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SENT *VIA* FEDEX

January 11, 2008

Robert L. Martin, Ph.D.
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

Re: GRAS Notice for Yeast Beta-Glucan

Dear Dr. Martin:

In accordance with proposed 21 CFR §170.36 [Notice of a claim for exemption based on a Generally Recognized As Safe (GRAS) determination] published in the *Federal Register* [62 FR 18938 (17 April 1997)], I am submitting in triplicate, as the notifier [Biothera, Inc., 3388 Mike Collins Drive, Eagan, MN, 55121], a Notice of the determination, on the basis of scientific procedures, that yeast beta-glucan, as defined in the enclosed documents, is GRAS under specific conditions of use as a food ingredient, and therefore, is exempt from the premarket approval requirements of the *Federal, Food, Drug and Cosmetic Act.* Information setting forth the basis for the GRAS determination, which includes a comprehensive summary of the data available and reviewed by an independent panel of experts (the Expert Panel) in support of the safety of yeast beta-glucan under the intended conditions of use, as well as *curricula vitae* evidencing the qualifications of the members of the Expert Panel for evaluating the safety of food ingredients, also is enclosed for review by the agency.

I trust that the enclosed Notice is acceptable. Should you have any questions or concerns regarding this GRAS Notice, please do not hesitate to contact me at any point during the review process so that we may provide a response in a timely manner.

Sincerely,

Dr. Donald J. Cox
Vice President of R&D and Business Development
Healthcare Group
Biothera, Inc.

Enclosures

3388 Mike Collins Drive
Eagan - Minnesota 55121

www.biotherapharma.com

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)]

Yeast beta-glucan, as defined in the report in Appendix I entitled, "**EXPERT PANEL CONSENSUS STATEMENT CONCERNING THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS OF YEAST BETA-GLUCAN FOR USE AS A FOOD INGREDIENT**", dated August 29, 2007, has been determined by Biothera, Inc (Biothera) to be 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, and on the consensus opinion of an independent panel of experts qualified by scientific training and expertise to evaluate the safety of yeast beta-glucan under the intended conditions of use. Therefore, the use of yeast beta-glucan as a food ingredient, as described below is exempt from the requirement of premarket approval

Signed,

11JAN08

Dr Donald J Cox
Vice President of R&D and Business Development
Healthcare Group
Biothera, Inc

Date

RECEIVED
JAN 16 2008
BY:

B. Name and Address of Notifier

Donald J Cox, Ph.D
Vice President of R&D and Business Development
Healthcare Group
Biothera, Inc
3388 Mike Collins Drive
Eagan, MN 55121

C. Common Name of the Notified Substance

Yeast beta-glucan

D. Conditions of Intended Use in Food

Biothera intends to market yeast beta-glucan, derived from food-grade bakers yeast (*Saccharomyces cerevisiae*), as a food ingredient in the United States in a variety of food products including baked goods and baking mixes, beverages and beverage bases, cereal and

cereal products, dairy product analogs, milk and milk products, plant protein products, processed fruits and fruit juices, soft candy, and soup and soup mixes at a level of up to 200 mg/serving (see Table 2 of Appendix I) Yeast beta-glucan is not intended for use in meat or meat-containing products.

The consumption of yeast beta-glucan from all proposed food uses was estimated using the United States Department of Agriculture 1994-1996 Continuing Survey of Food Intakes by Individuals (USDA CSFII 1994-1996) survey (USDA, 2000). Under the intended conditions of use, the total population all-user mean intake of yeast beta-glucan was estimated to be 413.02 mg/person/day (8.90 mg/kg body weight/day), with an estimated heavy consumer (90th percentile) all-user intake of 827.32 mg/person/day (20 66 mg/kg body weight/day). On an absolute basis, the greatest mean and 90th percentile all-user intakes of yeast beta-glucan were estimated to occur in male teenagers, at 580 95 and 1,186.49 mg/ person/day, respectively (see Table 3 of Appendix I) On a body weight basis, the greatest mean and 90th percentile all-user intakes of yeast beta-glucan were highest in infants, with intakes of 27.88 and 53.96 mg/kg body weight/day, respectively (see Table 4 of Appendix I); however, it should be noted that the intended food uses will not be marketed directly for use in infant products (*i e* , yeast beta-glucan is not intended to be incorporated in infant formula/foods or toddler foods), and hence the actual infant and toddler consumption of yeast beta-glucan is expected to be limited

E. Basis for the GRAS Determination

Pursuant to 21 CFR §170.30, yeast beta-glucan has been determined by Biothera to be GRAS 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 yeast beta-glucan as a component of food The safety of yeast beta-glucan is based on data generally available in the public domain on the ingredient itself and other yeast-derived beta-glucan ingredients, as discussed herein and in the accompanying documents [see Appendix I, **EXPERT PANEL CONSENSUS STATEMENT CONCERNING THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS OF YEAST BETA-GLUCAN FOR USE AS A FOOD INGREDIENT**].

F. Availability of Information

The data and information that serve as the basis for this GRAS Notice 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:

Biothera, Inc.
3388 Mike Collins Drive
Eagan, MN
55121

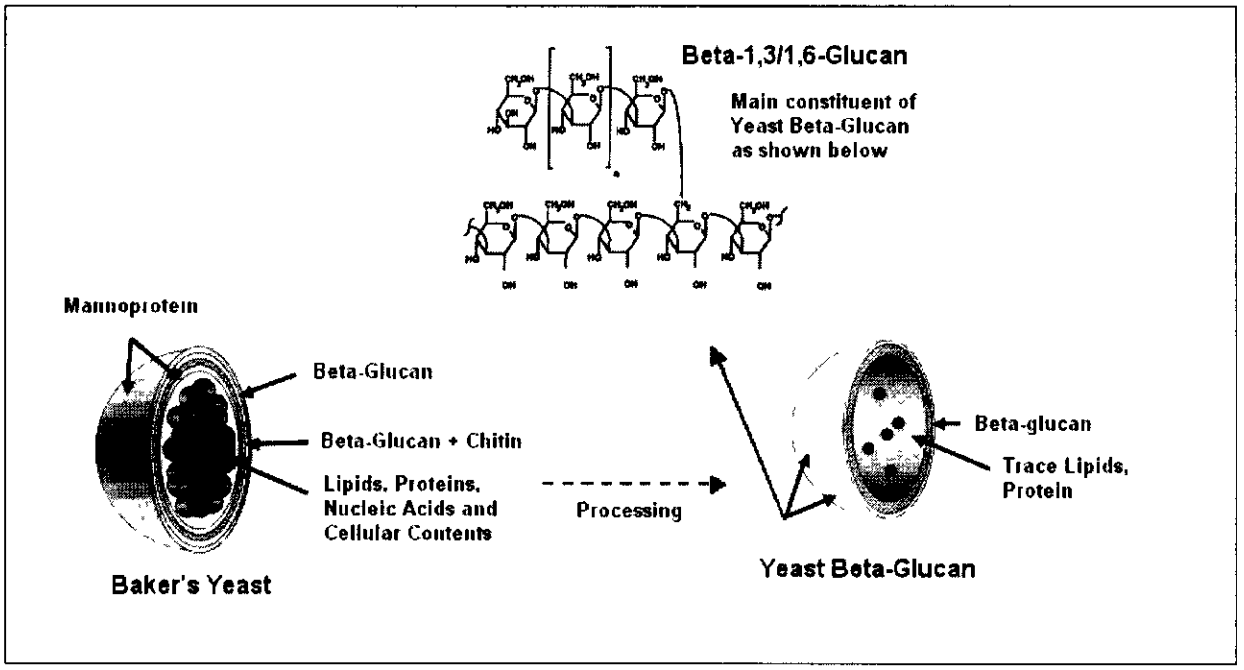
Should the FDA have any questions or additional information requests regarding this Notice, Biothera also will supply these data and information.

II. Detailed Information About the Identity of the Substance

A. Identity

The common or usual name of this product is yeast beta-glucan. Biothera's yeast beta-glucan is a dried spray-dried yeast extract powder with fine beige to tan coloration. The ingredient contains at least 70% insoluble beta-1,3/1,6-glucan, and comprises a physical make-up that is essentially represented as a mixture of hollow spheres or "ghost" cells as depicted in Figure 1 In addition to trace amounts of protein and lipids, small amounts of beta-1,6-glucan and chitin also are expected to be present in the final product

Figure 1 Pictorial Representation of Yeast Beta-Glucan



A typical preparation of Biothera's yeast beta-glucan consists of "hollow" yeast cell wall spheres approximately 2 to 4 microns in diameter

Common or Usual Name: Yeast beta-glucan
Chemical Name: (1-3),(1-6)-β-D-glucan, Poly-(1-6)-β-D-glucopyranosyl-(1,3)-β-D-glucopyranose

Chemical Abstracts Service (CAS) Number: Not available
Empirical Formula and Formula Weight: Not available

Structural Formula: See Figure 1.

B. Manufacturing

Yeast beta-glucan is manufactured according to current Good Manufacturing Practices (cGMP) using appropriate food grade reagents and ingredients The S. cerevisiae used in the production of yeast beta-glucan is standard food-grade Baker's yeast, which is grown at Biothera's production plant under controlled conditions in stainless steel fermentation vessels The yeast cells are lysed to extract the beta-glucan component of the cell wall, which is purified to produce the final ingredient. Autolysis of the fermentation mixture occurs in the fermentation vessel where the cells are lysed using a thermal process that takes place over several days. The yeast extract is then separated from the cell wall using centrifugal separation Following centrifugation, the total solids content of the cell wall is 10 to 12% of the original mass. The cell wall isolate then undergoes a caustic treatment to strip the mannosylated cell wall proteins, which are linked to the cell wall by alkali sensitive bonds. This step also removes any residual cellular lipids trapped within the cell wall that become soluble under alkaline pH Subsequently, the ingredient undergoes an acid treatment, which results in the depolymerization and deacetylation of chitin to form free glucosamine hydrochloride, and essentially results in the removal of most of the chitin. Next, the yeast wall slurry undergoes subsequent flash sterilization and pH adjustment steps resulting in a sterile solution with an approximate pH range 5-6. The resulting mixture contains between 6 to 12% of the original solids and is essentially pure beta-1,3/1,6-glucan. The mixture is then spray-dried, and once dry, the powder is sieved through a mesh sifter. The final beta-1,3/1,6-glucan product is then packaged into cardboard boxes with 10 kg double inner bags made out of polyethylene

C. Specifications for Food Grade Material

In order to ensure consistent product, Biothera has established specifications for the final ingredient (see Table 1), which are similar to those described for bakers yeast glycan (U.S. FDA, 2007b). Representative lots are routinely assayed to ensure compliance with final product chemical, physical, and microbiological specifications. The ingredient comprises mainly carbohydrates (at least 80%), with minor amounts of protein and fat, all of which already are present in the human diet *via* the consumption of bakers yeast and ingredients derived thereof. Biothera's yeast beta-glucan meets appropriate food-grade specifications and all processing aids used in the manufacture of the ingredient (*i e.,* pH-adjusting agents) are appropriate for food use. The results of studies of the stability of yeast beta-glucan indicated that the ingredient is very stable under normal storage conditions (*i.e.*, up to 5 years).

Table 1 Product Specifications for Biothera's Yeast Beta-Glucan

Specification Parameter	Specification	Method of Analysis
Physical Specifications		
Description	Fine beige/tan powder	Visual inspection
Taste	Bland	Taste
Odor	Faint/mild	Olfactory
Chemical Specifications		
Total Carbohydrate (%)	At least 80	By difference
Beta-glucan (1,3/1,6) (%)	At least 70[a,b]	Internal Method
Protein (%)	<10	AOAC Method 990 03
Fat (%)	<20	AOAC Method 989 05
Ash (%)	<5	AOAC Method 942 05
Moisture (%)	<8	AOAC Method 930.15
Lead (ppm)	<0 5	AOAC Method 984 27
Microbiological Specifications		
Aerobic Plate Count (CFU/g)	<20,000	AOAC Method 966 23
Yeast and Mold (CFU/g)	≤25	U S. FDA BAM, 7th ed.
Coliforms (CFU/g)	<10	AOAC Method 966 24
Escherichia coli	Negative	AOAC Method 966 08
Salmonella sp	Negative	AOAC Method 966 24

AOAC = Association of Analytical Communities; CFU = colony-forming units; U.S FDA BAM = U.S. Food and Drug Administration standard bacterial analytical manual methodologies (U.S. FDA, 1998)
[a] For commercial purposes, the product will be designated WGP® 3-6 if it contains a beta-glucan content of at least 75%, and otherwise will be designated BetaRight® 3-6.
[b] Small amounts of beta-1,6-glucan and chitin also are expected to be present in the final product

The final yeast beta-glucan ingredient is a fine beige to tan powder containing at least 70% insoluble beta-1,3/1,6-glucan and is sold as BetaRight® 3-6 (at least 70% beta-glucan) or WGP® 3-6 (at least 75% beta-glucan). Although BetaRight® 3-6 and WGP® 3-6 exist as separate commercial products, it should be noted that only one cGMP manufacturing process is used in the manufacture of Biothera's yeast beta-glucan ingredient(s), and the final ingredient is designated as either BetaRight® 3-6 or WGP® 3-6 based on the beta-glucan content of the final product.

Volatile organic compounds (VOCs) were identified as a by-product of the production process used to make the yeast beta-glucan ingredient (*i.e.*, small amounts of methanol, ethanol, isopropanol, acetone, and hexane can be detected in the final product), even though no organic solvents are used at any stage of the manufacturing process. Biothera determined that the VOCs are produced during the manufacturing process *via* fatty acid decomposition reactions as a result of removal of the lipids using an alkali wash procedure, and that the presence of trace VOCs are common to many yeast food ingredients and beta-glucan dietary supplements. The

levels of these compounds are present in a highly consistent manner from batch-to-batch, and the maximum level of VOC production will be restricted by quality control procedures that limit the levels of primary reactant (the lipid content) required for VOC formation in the final product to no more than 7%, which is well below the specification for this parameter Based on the levels of VOCs in the final product and the fact that the estimated intakes of these compounds will be below upper limits established by the U.S. Environmental Protection Agency and relevant pre-clinical toxicological information, the exposure to VOCs from the consumption of yeast beta-glucan from the estimated intake is not expected to produce adverse effects on human health.

III. Self-Limiting Levels of Use

The levels of use of yeast beta-glucan will be limited due to food formulation issues, as the ingredient will impart undesirable characteristics to the food regarding taste, flavor, and viscosity Specific thresholds for these effects have not been determined.

IV. Basis for GRAS Determination

Pursuant to 21 CFR §170 30, yeast beta-glucan, under the intended conditions of use specified herein and defined in Appendix I **[EXPERT PANEL CONSENSUS STATEMENT CONCERNING THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS OF YEAST BETA-GLUCAN FOR USE AS A FOOD INGREDIENT]** has been determined by Biothera to be GRAS 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 yeast glucan as a component of food.

