mattis, P. A., Standert, F. G., D'Aguanno, M., Doull, J., Newberne, J. W., and Zapp, J. A. Jr., Evaluation of safety of chemical agents in human subjects, *Toxicology and Applied Pharmacology*: 32, 449-450 (1980).
80. Doull, J., Klaassen, C. D., and Amdur, M. O. (eds.). *Casarett and Doull's Toxicology: The Basic Science of Poisons*, 2nd Ed., Macmillan Publishing Co., Inc., N.Y. (1980).
81. Klaassen, C. D., and Doull, J. Evaluation of safety: toxicologic evaluation. In *Casarett and Doull's Toxicology: The Basic Science of Poisons* (J. Doull, C. D. Klaassen and M. Amdur, eds.), pp. 28-55, Macmillan Publishing Co., Inc., N.Y. (1980).
82. Walaszek, E. J., Nelson, S., Doull, J., Fishman, S. S., and Killiam, K. K. Jr., Computerized academe: an update of "CATS" in pharmacology teaching, *Proc. Western Pharmacology Society*,: 23, 127 (1980).
83. Misawa, M., Doull, J., and Uyeki, E. M. Mechanisms of teratology induced by organophosphates. 8th Int. Congress of Pharmacology, July 19-24, Tokyo, Japan (1981).
84. Eigenberg, D., Pazdernik, T., and Doull, J. Hemoperfusion: a possible alternative method for treating organophosphate insecticide poisoning. *The Toxicologist* 1: 136 (1981).
85. Misawa, M., Doull, J., Kitos, P. A., and Uyeki, E. M. Teratogenic effects of cholinergic insecticides in chick embryos. I. Diazinon treatment on acetylcholinesterase and choline acetyltransferase activities. *Toxicol. Appl. Pharmacol.* 57: 20-29 (1981).
86. Doull, J., Food safety and toxicology, in *Food Safety*, H. R. Roberts Ed., Chapter 7: 295 (1981).

87. Misawa, M., Doull, J., and Uyeki, E., Teratogenic effects of cholinergic insecticides in chick embryos, III Development of cartilage and bone, *Jour. Tox. and Env. Health* 10: 551 (1982).
88. Uyeki, E. M., Doull, J., Cheng, C. C., and Misawa, M., Teratogenic and anti-teratogenic effects of nine nicotinamide analogs in chick embryos, *J. Toxicol. Envir. Health* :9, 963-973 (1983).
89. Doull, J. Assessing pesticide toxicity in man and correlations with laboratory animal studies. In J. Miyamoto et al. (ed.). *IUPAC Pesticide Chemistry*, Kyoto, Japan, Pergamon Press (1983).
90. Eigenberg, D. A., Pazdernik, T. L., and Doull, J., Hemoperfusion and pharmacokinetic studies with methamidophos in the rat, *Fund. Appl. Tox* 3: 496 (1983).
91. Nisho, A., Nakanishi, S., Doull, J., and Uyeki, E. M., Enhanced chondrocytic differentiation in chick limb bud cultures by inhibitors of poly (ADP-ribose) synthetase, *Biochem. Biophys. Res. Communications* : 111, 750-759 (1983).
92. Doull, J (Chair). et. al., The relevance of mouse liver hepatoma to human carcinogenic risk, *Report of an international expert committee to The Nutrition Foundation*, September (1983).
93. Eigenberg, D. A., Pazdernik, T. L., and Doull, J., Hemoperfusion and pharmacokinetic studies with parathion and paroxon in the rat and dog, *Drug. Metabolism and Disposition*: 11, 366- 370 (1983).
94. Doull, J. The past, present and future of toxicology. *Pharm. Rev.* 36: 15S-18S (1984).
95. Doull, J (chair) et. al., Report of the NTP ad hoc panel on chemical carcinogenesis testing and evaluation, *Report to the Board of Scientific Councilors of the National Toxicology Program*, (1984).
96. Doull, J. (co-chair) et. al., *Toxicity testing; Part 2, strategies to determine needs and priorities*, Nat. Acad. Press., Washington, D.C., (1984).

97. Doull, J., *NTP Blue Ribbon Panel Report; Report from the chairman, Toxicology Forum.*, (1985).
98. Walaszek, E. J., and Doull, J., Use of computers in the teaching of pharmacology, *Physiologist* : 28, 419-421 (1985).
99. Doull, J., The Future of Toxicology, *Vet. Hum. Toxicology*, 27(3) 210-2 (1985).
100. Klaassen, C. D., Amdur, M. O., and Doull, J. (eds.). *Casarett and Doull's Toxicology: The Basic Science of Poisons*, 3rd Ed., Macmillan Publishing Co., Inc., N.Y. (1986).
101. Doull, J., and Bruce, M. C. Origin and scope of toxicology. In *Casarett and Doull's Toxicology: The Basic Science of Poisons* (C. D. Klaassen, M. O. Amdur and J. Doull, eds.), pp. 3-10, Macmillan Publishing Co., Inc., N.Y. (1986).
102. Doull, J., *Introduction to Toxic Substances and Human Risk*, Tardiff, R. G., and Rodricks, J. V., Eds., pp 3, Plenum Publishing Co., Inc. (1987).
103. Doull, J., The mouse in safety evaluation, *Arch. Tox. Suppl.* 10: 3 (1987).
104. Doull, J.(Chair), *Complex Mixtures*, Committee on Methods for the In Vivo Toxicity Testing of Complex Mixtures, National Research Council, National Academy of Sciences, National Academy Press, Wash. D. C., (1988).
105. Doull, J., *Understanding Risk, Scientific Sources of Confusion*, *Health and Environment Digest* 4: No. 2, 3-5 (1990).
106. Zimmerman, R., Borzelleca, J., Crump, K., Doull, J., Gardner, D., Gardner, H., Hughes, D., Munro, I.c., Parke, D.M., Rodricks, J., Tardiff, R.G., and Travis, C., (Eds) *Governmental Management of Chemical Risk*, Lewis Pub., (1990)
107. Woods, L. A., and Doull, J. Gras evaluation of flavoring substances by the expert panel of FEMA. *Reg. Tox. Pharm.* 14: 48-58 (1991).
108. Amdur, M. O., Doull, J. and Klaassen, C. D. (eds), *Casarett and Doull's Toxicology: The Basic Science of Poisons*, 4th Ed., Pergamon Press, Inc., New York, (1991).

109. Gallo, M. and Doull, J. History and Scope of Toxicology, in Casarett and Doull's Toxicology: The Basic Science of Poisons (Amdur, M. O., Doull, J. and Klaassen, C. D. eds), pp 3-11, Pergamon Press Inc., New York, (1991).
110. Levine, R. S. and Doull, J. Global estimates of acute pesticide morbidity of mortality. *Rev. Env. Contam. and Toxicol.*: 129, 29-50 (1992).
111. Doull, J. Toxicology and exposure limits. *Appl. Occup. Environ. Hyg.* 7: 583-585 (1992).
112. Doull, J. Assessment of acute toxicity of pesticides on humans and domestic animals. In *Methods to Assess Adverse Effects of Pesticides on Non-target Organisms* (R. G. Tardiff, ed.), Chapter 10, John Wiley & Sons Ltd., West Sussex, England (1992).
113. Doull, J., et. al., Task Force Report on Water Quality: Agriculture's Role. *Cast Report 120*, Ames Iowa (1992)
114. Waddell, W. J., Borzelleca, J. F., Doull, J., Grasso, P, LeBourhis, B., Levy, P. S., and Tamburo, C. H., Alcohol and Cancer, *Br. J. Cancer*: 66, 1200 (1992).
115. Doull, J., Hazard and dose response assessment, Conference on the risk assessment paradigm after 10 years., Wright Patterson, OH, April 5-8 (1993).
116. Doull, J., Extrapolation of animal results to man, *J. Toxicol. Sci.*, 18, 69-71 (1993).
117. Rozman, K. K., Roth, W. L., Greim, H., Stahl, B. U. and Doull, J. Relative potency of chlorinated dibenzo-p-dioxins (CDDs) in acute, subchronic and chronic (carcinogenicity) toxicity studies: implications for risk assessment of chemical mixtures. *Toxicology* 77: 39-50 (1993).
118. Zapp, J. A., and Doull, J., Industrial Toxicology: Retrospect and Prospect, in *Patty's Industrial Hygiene and Toxicology*, Clayton G. D., and Clayton, F. E., Eds. Chap. 1 Vol. 2, Part 1: 1 (1993).

119. Andersen, R.A., Colton, T., Doull, J., Marks, J. G., and Smith, R. G., Designing a biological monitoring program to assess community exposure to chromium: Conclusions of an Expert Panel, *J. Tox. Env. Health* 40: 555-583, (1993).
120. Doull, J., Principles of risk assessment: Overview of the risk assessment process, Proceeding of Conf. on Chemical Risk Assessment in the DoD, Science, Policy and Practice, AL-TR-1993-001, NMRI-93-10, (1993).
121. Doull, J., The ACGIH approach and practice, *Appl. Occup. Environ. Hyg.*, 9(1): 23 (1994).
122. Munro, I. et. al., Interpretive Review of the Potential Adverse Effects of Chlorinated Organic Chemicals on Human Health and the Environment; Report of an Expert Panel. *Reg. Toxicology and Pharmacology*, 20: part 2, 1-1056 (1994).
123. Craun, G. F., Bull, R. J., Clark, R. M., Doull, J., Grabow, W., Marsh, G. M., Okun, D. A., Regli, S., Sobsey, M. D., and Symonds, J. M., Balancing chemical and microbial risks of drinking water; Part 1, Benefits and potential risks, *J. Water SRT* 43 #4: p 193 (1994).
124. Craun, G. F., Bull, R. J., Clark, R. M., Doull, J., Grabow, W., Marsh, G. M., Okun, D. A., Regli, S., Sobsey, M. D., and Symonds, J. M., Balancing chemical and microbial risks of drinking water; Part 2, Managing the risks, *J. Water SRT* 43 #5: p207 (1994).
125. Doull, J., et. al., Science and Judgement in Risk Assessment, National Academy Press, (1994).
126. Doull, J., Chlorinated organic chemicals: Occupational aspects, *Toxicology Forum.*, Berlin Germany. Sept. 19-21 (1994).
127. Neal, R. A., and Doull, J., Commentary: The Discipline of Toxicology, *Fundamental and Applied Toxicology* 24: 151-153, (1994).
128. Doull, J., Recommended Limits for Exposure to Chemicals, in Casarett and Doull's *Toxicology: The Basic Science of Poisons*, 5th Ed., Klaassen, C. D. ed, Appendix A, McGraw-Hill, New York, NY (1995).