The safety of yeast beta-glucan is based on data generally available in the public domain on the ingredient itself and other yeast-derived beta-glucan ingredients. These data include a published subchronic oral toxicity study of WGP® 3-6 in rats in which no compound-related toxicity was observed at the highest permissible dose (Babíček *et al* , 2007) and pre-clinical studies of other beta-1,3-glucan test articles, as well as other scientific data pertaining to the safety of yeast beta-glucan, and in particular, published clinical trials of beta-glucan ingredients. The safety of yeast beta-glucan is supported by the compositional similarity of the ingredient to bakers yeast glycan, which is approved by the FDA for direct addition as a multi-purpose food additive to various food products including salad dressing, frozen desserts, sour cream and cheese spread analogs, and flavored snack dips (21 CFR §172.898) (U.S. FDA, 2007b), as well as the background consumption of bakers yeast and ingredients derived thereof Additionally, the safety of Biothera's yeast beta-glucan is supported by unpublished human trials of the ingredient. Moreover, bakers yeast, has been used for over a thousand years as a food ingredient, and its most common present day and historical uses are in the production of bread and in the fermentation process of wine and beer (Mortimer, 2000), and significant levels of beta-1,3-glucans also occur naturally in a number of foods, such as edible mushrooms, celery,

chi-chian leaves, carrot, radish, and soybeans (Ko and Lin, 2004) Therefore, the consumption of Biothera's yeast beta-glucan will not result in exposure to any substance that is not already present in the human diet as a result of the inherent composition and use of bakers yeast glycan and its source, *S. cerevisiae*, as well as other natural foods In addition, all of the components of yeast beta-glucan (*i.e.*, carbohydrates, proteins, and fats) are expected to be subject to known metabolic processes. Using these data to support the safety of the ingredient, yeast beta-glucan is GRAS based on scientific procedures. A summary of this information is provided in Appendix I **[EXPERT PANEL CONSENSUS STATEMENT CONCERNING THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS OF YEAST BETA-GLUCAN FOR USE AS A FOOD INGREDIENT]**.

V. References

Babiček, K., Čechová, I.; Simon, R R., Harwood, M., Cox, D.J. 2007. Toxicological assessment of a particulate yeast (1,3)-β-D glucan in rats. Food Chem Toxicol 45(9)·1719-1730.

Ko, Y.-T ; Lin, Y.-L. 2004. 1,3-β-glucan quantification by a fluorescence microassay and analysis of its distribution in foods J Agric Food Chem 52(11):3313-3318.

Mortimer, R K 2000. Evolution and variation of the yeast (*Saccharomyces*) genome Genome Res 10(4)·403-409 & [Erratum, 10(6)891].

USDA 2000. 1994-1996, 1998 Continuing Survey of Food Intakes by Individuals (CSFII) and Diet and Health Knowledge Survey (DHKS) (On CD-ROM). U.S. Department of Agriculture (USDA); Riverdale, Maryland. [PB2000-500027].

U S FDA. 1998. Bacteriological Analytical Manual [BAM] (8th Ed.). U.S. Food and Drug Administration (U.S FDA), Center for Food Safety and Applied Nutrition (CFSAN), College Park, Maryland. Available from· http·//www.cfsan.fda.gov/~ebam/bam-toc html.

U.S. FDA. 2007a. Part 170—Food labeling 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 Government Printing Office (GPO); Washington, DC, pp 13-15

U.S. FDA 2007b. Part 172—Food additives permitted for direct addition to food for human consumption. §172.898—Bakers yeast glycan. In. U.S. Code of Federal Regulations (CFR). Title 21—Food and Drugs (U S Food and Drug Administration). U.S. Government Printing Office (GPO), Washington, DC, p 120.

APPENDIX I

EXPERT PANEL CONSENSUS STATEMENT CONCERNING THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS OF YEAST BETA-GLUCAN FOR USE IN AS A FOOD INGREDIENT

Appendix 1

EXPERT PANEL CONSENSUS STATEMENT CONCERNING THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS OF YEAST BETA-GLUCAN FOR USE AS A FOOD INGREDIENT

INTRODUCTION

At the request of Biothera Inc. (Biothera), 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 to conduct a critical and comprehensive evaluation of the available pertinent data and information on yeast beta-glucan, and determine whether, under the conditions of intended use as a food ingredient, yeast beta-glucan, derived from bakers yeast, *Saccharomyces cerevisiae*, would be safe and Generally Recognized as Safe (GRAS) based on scientific procedures. In the United States, bakers yeast extract is affirmed as GRAS for direct addition to food, and bakers yeast protein and glycan are permitted direct food additives. The Panel consisted of the below-signed qualified scientific experts. Prof Joseph F. Borzelleca, Ph.D. (Virginia Commonwealth University, Medical College of Virginia), Prof. Robert J. Nicolosi, Ph.D (University of Massachusetts Lowell), and Prof Gary M Williams, M.D (New York Medical College) *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 Biothera and compiled by Cantox Health Sciences International (Cantox). In addition, the Panel evaluated other information deemed appropriate or necessary, including scientific data obtained from the literature and other published sources through September 2006 by Cantox. The information evaluated by the Panel included data pertaining to the method of manufacture and product specifications of the yeast beta-glucan ingredient, supporting analytical data, information establishing the compositional similarity of Biothera's yeast beta-glucan to bakers yeast glycan, the intended use levels of yeast beta-glucan in specified food products, consumption estimates for all intended uses, background dietary consumption of bakers yeast and ingredients derived thereof, and a comprehensive assessment of the available scientific literature pertaining to the safety of yeast and other beta-glucan ingredients.

Following independent critical evaluation of such data and information, the Panel convened on 27 November 2006 and unanimously concluded that the proposed uses in traditional foods described herein for yeast beta-glucan derived from *S. cerevisiae*, meeting appropriate food-grade specifications and manufactured according to current Good Manufacturing Practice (cGMP), are safe. The Panel further concluded that these uses are GRAS based on scientific procedures. A summary of the basis for the Panel's conclusion is provided below

MANUFACTURING AND COMPOSITION

The *S. cerevisiae* used in the production of yeast beta-glucan is standard food-grade bakers yeast, which is grown at Biothera's production plant under controlled conditions in stainless steel fermentation vessels. The yeast cells are lysed to extract the beta-glucan component of the cell wall, which is purified to produce the final ingredient Yeast beta-glucan is manufactured according to cGMP and comprises mainly carbohydrates (at least 80%), with minor amounts of protein and fat, all of which already are present in the human diet *via* the consumption of bakers yeast and ingredients derived thereof The final yeast beta-glucan ingredient is a fine beige to tan powder containing at least 70% insoluble beta-1,3/1,6-glucan and is sold as BetaRight® 3-6 (at least 70% beta-glucan) or WGP® 3-6 (at least 75% beta-glucan). Although BetaRight® 3-6 and WGP® 3-6 exist as separate trade products, it should be noted that only one cGMP manufacturing process is used in the manufacture of Biothera's yeast beta-glucan ingredient(s), and the final ingredient is designated as either BetaRight® 3-6 or WGP® 3-6 based on the beta-glucan content of the final product

In order to ensure consistent product(s), Biothera has established specifications for the final ingredient(s) (see Table 1), which are similar to those described for bakers yeast glycan (U S FDA, 2007a). Cantox reviewed batch analysis data submitted by Biothera and concluded that a consistent product can be produced. Representative lots are routinely assayed to ensure compliance with final product chemical, physical, and microbiological specifications Biothera's yeast beta-glucan meets appropriate food-grade specifications and all processing aids used in the manufacture of the ingredient (*i.e* , pH-adjusting agents) are appropriate for food use. The results of studies of the stability of yeast beta-glucan indicated that the ingredient is very stable under normal storage conditions (*i.e* , up to 5 years)

Table 1 Product Specifications for Biothera's Yeast Beta-Glucan

Specification Parameter	Specification	Method of Analysis
Physical Specifications		
Description	Fine beige/tan powder	Visual inspection
Taste	Bland	Taste
Odor	Faint/mild	Olfactory
Chemical Specifications		
Total Carbohydrate (%)	At least 80	By difference
Beta-glucan (1,3/1,6) (%)	At least 70[a]	Internal Method
Protein (%)	<10	AOAC Method 990 03
Fat (%)	<20	AOAC Method 989 05
Ash (%)	<5	AOAC Method 942 05
Moisture (%)	<8	AOAC Method 930 15
Lead (ppm)	<0 5	AOAC Method 984 27

Table 1 Product Specifications for Biothera's Yeast Beta-Glucan		
Specification Parameter	**Specification**	**Method of Analysis**
Microbiological Specifications		
Aerobic Plate Count (CFU/g)	<20,000	AOAC Method 966 23
Yeast and Mold (CFU/g)	≤25	U S FDA BAM, 7th ed
Coliforms (CFU/g)	<10	AOAC Method 966 24
Escherichia coli	Negative	AOAC Method 966 08
Salmonella sp	Negative	AOAC Method 966 24

AOAC = Association of Analytical Communities, BAM = standard bacterial analytical manual methodologies (U S FDA, 1998), CFU = colony-forming units, U S EPA = U S Environmental Protection Agency, U S FDA = U S Food and Drug Administration

[a] For trade purposes, the product will be designated WGP® 3-6 if it contains a beta-glucan content of at least 75%, and otherwise will be designated BetaRight® 3-6

Volatile organic compounds (VOCs) were identified as a by-product of the production process used to make the yeast beta-glucan ingredient, and small amounts of methanol, ethanol, isopropanol, acetone, and hexane can be detected in the final product (<744 ± 70 ppm, on average), even though no organic solvents are used at any stage of the manufacturing process Biothera determined that the VOCs are produced during the manufacture of the yeast beta-glucan ingredient *via* fatty acid decomposition reactions as a result of removal of the lipids using an alkali wash procedure. Biothera also determined that the presence of trace VOCs are common to many yeast food ingredients and beta-glucan dietary supplements. As the VOC are produced during a GMP production process, the levels of these compounds are therefore present in a highly consistent manner from batch-to-batch. In addition, the maximum level of VOC production will be restricted by quality control procedures that limit the levels of primary reactant (the lipid content) required for VOC formation in the final product to no more than 7%, which is well below the specification for this parameter Based on the level of VOCs in the final product and the fact that the estimated intakes of these compounds will be below upper limits established by the U S Environmental Protection Agency (EPA) and relevant pre-clinical toxicological information, the exposure to VOCs from the consumption of yeast beta-glucan from the estimated intake is not expected to produce adverse effects on human health.

INTENDED USE AND ESTIMATED EXPOSURE OF YEAST BETA-GLUCAN

Biothera intends to market yeast beta-glucan as a food ingredient in the United States in a variety of food products including baked goods and baking mixes, beverages and beverage bases, cereal and cereal products, dairy product analogs, milk and milk products, plant protein products, processed fruits and fruit juices, soft candy, and soup and soup mixes at a level of 200 mg/serving. The individual proposed food-uses and use-levels are summarized below in Table 2 The use of yeast beta-glucan in food and beverage products is self-limiting due to certain food formulation issues, such as taste, flavor, and viscosity.

Table 2 Proposed Food Uses and Use Levels for Yeast Beta-Glucan				
Food Category	**Proposed Food-Use**	**RACC[a] (g or mL)**	**Yeast Beta-Glucan Level[b]**	
			(mg/serving)	**(%)**
Baked Goods and Baking Mixes	Cookies	30 to 40	200	0 5 to 0 667
Beverages and Beverage Bases	Meal Replacement Beverages (not Milk-Based)	240	200	0 083
Cereal and Cereal Products	Nutritional Bars (Breakfast, Granola, Protein)	40	200	0 500
Dairy Product Analogs	Soy Milk	240	200	0 083
Milk and Milk Products	Meal Replacement Beverages	240	200	0 083
	Probiotic Beverages	240	200	0 083
	Yogurt	225	200	0 089
	Yogurt Beverages	240	200	0 083
Plant Protein Products	Soy Protein Bars	40	200	0 500
Processed Fruits and Fruit Juices	Fruit Beverages (Drinks, Juices, Smoothies)	240	200	0 083
Soft Candy	Chocolate Confections	40	200	0 500
Soup and Soup Mixes	Soups	245	200	0 082

[a] RACC = Reference Amounts Customarily Consumed Per Eating Occasion [21 CFR §101 12 (U S FDA, 2007b)] When a range of values is reported for a proposed food use, particular foods within that food use may differ with respect to their RACC

[b] The intended use levels of up to 200 mg/serving comprise the maximum use level for each trade ingredient separately (*i e* , BetaRight® 3-6 or WGP® 3-6) or for both ingredients combined (*i e* , up to 200 mg BetaRight® 3-6 and WGP® 3-6 combined), therefore, for the purpose of this report, the intended uses of the ingredient(s) are stated simply as yeast beta-glucan

Using the United States Department of Agriculture (USDA) 1994-1996 Continuing Survey of Food Intakes by Individuals (USDA CSFII 1994-1996) survey (USDA, 2000), under the conditions of intended use, the total population all-user mean intake of yeast beta-glucan was estimated to be 413.02 mg/person/day (8 90 mg/kg body weight/day), with an estimated heavy consumer (90th percentile) all-user intake of 827 32 mg/person/day (20 66 mg/kg body weight/day). On an absolute basis, the greatest mean and 90th percentile all-user intakes of yeast beta-glucan were estimated to occur in male teenagers, at 580 95 and 1,186.49 mg/person/day, respectively (see Table 3). On a body weight basis, the greatest mean and 90th percentile all-user intakes of yeast beta-glucan were highest in infants, with intakes of 27 88 and 53 96 mg/kg body weight/day, respectively (see Table 4), however, it should be noted that the intended food uses will not be marketed directly for use in infant products (*i e* , yeast beta-glucan is not intended to be incorporated in infant formula/foods or toddler foods), and hence the actual infant and toddler consumption of yeast beta-glucan is expected to be limited.