129. Doull, J., Keynote Address: Improving the science and art of risk assesment, *Drug Metabolism Reviews*: 28 (1&2) , 1-7, (1996).
130. Smith, R.L., Newberne, P., Adams, T.B., Ford, R.A., Halligan, J.B., and the FEMA Expert Panel, GRAS Flavoring Substances 17, *Food Technol.*:50(10), 72-81 (1996).
131. Doull, J., Is it safe? *Vet. and Human Toxicol.*, 38: 456-458 (1996).
132. Smith, R.L., Newberne, P., Adams, T.B., Ford, R.A., Halligan, J.B., and the FEMA Expert Panel, Correction in GRAS Flavoring Substances 17, *Food Technol.*:51(2), 22 (1996).
133. Rozman, K. K., Kerecsen, L., Viluksela, M. K., Osterle, D., Deml, E., Viluksela, M., Stahl, B.U., Greim, H., and Doull, J., A toxicologist's view of cancer risk assessmenmt, *Drug Metabolism Reviews*:28 (1-2), 28-52, (1996).
134. Doull, J., Rozman, K. K., and Lowe, M. C., Hazard evaluation in risk assessment: What ever happened to sound scientific judgement and weight of evidence?, *Drug Metabolism Reviews*:28 (1&2), 285-289, (1996).
135. Doull, J., Toxicology in the 21th Century, *Science (Kexue)*: 48 No. 2, 14-16 (1996).
136. Doull, J., Is it Safe?, CIIT Founder's Award Address, *CIIT Activities*, Vol 16, May (1996).
137. Doull, J., et. al. ,IOM Committee to study in theractions of drugs, biologics and chemicals in the US Military Forces, *Interactions of Drugs, Biologics and Chemicals in the U.S. Military Forces*. (Eds. Petersdorf, R.G., Page, W.E., and Thaul, S.), NAS Press, Washington, D.C., (1996).
138. Omenn, G. S., Kessler, A. C., Anderson, N. T., Chiu, P., Doull, J., Goldstein, B., Lederberg, J., McGuire, S., Rall, D., Weldon, V. V.,*Risk Assessment and Risk Management in Regulatory Decision-Making*, Draft Report of the Commission on Risk Assessment and Risk Management, June (1996).

139. Doull, J., Specificity and dosimetry of toxicologic responses, *Reg. Tox and Pharm.*, 24, S55-57, (1996).
140. Doull, J., *Cancer Prevention: What really matters. Fed. Proc.*, 44 (1996).
141. Doull, J., How we use epidemiologic and toxicologic information to help us decide questions regarding the safety of chemicals, *Sustain*, 1: 12 (1996).
142. Doull, J., Risk Assessment, Improving the Science and the Art in Proceeding of the Arkansas Toxicology Symposium Honoring the Contributions of John Doull Ph.D., M.D., Little Rock Arkansas, Nov. 10, 1994., *Drug Metabolism Rev.*, 28, 1-255 (1996).
143. Adams., T. B., Hallagan, J. B., Putnam, J. M., Gierke, T. L., Doull, J., Munro, I. C., Newberne, P., Portoghese, P. S., Smith, R. L., Wagner, B. M., Weil, C. S., Woods, L. A., and Ford, R. A., The FEMA GRAS assessment of alicyclic substances used as flavor substances, *Food, Chem. Toxicol.*, 34, 763-828 (1996).
144. Smith, R. L., Newberne, P., Adams., T. B., Ford, R. A., Hallagan, J. B., and the FEMA Expert Panel, Recent Progress in Consideration of Flavour Ingredients Under the Food Additive Ammendments : #17 Gras Substances. (1997).
145. Doull, J., Back to Basics, American College of Toxicology Award Lecture, *Int. J. Toxicology* , 16, 191 (1997).
146. Risk Commission, U.S. Commission on Risk Assessment and Risk Management Final Report, Vol 1, Framework for Environmental Health Management, GPO #005-000-00567-2, Washington, D.C., U. S. Commission on Risk Assessment and Risk Management (1997).
147. Doull, J., *Mixtures in Encyclopedia of Toxicology*, R. Wexler Ed., Academic Press, San Diego CA (1997).
148. Risk Commission, U.S. Commission on Risk Assessment and Risk Management Final Report, Vol 2., *Risk Assessment and Risk Management in Regulatory Decision Making*, GPO #055-000-00568-1, Washington D. C., U. S. Commission on Risk Assessment and Risk Management, (1997).

149. Adams, T. B., Doull, J., Goodman, J. I., Munro, I. C., Newberne, P., Portoghese, P. S., Smith, R. L., Wagner, B. M., Weil, C. S., Woods, L. A., and Ford, R. A., The FEMA GRAS Assessment of Furfural Used as a Flavor Ingredient, *Food and Chem. Toxicol.*, Aug 35(8), 739-751 (1997).
150. Rozman, K., and Doull, J., *General Principles of Toxicology, Chapter 1 in Environmental Toxicology* (J. Rose Ed), Gordon & Breach, Amsterdam (1998).
151. Newberne, P., Smith, R. L., Doull, J., Goodman, J.I., Munro, I.C., Portoghese, P.S., Wagner, B. M., Weil, C. S., Woods, L.A., Adams, T. B., Halligan, J.B., and Ford, R.A., GRAS Flavoring Substances 18, *Food Technol.*; 52(9), 65-92 (1998).
152. Byrd, D.M., Allen, D. O., Beamer, R. L., Beahc, H. R., Bylund, D. B., Doull, J., Fleming, W.W., Guengerich, F. P., Hornbrook, R., Lasagna, L., Lum, B. K., Michaelis, E. K., Morgan, E. T., Polan, S. O., Rozman, K. K., Smith, J. B., Swanson, H.I., Waddell, W., and Wilson, J. D., The dose response model for dioxin, *Risk Analysis*, Feb 18(1), 1-2 (1998).
153. Adams, T.B., Greer, D.B., Doull, J., Munro, I.C., Newberne, P., Portoghese, P.S., Smith, R. L., Wagner, B. M., Weil, C. S., Woods, L. A., and Ford, R. A., The FEMA GRAS assessment of lactones used as flavor ingredients., *Food and Chem. Toxicol.*, Apr 36(4), 249278 (1998).
154. Newberne, P, Smith, R. L., Doull, J., Goodman, J. I., Munro, I.C., Portoghese, P. S., Wagner, B. M., Weil, C., S., Woods, L. A., Adams, T.,B., Lucas, C.D., and Ford, R.A., The FEMA GRAS assessment of trans-anethole used as a flavoring substance, *Food Chem. Toxicology*, Jul (37)7 789-811 (1999).
155. Doull J., Cattley, R., Elcombe, C., Lake, B. G., Swenberg, J., Wilkinson, C., Williams, G., and van Gemert, M., A cancer risk assessment of di(2-ethylhexyl)phthalate: Application of the new US EPA Risk Assessment Guidelines., *Regulatory Toxicol. Pharmacol.*, June (29)3, 327-357 (1999).
156. Newberne, P., Smith, R. L., Doull, J., Goodman, J.I., Munro, I.C., Portoghese, P.S., Wagner, B. M., Weil, C. S., Woods, L.A., Adams, T. B., Halligan, J.B., and Ford, R.A., Correction to GRAS Flavoring Substances 18; *Food Technol.*;53 (3), 104 (1999).

157. Hopke, P.K., Borak, T.B., Doull, J., Cleaver, J. E., Eckerman, K. F., Gunersen, L. C. S., Harley, N.H., Hess, C. T., Kinner, N. E., Kopecky, K. J., McKone, T. E., Sextro, R.G., and Simon, S.L., Health risks due to radon in drinking water., *Envir. Sci. Technol.*, 34 No.8, 921-926, Nov. (1999).
158. Doull, J., Risk Characterization, Introduction, *Inhal. Tox.*, 11, 573 (1999)
159. Rozman, K. K., and Doull, J., Hormesis, regulation, toxicity and risk assessment. *Belle Newsletter*, 8(1), 2-6 (1999).
160. Doull, J., Profiles in Toxicology, Kenneth Patrick DuBois (August 9, 1917-January 24, 1973), *Toxicological Sciences*, 54, 1-2 (2000)
161. Doull, J., A window of opportunity for toxicology, Chapter 1 in *Toxicology and Risk Assessment*, H. Salem and E. J. Olajos Eds., Taylor and Francis, Philadelphia, (2000).
162. Newberne, P., Smith, R.L., Doull, J., Feron, V.J., Goodman, J.I., Munro, I.C.,Portoghese, P.S., Waddell, W.J., Wagner, B.M., Weil, C.S., Adams, T.B., and Halligan J.B.,GRAS Flavoring Substances 19, *Food Technol.*; 54(6), 66-84 (2000).
163. Doull, J., and Rozman, K.K., Using Haber's Law to define the Margin of Exposure, *Toxicology*, 149,1-2 (2000).
164. Rozman, Karl K., and Doull, J., Dose and Time as Variables of Toxicity,*Toxicology*, 149, 169-178 (2000).
165. Krewski. D., et. al., Acute Exposure Guideline Levels for Selected Airborne Chemicals, Vol. 1., Nat. Acad. Press., Washington, D.C., (2000).
166. Storm, J.E., Rozman, K.K., and Doull, J., Occupational exposure limits for 30 organophosphate pesticides based on inhibition of red blood cell acetylcholinesterase. *Toxicology*, 150 (1-3), 1-29 (2000).
167. Rozman, K. K., and Doull, J. The Role of Time as a Quantifiable Variable of Toxicity and the Experimental Conditions when Haber's $c \times t$ Product Can Be Observed: Implications for Therapeutics, *J. Pharmacol. & Therap.*, 296 #3, (2001).