Table 3	Summary of the Estimated Daily Intake of Yeast Beta-Glucan from All Proposed Food Categories in the U.S. by Population Group (1994-1996, 1998 USDA CSFII Data)						
Population Group	Age Group (Years)	% Users	Actual # of Total Users	All-Person Consumption		All-Users Consumption	
				Mean (mg)	90th Percentile (mg)	Mean (mg)	90th Percentile (mg)
Infant	0 to 2	71 6	2,564	273 25	636 11	350 34	693 21
Child	3 to 11	98 4	6,205	475 32	869 07	484 94	870 62
Female Teenager	12 to 19	91 5	642	403 57	856 81	441 20	886 05
Male Teenager	12 to 19	91 7	638	531 93	1,134 57	580 95	1,186 49
Female Adult	20 and Up	85 0	3,887	291 07	642 50	339 21	673 10
Male Adult	20 and Up	81 6	3,876	354 34	827 75	433 08	906 93
Total Population	All Ages	86 4	17,812	356 92	786 22	413 02	827 32

Table 4	Summary of the Estimated Daily Per Kilogram Body Weight Intake of Yeast Beta-Glucan from All Proposed Food Categories in the U.S. by Population Group (1994-1996, 1998 USDA CSFII Data)						
Population Group	Age Group (Years)	% Users	Actual # of Total Users	All-Person Consumption		All-Users Consumption	
				Mean (mg/kg)	90th Percentile (mg/kg)	Mean (mg/kg)	90th Percentile (mg/kg)
Infant	0 to 2	71 6	2,564	21 70	50 50	27 88	53 96
Child	3 to 11	98 4	6,205	19 69	37 87	20 10	38 02
Female Teenager	12 to 19	91 5	642	7 49	17 47	8 21	17 72
Male Teenager	12 to 19	91 7	638	8 72	18 43	9 54	19 91
Female Adult	20 and Up	85 0	3,887	4 54	10 27	5 29	10 83
Male Adult	20 and Up	81 6	3,876	4 42	10 51	5 40	11 53
Total Population	All Ages	86 4	17,812	7 68	18 77	8 90	20 66

S cerevisiae, more commonly referred to as bakers yeast, has been used for over a thousand years as a food ingredient, and its most common present day and historical uses are in the production of bread and in the fermentation process of wine and beer (Mortimer, 2000). As mentioned, bakers yeast and various ingredients derived from bakers yeast are permitted for use as direct ingredients in certain food products for sale in the U S (U S FDA, 2007a)[1], and significant levels of beta-1,3-glucans also occur naturally in a number of foods, such as edible mushrooms, specifically the Shiitake (*Lentinus edodes*), Maitake (*Grifola frondosa*), Wood

[1] According to a survey of industrial food additive use in the United States, the use of bakers yeast in foods was reported to be 58,900 pounds/year, which on a *per capita* basis would correspond to 3.07 mg/person/day (0 04 mg/kg body weight/day) (Lucas *et al* , 1999)

Cauliflower (*Sparassis crispa Fr*), and snow mushroom (*Tremella fuciformis*) varieties (Ko and Lin, 2004) Several non-fungus-derived food sources, including celery, chi-chian leaves, carrot, and radish, contain nearly 20% beta-1,3-D-glucan in their total carbohydrate fraction, and soybeans contain up to 0.8% beta-1,3-D-glucan (dry weight) (Ko and Lin, 2004). Moreover, Biothera markets their WGP 3-6® ingredient (as Imucell WGP® 3-6) as a dietary ingredient for use in dietary supplement products, and various other yeast beta-glucan supplements are marketed in the U.S. Therefore, all of the components present in Biothera's yeast beta-glucan are already present in the diet

BASIS FOR GRAS STATUS OF YEAST BETA-GLUCAN

The safety of yeast beta-glucan is based on data generally available in the public domain on the ingredient itself and other yeast-derived beta-glucan ingredients The safety of yeast beta-glucan is supported by the compositional similarity of the ingredient to bakers yeast glycan, which is approved by the U.S. Food and Drug Administration (FDA) for direct addition as a multi-purpose food additive (21 CFR §172 898) to various food products including salad dressing, frozen desserts, sour cream and cheese spread analogs, and flavored snack dips (U.S. FDA, 2007a), the background consumption of bakers yeast and ingredients derived thereof; and other scientific data pertaining to the safety of yeast beta-glucan, including unpublished human trials of the ingredient. Moreover, the consumption of Biothera's yeast beta-glucan will not result in exposure to any substance that is not present in bakers yeast glycan or its source, *S. cerevisiae*, which are already present in the human diet, and all of the components of yeast beta-glucan (*i.e.*, carbohydrates, proteins, and fats) are expected to be subject to known metabolic processes Using these data to support the safety of the ingredient, yeast beta-glucan is GRAS based on scientific procedures. A summary of this information is provided below.

Compositional Similarity of Yeast Beta-Glucan to Bakers Yeast Glycan

As stated in the *Code of Federal Regulations* (CFR), "the FDA believes that in certain instances the concept of equivalence may have applicability to the technical element of a GRAS determination" (U S. FDA, 1997). Substantial equivalence is referred to in the joint Food and Agriculture Organization (FAO) and World Health Organization (WHO) report as embodying "the concept that if a new food or food component is found to be substantially equivalent to an existing food or food component, it can be treated in the same manner with respect to safety (*i.e* , the food or food component can be concluded to be as safe as the conventional food or food component" (FAO/WHO, 1996; U.S. FDA, 1997).

In establishing the equivalence of a product to an existing food product it is important to determine that any differences in the new food product do not outweigh the similarities between the two products. Thus, the FDA has stated that a critical factor that must be determined when

applying the concept of equivalence is any difference in composition between the substances being compared (U.S. FDA, 1997)

Biothera's yeast beta-glucan and bakers yeast glycan can both be defined as the dried cell wall of the yeast, *S cerevisiae* The cell wall of *S cerevisiae* is predominantly composed of linear helical chains of beta-D glucose molecules bonded through 1,3 linkages, and characteristic of *S cerevisiae*, these glucan chains also contain a number of 1,6 branch points. Both food ingredients are composed almost entirely of carbohydrates, as both products are approximately 80% pure carbohydrate on a dry weight basis, and the ingredients' product specifications include similar limits for chemical and microbiological parameters. A comparison of the specifications for yeast beta-glucan and bakers yeast glycan is presented in Table 5.

Table 5 Comparison of Biothera's Yeast Beta-Glucan with Bakers Yeast Glycan

Specification	Yeast Beta-Glucan	Bakers Yeast Glycan*
Description	Fine beige/tan powder	Comminuted, washed, pasteurized, and dried cell walls of the yeast, *Saccharomyces cerevisiae*
Organism	*S cerevisiae*	*S cerevisiae*
Total Carbohydrate (%)	At least 80	At least 85
Beta-glucan (%)	At least 70	At least 57 [a]
Protein (%)	<10	na
Fat (%)	<20	na
Ash (%)	<5	na
Moisture (%)	<8	na
Lead (ppm)	<0 5	<0 2
Mercury (ppm)	<0 05	<0 05
Arsenic (ppm)	<0 1 [b]	<0 4
Selenium (ppm)	N/A	<0 09
Cadmium (ppm)	<1 [b]	<13
Zinc (ppm)	N/A	<10
Aerobic Plate Count (CFU/g)	<20,000	<10,000
Yeast and Mold (CFU/g)	≤25	<10
Coliforms (CFU/g)	<10	na
Escherichia coli	Negative	Negative
Salmonella sp	Negative	Negative
Coagulase positive *Staphylococci*, *Clostridium perfringens*, *Clostridium botulinum*, or any other recognized pathogen or harmful microbial toxin	N/A	Negative

CFU = colony forming units, N/A = not analyzed for by Biothera, na = not available per 21 CFR §172.898
*All parameters specified under 21 CFR §172 898 for bakers yeast glycan Additional details were not available
[a] The total carbohydrate fraction comprises beta-glucan and mannose units in approximately a 2 1 ratio
[b] Derived from certificates of analysis for various batches of Biothera's yeast beta-glucan

The primary difference between the two products pertains to the carbohydrate composition Bakers yeast glycan contains mannose at a ratio of 1:2 to beta-glucan, whereas mannose is not expected to be present in Biothera's yeast beta-glucan. Given that the total carbohydrate level present in bakers yeast glycan is at least 85%, and using a ratio of 1·2 of mannose to beta-glucan, the level of beta-glucan present in bakers yeast glycan is expected to be at least 56%, which is only slightly less than the beta-glucan level of Biothera's yeast beta-glucan ingredient (*i.e.*, at least 70%)

Pursuant to the CFR, bakers yeast glycan is permitted for use in salad dressing at a level not to exceed 5% of the finished product and also is permitted for use in frozen desserts, sour cream analogs, cheese spread analogs, and cheese flavored and sour cream flavored snack dips at levels that are not to exceed good manufacturing practice. These levels are at least 10-fold higher than the proposed levels of use of yeast beta-glucan in any one food category, and thus the intended conditions of use of yeast-beta glucan are not anticipated to represent an exposure that would be substantially different than exposure from the permitted uses of bakers yeast glycan.

In conclusion, based on the fact that both ingredients are derived from the cell wall of *S. cerevisiae* and analytically are similar in composition, and that the consumption of Biothera's yeast beta-glucan would result in comparable exposure to beta glucan and other constituents present in bakers yeast glycan (minus mannose), the compositional similarity of Biothera's yeast beta-glucan to bakers yeast glycan as permitted for use by the FDA and regulated under 21 CFR §172.898 (U S FDA, 2007a) supports the safe use of the ingredient in food.

Absorption, Distribution, Metabolism, and Excretion of Yeast Beta-Glucan

Biothera's ingredient is an insoluble yeast beta-glucan cell wall particulate carbohydrate. Humans are unable to digest carbohydrate polymers with beta-glucosidic linkages (Wisker *et al.*, 1985), and therefore absorption by the intestinal epithelium and significant systemic exposure to particulate yeast glucans will not occur (Lehne *et al*, 2005, Rice *et al*, 2005) Some systemic exposure following oral administration does occur, however, and is likely a rate-limited process[2] that is regulated by processing within the Peyer's patches of the small intestine and transport to the reticuloendothelial system *via* macrophages (Beier and Gebert, 1998; Hong *et al.*, 2004). Oxidative degradation of the glucan particle then occurs over several days (Hong *et al*, 2004). This is in contrast to exposure to yeast beta-glucans *via* intraperitoneal or intravenous routes, which results in significant accumulation of the carbohydrate within the organs of the reticuloendothelial system, however, due to minimal (if any) bioavailability of

[2] Although there is no direct empirical evidence to substantiate this, there is no reason to believe these compounds would be handled any differently than the consumption of Bakers yeast In addition, it should also be emphasized that the Peyer's patches are sensory organs and do not display dietary uptake functions

orally-administered yeast beta-glucan, parenteral routes of exposure are inappropriate for the safety evaluation of food ingredients that are ingested and not absorbed.

Toxicological Studies

A critical evaluation of the available acute, sub-chronic, and chronic oral toxicity data on yeast beta-glucans indicated that insoluble particulate yeast beta-1,3-glucans are of low toxicity. In addition, available information on *S cerevisiae*-derived particulate beta-1,3-glucans was evaluated for the purpose of supporting the safety of Biothera's yeast beta-glucan These studies are summarized below. Yeast beta-glucan cannot be detected in the plasma following oral administration (Lehne *et al*, 2005, Rice *et al.*, 2005) due to minimal or no absorption from the gastrointestinal tract. Studies involving parenteral exposure to yeast beta-glucans were identified and reviewed for the purpose of this report, but were not considered in the safety assessment of yeast beta-glucan under the conditions of use in food

Acute Toxicity Studies

The administration of a single oral dose of 2,000 mg yeast beta-glucan (as WGP® 3-6)/kg body weight was well tolerated in BrlHan WIST@Jcl rats, and no clinical or histopathological evidence of toxicity was observed (OECD, 2001; Babíček *et al*, 2007), which is consistent with the fact that orally administered yeast beta-glucans are not digested or absorbed to any significant degree

Studies of acute parenteral exposure to soluble beta-glucan also indicated that yeast-derived beta-glucan[3] was well tolerated in mice and rats following single intravenous doses of up to 1,000 and 500 mg/kg body, respectively, and following intraperitoneal administration of 250 mg yeast beta-glucan/kg body weight for a period of 7 days in mice, although significantly reduced weight gain was observed in guinea pigs under the same study conditions (Williams *et al*, 1988).

Sub-Chronic/Chronic Toxicity Studies

A sub-chronic oral toxicity study of yeast beta-glucan (as WGP® 3-6) administered by gavage was conducted in Fisher CDF(F-344)/CrlBR rats The animals (10/sex/group) were administered 0, 2, 33 3, or 100 mg/kg body weight/day of WGP® 3-6 for 91 consecutive days (OECD, 1998, Babíček *et al.*, 2007). Separate control and treatment (100 mg/kg body weight/day) recovery groups for each sex also were included, and were maintained for an additional 14 days without dosing following the treatment period This study was conducted consistent with Organisation for Economic Co-operation and Development (OECD) Guideline 408, which states that the maximum volume to be administered by gavage is not to exceed 10

[3] Based on references in the document, it appears that the glucan used in the experiment was a soluble beta-glucan preparation derived from *S cerevisiae*, however, detailed descriptions of the test article were not reported

mL/kg body weight Based on maximum flowable concentration , the authors stated that 100 mg/kg body weight was the highest permissible dose that could be administered by gavage Although no information was presented by the authors regarding the use of gavage *versus* inclusion of yeast beta-glucan in the food, it is known that yeast beta-glucan is bitter tasting at high doses and thus palatability issues may have prevented administration of the test article in the diet.

WGP® 3-6 was well tolerated throughout the treatment period, and no mortality, signs of morbidity, or significant differences in weight gain or food consumption were observed. A few sporadic, statistically significant, increases in red blood cell (RBC) count, mean corpuscular volume (MCV), and hematocrit (Hct) occurred in males in the highest dose group (100 mg/kg body weight/day) compared to controls; however, the differences were less than 10% and did not exceed the maximums of physiological and historical control data ranges, and the same effect was not observed in the corresponding recovery group Similarly, a dose-dependent difference in clotting times observed in male animals compared to controls that was significant at the 2 highest doses (33 3 and 100 mg/kg body weight/day; decreased by 33 and 44%, respectively) was within the historical control range, was not present in both sexes, and returned to baseline levels following withdrawal of dosing. Moreover, the authors reported that the clotting times were unexpectedly elevated in the control group; therefore, the effect was considered to be clinically non-significant. Similar to the males, a statistically significant increase in MCV was observed in females, however, the effect was modest (6%) and occurred equally in all dose groups. Isolated statistically significant changes were observed for some clinical chemistry parameters (bilirubin, glucose, sodium, potassium, cholesterol, low-density lipoprotein cholesterol, urea, and total protein); however, since the changes were within historical control values, were not dose responsive, and did not occur in both sexes, the effects were considered to be of no toxicological significance. Infrequent non-dose-related findings of very fine nodular adhesions were detected on the spleen capsule of 4 treatment animals, and 1 male in the control group developed a malignant lymphoma. No pathological findings were present in any animals subjected to necropsy after termination of the recovery period. There were some slight (≤10%) but statistically significant changes in the absolute weights and relative organ weights in treatment *versus* control groups; however, these effects were sporadic, the differences in organ weights were not connected with any pathologic processes (*i e.*, the incidence of histopathological findings for controls and high-dose animals were similar), and no connection with potential effects of WGP® 3-6 was observed. Moreover, all mean values of absolute weights were within the limits of historical variability The findings occurring more frequently (*i e* , calcifications in the female renal tubules, small hyaline casts in the male renal tubules, small foci of fibrous adhesions on the spleen capsule) were observed randomly at similar frequencies in animals of the control groups and animals treated with the test item. The authors also stated that neither proliferative, hyperplastic, nor hypertrophic alterations were observed in lymphoid organs. Based on clinical, pathological, and statistical evaluations, the authors concluded that no compound-related toxicity was observed over the 91-day

administration period, and the no observed adverse effect level (NOAEL) of WGP® 3-6 was reported to be 100 mg/kg body weight/day, the highest permissible dose tested

Feletti *et al.* (1992) investigated the effects of chronic (52 weeks) oral administration of an insoluble yeast beta-glucan granulate (99 4% purity) derived from *Candida albicans* in Sprague-Dawley rats. Animals (20/sex/group) were administered the test material by gavage over a period of 52 weeks at doses of 0, 50, 100, or 200 mg total beta-glucan/kg body weight/day. Separate recovery control groups also were included in the study No compound-related abnormalities in the clinical measures or deaths were observed over the experimental period, nor were significant differences in body weight, food consumption, or water intake observed between the control and treatment groups. There also were no significant differences in the hematology, blood chemistry, urinalysis, or organ weight measurements. The only finding attributed to beta-glucan administration was soft stools or diarrhea and cecal enlargement with variable hyperplasia of the colon mucosa in the high-dose group (200 mg/kg body weight/day), an effect that returned to normal after the cessation of treatment Based on observations of cecal enlargement at the highest dose, the authors determined the no observed effect level (NOEL) to be 100 mg/kg body weight/day. However, cecal enlargement is a well established response in rodents consuming large quantities of polyols (Newberne *et al.*, 1988), and is not considered toxicologically significant and not relevant to humans (WHO, 1987). A no observed adverse effect level (NOAEL) of 200 mg/kg body weight/day, the highest dose tested, is more appropriate

Williams *et al.* (1988) reported on a series of sub-chronic parenteral toxicity studies of soluble beta-glucan in ICR/HSD mice Bi-weekly intravenous administration of yeast-derived beta-glucan at doses of 0, 40, 200, or 1,000 mg/kg body weight to males (5/group) in 2 separate 30- and 60-day experiments did not significantly alter body weights or liver, lung, or kidney weights in mice, although, following 30 days of treatment, a non-dose-related significant increase in spleen weight was reported in mice receiving 40 or 1,000 mg/kg body weight/day compared to the control group A similar effect was observed during the 60-day study, with spleen weights increasing in a dose-dependent manner and achieving statistical significance at the highest dose (1,000 mg/kg body weight/day). No deaths occurred and there were no behavioral or appearance changes observed in any group for either experiment. The 30- and 60-day 1,000 mg/kg body weight/day dose groups showed significant histological changes in the liver, with an observation of granuloma formation and mononuclear infiltrate consisting of monocytes and an unidentified cell type the authors speculated might have been of lymphocyte origin. There were no significant histopathological changes in the lung, kidney, or spleen at any dose level for either the 30- or 60-day animals These studies are not relevant to the safety assessment of yeast beta-glucan under the intended conditions of use in food.

Mutagenicity/Genotoxicity Studies

No mutagenicity or genotoxicity studies for yeast beta-glucan were identified in the literature, although two studies indicated that yeast-derived beta-glucans display anti-mutagenic properties *in vitro* (Zhang and Ohta, 1993; Miadoková *et al.*, 2005) In addition, numerous studies document the antioxidant, chemoprotectant, and anti-cancer properties of various yeast beta-glucans *in vitro* and in animal models (Chorvatovičová and Navarová, 1992; Gomaa *et al.*, 1992, Cheung *et al* , 2002; Križková *et al* , 2003; Slameňová *et al.*, 2003, Hong *et al* , 2004; Allendorf *et al.*, 2005, Gu *et al.*, 2005), and the mushroom beta-glucan, lentinan, has been used in Japan for the treatment of cancer for a number of years (Matsuoka *et al.*, 1997; Nakano *et al* , 1999; Yoshino *et al.*, 2000).

Reproductive and Developmental Toxicity Studies

No reproductive or developmental toxicity studies of orally administered yeast beta glucans were identified in the literature Studies in CrL COBS CD (SD) BR rats investigating the potential reproductive and developmental toxicity of intravenous lentinan administration were reported by Cozens *et al.* (1981a,b,c,d). These studies were designed to assess the effects of lentinan administration in males and females prior to mating, and/or to assess the effects of lentinan *in utero* and post-natally by administration of lentinan to females during gestation and post-partum. Significant gonadal damage and impaired reproductive capacity was observed in male rats administered lentinan at doses equal to or greater than 0 10 mg/kg body weight/day, while a dose of 0 01 mg/kg body weight/day in male rats resulted in some morphological evidence of gonadal damage without resulting reproductive capacity. No significant differences in reproductive capacity of the females or in parameters of fetal development were observed. In rabbits, intravenous administration of up to 1 0 mg lentinan/kg body weight/day to dams during gestation did not result in any significant compound-related effects on developmental parameters (Cozens *et al.*, 1981d). Similar to observations in sub-chronic dog and monkey studies (Chesterman *et al.*, 1981, Sortwell *et al.*, 1981), significant dose-dependent increases in spleen weights were reported in both males and females receiving lentinan at intravenous doses of 0 10 mg/kg body weight/day and higher (Cozens *et al.*, 1981a,b,c), and lentinan at doses above 0 5 mg/kg body weight/day resulted in reticuloendothelial toxicity. Similarly, significantly increased spleen weights were reported in rabbits receiving 30 mg/kg body weight/day of lentinan (Cozens *et al.*, 1981d) Although lentinan is a 1,3/1,6-beta glucan, the compound is not yeast-derived and is at least an order of magnitude higher in molecular weight than *S cerevisiae*-derived beta-glucans, and the product used in the identified systemic reproductive studies was partially soluble, compared to the insoluble yeast beta-glucan particulate produced by Biothera Therefore, although some toxic effects were observed in association with systemic lentinan exposure, the studies are not considered in the safety assessment of yeast beta-glucans under the intended conditions of use in foods because the test compounds are different and the route of exposure for lentinan is inappropriate

Studies in Humans

In a double blind, placebo-controlled clinical trial with 20 healthy volunteers, treatment subjects consumed a single capsule providing 250 mg WGP® 3-6/day for 10 days (BEI, 2005a). Blood collection was performed on Day 0 prior to treatment and on Day 10, and the subjects were monitored for 30 days for clinical observations In addition to standard clinical chemistry and hematology, a number of immunological parameters also were determined. No significant differences in white blood cell differential count, whole blood phenotyping, or natural killer (NK) cell activity were observed Assessed by flow cytometry, the phagocytosis of *Staphylococcus aureus* beads was significantly increased by WGP® 3-6 treatment. Serum tumor necrosis factor (TNF)-alpha levels were increased 6-fold relative to baseline levels, but no effects on interleukin (IL)-1 or interferon (INF)-gamma were reported. The blood chemistry profiles were within normal ranges for most subjects with the following exceptions: 6 of 10 subjects had increased potassium levels; glucose increased in one subject and decreased in another, and calcium levels were increased in 1 patient. Overall, WGP® 3-6 at a dose of 250 mg/person/day for 10 days was safe and well tolerated and blood biochemistry parameters were essentially unaffected by beta-glucan treatment

A second placebo-controlled double blind study was performed with 62 subjects to assess the safety and impact of WGP® 3-6 on immune biomarkers in subjects exposed to rhinovirus (common cold) (BEI, 2005b). All volunteers were pre-screened to exclude subjects that exhibited levels of rhinovirus antibodies, and each participant consumed 2 daily doses of 250 mg of WGP® 3-6 per day for 10 days. Standard safety endpoints and a number of immune-related hematological biomarkers were measured. WGP® 3-6 supplementation insignificantly increased the NK cell number relative to the placebo, while no significant effects on T cells or cytokine levels were observed. Overall, WGP® 3-6 was well tolerated and no adverse effects attributable to the test article were reported

Nicolosi *et al* (1999) reported on a clinical study that investigated the safety and potential cholesterol-lowering effect of an oral insoluble particulate yeast beta-glucan at a dose of 15 g/person/day (approximately 150 mg/kg body weight/day) in 15 free-living, obese, hypercholesterolemic men over a period of 8 weeks The beta-glucan test article was not well characterized in the published study article, however, the authors indicated that the product was 85 to 90% pure beta-glucan, consisting of beta-1,3 linkages and forming distinct hollow microsphere structures that were readily miscible in water and communication with Biothera confirmed that the yeast beta-glucan preparation used in the study was identical to WGP® 3-6. Compared to average baseline values, the consumption of yeast beta-glucan decreased plasma total cholesterol levels by 8% at Week 7 and by 6% at Week 8. Following discontinuation of beta-glucan treatment, total cholesterol levels returned to baseline values, however, a significant increase (16%) in high-density lipoprotein (HDL)-cholesterol was reported at week 12. No significant change in low-density lipoprotein cholesterol was observed throughout any of the time-points. The mean ratio of total cholesterol to HDL cholesterol declined significantly

from baseline on Weeks 7 and 8, but returned to baseline levels by Week 12. Side effects typically reported with fiber consumption, such as diarrhea, nausea, abdominal discomfort, abdominal distension, and flatulence, were minimal The results of this study indicate that high doses of yeast beta-glucan (15 g/person/day) were well tolerated in adults.

The safety of oral supplementation with a "soluble" branched beta-1,3-glucan (SBG)[4] derived from *S. cerevisiae* was investigated by Lehne *et al.* (2005) in an open dose-escalation study in 18 healthy volunteers Subjects (6/group) were randomized to receive 100, 200, or 400 mg SBG/person for a period of 4 consecutive days. Data collected included routine hematological data, clinical chemistry data, urinalysis, blood and saliva levels of total immunoglobulin (Ig) A, IgG, IL-6 and TNF-alpha, saliva levels of IL-1β, vital signs, and oral cavity observations. On Days 1 (before and 1 hour after administration), 2, 5, and 8, plasma concentrations of beta 1,3-D-glucan were measured Plasma concentrations of beta-1,3-D-glucan did not differ between the pre-study values and the values recorded on Days 5 and 8, demonstrating that there was no systemic absorption of beta-1,3-D-glucan following oral supplementation with SBG. No abnormalities in vital signs were observed and no adverse event was considered related to SBG administration. Minor mucosal lesions of the oral cavity were observed in 7 subjects but were considered normal physiological variations. Increased C-reactive protein, fibrinogen, and abnormal differential counts of leucocytes were observed in 5 subjects with pre-existing respiratory infections, including 1 with herpes labialis. All other hematological and biochemical parameters were within normal physiological ranges throughout the study There was a significant increase in the saliva IgA value on Day 5 compared to Day 1 in the 400 mg SBG/day dose group, but no other significant differences in serum or saliva IgA or IgG values were reported. There were no significant changes in IL-1β, IL-6, or TNF-α between treatment groups.

Other Considerations

Potential Hypersensitivity/Allergenicity of Yeast Beta-Glucan

In a study conducted by Instanes *et al.* (2004), injection (into the fat pad of the hind foot) of a beta-1,3-glucan extract derived from *S. cerevisiae* was reported to increase the allergic response to ovalbumin (OVA) immunization in female balb/c mice, although no IgE or IgG1 anti-OVA antibodies were observed for animals receiving beta-glucan in the absence of OVA. Similar yet more modest delayed hypersensitivity reactions were reported by Tokunaka *et al.* (2000), where a significant increase in IgG production was observed in ICR mice following the intraperitoneal administration of a soluble beta-D glucan (from *Candida* and *Sclerotina* yeasts)

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[4] The SBG was formulated as a water suspension that subjects were instructed to use as a mouthwash for 2 minutes before swallowing Although the beta-glucan was stated to be soluble, the mouthwash solution was characterized as "hazy" by the authors and suggests that the glucan test material was actually poorly soluble in water, and a significant percentage of the glucan would therefore have been in a particulate form

used as an adjuvant with bovine serum albumin antigen. Delayed hypersensitivity reactions also were observed by Perez *et al* (1984) in C3H/He mice administered insoluble beta-glucan (derived from *S cerevisiae*) *via* intraperitoneal or subcutaneous routes before and in conjunction with immunizing doses of sheep RBC.

The effect of *S. cerevisiae*–derived beta-glucan on the immune response to OVA also was assessed by Li *et al.* (2005) in piglets. Upon weaning, 24 pigs were randomized to receive 1 of 2 diets supplemented with beta-glucan at 0 or 50 mg/kg feed (providing approximately 60 mg/kg body weight/day) for a period of 31 days. On Day 14, animals were injected with OVA and the antibody response was determined on Days 21 and 28. An increase in OVA response (20%) was observed on Day 21 for beta-glucan-treated animals, although the effect was transient and OVA antibody levels returned to baseline by Day 28. In a second study by Li *et al.* (2006), yeast beta-glucan (*S cerevisiae*-derived) was administered once again to weaned pigs at concentrations up to 200 ppm in the diet for a period of 35 days. The glucan diet was well tolerated at all feed supplementation levels, as evidenced by no compound-related changes in body weight, and had no effect on *ex vivo* lymphocyte proliferation relative to controls. In weanling crossbred male pigs receiving *S. cerevisiae* beta-glucan (312 mg/kg body weight/day) in the diet, improved growth and decreased stress response to endotoxin challenge was observed relative to control animals not receiving beta-glucan supplementation (Eicher *et al* , 2006)

In humans, positive skin prick tests to *S. cerevisiae* have been reported in as high a proportion as 70 to 94% of patients with atopic dermatitis Moreover, delayed hypersensitivity to intravenous beta glucan was observed in surgical trauma patients, however, the increased sensitivization effect resulted in a beneficial effect in trauma patients, as a significant decrease in mortality and overall septic morbidity was observed (Browder *et al* , 1990)

Although direct allergy to *S. cerevisiae* occurring from food consumption is rare, confirmed cases of food allergy to bakers yeast have been reported in the literature (Pajno *et al.*, 2005) The effects were not life threatening, however, and mechanistically, yeast allergy is typically a function of hypersensitivity to the enolase and/or mannan in the yeast, not the beta-glucan fraction (Kortekangas-Savolainen *et al* , 1993; Nittner-Marszalska *et al.*, 2001), and therefore, allergenicity and/or hypersensitivity to yeast beta-glucan is not anticipated to occur. Since the ingredient will be labeled as yeast beta-glucan, it is anticipated that individuals with yeast or beta-glucan allergy or sensitivity will avoid ingestion of this product

Mineral Binding

Although the consumption of dietary fiber has been reported to reduce the bioavailability of various minerals, the effect is predominantly a function of the phytate content of the food, and mechanistic evidence to support a direct role of indigestible fiber in the sequestering of minerals is conflicting at best (Greger, 1999). In fact, most studies suggest that various pectins, gums,

and indigestible sugars improve mineral bioavailability (Greger, 1999). For example, in a study by Mai *et al* (2002) designed to investigate the potential effects of brewer's yeast and 2 of its components (glucan and mannan) on the absorption of radiolabeled iron in anemic rats, 5 groups of anemic male 4-week-old Sprague-Dawley rats (5 to 6 animals/group) were provided single gavage doses of a control mixture, a glucan mixture (14 mg/rat), a yeast cell wall mixture (50 mg/rat), a mixture of glucan and mannan (14 and 7 mg/rat), or a yeast cytoplasm mixture (50 mg/rat). Glucan treatment significantly increased the blood iron levels relative to controls and also significantly increased kidney and small intestine levels of radiolabeled iron. The authors reported that the glucan and yeast cell wall treatments stimulated the incorporation of dietary iron into iron stores, and that beta-glucan was responsible for this effect. Increased bioavailability similar to the effects reported by Mai *et al.* (2002) has been reported by others (*e g* , Greger, 1999) It is unlikely that the consumption of yeast beta-glucans would impair mineral bioavailability under their intended conditions of use in food

Plasma Cholesterol, Bile Acid Secretion and Short Chain Fatty Acid Production

A study designed to investigate the effect of various crude and refined soluble and insoluble yeast (*Kluyveromyces marxianus*) cell wall preparations on plasma cholesterol, fecal sterol excretion, and short chain fatty acid production was performed by Yoshida *et al.* (2005) in which 5-week-old male Wistar (8/group) rats fed a high-cholesterol diet supplemented with 50 g/kg feed [approximately 5,000 mg/kg body weight/day (U S. FDA, 1993)] of the various test articles over a period of 14 days were reported not to exhibit any significant differences in weight gain, however, total cholesterol was significantly decreased with both insoluble yeast cell wall preparations, without any significant differences in HDL-cholesterol, triglyceride, or phospholipid levels Fecal sterol excretion was increased by the insoluble yeast cell wall supplementation, as were total neutral sterols, bile acids, and total sterols relative to controls. Total fecal short chain fatty acid (SCFA) excretion also was increased from insoluble yeast cell wall supplementation. No adverse effects on gastrointestinal function were observed, and the changes observed were overall of a beneficial nature.