168. Doull, J., *Toxicology Comes of Age*, *Ann. Rev. Pharm. Tox.*, 41, 1-21 (2001)
169. Rozman, K.K., and Doull J., *Paracelsus, Haber and Arndt, Toxicology*, 160 (1-3), 191-6 (2001).
170. Rozman, K. K., Doull, J., and Hayes, W. J., *Dose, Time and Other Factors Influencing Toxicity*. Chapter 2 in *Handbook of Pesticide Toxicology*, R. Krieger Ed., Academic Press, San Diego (2001).
171. J. Doull, *Recommended Limits for Occupational Exposure to Chemicals*, in *Casarett and Doull's Toxicology*, Curtis Klaassen Ed. , McGraw Hill, New York, (2001).
172. Krewski, D. et. al., *Standard Operating Procedures for Developing Acute Exposure Guidelines for Hazardous Chemicals*, Nat. Acad. Press, Washington DC. (2001).
173. Smith, R. L., Doull, J., Feron. V.J., Goodman, J. I., Munro, I.C., Newberne, P.M., Portoghese, P.S., Waddell, W.J., Wagner, T.B., Adams., T.B., and McGowen, M.M., *GRAS Flavoring Substances 20*, *Food Technology*; 55 #12, 34-55 (2001).
174. Morrow, P., E., Bruce, M. C., and Doull, J., *Profiles in Toxicology*, Louis James Casarett, *Tox. Sci.*, 63, 151-2 (2001).
175. Smith, R.L., Doull, J., Feron, V.J., Goodman, J. I., Marnett, L.J., Munro, I.C., Newberne, P., Portoghese, P.S., Waddell, W.J., Wagner, B.M., and Adams, T.B., *The FEMA GRAS assessment of pyrazine derivatives used as flavor ingredients*, *Food Chem. Toxicol.*: 40 (4), 429-451 (2002)
176. Haighton, L.A., Hlywka, J.J., Doull, J., Kroes, R.L., Lynch, B.S., and Munro, I. C., *Evaluation of the Carcinogenicity of Bisphenol A to Rodents and Relevance of Findings to Humans*, *Tox Sci.*, 66, 185 (2002)
177. Haighton, L.A., Hlywka, J.J., Doull, J., Kroes, R., Lynch, B.S., and Munro, I.C., *An Evaluation of the Possible Carcinogenicity of Bisphenol A to Humans*, *Regul. Tox. Pharm.*: 35, 238-254 (2002)

178. Munro, I.C., Haighton, L.A., Hlywka, J.J., Lynch, B.S., Doull, J., and Kroes, R., Carcinogenicity Bioassay of Bisphenol A., *Toxicol. Sci.* 56, 356 (2002)
179. Munro, I.C., Haighton, L.A., Hlywka, J.J., Lynch, B.S., Doull, J., and Kroes, R., Response to Carcinogenicity of Bisphenol A., Revisited, *Toxicol. Sci.*, 70, 283-285 (2002)
180. Rozman, K.K. and Doull, J.: Derivation of an occupational exposure limit (OEL) for n-Propyl Bromide. *App. Occ. Env. Hyg.* (in press), 2002.
181. Munro, I.C., Haighton, L.A., Hlywka, J.J., Lynch, B.S., Doull, J., and Kroes, R., Response to ; Does Exposure to Bisphenol A Represent a Human Health Risk?, *Reg. Toxicol. Pharm.*, 37, 409-10 (2003)
182. Smith, R.L., Cohen, S.M., Doull, J., Feron, V.J., Goodman, J.L., Marnett, L.J., Portoghese, P.S., Waddell, W.J., Wagner, B.M., and Adams, T.B., Grass Flavoring Substances 21, *Food Technology*, 57, #5, 1-11, (2003)
183. Doull, J., The Red Book and Other Risk Assessment Milestones, *Hum. And Ecolog. Risk Assessment*, 9, 1229-1238 (2003)
184. Golden, R., Doull, J., Waddell, W., and Mandel, J., Potential Human Cancer Risks from Exposure to PCB's: A Tale of Two Evaluations, *Crit. Rev. Toxicol.*, 33(5), 543-580 (2003)
185. Smith, R.L., Doull, J., Feron, V.J., Goodman, J. I., Marnett, L.J., Munro, I.C., Newberne, P., Portoghese, P.S., Waddell, W.J., Wagner, B.M., and Adams, T.B., Safety assessment of methyl eugenol and estragole used as flavor ingredients, *Food Chem. Toxicol.*, in press.
186. Smith, R.L., Doull, J., Feron, V.J., Goodman, J. I., Marnett, L.J., Munro, I.C., Newberne, P., Portoghese, P.S., Waddell, W.J., Wagner, B.M., and Adams, T.B., The FEMA GRAS Assessment of Aliphatic and Aromatic Sulfides and Thiols used as Flavor Ingredients, *Food Chem. Toxicol.*, submitted.
187. Haighton, L.A., Hlywka, J.J., Doull, J., Kroes, R.I., Lynch, B.S., and Munro, I. C., Letter to the Editor in response to the James Huff letter.

CURRICULUM VITAE

Dr. Eric A. Johnson

Education:

Positions:

Awards and Other Professional Activities

1975 to 1976, President's Undergraduate Fellowship, University of California-Davis
1976, Western United States Undergraduate Research Award, Institute of Food Technologists
1976, Jastro-Shields Scholarship, University of California-Davis
1977, Sigma XI Grant-in-Aid of Research
1977 to 1978, SeaGrant Graduate Fellowship
1980 to 1981, Department of Energy Graduate Fellowship
1981 to 1983, National Distiller's Graduate Fellowship
1982 to 1983, National Science Foundation Research Grant, 1982 - 1983.
1996, Chair Elect, Division P (Food Microbiology), American Society for Microbiology
1999, Educator Award, International Association for Food Protection
2000, Elected to Fellowship in the American Academy of Microbiology
2001 to 2005, Editor for Applied and Environmental Microbiology
2001, Appointed to AIBS panel to review DOD Toxicology Program, Fort Detrick, Maryland
2001, Involved in CDC program for bioterrorism preparedness
2001-2002, NIH study panel for bioterrorism related research proposals
2002-present, NIH-NIAID review panel, Small Business: Infectious Diseases and Microbiology
2002-present, NIH-NIAID review panel, Bacterial Biodefense
2004, ASM Waksman Foundation for Microbiology Lecturer

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Journal publications

- Johnson, E.A., D.E. Conklin and M.J. Lewis. 1977. The yeast *Phaffia rhodozyma* as a dietary pigment source for salmonids and crustaceans. J. Fish. Board Can. 34:2417-2421.
- Johnson, E.A. and H.J. Phaff. 1978. *Rhodotorula fujisanensis*, a new taxonomic combination. Curr. Microbiol. 1:223-225.
- Johnson, E.A., T.G. Villa, M.J. Lewis and H.J. Phaff. 1978. Simple method for the isolation of astaxanthin from the yeast *Phaffia rhodozyma*. Appl. Environ. Microbiol. 35:1155-1159.
- Johnson, E.A., T.G. Villa, M.J. Lewis, H.J. Phaff. 1979. Lysis of the cell wall of the yeast *Phaffia rhodozyma* by a lytic enzyme complex from *Bacillus circulans* WL-12. J. Appl. Biochem. 1:273-282.
- Johnson, E.A. and M.J. Lewis. 1979. Astaxanthin formation by the yeast *Phaffia rhodozyma*. J. Gen. Microbiol. 115:173-183.
- Johnson, E.A., M.J. Lewis, and C.R. Grau. 1980. Pigmentation of egg yolks with astaxanthin from the yeast *Phaffia rhodozyma*. Poultry Sci. 59:1777-1782.
- Nelson, K., D. Hedgecock, W. Borgeson, E. Johnson, R. Daggett and D. Aronstein. 1980. Density-dependent growth inhibition in lobsters, *Homarus* (Decapoda, Nephropidae) Biol. Bull. 159:162-176.
- Johnson, E.A., T.G. Villa and M.J. Lewis. 1980. *Phaffia rhodozyma* as an astaxanthin source in salmonid diets. Aquaculture 20:123-134.
- Johnson, E.A. and A.L. Demain. 1981. Chemically defined minimal medium for growth of the anaerobic cellulolytic thermophile *Clostridium thermocellum*. Appl. Environ. Microbiol. 41:1060-1062.
- Johnson, E.A., M. Sakajoh, G. Halliwell, A. Madia and A. L. Demain. 1982. Saccharification of complex cellulosic substrates by the cellulase system from *Clostridium thermocellum*. Appl. Environ. Microbiol. 43:1125-1132.
- Johnson, E.A. and A.L. Demain. 1983. Probable involvement of sulfhydryls and iron in the cellulase of *Clostridium thermocellum*. Arch. Microbiol. 137:135-138.
- Duong, T.-V., E.A. Johnson and A.L. Demain. 1983. Thermophilic, anaerobic and cellulolytic bacteria. Topics Enzyme Biotech. 7:156-195.
- Johnson, E.A., S.K. Burke, R.G. Forage and E.C.C. Lin. 1984. Purification and properties of dihydroxyacetone kinase from *Klebsiella pneumoniae*. J. Bacteriol. 160:55-60.
- Johnson, E.A. and A.L. Demain. 1984. Probable involvement of sulfhydryl groups and a metal as essential components of the cellulase of *Clostridium thermocellum*. Arch. Microbiol. 137:135-138.