In an experiment by Nakamura *et al.* (2001a), brewer's yeast cell wall beta-glucan derived from *S cerevisiae* provided *via* the diet at levels of 0, 2, 3, or 5% [0, 2,000, 3,000 and 5,000 mg/kg body weight/day, respectively (U S FDA, 1993)] was reported to positively affect experimentally-induced constipated rats, as significant increases in number of feces, fecal dry weight, and fecal water content were observed relative to a no-fiber diet, and in most cases, relative to cellulose positive controls Similar to the experiment by Yoshida *et al.* (2005), generalized increases of volatile fatty acids were observed, an effect characterized by significant increases in butyrate, propionate, and acetate production relative to both positive and normal controls

In a similar study, Nakamura *et al.* (2001b) assessed the effect of yogurt supplemented with 0, 1, 3, or 5% brewer's yeast cell wall [approximately 0, 1,000, 3,000 or 5,000 mg/kg body

weight/day (U.S. FDA, 1993)] on experimentally-induced constipation and intestinal microflora in rats (8 to 10 animals/group). The yeast cell wall administration increased fecal frequency in non-constipated rats and resulted in a dose-responsive increase in fecal frequency and fecal volume in constipated rats at the highest dose without effects on fecal water content, and increased fecal SCFA (*i.e.*, acetic, proprionic, and butyric acids) production was observed in a dose-dependent manner. In addition, treatment significantly increased the number of *Lactobacilli*, *Eubacteria*, and total anaerobes in the gastrointestinal tract relative to cellulose controls without effects on the microbial populations of *Bifidobacterium* or *Bacterioideceae*. The authors concluded that the yeast cell wall was fermented by intestinal bacteria, and that the effect resulted in the alleviation of loperimide-induced constipation and an improved bowel environment. Similar results were reported by McBurney (1991) in an *in vitro* experiment in which various fiber sources were fermented with human fecal microbiota, and the highest level of SCFA was observed in the beta-glucan group (compared to a mixed fiber and psyllium group) In contrast, yeast glucan was the least effective fiber in terms of water holding capacity.

The results from these studies demonstrate that yeast beta-glucans were substrates of bacterial metabolism. The metabolic products were characterized primarily as acetate, propionate, and butyrate, with lesser amounts of other endogenous SCFA. These metabolic compounds are not toxic, and humans are routinely exposed to these SCFA through the routine consumption of food products containing indigestible fibers such as cellulose An additional gastrointestinal effect reported was increased laxation, which was probably mediated by osmotic effects resulting in fecal overloading. This effect is not considered adverse.

SUMMARY

Yeast beta-glucan is isolated from the cell wall of bakers yeast (*S cerevisiae*) and is composed primarily of beta-1,3-glucan (at least 70%). The ingredient, which will be marketed as BetaRight® 3-6 (containing at least 70% beta-glucan) or WGP® 3-6 (containing at least 75% beta-glucan), is intended for use in a number of food products, including cookies, meal replacement beverages, breakfast, granola and protein nutritional bars, soy milk, probiotic beverages, yogurt, and yogurt beverages, fruit beverages, drinks, juices, and smoothies, soft candy, and soups at a level of 200 mg per serving. Under the conditions of intended use, total population all-user mean and 90th percentile daily intakes of yeast beta-glucan are estimated to be 413 02 and 827 32 mg/person/day, respectively (corresponding to 8.90 and 20.66 mg/kg body weight/day). Yeast beta-glucan is produced in accordance with cGMP, is highly stable under appropriate storage conditions, and the final product meets appropriate food-grade specifications Small amounts of VOC are produced during the manufacturing process of Biothera's yeast-derived beta-glucans *via* the degradation of fatty acids, despite the fact that no VOC are used in the production of the ingredient. However, this is not uncommon in yeast beta-glucan products and Biothera demonstrated that a number of currently-marketed yeast glucan food and dietary ingredients contain VOC at levels that are comparable to Biothera's yeast beta-

glucan. Based on established limits and available safety data for each VOC, the levels present in yeast beta-glucan are not expected to be of concern under the intended conditions of use of the ingredient in food.

The proposed uses of yeast beta-glucan are safe and also are GRAS based on scientific procedures The safety of yeast beta-glucan is based on pre-clinical and clinical safety data. Yeast beta-glucan, like many other dietary fibers, is not absorbed following consumption (Hong *et al.*, 2004; Lehne *et al* , 2005), and there is little risk of systemic toxicity. Any effects would be generally limited to those on the structure and function of the gastrointestinal tract, which would be effects that are typical of indigestible fiber Degradation of yeast beta-glucan occurs primarily in the large intestine where microflora fermentation occurs, resulting in the generation of short-chain fatty acids, which are subsequently absorbed and utilized in well-characterized biochemical pathways Small amounts of yeast beta-glucan may enter the systemic circulation *via* transport by macrophage cells to the bone marrow, spleen, and lymph nodes, where the beta-glucan is completely degraded.

A single oral dose of 2,000 mg WGP® 3-6/kg body weight to rats was well tolerated, and daily oral gavage dosing of WGP® 3-6 for 91 days in rats was without evidence of systemic or local (gastrointestinal) toxicity at the highest possible dose of 100 mg/kg body weight/day, which was determined by the authors to be the NOAEL under the conditions of this study (Babíček *et al.*, 2007) Feletti *et al.* (1992) reported on a 52-week study in rats using an oral particulate glucan (derived from *C albicans*) and no systemic toxicity was observed at the highest oral dose tested, 200 mg/kg body weight/day, which is the NOAEL

No adverse clinical effects or changes in biochemistry or hematology parameters were reported following WGP® 3-6 supplementation at quantities up to 500 mg/person/day for a period of 10 days to healthy human volunteers (BEI, 2005a,b) Higher doses of WGP® 3-6 were well tolerated in humans in a study by Nicolosi *et al.* (1999) in which daily oral supplementation with 15 g of WGP® 3-6 over a period of 8 weeks in 15 free-living obese hypercholesterolemic men was without any adverse effects typical of fiber consumption (*e.g* , diarrhea, nausea, abdominal discomfort and or distension, and flatulence)

Although WGP 3-6 has been shown to be taken up by immune cells, and to display immune modulation effects in rodents, the observations are difficult to extrapolate to humans, and overall, there is no evidence to suggest that Biothera's yeast glucans would adversely affect the immune system in humans The administration of WGP® 3-6 (250 mg/person) in healthy volunteers had no effect on total and differential white blood cell count, and no effects on whole blood phenotyping or NK cell activity The only effect observed during this study was an enhanced phagocytic capacity, suggesting enhanced macrophage activity and/or function. In healthy subjects exposed to rhinovirus, WGP® 3-6 at a level of 500 mg/person had no effects on NK cell numbers relative to placebo, and no significant effects on T cell number or cytokine levels were observed. Increased hypersensitivity effects have been reported in both humans

and animals (Perez *et al.*, 1984, Browder *et al.*, 1990; Instanes *et al.*, 2004), however, the effects are limited to the use of soluble yeast glucans and administration *via* parenteral routes. Allergenicity to bakers yeast has been reported in the literature (Pajno *et al.*, 2005), although its occurrence appears to be rare, and mechanistically is related to IgE reactivity to the mannan or enolase content of the cell rather than beta-glucan (Kortekangas-Savolainen *et al.*, 1993; Nittner-Marszalska *et al* , 2001)

In general, systemic toxicity is limited to parenteral administration as, with the exception of small amounts of gut-associated-lymphoid-tissue-mediated uptake, beta-glucans are not absorbed from the gastrointestinal tract and thus, systemic exposure to yeast beta-glucan following oral administration will not occur to any significant degree Therefore, the observations associated with the administration of various beta-glucans *via* parenteral routes would not be expected under the proposed conditions of use of yeast beta-glucan in foods

The safety of the yeast beta-glucan is supported by its essentially equivalent composition to bakers yeast glycan, which is the comminuted, washed, pasteurized, and dried cell walls of *S cerevisiae* and is approved for use by the FDA for direct addition to food as a multi-purpose food additive Both ingredients are derived from the cell walls of *S. cerevisiae*, contain at least 80% carbohydrate (dry weight basis), and are produced consistent with cGMP, and with similar product specifications, both ingredients meet food-grade specifications This essential equivalency between yeast beta–glucan and bakers yeast glycan supports the GRAS status of the proposed uses of Biothera's yeast beta-glucan

CONCLUSION

We, the Expert Panel, have independently and collectively critically evaluated the data and information summarized above and conclude that the proposed uses of Biothera's yeast beta-glucan derived from bakers yeast, *Saccharomyces cerevisiae*, meeting appropriate food-grade specifications and manufactured in accordance with cGMP, are safe and suitable. We further conclude that these proposed uses of Biothera's yeast beta-glucan are Generally Recognized as Safe (GRAS) based on scientific procedures It is our opinion that other qualified experts would concur with these conclusions

Prof Joseph F. Borzelleca, Ph D
Virginia Commonwealth University, Medical College of Virginia

31 August 2007
Date

Prof. Robert J. Nicolosi, Ph D.
University of Massachusetts Lowell

04 September 2007
Date

Gary M. Williams, M.D.
New York Medical College

10 September 2007
Date

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REFERENCES

Allendorf, D.J., Yan, J ; Ross, G.D ; Hansen, R.D , Baran, J.T., Subbarao, K., Wang, L ; Haribabu, B. 2005. C5a-mediated leukotriene B_4-amplified neutrophil chemotaxis is essential in tumor immunotherapy facilitated by anti- tumor monoclonal antibody and β-glucan J Immunol 174(11)·7050-7056.

Babíček, K ; Čechová, I., Simon, R.R ; Harwood, M , Cox, D.J. 2007 Toxicological assessment of a particulate yeast (1,3)-β-D glucan in rats Food Chem Toxicol [In Press].

BEI. 2005a Effect of Immunocell™ WPG® 3-6 Beta-Glucan Given per os (PO) on the Immune System of Healthy Human Volunteers: Confidential Biopolymer Engineering, Inc , Eagan, Minn

BEI 2005b Final Report on the Evaluation of the Efficacy of β-1,3/β1,6 Glucan for Prevention of Experimental Rhinovirus Infection (Common Cold) in Human Volunteers Confidential. Biopolymer Engineering, Inc., Eagan, Minn

Beier, R., Gebert, A. 1998. Kinetics of particle uptake in the domes of Peyer's patches. Am J Physiol 275(1, Part 1).G130-G137

Browder, W.; Williams, D., Preus, H ; Olivero, G., Enrichens, F., Mao, P.; Franchello, A. 1990 Beneficial effect of enhanced macrophage function in the trauma patient. Ann Surg 211(5)·605-612 & Discussion pp 612-613.

Chesterman, H ; Heywood, R , Allen, T.R., Street, A E ; Edmondson, N.A., Prentice, D.E. 1981. The intravenous toxicity of lentinan to the beagle dog Toxicol Lett 9(1):87-90.

Cheung, N.-K V , Modak, S , Vickers, A , Knuckles, B 2002 Orally administered β-glucans enhance anti-tumor effects of monoclonal antibodies Cancer Immunol Immunother 51(10).557-564

Chorvatovičová, D ; Navarová, J. 1992 Suppressing effects of glucan on micronuclei induced by cyclophosphamide in mice. Mutat Res 282(3).147-150

Cozens, D D.; Masters, R.E., Clark, R., Offer, J.M. 1981a. The effect of lentinan on fertility and general reproductive performance of the rat Toxicol Lett 9(1):55- 64

Cozens, D D., Hughes, E W ; Clark, R.; Offer, J.M 1981b. The effect of lentinan on the in utero foetal development of the rat and on postnatal development of the F1 offspring. Toxicol Lett 9(1):77-80

Cozens, D.D., Hughes, E W ; Clark, R., Offer, J.M. 1981c The effect of lentinan on the in utero embryonic and foetal development of the rat and on postnatal development of the F1 offspring. Toxicol Lett 9(1) 71-76

Cozens, D.D., Masters, R.E ; Clark, R 1981d. The effect of lentinan on pregnancy of the New Zealand white rabbit Toxicol Lett 9(1) 65-69.

Eicher, S.D., McKee, C A , Carroll, J.A , Pajor, E A. 2006. Supplemental vitamin C and yeast cell wall β-glucan as growth enhancers in newborn pigs and as immunomodulators after an endotoxin challenge after weaning J Anim Sci 84(9) 2352-2360.

FAO/WHO 1996 Biotechnology and Food Safety. Report of a Joint FAO/WHO Consultation, Sep. 30-Oct. 4, 1996, Rome, Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO), Geneva, Switz , FAO Food and Nutrition Paper No. 61

Feletti, F , De Bernardi di Valserra, M., Contos, S., Mattaboni, P ; Germogli, R. 1992 Chronic toxicity study on a new glucan extracted from Candida albicans in rats Arzneimittelforschung 42(11):1363-1367.

Gomaa, K , Kraus, J., Rosskopf, F , Roper, H.; Franz, G. 1992. Antitumour and immunological activity of a β1→3/1→6 glucan from *Glomerella cingulata.* J Cancer Res Clin Oncol 118(2):136-140.

Greger, J L. 1999 Nondigestible carbohydrates and mineral bioavailability. J Nutr 129(7S)·1434S-1435S.

Gu, Y -H., Takagi, Y., Nakamura, T., Hasegawa, T.; Suzuki, I., Oshima, M., Tawaraya, H ; Niwano, Y 2005 Enhancement of radioprotection and anti-tumor immunity by yeast-derived β-glucan in mice. J Med Food 8(2) 154-158

Hong, F., Yan, J., Baran, J.T., Allendorf, D J.; Hansen, R.D., Ostroff, G.R ; Xing, P X ; Cheung, N.-K V , Ross G D 2004 Mechanism by which orally administered β-1,3-glucans enhance the tumoricidal activity of antitumor monoclonal antibodies in murine tumor models. J Immunol 173(2):797-806.