- Johnson, E.A., F. Bouchot, and A.L. Demain. 1985. Regulation of cellulase formation in *Clostridium thermocellum*. J. Gen. Microbiol. 131:2303-2308.
- Johnson, E.A., R.L. Levine and E.C.C. Lin. 1985. Inactivation of glycerol dehydrogenase and the role of divalent cations. J. Bacteriol. 164:479-482.
- Johnson, E.A. and E.C.C. Lin. 1987. *Klebsiella pneumoniae* 1, 3-propanediol oxidoreductase. J. Bacteriol. 169:2050-2054.
- Hughey, V.L. and E.A. Johnson. 1987. Antimicrobial activity of egg white lysozyme against bacteria involved in food spoilage and foodborne disease. Appl. Environ. Microbiol. 53:2165-2170.
- Nelson, K., B. Heyer, E. Johnson, D. Hedgecock, and E. S. Chang. 1988. Photoperiod-induced changes in hemolymph vitellogenins in female lobsters (*Homarus americanus*). Comp. Biochem. Phys. 90B:809-821.
- Kihm, D.J., M.T. Hutton, J.H. Hanlin, and E.A. Johnson. 1988. Zinc stimulates sporulation in *Clostridium botulinum* 113B. Curr. Microbiol. 17:193-198.
- Whitmer, M.E. and E.A. Johnson. 1988. Development of improved defined media for *Clostridium botulinum* serotypes A, B, and E. Appl. Environ. Microbiol. 54:753-759.
- Hammer, B.A. and E.A. Johnson. 1988. Purification, properties, and metabolic roles of NAD⁺-glutamate dehydrogenase in *Clostridium botulinum* 113B. Arch. Microbiol. 150:460-464.
- Hughey, V.L., P.A. Wilger, and E.A. Johnson. 1989. Antibacterial activity of hen egg white lysozyme against *Listeria monocytogenes* Scott A in foods. Appl. Environ. Microbiol. 55:631-638.
- An, G.-H. and E.A. Johnson. 1989. Isolation of *Phaffia rhodozyma* mutants with increased astaxanthin content. Appl. Environ. Microbiol. 55:116-124.
- Sprenger, G.A., B.M. Hammer, E.A. Johnson, and E.C.C. Lin. 1989. Anaerobic growth of *Escherichia coli* on glycerol by importing genes of the *dha* regulon from *Klebsiella pneumoniae*. J. Gen. Microbiol. 135:1255-1262.
- Patterson-Curtis, S.I. and E.A. Johnson. 1989. Regulation of neurotoxin and protease formation in *Clostridium botulinum* Okra B and Hall A by arginine. Appl. Environ. Microbiol. 55:1544-1548.
- Rengpipat, S. and E.A. Johnson. 1989. Characterization of a *Lactobacillus* strain producing white crystals on Cheddar cheese. Appl. Environ. Microbiol. 55:2579-2582.
- Johnson, E.A. 1989. A pigment source in salmonid feed. Feed Management. 40:18-21.
- An, G.-H. and E.A. Johnson. 1990. Influence of light on growth and pigmentation of the yeast *Phaffia rhodozyma*. Antonie van Leeuwenhoek 57:191-203.

- Johnson, E.A., J.H. Nelson, and M. Johnson. 1990a. Microbiological safety of cheese made from heat-treated milk, Part I. Executive summary, introduction, and history. *J. Food Prot.* 53:441-452.
- Johnson, E.A., J.H. Nelson, and M. Johnson. 1990b. Microbiological safety of cheese made from heat-treated milk, Part II. Microbiology. *J. Food Prot.* 53:519-540.
- Johnson, E.A., J.H. Nelson, and M. Johnson. 1990c. Microbiological safety of cheese made from heat-treated milk, Part III. Technology, discussion, recommendations, bibliography. *J. Food Prot.* 53:610-623.
- Kihm, D., M.T. Hutton, J.H. Hanlin, and E.A. Johnson. 1990. Influence of transition metals added during sporulation on heat resistance of *Clostridium botulinum* 113B spores. *Appl. Environ. Microbiol.* 56:681-685.
- Schantz, E.J. and E.A. Johnson. 1990. Dose standardisation of botulinum toxin. *Lancet* 335:421.
- Kihm, D. and E.A. Johnson. 1990. Hydrogen gas accelerates thermal inactivation of *Clostridium botulinum* spores. *Appl. Microbiol. Biotech.* 33:705-708.
- Leyer, G. and E.A. Johnson. 1990. Repression of toxin production by tryptophan in *Clostridium botulinum* type E. *Arch. Microbiol.* 154:443-447.
- An, G.-H., J. Bielich, R. Auerbach, and E.A. Johnson. 1991. Isolation and characterization of carotenoid hyperproducing mutants of yeast by flow cytometry and cell sorting. *Bio/Tech.* 9:70-73.
- Malizio, C.J. and E.A. Johnson. 1991. Evaluation of the botulism hazard from vacuum-packaged enoki mushrooms (*Flammulina velutipes*). *J. Food Prot.* 54:20-21, 23.
- Goodnough, M.C., and E.A. Johnson. 1991. Control of *Salmonella enteritidis* infections in poultry by polymyxin B and trimethoprim. *Appl. Environ. Microbiol.* 57:785-788.
- Lin, W.-J. and E.A. Johnson. 1991. Transposon Tn916 mutagenesis in *Clostridium botulinum*. *Appl. Environ. Microbiol.* 57:2946-2950.
- Premaratne, R.J., W.-J. Lin, and E.A. Johnson. 1991. Development of an improved chemically defined minimal medium for *Listeria monocytogenes*. *Appl. Environ. Microbiol.* 57:3046-3048.
- Borodic, G., B. Pearce, E.J. Schantz, and E.A. Johnson. 1991. Botulinum toxin: Clinical and scientific aspects. *Opth. Clin. N. America* 4:491-503
- Johnson, E.A. and G.-H. An. 1991. Astaxanthin from Microbial Sources. *Crit. Rev. Biotech.* 11:297-326.
- Schantz, E.J. and E.A. Johnson. 1992. Properties and use of botulinum toxin and other microbial neurotoxins in medicine. *Microbiol. Rev.* 56:80-99.

- Wang, L.-L. and E.A. Johnson. 1992. Inhibition of *Listeria monocytogenes* by fatty acids and monoglycerides. *Appl. Environ. Microbiol.* 58:624-629.
- Leyer, G.J. and E.A. Johnson. 1992. Acid adaptation promotes survival of *Salmonella* in cheese. *Appl. Environ. Microbiol.* 58:2075-2080.
- Patterson-Curtis, S.I. and E.A. Johnson. 1992. Roles of arginine in growth of *Clostridium botulinum* Okra B. *Appl. Environ. Microbiol.* 58:2334-2337.
- Goodnough, M.C. and E.A. Johnson. 1992. Stabilization of botulinum toxin during lyophilization. *Appl. Environ. Microbiol.* 58:3426-3428.
- Schroeder, W.A. and E.A. Johnson. 1993. Antioxidant role of carotenoids in *Phaffia rhodozyma*. *J. Gen. Microbiol.* 139:907-912.
- Larson, A.E., E.A. Johnson, and J.H. Nelson. 1993. Behavior of *Listeria monocytogenes* and *Salmonella heidelberg* in rennet whey containing added sodium chloride or potassium chloride. *J. Food Prot.* 56:385-389.
- Zhou, Y. and E.A. Johnson. 1993. Genetic transformation of *Clostridium botulinum* Hall A by electroporation. *Biotech. Lett.* 15:121-126.
- Leyer, G.J. and E.A. Johnson. 1993. Acid adaptation induces cross protection against environmental stresses in *Salmonella typhimurium*. *Appl. Environ. Microbiol.* 59:1842-1847.
- Wang, L.-L., B.-K. Yang, K.L. Parkin, and E.A. Johnson. 1993. Inhibition of *Listeria monocytogenes* by monoacylglycerols synthesized from coconut oil and milkfat by lipase-catalyzed glycerolysis. *J. Agric. Food Chem.* 41:1000-1005.
- Goodnough, M.C., H. Sugiyama, and E.A. Johnson. 1993. Colony immunoblot assay of botulinum toxin. *Appl. Environ. Microbiol.* 59:2339-2342.
- Malizio, C.J., J. Harrod, K.M. Kaufman, and E.A. Johnson. 1993. Arginine promotes toxin formation in cheddar cheese by *Clostridium botulinum*. *J. Food Prot.* 56:769-772.
- Zhou, Y., H. Sugiyama, and E.A. Johnson. 1993. Transfer of toxigenicity from *Clostridium butyricum* to a nontoxigenic *Clostridium botulinum* type E-like strain. *Appl. Environ. Microbiol.* 59:3825-3831.
- Schiavo, G., C. Malizio, W.S. Trimble, P. Polverino de Laureto, G. Milan, H. Sugiyama, E.A. Johnson, and C. Montecucco. 1994. Botulinum G neurotoxin cleaves VAMP/synaptobrevin at a single ala-ala peptide bond. *J. Biol. Chem.* 269:20213-20216.
- Kihm, D.J., G.J. Leyer, G.-H. Hwan, and E.A. Johnson. 1994. Sensitization of heat-treated *Listeria monocytogenes* to added lysozyme in milk. *Appl. Environ. Microbiol.* 60:3854-3861.

- Borodic, G, L.B. Pearce, and E.A. Johnson. 1994. Antibodies to botulinum toxin. *Ophthalmology* 101:1158.
- Luchansky, J.B. and E.A. Johnson. 1995. Trends and tactics for reducing fat and cholesterol—addressing dairy issues. *Prepared Foods* 164(8):73.
- Pearce, L.B., G.E. Borodic, E.A. Johnson, E.R. First, and R. MacCallum. 1995. The median paralysis unit: a more pharmacologically relevant unit of biological activity for botulinum toxin. *Toxicon* 33:217-227.
- Borodic, G.E., B. Pearce, D. Duane, and E. Johnson. 1995. Antibodies to botulinum toxin. *Neurology* 45:204.
- Zhou, Y., H. Sugiyama, H. Nakano, and E.A. Johnson. 1995. The genes for *Clostridium botulinum* type G toxin complex are on a plasmid. *Infect. Immun.* 63:2087-2091.
- Schroeder, W.A. and E.A. Johnson. 1995. Carotenoids protect *Phaffia rhodozyma* against singlet oxygen damage. *J. Ind. Microbiol.* 14:502-507.
- Schroeder, W.A. and E.A. Johnson. 1995. Singlet oxygen and peroxy radicals regulate carotenoid biosynthesis in *Phaffia rhodozyma*. *J. Biol. Chem.* 270:18374-18379.
- Leyer, G.J., L.-L. Wang, and E.A. Johnson. 1995. Acid adaptation of *Escherichia coli* O157:H7 increases survival in acid foods. *Appl. Environ. Microbiol.* 61:3752-3755.
- Lin, W.-J. and E.A. Johnson. 1995. Genome analysis of *Clostridium botulinum* type A by pulsed field gel electrophoresis. *Appl. Environ. Microbiol.* 61:4441-4447.
- Johnson, E.A. and W.A. Schroeder. 1995. Astaxanthin from the yeast *Phaffia rhodozyma*. *Studies in Mycology* 38:81-90.
- Johnson, E.A. and W.A. Schroeder. 1995. Microbial carotenoids. *Adv. Biochem. Eng./Biotech.* 53:119-178.
- Nickelson, R., J. Luchansky, C. Kaspar, and E. Johnson. 1996. Dry fermented sausage and *E. coli* O157:H7. National Cattlemen's Beef Association, Chicago, IL. Research Report No. 11-316.
- Hutson, R.A., Y.-T. Zhou, E.A. Johnson, M.D. Collins, C.L. Hatheway, and H. Sugiyama. 1996. Genetic characterization of *Clostridium botulinum* type A containing silent type B neurotoxin gene sequences. *J. Biol. Chem.* 271:10786-10792.
- Borodic, G., E. Johnson, M. Goodnough, and E. Schantz. 1996. Botulinum toxin therapy, immunologic resistance, and problems with available materials. *Neurology* 46:26-29.
- Schroeder, W.A., P. Calo, M. DeClercq, and E.A. Johnson. 1996. Selection for carotenogenesis in the yeast *Phaffia rhodozyma* by singlet oxygen. *Microbiol.* 142:2923-2929.

- Larson, A.E., R.R.Y. Yu, O.A. Lee, S. Price, G.J. Haas, and E.A. Johnson. 1996. Antimicrobial activity of hop extracts against *Listeria monocytogenes* in media and in food. *Int. J. Food Microbiol.* 33:195-207
- Pellizzari, R., O. Rossetto, L. Lozzi, S. Giovedi, E.A. Johnson, C.C. Shone, and C. Montecucco. 1996. Structural determinants of the specificity for synaptic vesicle-associated membrane protein/synaptobrevin of tetanus and botulinum type B and G neurotoxins. *J. Biol. Chem.* 271:20353-20358.
- An, G.-H., K.-W. Chang, and E.A. Johnson. 1996. Effect of oxygen radicals and aeration on carotenogenesis and growth of *Phaffia rhodozyma* (*Xanthophyllomyces dendrohous*). *J. Microbiol. Biotech.* 6:103-109.
- Gaumnitz, E., P. Bass, M. Sweet, M.C. Goodnough, E.A. Johnson, C. Singaram. 1996. Mechanism of botulinum toxin-induced LES relaxation in opossum involves cholinergic and peptidergic neurons. *Gastroenterology.* 110:668.
- Wang, L.-L. and E.A. Johnson. 1997. Control of *Listeria monocytogenes* by monoglycerides in foods. *J. Food Prot.* 60:131-138.
- Leyer, G.J. and E.A. Johnson. 1997. Acid adaptation sensitizes *Salmonella typhimurium* towards hypochlorous acid. *Appl. Environ. Microbiol.* 63:461-467.
- Schantz, E.J. and E.A. Johnson. 1997. Botulinum toxin: The story of its development for the treatment of human disease. *Perspectives Biol. Med.* 40:317-327.
- Larson, A.E., E.A. Johnson, C. Barmore, and M. Hughes. 1997. Evaluation of the botulism hazard from vegetables in modified atmosphere packaging. *Journal of Food Protection* 60:1208-1214
- Johnson, E.A., W.-J. Lin, Y.-T. Zhou, and M. Bradshaw. 1997. Characterization of neurotoxin mutants in *Clostridium botulinum* type A. *Clin. Infect. Dis.* 25(Suppl 2):S168-70.
- Gu, W.-L., An, G.-H., and E.A. Johnson. 1997. Ethanol increases carotenoid production in *Phaffia rhodozyma*. *J. Indust. Microbiol. Biotechnol.* 19:113-117.
- Ingham, S., A. Larson, M. Smukowski, K. Houck, E. Johnson, M. Johnson, and R. Bishop. 1997. Potential uses of microbiological testing in cheese plant HACCP and quality assurance systems. *Dairy Food Environ. Sanitat.* 17:774-780.
- Torbey, C., E. Gaumnitz, P. Bass, M. Sweet, M. Goodnough, E. Johnson, and C. Singaram. 1997. Pharmacological effects of botulinum toxin on rat jejunal smooth muscle. *Digestion.* 7:34-38.
- Gaumnitz, E.Z., P. Bass, M.C. Goodnough, E.A. Johnson, C. Singaram. 1997. Physiologic effects of botulinum toxin in opossum lower esophageal sphincter. *Gastroenterology.* 34:128-129.

- K.A. Glass, K.M. Kaufman, and E.A. Johnson. 1998. Survival of bacterial pathogens in pasteurized process cheese slices stored at 30°C. *J. Food Prot.* 61:290-294.
- Angulo, F.J., J. Getz, J.P. Taylor, K.A. Hendricks, C.L. Hatheway, S.B. Barth, H.M. Solomon, A.E. Larson, E.A. Johnson, L.N. Nickey, and A.A. Ries. 1998. A large outbreak of botulism: The hazardous baked potato. *J. Infect. Dis.* 178:172-177.
- Bradshaw, M., M.C. Goodnough, and E.A. Johnson. 1998. Conjugative transfer of the *E. coli*-*C. perfringens* shuttle vector pJIR1457 to *Clostridium botulinum* type A strains. *Plasmid* 40:233-237.
- Sofos, J.N., L.R. Beuchat, P.M. Davidson, and E.A. Johnson. 1998. Interpretative Summary. Naturally Occurring Antimicrobials In Food. *Regulatory Toxicol. Pharmacol.* 28:71-72.
- Maksymowych, A.B., M. Reinhard, C.J. Malizio, M.C. Goodnough, E.A. Johnson, and L.L. Simpson. 1999. Pure botulinum toxin is absorbed from the stomach and small intestine and produces peripheral neuromuscular blockade. *Infect. Immun.* 67:4708-4712.
- Larson A.E. and E.A. Johnson. 1999. Evaluation of botulinum toxin formation in packaged fresh-cut cantaloupe and honeydew melons. *J. Food Protect.* 62:948-952.
- Nelson, J.A., D.A. Wubah, M.E. Whitmer, E.A. Johnson, and D.J. Stewart. 1999. Wood-eating catfishes of the genus *Panaque*: gut microflora and cellulolytic enzyme activities. *J. Fish Biol.* 54:1069-1082.
- Glass, K.A., K.M. Kaufman, A.L. Smith, E.A. Johnson, J.H. Chen, and J.H. Hotchkiss. 1999. Toxin production by *Clostridium botulinum* in pasteurized milk treated with carbon dioxide. *J. Food Prot.* 62:872-876.
- Larson, A.E., E.A. Johnson, and J.H. Nelson. 1999. Survival of *Listeria monocytogenes* in commercial cheese brines. *J. Dairy Sci.* 82:1860-1868.
- Johnson, E.A. 1999. Clostridial toxins as therapeutic agents: benefits of nature's most toxic proteins. *Annu. Rev. Microbiol.* 53:551-575.
- Johnson, E.A. 1999. Biomedical aspects of botulinum toxin. *J. Toxicol. -Toxin Reviews* 18:1-15.
- Boekhout, T.J. W. Fell, C.P. Kurtzman, and E.A. Johnson. 1999. Proposal to reject the name *Rhodomyces dendrorhous* (Fungi, Basidiomycota). *Taxon* 48:147-148.
- An, G.-H., M.-H. Cho, and E.A. Johnson. 1999. Monocyclic carotenoid biosynthetic pathway in the yeast *Phaffia rhodozyma* (*Xanthophyllomyces dendrorhous*). *J. Biocsci. Bioeng.* 88:189-193.
- Malizio, C.J., M.C. Goodnough, and E.A. Johnson. 2000. Purification of botulinum type A neurotoxin. *Meth. Molec. Biol.* 145:27-39.
- An, G.-H., O.-S. Suh, H.-C. Kwon, K. Kim, and E.-A. Johnson. 2000. Quantification of

carotenoids in cells of *Phaffia rhodozyma* by autofluorescence. *Biotechnol. Lett.* 22:1031-1034.