Instanes, C., Ormstad, H.; Rydjord, B., Wiker, H.G., Hetland, G 2004. Mould extracts increase the allergic response to ovalbumin in mice. Clin Exp Allergy 34(10).1634-1641.

Ko, Y.-T ; Lin, Y -L 2004 1,3-β-glucan quantification by a fluorescence microassay and analysis of its distribution in foods J Agric Food Chem 52(11) 3313-3318

Kortekangas-Savolainen, O ; Kalimo, K ; Lammintausta, K ; Savolainen, J. 1993. IgE-binding components of baker's yeast (*Saccharomyces cerevisiae*) recognized by immunoblotting analysis Simultaneous IgE binding to mannan and 46-48 kD allergens of *Saccharomyces cerevisiae* and *Candida albicans* Clin Exp Allergy 23(3)·179-184 [Abstract Only].

Krížková, L , Ďuračková, Z , Šandula, J.; Slameňová, D.; Sasinková, V ; Sivoňová, M., Krajčovič, J 2003 Fungal β-(1-3)-D-glucan derivatives exhibit high antioxidative and antimutagenic activity in vitro. Anticancer Res 23(3B):2751-2756

Lehne, G ; Haneberg, B., Gaustad, P , Johansen, P.W., Preus, H., Abrahamsen, T.G. 2005. Oral administration of a new soluble branched β-1,3-D-glucan is well tolerated and can lead to increased salivary concentrations of immunoglobulin A in healthy volunteers Clin Exp Immunol 143(1):65-69

Li, J , Xing, J., Li, D , Wang, X , Zhao, L , Lv, S , Huang, D 2005 Effects of β-glucan extracted from *Saccharomyces cerevisiae* on humoral and cellular immunity in weaned piglets. Arch Anim Nutr 59(5) 303-312.

Li, J., Li, D F ; Xing, J.J.; Cheng, Z B ; Lai, C H 2006 Effects of β-glucan extracted from *Saccharomyces cerevisiae* on growth performance, and immunological and somatotropic responses of pigs challenged with *Escherichia coli* lipopolysaccharide J Anim Sci 84(9) 2374-2381.

Lucas, C D ; Putnam, J M , Hallagan, J B 1999. Flavor and Extract Manufacturers' Association of the United States 1995 Poundage and Technical Effects Update Survey. Flavor and Extract Manufacturers' Association (FEMA); Washington, DC

Mai, T.T.T , Igarashi, K., Hirunuma, R ; Takasaki, S., Yasue, M., Enomoto, S ; Kimura, S., Nguyen, C V. 2002 Iron absorption in rats increased by yeast glucan Biosci Biotechnol Biochem 66(8):1744-1747

Matsuoka, H., Seo, Y., Wakasugi, H.; Saito, T., Tomoda, H. 1997 Lentinan potentiates immunity and prolongs the survival time of some patients. Anticancer Res 17(4A):2751-2755

McBurney, M.I. 1991 Potential water-holding capacity and short-chain fatty acid production from purified fiber sources in a fecal incubation system. Nutrition 7(6) 421-424

Miadoková, E.; Svidová, S., Vlčková, V , Dúhová, V ; Pražmáriová, E , Tothová, K , Nad'ová, S , Kogan, G ; Rauko, P. 2005. The role of natural biopolymers in genotoxicity of mutagens/carcinogens elimination. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 149(2) 493-496

Mortimer, R.K. 2000. Evolution and variation of the yeast (*Saccharomyces*) genome. Genome Res 10(4):403-409 & [Erratum, 10(6)891].

Nakamura, T , Agata, K., Mizutani, M ; Iino, H. 2001a. Effects of brewer's yeast cell wall on constipation and defecation in experimentally constipated rats Biosci Biotechnol Biochem 65(4):774-780.

Nakamura, T ; Nishida, S., Mizutani, M ; Iino, H. 2001b. Effects of yogurt supplemented with brewer's yeast cell wall on constipation and intestinal microflora in rats. J Nutr Sci Vitaminol (Tokyo) 47(6):367-372

Nakano, H., Namatame, K., Nemoto, H., Motohashi, H ; Nishiyama, K , Kumada, K. 1999. A multi-institutional prospective study of lentinan in advanced gastric cancer patients with unresectable and recurrent diseases: effect on prolongation of survival and improvement of quality of life Kanagawa Lentinan Research Group. Hepatogastroenterology 46(28):2662-2668.

Newberne, P M., Conner, M.W., Estes, P. 1988 The influence of food additives and related materials on lower bowel structure and function. Toxicol Pathol 16(2) 184-197

Nicolosi, R ; Bell, S J., Bistrian, B R., Greenberg, I ; Forse, R.A., Blackburn, G L 1999 Plasma lipid changes after supplementation with β-glucan fiber from yeast Am J Clin Nutr 70(2).208-212

Nittner-Marszalska, M., Wójcicka-Kustrzeba, I.; Bogacka, E., Patkowski, J., Dobek, R. 2001. Skin prick test response to enzyme enolase of the baker's yeast (Saccharomyces cerevisiae) in diagnosis of respiratory allergy. Med Sci Monit 7(1) 121-124

OECD 1998 Repeated dose 90-day oral toxicity study in rodents In· OECD Guidelines for the Testing of Chemicals Organization for Economic Co-operation and Development (OECD); Paris, France, OECD Guideline No 408 [Adopted: 21st September 1998].

OECD. 2001 Acute oral toxicity – Fixed dose procedure. In: OECD Guidelines for the Testing of Chemicals. Organisation for Economic Co-Operation and Development (OECD), Paris, France, Guideline Test No. 420 [Adopted 17th December 2001].

Ono, Y ; Takeuchi, Y ; Hisanaga, N 1981. A comparative study on the toxicity of n-hexane and its isomers on the peripheral nerve. Int Arch Occup Environ Health 48(3) 289-294

Pajno, G B ; Passalacqua, G ; Salpietro, C ; Vita, D ; Caminiti, L., Barberio, G. 2005. Looking for immunotolerance. a case of allergy to baker's yeast (*Saccharomyces cerevisiae*) Allerg Immunol (Paris) 37(7) 271-272 [Abstract Only]

Pérez, H A ; Bolívar, J ; San Blas, G 1984. The immunomodulatory effect of yeast glucan on delayed hypersensitivity. J Immunopharmacol 6(4) 305-321

Rice, P J ; Adams, E L ; Ozment-Skelton, T ; Gonzalez, A.J., Goldman, M.P., Lockhart, B E , Barker, L A , Breuel, K.F., DePonti, W K.; Kalbfleisch, J H.; Ensley, H.E., Brown, G.D., Gordon, S ; Williams, D L 2005 Oral delivery and gastrointestinal absorption of soluble glucans stimulate increased resistance to infectious challenge. J Pharmacol Exp Ther 314(3).1079-1086.

Slameňová, D , Lábaj, J ; Križková, L ; Kogan, G , Šandula, J., Bresgen, N , Eckl, P 2003 Protective effects of fungal (1→3)-β-D-glucan derivatives against oxidative DNA lesions in V79 hamster lung cells Cancer Lett 198(2):153-160.

Sortwell, R J ; Dawe, S.; Allen, D G.; Street, A.E ; Heywood, R., Edmondson, N.A , Gopinath, C 1981. Chronic intravenous administration of lentinan to the rhesus monkey. Toxicol Lett 9(1)·81-85

Tokunaka, K., Ohno, N.; Adachi, Y., Tanaka, S., Tamura, H , Yadomae, T 2000 Immunopharmacological and immunotoxicological activities of a water-soluble (1→3)-β-D-glucan, SCBG from *Candida* spp. Int J Immunopharmacol 22(5):383-394.

U S. FDA. 1993. Appendix I. Table 14. Conversion table for test chemical treatment doses used in PAFA. In: Priority Based Assessment of Food Additives (PAFA) Database U S Food and Drug Administration (FDA), Center for Food Safety and Applied Nutrition (CFSAN); Washington, DC, p 58

U S. FDA 1997. Substances generally recognized as safe; Proposed rule (21 CFR Parts 170, 184, 1986, and 570). Fed Regist (US) 62(74).18937-18964

U S FDA. 1998 Bacteriological Analytical Manual [BAM] (8th Ed). U.S. Food and Drug Administration (U.S FDA), Center for Food Safety and Applied Nutrition (CFSAN); College Park, Maryland. Available from http //www cfsan.fda gov/~ebam/bam-toc html.

U S. FDA. 2007a. Part 172—Food additives permitted for direct addition to food for human consumption §172 898—Bakers yeast glycan. In: U S Code of Federal Regulations (CFR) Title 21—Food and Drugs (U.S. Food and Drug Administration). U S Government Printing Office (GPO); Washington, DC, p. 120

U S FDA 2007b. Part 101—Food labeling. § 101.12—Reference amounts customarily consumed per eating occasion In. U.S. Code of Federal Regulations (CFR) Title 21—Food and Drugs (U.S. Food and Drug Administration). U.S. Government Printing Office (GPO), Washington, DC, pp 46-56

USDA. 2000. 1994-1996, 1998 Continuing Survey of Food Intakes by Individuals (CSFII) and Diet and Health Knowledge Survey (DHKS) (On CD-ROM). U.S. Department of Agriculture (USDA); Riverdale, Maryland. [PB2000-500027]

WHO 1987. Toxicological versus physiological responses. In: Principles for the Safety Assessment of Food Additives and Contaminants in Food. World Health Organization (WHO), International Programme on Chemical Safety (IPCS); Geneva. Environmental Health Criteria, No. 70, p. 82.

Williams, D L., Sherwood, E.R., Browder, I W , McNamee, R.B., Jones, E L , Di Luzio, N.R. 1988. Pre-clinical safety evaluation of soluble glucan. Int J Immunopharmacol 10(4) 405-414.

Wisker, E , Feldheim, W ; Pomeranz, Y., Meuser, F. 1985. Dietary fiber in cereals. In· Pomeranz, Y (Ed) Advances in Cereal Science and Technology American Association of Cereal Chemists, St Paul, Minn., Vol VII, pp. 169-238.

Yoshida, Y ; Yokoi, W , Ohishi, K., Ito, M , Naito, E.; Sawada, H. 2005 Effects of the cell wall of *Kluyveromyces marxianus* YIT 8292 on the plasma cholesterol and fecal sterol excretion in rats fed on a high-cholesterol diet. Biosci Biotechnol Biochem 69(4):714-723

Yoshino, S.; Tabata, T ; Hazama, S., Iizuka, N., Yamamoto, K ; Hirayama, M ; Tangoku, A., Oka, M 2000 Immunoregulatory effects of the antitumor polysaccharide lentinan on Th1/Th2 balance in patients with digestive cancers. Anticancer Res 20(6C)·4707-4711.

Zhang, X.B., Ohta, Y. 1993 Antimutagenicity of cell fractions of microorganisms on potent mutagenic pyrolysates. Mutat Res 298(4)·247-253

Attachment 1

ATTACHMENT 1

***CURRICULUM VITAE* OF EXPERT PANEL MEMBERS**

Joseph Francis Borzelleca

Educational Background·

Academic Appointments

Professional Certification

Fellow, Academy of Toxicological Sciences

Professional Affiliations

Societies

Academy of Toxicological Sciences* **

American Association for the Advancement of Science

American Chemical Society

American College of Toxicology*

American Society of Pharmacology and Experimental Therapeutics**

(Environmental Pharmacology Committee, Liaison Committee, SOT, Toxicology Committee)

International ›ciety of Regulatory Toxicology and Pharmacology*

(Mem ›r of Council)

Sigma XI

Society o xperimental Biology and Medicine*

(Cour ›or, Program Chairman of Southeastern Section)

Society for R Analysis

Society of T(:ology* **
(Mer r and/or Chairman Awards, Education, Legislative Affairs, Membership,
Nom ıng Committees, Secretary of the Society, Councilor, and President, President,
Fooc ›fety Specialty Section)

Virginia Aca ıy of Science*

(Cha an, Medical Sciences Division)

* Held electe fice
** Held appo d office or position

Board of Dir tors

ILSI

Board of Sci ıtific and Policy Advisors

American Council on Science and Health

Journals

Editor, Food (emical Toxicology,

Editorial Boa d

Environme ıtal Carcinogenesis Reviews,

Journal of Environmental Pathology, Toxicology and Oncology

Journal of Environmental Science and Health,

Journal of the American College of Toxicology,

Journal of Toxicology Cutaneous and Ocular Toxicology,

Journal of Applied Toxicology,

Pharmac ›gy,

Pharmac ›gy and Drug Development,

Toxicolog and Applied Pharmacology,

Consultantships (Past, Present)

Governmental

- Food and Drug Administration
- National Institute of Mental Health
- National Cancer Institute
- Environmental Protection Agency
- Department of Labor - OSHA (Chairman, Carcinogens Standards Committee)
- U S Army - Research and Development Command

Non-Governmental

- National Academy of Sciences - NRC
  - Committee on Toxicology (Member, Chairman)/Board on Toxicology and Environmental Health Hazards
  - Safe Drinking Water Committee
  - Evaluation of Household Substances Committee (1138 Committee)
  - Food Protection Committee
  - Food Additives Survey Committee
  - Committee on Risk-Based Criteria for Non-RCRA Hazardous Wastes
  - Committee on Risk Assessment of Flame-Retardant Chemicals
- Federation of American Societies of Experimental Biology
  - Select Committee on GRAS Substances
  - Flavors and Extracts
  - Biotechnology Product Safety
  - Caprenin GRAS Committee
- World Health Organization
  - Joint Meeting on Pesticide Residues (JMPR) (Member, Chairman)
- NATO/CCMS Drinking Water Committee

Industrial

- Chemical Companies, Trade Associations

University Activities

Related to Instruction

Prepared a laboratory manual in pharmacology (animal and human studies) (1960)
Introduced the use of closed circuit TV and TV tapes in pharmacology (11960)
Introduced clinical pharmacological experiments into the medical and dental programs (1960)

Planning and participation in continuing education program
(Schools of Dentistry, Medicine and Pharmacy)

Planning and administering each of the three major efforts in pharmacology

(dental, medical, pharmacy) since

Graduate Program - assisted in developing graduate training program in toxicology

Current Teaching Activities

Presents lectures on Toxicological Issues, Food Intake and Control

Not Directly Related to Instruction

Elected senator from the graduate school, then vice-president of the University Senate
Served on various committees (e g Curriculum, Search, Animal Care) in each of the four major schools (Dentistry, Graduate, Medical, Pharmacy)

Research

Research was continuously funded from Sources of support included governmental (U S P H S , N I H, E P A , N I D A) and non-governmental (industrial) A list of publications is attached)

Awards

DOD - US Army - Chemical Research Development and Engineering Center

Distinguished Service Award,

National Italian - American Foundation Award

Excellence in Medicine and Community Service,

Thomas Jefferson University

Distinguished Alumnus Award,

Virginia Commonwealth University - School of Basic Health Sciences

Outstanding Faculty Award,

000042 Virginia Commonwealth University - School of Basic Health Sciences, Dept of Pharmacology and Toxicology

Professor of the Year-

American College of Toxicology

Distinguished Service Award-

Virginia's Life Achievement in Science Award-

Bernard L Oser Food Ingredient Safety Award by the Institute of Food Technologists

PUBLICATIONS

Borzelleca, J F and Manthei, R W Factors influencing pentobarbital sleeping time in mice Arch Int Pharmacodyn. 111.296, 1957

Borzelleca, J F Studies of the contribution of bladder absorption to the physiological changes induced by pentobarbital J Pharm Exp Ther 129 305, 1960

Borzelleca, J F The absorption of nicotine from the urinary bladder of the dog Arch Int Pharmacodyn 133 444, 1961

Borzelleca, J F , Bowman, E R and McKennis, H , Jr The cardiovascular and respiratory effects of (-)-cotinine J Pharmacol Exp Ther 137 313,1962

Borzelleca, J F. Drug absorption from the urinary tract of the rat Nicotine Arch Int Pharmacodyn 143.595,1963

Borzelleca, J F Influence of saline and glucose infusions on the course of barbiturate intoxication Arch Int Pharmacodyn 146 163, 1963

Larson, P S , Borzelleca, J F , Bowman, E R , Crawford, E M , Smith, R B , Jr and Henningar, G R Toxicologic studies on a preparation of p-tertiary octylphenoxy-polyethoxy ethanols (Triton X-405) Toxicol Appl Pharmacol 5 782, 1963

Borzelleca, J F , Larson, P S , Henningar, G R , Hug, E G , Crawford, E M and Smith, R B , Jr Studies on the chronic oral toxicity of monomeric ethyl acrylate and methyl methacrylate Toxicol Appl Pharmacol 6 29,1964

Borzelleca, J F and Cherrick, H The excretion of drugs in saliva Antibiotics J Oral Therap Pharmacol. 2 180,1965.

Borzelleca, J F and Lester, D Acute toxicity of some perhalogenated acetones Toxicol Appl Pharmacol 7 592,1965

Borzelleca, J F Drug movement from the isolated urinary bladder of the rabbit Arch Int Pharmacodyn 154 40,1965

Borzelleca, J F Rabbit urinary bladder potentials Invest Urol 3 77, 1965

Borzelleca, J F Studies on the mechanisms of drug movement from the isolated urinary bladder J Pharmacol Exp Ther 148 111, 1965

Lowenthal, W and Borzelleca, J F Drug absorption from the rectum. I. J Pharm Sci 54.1790, 1965

Ambrose, A.M , BorzelleGa, J F , Larson, P S , Smith, R B , Jr and Hennigar, G R Toxicologic studies on monochloroacetaldehyde 2,4-dinitrophenylhydrazone, a foliar fungicide Toxicol Appl Pharmacol. 8 472, 1966

Borzelleca, J F and Doyle, C H Excretion of drugs in saliva Salicylate, barbiturate, sulfanilamide J Oral Therap Pharmacol 3 104, 1966

Borzelleca, J F and Lowenthal, W Drug absorption from the rectum II J Pharm Sci 55 151, 1966

Wooles, W R and Borzelleca, J F Prolongation of barbiturate sleeping time in mice by stimulation of the reticuloendothelial system J Reticuloendo Soc 3 41, 1966

Wooles, W R , Borzelleca, J F and Branham, G W The effects of acute and prolonged salicylate administration on liver and plasma triglyceride levels and dietary-induced hypercholesterolernia Toxicol Appl Pharmacol 10 1 1967

Borzelleca, J F , Harris, T and Bernstein, S The effect of DIVISO on drug movement through the wall of the urinary bladder of the rabbit J. Invest Urol 6 43, 1968

Borzelleca, J F · The excretion of glucose in saliva Dog J Oral Therap Pharmacol 4 338, 1968

Kim, K S , Borzelleca, J F , McKennis, H and Bowman, E R Pharmacological effects of some nicotine metabolites and related compounds J Pharmacol Exp Ther 161 59, 1968

Marcus, S and Borzelleca, J F Observations of reserpine-induced bradycardia. Arch Int Pharamacodyn 174 12,1968

Schwartz, S L and Borzelleca, J F Adrenergic blood pressure response in the shark Science 163 395, 1969

Ambrose, A M., Borzelleca, J F , Larson, P S and Hennigar, G R The toxicology of a foliar fungicide, GC4072. Toxicol Appl. Pharmacol 17 323, 1970

BorzelleGa, J F and Putney, J W , Jr A model for the movement of salicylate across the parotid epithelium J Pharmacol Exp Ther 174 527, 1970

Borzelleca, J F and Putney, J W , Jr Studies on the biotransformation of salicylic acid by the salivary gland Arch Int Pharmacodyn 188 127, 1970

Lowenthal, W , BorzelleGa, J F and Corder, C D , Jr Drug absorption from the rectum 111 Aspirin and some aspirin derivatives J Pharm Sci 59 1353, 1970

Putney, J W , Jr and Borzelleca, J F A method for the determination of small quantities of salicylate metabolites in the presence of a great excess of salicylic acid Arch Int Pharmacodyn 188 119, 1970

Wynn, J E , van't Riet, B and Borzelleca, J F Excretion and toxicity of EGTA and EDTA after oral administration to rats Toxicol Appl Pharmacol 16 807, 1970

Ambrose, A M , Larson, P S., Borzelleca, JR, Smith, R B , Jr and Hennigar, G R Toxicologic studies on 2,4-dichlorophenyl-p-nitrophenyl ether Toxicol Appl Pharmacol. 19 263, 1971

Borzelleca, J F , Larson, P S , Crawford, E M , Hennigar, G R , Jr , Kuchar, E J and Klein, H.H Toxicologic and metabolism studies on pentachloronitrobenzene Toxicol Appl Pharmacol 18 522, 1971

Putney, J W , Jr and Borzelleca, J F On the mechanisms of 14C- salicylic acid distribution in rat submaxillary gland *in vitro* J Pharmacol Exp Ther 117 263, 1971

Putney, J W , Jr and Borzelleca, J F On the mechanisms of 14C-nicotine distribution in rat submaxillary gland *in vitro* J Pharmacol Exp Ther 178 180, 1971

Ambrose, A M , Larson, P S , Borzelleca, J F and Hennigar, G R Toxicologic studies on 3',4'-dichloropropionanilide Toxicol. Appl. Pharmacol 23 650, 1972

Egle, J L., Jr., Putney, J W , Jr and Borzelleca, J F Cardiac rate and rhythm in mice affected by haloalkane propellants J A M A 222 786, 1972

Putney, J W , Jr and Borzelleca, J F On the mechanisms of 14C-salicylic acid excretion by the rat submaxillary gland. J Phamacol Exp Ther 182 515, 1972.

Putney, J W , Jr and Borzelleca, J F Active accumulation of 14C-salicylic acid by rat kidney cortex *in vitro*. J Pharmacol Exp Ther 186 600, 1973

Borzelleca, JR Safety evaluation and toxicological tests and procedures J A O A C 58 692, 1975

Adams, M D , Wedig, J H , Jordan, R L , Smith, L W , Henderson, R and Borzelleca, J F Urinary excretion and metabolism of salts of 2-pyridinethiol-l -oxide following intravenous administration to female Yorkshire pigs Toxicol Appl Pharmacol 36 523,1976

Allen, M A , Wrenn, J M., Putney, J W , Jr and Borzelleca, J F A study of the mechanism of transport of dipheny1hydantoin in the rat submaxillary gland *in vitro* J Pharmacol Exp Ther 197 408, 1976

Ambrose, A.M , Larson, P S , Borzelleca, J F and Hennigar, G R Long-term toxicologic assessment of nickel in rats and dogs J Food Science and Technology 13 181, 1976

Egle, J L , Jr., Long, J E , Simon, G S and Borzelleca, J F An evaluation of the cardiac sensitizing potential of a fabric protector in aerosol form, containing 1,1,1-trichloroethane Toxicol Appl Pharmacol 38 369,1976

EGLE, J L , Jr , Fernandez, S B , Guzelian, P S and Borzelleca, J F Distribution and excretion of chlordecone (Kepone) in the rat Drug Metab Dispos 6 91, 1976

Munson, A E , Barrett, B A and Borzelleca, J. F *In vitro* experimental approaches to detection of sensitive agents In Cutaneous Toxicity, (V Drill, ed), Academic Press, Inc , San Francisco, p 175, 1977

Weinberg, A.D , Dimen, E.M , Borzelleca, J F and Harris, L.S Weight and activity in male mice after daily inhalation of cannabis smoke in an automated smoke exposure chamber J Pharm & Pharmac 29 477, 1977

Weinberg, A D , Dimen, E M , Simon, G S , Harris, L S and Borzelleca, J.F Measurements of weight and activity in male mice following inhalation of cannabis smoke in a controlled smoke exposure chamber Toxicol Appl Pharmacol 42 301, 1977

Allen, M A , Wrenn, J M , Putney, J W , Jr and BorzelleGa, J F A study of the mechanisms of transport of benzy1penicillin in the rat submaxillary gland Arch Int Pharmacodyn 233 180, 1978

Bowman, F J , Borzelleca, J F and Munson, A E The toxicity of some halomethanes in mice Toxicol Appl Pharmacol 44 213,1978

Egle, J L , Jr , Fernandez, S B , Guzelian, P S and Borzelleca, J F Distribution and excretion of chlordecone (Kepone) in the rat Drug Metab Dispos 6 91, 1978

McConnell, W R and Borzelleca, J F A study of the mechanism of transport of A9-tetrahydrocannabinol in the rat submaxillary gland *in vivo* Arch Int Pharmacodyn 235 180, 1978

McConnell, W R , Dewey, W L , Harris, L S and Borzelleca, J F A study of the effect of delta-9-tetrahydrocannabinol (delta-9-THC) on mammalian salivary flow J Pharmacol Exp Ther 206 567, 1978

Schumann, A M and Borzelleca, J F An assessment of the methemoglobin and Heinz body inducing capacity of pentachloronitrobenzene in the cat Toxicol Appl. Pharmacol 44 523, 1978

Simon, G S , Tardiff, R G and Borzelleca, J F Potential mutagenic and adverse male reproductive effects of 1,2,3,4-tetrabromobutane A dominant lethal study in the rat Toxicol Appl Pharmacol 44 661, 1978

Carmines, E L , Carchman, R A and Borzelleca, J F Kepone Cellular sites of action Toxicol Appl Pharmacol 49 543, 1979

Egle, J L , Jr , Guzelian, P S and Borzelleca, J F Time course of the acute toxic effects of sublethal doses of chlordecone (Kepone) Toxicol Appl Pharmacol 48 533, 1979

Larson, P S , Egle, J L , Jr , Hennigar, G R and Borzelleca, J F Acute and subchronic toxicity of mirex in the rat, dog, and rabbit Toxicol Appl Pharmacol 49 271, 1979

Larson, P S , Egle, J L , Jr , Hennigar, G R , Lane, R W and Borzelleca, J F Acute, subchronic and chronic toxicity of chlordecone Toxicol Appl Pharmacol 48 29, 1979

Simon, G S , Kuchar, E J , Klein, H H and Borzelleca, J F Distribution and clearance of pentachloronitrobenzene in chickens Toxicol Appl Pharmacol 50 401,1979

Simon, G S , Tardiff, R G and Borzelleca, J F Failure of hexachlorobenzene to induce dominant lethal mutations in the rat Toxicol Appl Pharmacol 47 415, 1979

Borzelleca, J F and Skalsky, H L The excretion of pesticides in saliva and its value in assessing exposure J Environ Sci Health, B15(6), 843, 1980

Borzelleca, J F , Egle, J L , Jr , Hennigar, G R , Klein, H H , Kuchar, E J , Lane, R W and Larson, P S A toxicologic evaluation of 5-ethoxy-3- trichloromethyl-1,2,4-triadiazole (ETMT) Toxicol Appl Pharmacol 56 164,1980

000046 Carmines, E L , Carchman, R A and Borzelleca, J F A method for the evaluation of dose-effect data utilizing a programmable calculator J Environ Path and Tox 4 23, 1980

Kessler, F K , Laskin, D L , Borzelleca, J F and Carchman, R A Assessment of somatogenotoxicity of povidone-iodine using two *in vitro* assays J Environ Path and Tox 3 327, 1980

Skalsky, H L , Wrenn, J M and Borzelleca, J F *In vitro* and *in vivo* evaluation of the movement of Kepone in the rat submaxillary gland J Environ Path and Tox 3 529, 1980

Smith, L W and Borzelleca, J F Excretion of cadmium and mercury in rat saliva Toxicol Appl. Pharamacol 54 134, 1980

Smith, L W and Borzelleca, J F *In vitro* stimulation of oxygen consumption in rat submaxillary gland by pilocarpine. J. Dent Res (59)9 1539, 1980

Smith, L W and Borzelleca, J F Movement of cadmium in rat submaxillary slices Toxicol Appl Pharmacol 55 403, 1980

Smith, L W and Borzelleca, J F Movement of mercury in rat submaxillary slices Toxicology 18 169, 1980

Borzelleca, J F Report of the NATO/CCMS drinking water pilot study on health aspects of drinking water contaminants Sci of the Total Environ 18 205, 1981

Carmines, E L , Carchman, R A and BorzelleGa, J F Investigations into the mechanism of paraquat toxicity utilizing a cell culture system Toxicol Appl Pharmacol 58 353, 1981

Simon, G S , Borzelleca, J F and Dewey, W L Narcotics and diabetes 11 Streptozotocin-induced diabetes selectively alters the potency of certain narcotic analgesics Mechanism of diabetes morphine interaction J Pharmacol Exp Ther 218 324, 1981

Balster, R L and Borzelleca, J F The behavioral toxicity of trihalomethane contaminants of drinking water in mice Environ Health Perspec. 46 127, 1982

Kauffmann, B M , White, K L , Jr , Sanders, V M , Douglas, K A , Sain, L E , Borzelleca, J F and Munson A E Humoral and cell-mediated immune status in mice exposed to chloral hydrate Environ Health Perspec 44 147, 1982

Lane, R W , Riddle, B L and Borzelleca, J F Effects of 1,2-dichloroethane and 1,1,1-trichloroethane in drinking water on reproduction and development in mice Toxicol Appl Pharmacol 63 409, 1982

Munson, A.E , Sain, L E , Sanders, V M , Kauffmann, B M , White, K L , Jr , Page, D G , Barnes, D W , and Borzelleca, J F Toxicology of organic drinking water contaminants trichloromethane, bromodichloromethane, dibromochloromethane and tribromomethane Environ Health Perspec 46 117, 1982

Sanders, V M , Kauffmann, B M , White, K.L , Douglas, K A , Barnes, D W , Sain, L.E , Bradshaw, T J , Borzelleca, J F and Munson, A E Toxicology of chloral hydrate in the mouse Environ Health Perspec 44 137, 1982

Sanders, V M , Tucker, A N , White, K L , Jr , Kauffmann, B M , Hallett, P , Carchman, R A , Borzelleca, J F and Munson, A E Humoral and cell-mediated immune status in mice exposed to trichloroethylene in the drinking water Toxicol Appl Pharmacol 62. 358, 1982

Borzelleca, J F A review of volatile organic contaminant data Proc. AWWA Water Quality Tech Conf 225, 1983