Dineen, S.S., M. Bradshaw, and E.A. Johnson. 2000. Cloning, nucleotide sequence, and expression of the gene encoding the bacteriocin boticin B from *Clostridium botulinum* strain 213B. *Appl. Environ. Microbiol.* 66:5480-5483.

Pariza, M.W. and E.A. Johnson. 2001. Evaluating the safety of microbial enzyme preparations used in food processing: Update for a new century. *Regulat. Toxicol. Pharmacol.* 33:1-14.

Peck, R.F., C. Echavarri-Ersasun, E.A. Johnson, W.V. Ng, S.P. Kennedy, L. Hood, S. DasSarma, and M.P. Krebs. 2001. *brp* and *blh* are required for synthesis of the retinal cofactor of bacteriorhodopsin in *Halobacterium salinarum*. *J. Biol. Chem.* 276:5739-5744.

Johnson, E.A. and M. Bradshaw. 2001. *Clostridium botulinum*: A metabolic and cellular perspective. *Toxicon* 39:1703-1722.

Borodic, G E., M. Acquadro, and E.A. Johnson 2001. Botulinum toxin therapy for pain and inflammatory disorders: mechanisms and therapeutic effects. *Expert. Opin. Invest. Drugs* 10:1531-1544.

Rigoni, M., Caccin, P., Johnson, E.A., Montecucco, C , Rossetto, O. 2001. Site-directed mutagenesis identifies active-site residues of the light chain of botulinum neurotoxin type A. *Biochem. Biophys. Res. Commun.* 288(5):1231-1237.

Finegold, S.M., D. Molitoris, Y. Song, C. Liu, M.-L. Vaisanen, E. Bolte, M. McTeague, R. Sandler, H. Wexler, E. Marlowe, M.D. Collins, P. Lawson, P. Summanen, M. Baysallar, T. Tomzynski, E.A. Johnson, R. Rolfe, H. Shah, P. Manning, and A. Kaul. 2002. Gastrointestinal studies in late-onset autism. *Clin. Infect. Dis.* 35(Suppl.1):S6-S16.

Glass, K.A., D.A. Granberg, A.L. Smith, A.M. McNamara, M. Hardin, J. Mattias, K. Ladwig, and E.A. Johnson. 2002. Inhibition of *Listeria monocytogenes* by sodium diacetate and sodium lactate on wieners and cooked bratwurst. *J. Food Prot.* 65:116-23.

Goodnough M.C., G. Oyler , P.S. Fishman, E.A. Johnson, E.A. Neale, J.E. Keller, W.H. Tepp, M. Clark, S. Hartz. 2002. Development of a delivery vehicle for intracellular transport of botulinum neurotoxin antagonists. *FEBS Lett.* 513:163-8.

Peck, R.F., E.A. Johnson, and M.P. Krebs. 2002. Identification of a lycopene beta-cyclase required for bacteriorhodopsin biogenesis in the Archaeon *Halobacterium salinarum*. *J. Bacteriol.* 184:2889-2897.

Dineen, S.S., M. Bradshaw, and E.A. Johnson. 2003. Neurotoxin gene clusters in *Clostridium botulinum* type A strains: sequence comparison and evolutionary implications. *Curr. Microbiol.* 46:345-352.

Foran, P.G., N. Mohammed, G.O. Lisk, S. Nagwaney, G.W. Lawrence, E. Johnson, L. Smith, K.R. Aoki, and J.O. Dolly. 2003. Evaluation of the therapeutic usefulness of botulinum neurotoxin B, C1, E,

and F compared with the long lasting type A-Basis for distinct durations of inhibition of exocytosis in central neurons. *J. Biol. Chem.* 278(2):1363-1371.

Brehm-Stecher, B.F and E.A. Johnson. 2003. Sensitization of *Staphylococcus aureus* and *Escherichia coli* to antibiotics by the sesquiterpenoids nerolidol, farnesol, bisabolol, and apritone. *Antimicrob Agents Chemo.* 47:3357-3360.

Dong, M., D.A. Richards, M.C. Goodnough, W.H. Tepp, E.A. Johnson, and E.R. Chapman. 2003. Synaptotagmins I and II mediate entry of botulinum neurotoxin B into cells. *J. Cell Biol.* 162:1293-1303.

Johnson, E.A. 2003. *Phaffia rhodozyma*: colorful odyssey. *Int. Microbiol.* 6:169-174.

Ferreira, J.L., S. Maslanka, E. Johnson, and M. Goodnough. 2003. Detection of botulinum neurotoxins A, B, E, and F by amplified enzyme-linked immunosorbent assay: collaborative study. *J. AOAC Int.* 86:314-331.

Caccin, P., O. Rossetto, M. Rigoni, E. Johnson, G. Schiavo, and C. Montecucco. 2003. VAMP/synaptobrevin cleavage by tetanus and botulinum neurotoxins is strongly enhanced by acidic liposomes. *FEBS Lett.* 542:132-136.

Oost, T., C. Sukonpan, M. Brewer, M. Goodnough, W. Tepp, E.A. Johnson, and D.H. Rich. 2003. Design and Synthesis of Substrate-Based Inhibitors of Botulinum Neurotoxin Type B Metalloprotease. *Biopolymers* 71:602-619.

Echavarri-Erasun, C. and E.A. Johnson. 2004. Stimulation of astaxanthin formation in the yeast *Xanthophyllomyces dendrorhous* by the fungus *Epicoccum nigrum*. *FEMS Yeast Res.* 4:511-519.

Dineen, S.S., M. Bradshaw, C.E. Karasek, and E.A. Johnson. 2004. Nucleotide sequence and transcriptional analysis of the type A2 neurotoxin gene cluster in *Clostridium botulinum*. *FEMS Microbiol. Lett.* 235:9-16.

Puhar, A, E.A. Johnson, O. Rossetto, and C. Montecucco. 2004. Comparison of the pH-induced conformational change of different clostridial neurotoxins. *Biochem. Biophys. Res. Comm.* 319:66-71.

Glass, K.A. and E.A. Johnson. 2004. Factors that contribute to the botulinum safety of reduced-fat and fat-free process cheese products. *J. Food Prot.* 65:1687-1693.

Glass, K.A. and E.A. Johnson. 2004. Antibotulinum activity of process cheese ingredients. *J. Food Prot.* 67:1765-1769.

Sukonpan, C., T. Oost, M. Goodnough, W. Tepp, E.A. Johnson, and D.H. Rich. 2004. Synthesis of substrates inhibitors of botulinum neurotoxin type A metalloprotease. *J. Peptide Res.* 63:181-193.

- Moorthy, J., G.A. Mensing, D. Kim, S. Mohanty, D.T. Eddington, W.H. Tepp, E.A. Johnson, and D.J. Beebe. 2004. Microfluidic tectonics platform: a colorimetric, disposable botulinum toxin enzyme-linked immunosorbent assay system. *Electrophoresis* 25:1705-1713.
- Baldwin, M.R., M. Bradshaw, E.A. Johnson, and J.T. Barbieri. 2004. The C-terminus of botulinum neurotoxin type A light chain contributes to solubility, catalysis, and stability. *Protein Exp. and Purif.* 37:187-195.
- Glass, K.A. and E.A. Johnson. 2004. Antagonistic effect of fat on the antibotulinal activity of food preservatives and fatty acids. *Food Microbiol.* 21:675-682,
- Dong, M., W.H. Tepp, E.A. Johnson, and E.R. Chapman. 2004. Using fluorescent sensors to detect botulinum neurotoxin activity *in vitro* and in living cells. *PNAS* 101:14701-14706.
- Brehm-Stecher, B.F. and E.A. Johnson. 2004. Single-cell microbiology: tools, technologies, and applications. *Microbiol. Molecular Biology Reviews* 68:538-559.
- Bradshaw, M., S.S. Dineen, N.D. Maks, and E.A. Johnson. 2004. Regulation of neurotoxin complex expression in *Clostridium botulinum* strains 62A, Hall A-*hyper*, and NCTC 2916. *Anaerobe* 10:321-333.
- Brehm-Stecher, B.F. and E.A. Johnson. 2004. Rapid Nucleic Acid-Based Detection and Enumeration of *Listeria* spp. by Flow Cytometry, ILSI *Listeria* Research Update proceedings, Food Protection Trends. 24: 761-763
- Johnson, E.A., W.H. Tepp, M. Bradshaw, R.J. Gilbert, P.E. Cook, and E.D.G. McIntosh. 2005. Characterization of *Clostridium botulinum* strains associated with an infant botulism case in the United Kingdom. *J. Clin. Microbiol.* 43:2602-2607.
- Anne, C., S. Turcaud, A.G S. Blommaert, F. Darchen, E.A. Johnson, and B.P. Roques. 2005. Partial protection against botulinum B neurotoxin-induced blocking of exocytosis by a potent inhibitor of its metallopeptidase activity. *ChemBioChem* 6:1375-1380.
- Brehm-Stecher, B.F., Hyldig-Nielsen, J.J., and E.A. Johnson. 2005. Design and evaluation of 16S rRNA- targeted peptide nucleic acid probes for whole cell detection of the genus *Listeria*. *Applied and Environmental Microbiology* 71:5451-5457.
- Smith, T.J., J. Lou, I.N. Geren, C.M. Forsyth, R. Tsai, S.L. LaPorte, W.H. Tepp, M. Bradshaw, E.A. Johnson, L.A. Smith, and J.D. Marks. 2005. Sequence variation within botulinum neurotoxin serotypes impacts antibody binding and neutralization. *Infect. Immun.* 73:5450-5457.
- Baldwin, M.R., W.H. Tepp, C.L. Pier, M. Bradshaw, M. Ho, B.A. Wilson, R.B. Fritz, E.A. Johnson, and J.T. Barbieri. 2005. Characterization of the antibody response to the receptor binding domain of botulinum neurotoxin serotypes A and E. *Infect. Immun.* 73:6998-7005.

Borodic, G., M. Bartley, W. Slattery, M. Glasscock, E. Johnson, C. Malizio, M. Goodnough, M. Acquadro, and M. McKenna. 2005. Botulinum toxin for aberrant facial nerve regeneration; double-blind, placebo-controlled trial using subjective endpoints. *Plast. Reconstr. Surg.* 116:36-43.

Johnson, E.A. 2005. *Clostridium botulinum* neurotoxins--applications in medicine and potential agents of bioterrorism. *Clin. Microbiol. Newsletter.* 27:147-151.

Dong, M., F. Yeh, W.H. Tepp, C. Dean, E.A. Johnson, R. Janz, E.R. Chapman. 2006. SV2 is the protein receptor for botulinum neurotoxin A. *Science.* 312(5773):592-6..

Arndt, J.W., M.J. Jacobson, E E. Abola, C.M. Forsyth, W.H. Tepp, J.D. Marks, E.A. Johnson, and R.C. Stevens. 2006. A structural perspective of the sequence variability within botulinum neurotoxin subtypes A1-A4. *J. Mol. Biol.* 362(4):733-742. Epub 2006 July 27.

Hill, K.K., T.J. Smith, C.H. Helma, L.O. Ticknor, B.T. Foley, R.T. Svensson, J.L. Brown, E.A. Johnson, L.A. Smith, R.T. Okinaka, P.J. Jackson, and J.D. Marks. Genetic diversity among botulinum neurotoxin producing clostridial strains. *J. Bacteriol.* 189:818-832.

Chai, Q., J.W. Arndt, M. Dong, W H. Tepp, E.A. Johnson, E.R. Chapman, R.C Stevens. 2006. Structural basis of cell surface receptor recognition by botulinum neurotoxin B. *Nature.* 444(7122):1096-1100. Epub 2006 Dec 13.

Joon-Seo Park, Sarah Teren, William H. Tepp, David J. Beebe, Eric A. Johnson, and Nicholas L. Abbott "Formation of Oligopeptide-Based Polymeric Membranes at Interfaces between Aqueous Phases and Thermotropic Liquid Crystals" *Chemistry of Materials*, 2006, 18, 6147-6151.

Eubanks, L.M., M.S. Hixon, W. Jin, S. Hong, C.M. Clancy, W.H. Tepp, M.R. Baldwin, C.J. Malizio, M.C. Goodnough, J.T. Barbieri, E.A. Johnson, D.L. Boger, T.J. Dickerson, and K.D. Janda. 2007. An *in vitro* and *in vivo* disconnect uncovered through high-throughput identification of botulinum neurotoxin A antagonists. *PNAS*104:2602-2607.

Kale

Book Chapters:

Johnson, E.A. and M.W. Pariza. 1989. Microbiological principles for the safety of foods, p. 135-174. In: R.D. Middlekauff and P. Shubik (eds.), *Food Regulation Handbook*. Marcel Dekker, Inc., New York.

Johnson, E.A. 1990. Infrequent microbial infections, p 259-273. In: D.O. Cliver (ed.), *Foodborne Diseases* Academic Press, New York.

Johnson, E.A. 1990. *Bacillus cereus*, p. 127-135. In: D.O. Cliver (ed.), *Foodborne Diseases*. Academic Press, New York.

- Johnson, E.A. 1990. *Clostridium perfringens*, p. 229-240. In: D.O. Cliver (ed.), *Foodborne Diseases*. Academic Press, New York.
- Johnson, E.A. 1991. Microbiological safety of fermented foods, p. 135-169. In: J.G. Zeikus and E.A. Johnson (eds.), *Mixed Cultures in Biotechnology*. McGraw Hill, New York.
- Johnson, E.A. 1992. Use of botulinum toxin as a therapy agent, p. 95-105. In: T.G. Villa and J. Abalde (eds.), *Profiles in Biotechnology*. Servicio de Publicacions. Universidade de Santiago, Spain.
- Johnson, E.A. 1992. New advances in astaxanthin synthesis by *Phaffia rhodozyma*, p. 289-299. In: T.G. Villa and J. Abalde (eds.), *Profiles in Biotechnology*. Universidade de Santiago, Santiago de Compostela, Spain.
- Schantz, E.J., and E.A. Johnson. 1993. Quality of botulinum toxin for human treatment, p. 657-659. In: B.R. DasGupta (ed.), *Botulinum and Tetanus Neurotoxins. Neurotransmission and Biomedical Aspects*. Plenum Press, New York.
- E.J. Schantz and E.A. Johnson. 1994. Preparation and characterization of botulinum toxin type A for human treatment, p. 41-49. In: J. Jankovic and M. Hallett (eds.), *Therapy with Botulinum Toxin*. Marcel Dekker, New York.
- Johnson, E.A. 1994. Egg white lysozyme as a preservative for use in foods, p. 177-191. In: J.S. Sim and S. Nakai (eds.), *Egg uses and processing technologies New developments*. CAB International, UK.
- Goodnough, M.C., and E.A. Johnson. 1994. Recovery of botulinum toxin following lyophilization, p. 193-203. In: J. L. Cleland and R. Langer (eds.), *Formulation and delivery of proteins and peptides*. ACS Symposium Series 567, American Chemical Society, Washington, DC.
- Johnson, E.A., and M.C. Goodnough. 1995. Preparation and properties of botulinum toxin type A for medical use, p. 347-365. In: J. Tsui and D. Calne (eds.), *Handbook of Dystonia*. Marcel Dekker, New York.
- Johnson, E.A., and W.S. Schroeder. 1996. Biotechnology of astaxanthin production in *Phaffia rhodozyma*, p. 39-50. In: G.R. Takeoka, R. Teranishi, R.J. Williams, and A. Kobayashi (eds.), *Biotechnology for Improved Foods and Flavors*. ACS Symposium Series 637, Washington, DC.
- Goodnough, M.C., and E.A. Johnson. 1996. Botulism. In: *Topley and Wilson's Current Topics in Microbiology*. Arnold Publishing, London.
- Setlow, P., and E.A. Johnson. 1997. Spores and Their Significance, p. 30-65. In: M.P. Doyle, L.R. Beuchat, and T.J. Montville (eds.), *Food Microbiology: Fundamentals and Frontiers*. ASM Press, Washington, DC.

- Johnson, E.A. 1997. Extracellular virulence factors in clostridia, p. 35-48. In: J.I. Rood, B.A. McClane, J.G. Songer, and R.W. Titball (eds.), *The Clostridia: Molecular Biology and Pathogenesis*. Academic Press Ltd., San Diego.
- Hatheway, C.L., and E.A. Johnson. 1998. *Clostridium*: the spore-bearing anaerobes, p. 731-782. In: L. Collier, A. Balows, and M. Sussman (eds.), *Topley and Wilson's Microbiology and Microbial Infections, Ninth Edition, Volume 2: Systematic Bacteriology*. Arnold, London.
- Johnson, E.A., and M.C. Goodnough. 1998. Botulism, p. 723-741. In: L. Collier, A. Balows, and M. Sussman (eds.), *Topley and Wilson's Microbiology and Microbial Infections, Ninth Edition, Volume 3: Bacterial Infections*. Arnold, London.
- Sofos, J.N., L.R. Beuchat, P.M. Davidson, and E.A. Johnson. 1998. Naturally occurring antimicrobials in foods. Council for Agricultural Science and Technology, Task Force Report No. 132, Ames, Iowa.
- Johnson, E.A. 1999. *Clostridium botulinum*, p. 458-463. In: R.K. Robinson, C.A. Batt, and P.D. Patel (eds.), *Encyclopedia of Food Microbiology*. Academic Press, London.
- Johnson, E.A. 1999. Anaerobic Fermentations. In: A.L. Demain, J. Davies, et al. (eds.), *Manual of Methods for Industrial Microbiology, 2nd Edition*. ASM Press, Washington, DC.
- Malizio, C.J., M.C. Goodnough, E.A. Johnson. 1999. Purification of *Clostridium botulinum* type A neurotoxin, p. 27-39. In: O. Holst (ed.), *Bacterial Toxins Methods & Protocols*. The Humana Press, Inc., Totowa, NJ.
- Johnson, E.A. 2000. Neurotoxicogenic clostridia, p. 540-550. In: V.A. Fischetti et al. (eds), *Gram-Positive Pathogens*. American Society for Microbiology, Washington, DC.
- Johnson, E.A. 2000. Clostridia, p. 834-839. In J. Lederberg (ed.), *Encyclopedia of Microbiology, Volume one*. Academic Press, Inc., San Diego.
- Johnson, E.A. 2000. Pigments, Microbially Produced, p. 647-653. In J. Lederberg (ed.), *Encyclopedia of Microbiology, Volume one*. Academic Press, Inc., San Diego.
- Goodnough, M., W. Tepp, C. Malizio, and E. Johnson. 2000. Development of delivery vehicle targeting motor neurons. In: *Proceedings of Bioscience 2000*. Department of Defense press.
- Solomon, H.M., E.A. Johnson, D.T. Bernard, S.S. Arnon, and J.L. Ferreira. 2001. *Clostridium botulinum* and its toxins, p. 317-324. In: F.P. Downes and K. Ito, (eds.), *Compendium for the Microbiological Examination of Foods, 4th edition*. American Public Health Association, Washington, DC.
- K.A. Glass, and E.A. Johnson. 2001. Formulating low-acid foods for botulinal safety, p. 323-350. In: V.K. Juneja and J.N. Sofos (eds.), *Control of Foodborne Organisms*. Marcel-Dekker, New York.

Setlow, P., and E.A. Johnson. 2001. Spores and their significance, p. 33-70. In: M.P. Doyle, L.R. Beuchat, and T. Montville (eds.), *Food Microbiology: Fundamentals and Frontiers*. ASM Press, Washington, DC.

Echavarri-Erasun, C., and E.A. Johnson. 2002. Fungal carotenoids, p. 45-85. In: G.G. Khachatourians and D.K. Arora (eds.), *Applied Mycology & Biotechnology, vol. 2, Agriculture and Food Production* Elsevier Science, The Netherlands.

Johnson, E.A., M.C. Goodnough, C.M. Malizio, W.H. Tepp, S.S. Dineen, and M. Bradshaw. 2002. Hybrid and chimeric botulinum toxin molecules. pp. 477-484. In: M.F. Brin, M. Hallett, and J. Jankovic (eds.), *Scientific and Therapeutic Aspects of Botulinum Toxin*. Lippincott Williams & Wilkins, Philadelphia, PA.

Echavarri-Erasun, C. and E.A. Johnson. 2002. Food Spoilage Yeasts and Fungi, p. 469-475. In G.G. Khachatourians and D.K. Arora (eds.), *Applied Mycology and Biotechnology, Volume 2*. Elsevier Science.

Johnson, E.A. and E.J. Schantz. 2002. Seafood Toxins, p. 211-230. In D. Cliver and H. Riemann (eds.), *Foodborne Diseases, 2nd edition*. Elsevier Science.

Johnson, E.A. 2003. Microbial Adaptation and Survival in Foods, p. 75-103. In A.E. Yousef and V.K. Juneja (eds.), *Microbial Stress Adaptation and Food Safety*. CRC Press LLC, Boca Raton.

Johnson, E.A. 2003. Bacterial Pathogens and Toxins in Foodborne Disease, p. 25-45. In: J.P.F. D'Mello (ed.), *Food Safety: Contaminants and Toxins*, CABI International..

Johnson, E.A. and A.E. Larson. 2005. Lysozyme. P. 361-387. In P.M. Davidson, (ed.), *Antimicrobials in Foods, 3rd edition*. CRC Press, Boca Raton, FL.

Johnson, E. A. 2005. Clostridial Neurotoxins. In: P. Duerre, ed. *Handbook on Clostridia*, CRC Press, Boca Raton.

Johnson, E.A. 2005. Bacteriophages Encoding Botulinum and Diphtheria Toxins. In: M.K. Waldor, D.I. Friedman, and S.L. Adhya (eds.), *Phages: Their Role in Bacterial Pathogenesis and Biotechnology*, ASM Press, Washington, D.C.

Johnson, E. A. 2005. Clostridium botulinum and Clostridium tetani, p. 1035-1088. In: S.P. Borriello, P.R. Murray, G. Funke, eds., *Topley and Wilson's Microbiology and Microbial Infections*, eighth edition, Hodder Arnold, London.

Johnson, E.A., P. Summanen, and S.M. Finegold 2006. Clostridium. In: *Manual of Clinical Microbiology*, volume 9 ASM Press, Washington, D.C.

Johnson, E.A. and E.J. Schantz. 2006. Miscellaneous Natural Intoxicants. p. 663-709. In: *Foodborne Infections and Intoxications*, 3rd edition, Elsevier, Inc.

Johnson, E.A., G.E. Borodic, and M.A. Acquadro. 2006. Medical Applications of Botulinum Neurotoxins. p. 959-975. In: J.E. Alouf and M.R. Popoff (eds.), *Comprehensive Sourcebook of Bacterial Protein Toxins*, 3rd edition, Elsevier, Inc.

Johnson, E. A. 2006. Neurotoxicogenic clostridia, p. 688-703. In: V. A. Fischetti, R. P. Novick, J. J. Ferretti, D. A. Portnoy, and J. R. Rood, eds. *Gram-Positive Pathogens*, 2nd ed. ASM Press, Washington, DC.

Setlow, P., and E. A. Johnson. 2007. Spores and Their Significance, p. 35-67. In: M. P. Doyle and L. R. Beuchat, eds. *Food Microbiology Fundamentals and Frontiers*, 3rd edition, ASM Press, Washington, D.C.

Johnson, E.A. 2007. *Clostridium botulinum*, p. 401-421. In: M. P. Doyle and L. R. Beuchat. *Food Microbiology: Fundamentals and Frontiers*, 3rd edition, ASM Press, Washington, D.C.

Patents

Johnson, E.A., A.L. Demain, and A. Madia. Method of saccharifying cellulose. U.S. Patent #4,540,664, September 10, 1985.

Johnson, E.A., E. Dell'Acqua, T. Bruzzese, and H.H. van den Heuvel. Process for obtaining foods free of *Listeria* bacteria. U.S. Patent #4,810,508, March 7, 1989. European Patent #87115661.8.

Johnson, E.A., E. Dell'Acqua, and L. Ferrari. Process for bacterial decontamination of vegetable foods. U.S. Patent #5,019,411, May 28, 1991.

Johnson, E.A. and M.C. Goodnough. Method for controlling *Salmonella enteritidis* in poultry. U.S. Patent #5,132,288, July 21, 1992.

Johnson, E.A., D. Schreiber, K.P. Ho, W.T. Hall, H.-H. Yang, and B. Geldiay-Tuncer. Processes for in vivo production of astaxanthin and *phaffia rhodozyma* yeast of enhanced astaxanthin content. U.S. Patent #5,182,208, January 26, 1993.

Johnson, E.A., H.-H. Yang, B., Geldiay-Tuncer, W.T. Hall, D. Schreiber, and K. Ho. Processes for in vivo production of astaxanthin and *phaffia rhodozyma* yeast of enhanced astaxanthin content. U.S. Patent #5,356,809, October 18, 1994.

Fleno, B., I. Christensen, R. Larsen, S.R. Johansen, and E.A. Johnson. Astaxanthin-producing yeast cells, methods for their preparation and their use. U.S. Patent #5,356,810, October 18, 1994.

Johnson, E.A. and E. Dell'Acqua. Composition active against botulism. U.S. Patent #5,393,545, February 28, 1995.

Parreiras, J.F.M. and E.A. Johnson. Method of inhibiting pathogens and food spoilage bacteria. U.S. Patent #5,455,278, October 3, 1995.

Johnson, E.A. and M.C. Goodnough. Pharmaceutical composition of botulinum neurotoxin and method of preparation. U.S. Patent #5,512,547, April 30, 1996.

Fleno, B., I. Christensen, R. Larsen, S.R. Johansen, and E.A. Johnson. Astaxanthin-producing yeast cells, methods for their preparation and their use. U.S. Patent #5,599,711, February 4, 1997.

Fleno, B., I. Christensen, R. Larsen, S.R. Johansen, and E.A. Johnson. Astaxanthin-producing yeast cells, methods for their preparation and their use. U.S. Patent #5,679,567, October 21, 1997.

Johnson, E.A., M.C. Goodnough, and G.E. Borodic. Pharmaceutical composition containing botulinum B complex. U.S. Patent #5,696,077, December 9, 1997.

Fleno, B., I. Christensen, R. Larsen, S.R. Johansen, and E.A. Johnson. Astaxanthin-producing yeast cells, methods for their preparation and their use. U.S. Patent #5,709,856, January 20, 1998.

Fleno, B., I. Christensen, R. Larsen, S.R. Johansen, and E.A. Johnson. Astaxanthin-producing yeast cells methods for their preparation and their use. U.S. Patent #5,712,110, January 27, 1998.

Johnson, E.A. and M.C. Goodnough. Pharmaceutical compositions of botulinum toxin or botulinum neurotoxin and methods of preparation. U.S. Patent #5,756,468, May 26, 1998.

Johnson, E.A., H. Sugiyama, and C.J. Malizio. Purification of type G botulinum neurotoxin and pharmaceutical compositions thereof. U.S. Patent #5,846,929, December 8, 1998.

Johnson, E.A., M.C. Goodnough, and M. Bradshaw. Hybrid botulinal neurotoxins. U.S. Patent #5,939,070, August 17, 1999.

Johnson, E.A., M. Bradshaw, J.I. Rood, and D. Lyras. Expression system for clostridium species. U.S. Patent #5,955,368, September 21, 1999.

Fleno, B., I. Christensen, R. Larsen, S.R. Johansen, and E.A. Johnson. Astaxanthin-producing yeast cells, methods for their preparation and their use. U.S. Patent #5,972,642, October 26, 1999.

Johnson, E.A. and G.J. Haas. Antimicrobial activity of hops extract against *Clostridium botulinum*, *Clostridium difficile* and *Helicobacter pylori*. U.S. Patent #6,251,461, June 26, 2001.

Johnson, E.A. and B.F. Brehm-Stecher. Method of sensitizing microbial cells to antimicrobial compound. U.S. Patent #6,319,958, November 20, 2001.

Johnson, E.A., M.C. Goodnough, M. Bradshaw, and W.H. Tepp. Hybrid botulinal neurotoxins. U.S. Patent #6,444,209, September 3, 2002.

Johnson, E.A., M.C. Goodnough, C.J. Malizio, and A.B. Scott. Chimeric toxins. U.S. Patent #6,545,126, April 8, 2003.

Johnson, E.A. and G.J. Haas. Treating or preventing illness growth of Clostridium difficile. U.S. Patent #6,623,775, September 23, 2003.

Goodnough, M.C., E.A. Johnson, W.H. Tepp, and C.J. Malizio. Method of targeting pharmaceuticals to motor neurons. U.S. Patent #6,670,322, December 30, 2003.

SUBMISSION END

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