Charles, J L , Kram, D , Borzelleca, J F and Carchman, R A The kinetics of *in vivo* sister chromatid exchange induction in mouse bone marrow cells by alkylating agents. I Cyclophosphamide Environ Mut 5 825, 1983

Borzelleca, J F , Condie, L W and Hayes, J R. Toxicological evaluation of selected chlorinated phenols Proceedings of the 5th International Water Disinfection Conference, Williamsburg, VA, 1984

Borzelleca, J F Food safety regulations, research, and results Va Med 111 390, 1984

Seyler, D E , East, J M , Condie, L W and Borzelleca, J F The use of *in vitro* methods for assessing reproductive toxicity of dichlorophenols Tox Letters 20 309, 1984

Shopp, G M , White, K L , Jr , Holsapple, M P , Barnes, D W , Duke, S S , Anderson, A.C , Condie, L W , Jr , Hayes, J R and Borzelleca, J F Naphthalene toxicity in CDA mice general toxicology and immunotoxicology Fund Appl Toxicol 4 406, 1984

Borzelleca, J F and Hogan, G K Chronic toxicity/carcinogencity study of FD&C Blue No 2 in mice Food Chem Tox 23 719, 1985

Borzelleca, J F , Hayes, J R , Condie, L W. and Egle, J L , Jr Acute toxicity of monochlorophenols, dichlorophenols and pentachlorophenol in the mouse Toxicol Letters 29 39,1985

Borzelleca, J F , Hayes, J R , Condie, L W and Egle, J L Acute and subchronic toxicity of 2,4-dichlorophenol in CD-1 mice Fund Appl Toxicol 5 478, 1985

Borzelleca, J F , Hogan, G.K and Koestner A Chronic toxicity/carcinogencity study of FD&C Blue No 2 in rats Food Chem Tox 23 551, 1985

Hayes, J R and Borzelleca, J F Nutrient interaction with drugs and other xenobiotics, J Am Dietetic Assoc 85 3 335, 1985

Lane, R W , Simon, Glen, S S , Dougherty, R W , Egle, J L and Borzelleca, J F Reproductive toxicity and lack of dominant lethal effects of 2,4-dinitrotolune in the male rat Drug and Chem. Tox 4 265,1985

Borzelleca, J F , Goldenthal, E I and Wazeter, FX A multigeneration study of FD&C Blue No 2 in rats Food Chem Tox 24 159, 1986

Charles, J L , Jacobson-Kram, D , Condie, L W , Jr , Borzelleca, J.F and Carchman, R A The kinetics of *in vitro* sister chromatid exchange induction in mouse bone marrow cells by ethylnitrosourea and methylnitosourea Toxicol Appl Pharmacol 84 56, 1986

Hayes, J R , Condie, L W , Jr and Borzelleca J F The subchronic toxicity of tetrachorethylene (perchloroethylene) administered in the drinking water of rats Fund Appl Toxicol 7 119, 1986

Hayes, J R , Condie, L W , Jr and Borzelleca, J F Acute, 14-day repeated dosing and 90-day subchronic toxicity studies of carbon tetrachloride in CD-1 mice Fund Appl Toxicol 7 454, 1986

Hayes, J R., Condie, L.W , Jr and Borzelleca, J F . Acute, 14-day repeated dosing, and 90-day subchronic toxicity studies of potassium picloram Fund Appl Toxicol 7 464, 1986

Hayes, J R , Condie, L W , Jr and Borzelleca, J F Toxicology of haloacetonitriles Environ Health Perspec 69 183, 1986

Lane, R W , Sturm, R J , Borzelleca, J F and Carchman, R A Effect of *in vitro* differentiation on phorbol diester receptor number in human promyelocytic leukemia (HL-60) cells Cancer Res 46 3782,1986

Simon, G S , Egle, J L , Jr , Dougherty, R W and Borzelleca, J F Dominant lethal assay of chlordecone and its distribution in the male reproductive tissues of the rat Tox Letters 30 237, 1986

Tarka, S M , Jr , Applebaum, R S and Borzelleca, J F Evaluation of the perinatal, postnatal and teratogenic effects of coca powder and theobromine in Sprague-Dawley/CD rats Food Chem Tox 24 375, 1986

Tarka, S M , Jr , Applebaum, R S and Borzelleca, J F Evaluation of the teratogenic potential of cocoa powder and theobromine in New Zealand white rabbits Food Chem Tox 24 363, 1986

Borzelleca, J F , Capen, C C and Hallagan, J B Lifetime toxicity/carcinogenicity study of FD&C Red no 3 (erythrosine) in rats. Fd Chem. Toxic 25 723, 1987

Borzelleca, J F , Capen, C C , and Hallagan, J B Lifetime toxicity/carcinogenicity study of FD&C Red No 3 (erythrosine) in mice Fd Chem. Toxic 25 735, 1987

Hayes, J R , Condie, L W , Jr , Egle, J L , Jr and Borzelleca, J F The acute and subchronic toxicity in rats of trans-1,2 dichloroethylene in drinking water J Am Coll Toxicol 6 471, 1987

Borzelleca, J F and Hallagan, J B Chronic toxicity/carcinogenicity studies of FD&C Yellow No 5 (tartrazine) in rats Fd Chem Toxic 26 179, 1988

Borzelleca, J F , Condie, L W , Jr and Egle, J L Short-term toxicity (one- and ten-day gavage) of barium chloride in male and female rats J Am Coll Toxicol 7 675-685, 1988

Condie, L.W , Jr , Hill, J R and Borzelleca, J F Oral toxicology studies with xylene isomers and mixed xylenes Drug and Chem Tox 11 329, 1988

Borzelleca, J F and Hallagan, J B A chronic toxicity/carcinogenicity study of FD&C yellow no 5 (tartrazine) in mice Fd Chem Toxic 26 189, 1988

Borzelleca, J F , Clark, E C and Condie, L W , Jr. Short-term toxicity (1 and 10 days) of cadmium chloride in male and female rats gavage and drinking water J Am Coll Toxicol 8 377,1989

Borzelleca, J F , Condie, L W , Jr , Clarke, E C and Egle, J L Short-term toxicity (one and ten day gavage) of potassium dichromate in male and female rats J Am Coll Toxicol 8 1197,1989

Borzelleca, J F , Olson, J W A. and Reno, F A Lifetime toxicity/carcinogenicity study of FD&C red No 40 (allura red) in Sprague-Dawley rats Fd Chem Tox 27 701, 1989

Borzelleca, J F Status of colors and flavors used in the confectionery industry Proc 106th Annual Convention of the National Confectioners Association of the United States 33, 1989

Lamb, R G , Borzelleca, J F , Condie, L W and Gennings, C Toxic interactions between carbon tetrachloride and chloroform in cultured rat hepatocytes Toxicol Appl Pharmacol. 101 106, 1989

O'Hara, T M , Borzelleca, J F , Clark, E C , Sheppard, M A and Condie, L W , Jr.: A $CCl_4/CHCl_3$ interaction study in isolated hepatocytes selection of a vehicle Fund Appl Toxicol 13 605, 1989

Borzelleca, J F and Hallagan, J B Multigeneration study of FD&C red no 3 (erythrosine) in Sprague-Dawley rats Fd Chem Tox 28 813, 1990

Borzelleca, J F , Depukat, K and Hallagan, J B Lifetime toxicity/carcinogenicity studies of FD&C blue no 1 (brilliant blue FCF) in rats and mice Fd Chem Toxic 28 221,1990

Borzelleca, J F , O'Hara, T M , Gennings, C , Granger, R H , Sheppard, M A and Condie, L W Jr Interactions of water contaminants I Plasma enzyme activity and response surface methodology following gavage administration of CCl_4 and $CHCl_3$ or TCE singly and in combination in the rat Fund Appl Toxicol 14 477, 1990

Borzelleca, J F , Olson, J W A and Reno, F A Lifetime toxicity/carcinogenicity study of FD&C red no 40 (allura red) in mice Fd Chem Tox 29 313, 1991

O'Hara, T M , Sheppard, M A , Clarke, E C , Borzelleca J F , Gennings, C and Condie, L W , Jr A $CCl_4/CHCl_3$ interaction study in isolated hepatocytes non-induced, and phenobarbital pretreated cells J Appl Toxicol 11 147, 1991

Borzelleca, J F Assessment of Safety/Risk of Chemicals- Inception and Evolution of the ADI and Dose-Response Modeling Procedures- Commentary Tox Letters 59 1, 1991

Borzelleca, J F The safety evaluation of macronutrient substitutes CRC Critical Reviews in Food Science and Nutrition 32 127, 1992

Borzelleca, J F Macronutrient Substitutes Safety Evaluation Reg Tox Pharm 16 253, 1992

Waddell, W J , Borzelleca, J F , Doull, J., Grasso, P., LeBourhis, B , Levy, P S and Tamburro, C H Alcohol and Cancer Br J Cancer 66 1200, 1992

Borzelleca, J F Evaluation of the safety of tara gum as a food ingredient a review of the literature J. Am Coll Tox 12(1) 81,1993

Borzelleca, J F and Egle, J L Jr An evaluation of the reproductive and developmental effects of tara gum in rats J Am Coll Tox 12(1) 91, 1993

Borzelleca, J F. Interactions of environmental chemicals and toxins in Proceedings of the Second Princess Chulabhorn Science Congress " Environment, Science and Technology the Challenges of the 21st Century " 1993

Borzelleca, J F , Egle, J L., Jr , Harris, L S , Johnson, D N , Terrill, J B and Belleville, J A N Toxicological Evaluation of u-Agonists, Part 1 Assessment of Toxicity Following 30 Days of Repeated Oral Dosing of Male and Female Rats with Levo-Alpha-Acetylmethadol HCl (LAAM) J Appl Tox 14 (6)· 435,1994

Conn, R E , Kolstad, J J , Borzelleca, J F., Dixler, D.S., Filer, L J., Jr, LaDu, B N , Jr , and Pariza, M W Safety Assessment of Polylactide (PLA) for Use as a Food-contact Polymer Fd. Chem Tox 33 273-283, 1995

Hallagan, J B , Allen, D C , and Borzelleca, J F The safety and regulatory status of food, drug and cosmetics color additives exempt from certification Fd Chem Toxic 33 515, 1995

Borzelleca, J F Post-Marketing Surveillance of Macronutrient Substitutes Fd Tech 49 107-113, 1995

Borzelleca, J F , Egle, J L Jr , Harris, L S and Belleville, J A N Toxicological Evaluation of u-Agonists Part II Assessment of Toxicity Following 30 Days of Repeated Oral Dosing of Male and Female Rats with Levo-alpha-noracetylmethadol HCl (NorLAAM) J Appl Tox 15(5) 339-355, 1995

Moore, K A , Lichtman, A H , Poklis, A , and Borzelleca, J F alpha-Benzyl-N-methylphenethylamine (BNMPA), an impurity of illicit methamphetamine synthesis pharmacological evaluation and interaction with methamphetamine Drug and Alcohol Dependence 39 83-89, 1995

Borzelleca, J F , Filer, L J , Jr , Kinoshita, F K , Gerrish, T C , Kuo, P K , and LaDu, B N Evaluation of the safety of sodium pectate as a food ingredient Fd Chem Toxic 34 21-25, 1996

Borzelleca, J F A proposed model for safety assessment of macronutrient substitutes Reg Tox Pharm 23 S15-S18, 1996

Steinberg, M , Borzelleca, J F , et al A new approach to the safety assessment of pharmaceutical excipients Reg Tox Pharm 24 149-154, 1996

Berndt, W O , Borzelleca, J F , Flamm, W G , and Munro, I C Erythritol A Review of Biological and Toxicological Studies Reg Tox Pharm 24 S191-198, 1996

Hallagan, J B , LaDu, B N , Pariza, M W , Putnam, J M , and Borzelleca, J.F . Assessment of Cassia Gum Fd Chem Toxic 35 625-632,1997.

Graham, D M , Pariza, M W , Glaze, W H , Newell, G W , Erdman, JW, and Borzelleca, J F Use of Ozone in Food Processing Fd Tech June 1997

Pariza, M W , Borzelleca, J F et al Examination of Dietary Recommendations for Salt-Cured, Smoked, and Nitrite-Preserved Foods CAST Issue Paper Number 8, November 1997

Borzelleca, JF Paracelsus Herald of Modern Toxicology Toxicological Sciences 53· 2-4 1999

ABSTRACTS

Borzelleca, J F and Manthei, R W Influence of dehydration on pentobarbital sleeping time in mice Fed Proc 15 403, 1956

Borzelleca, J F The effect of blood pH on barbiturate sleeping time in mice Fed Proc 16 284,1957

Borzelleca, J F Drug absorption from the urinary bladder Fed Proc 18 370, 1959

Borzelleca, J F Nicotine absorption from the urinary bladder of the dog Fed Proc 19 391,1960

Borzelleca, J F , Bowman, E.R and McKennis, H , Jr Depressor effects arising from (-)-cotinine Pharmacologist 2 72, 1960

Borzelleca, J F Influence of saline infusions on the course of barbiturate intoxication Pharmacologist 3 63,1961

Borzelleca, J F Drug absorption from the urinary tract of the rat Nicotine Fed Proc 21 451, 1962

Borzelleca, J F Drug movement from the isolated urinary bladder of the rabbit Fed Proc 22 661, 1963

Borzelleca, J F Studies on the mechanisms of drug movement from the isolated urinary bladder Pharmacologist 6 178, 1964

Kim, K S , Borzelleca, J F , McKennis, H , Jr and Bowman, E R Effects of cotinine and other nicotine metabolites *in vitro* on duodenum and ileum segments Fed Proc 23 330, 1964

Borzelleca, J.F and Doyle, H Salivary excretion of drugs Fed Proc 24 546, 1965

Cherrick, H and Borzelleca, J F Salivary excretion of drugs Antibiotics. Toxicol Appl Pharmacol 7 481 1965

Wooles, W R and BorzelleGa, J F Prolongation of barbiturate sleeping time in mice by stimulation of the RES J R E S, 1 574,1965

Borzelleca, J F Salivary excretion of glucose, salicylate, penicillin Fed Proc 24 564, 1966.

Lowenthal, W and Borzelleca, J F Rectal absorption of salicylates Toxicol Appl Pharmacol 8 347, 1966

Bernstein, S and Borzelleca, J F The effect of dimethylsulfoxide on drug transfer from the urinary bladder Va J Sci 18 195, 1967

Kim, K S and Borzelleca, J F Pharmacological effects of some nicotine metabolites and related compounds Fed Proc 26 683, 1967

Mullen, K and Borzelleca, J F Predictive model for blood glucose concentration in the dog. Va J Sci 18 200,1967

Schwartz, S L and Borzelleca, J F Adrenergic blood pressure responses in the shark Proc Shark Res Panel of Am Inst Biol Sci , 26 April 1968

Schwartz, S L and Borzelleca, J F Adrenergic responses in the shark Toxicol Appl Pharmacol 12 307,1968.

Wynn, J E , van't Riet, B and Borzelleca, J F Excretion and toxicity of EGTA and EDTA after oral administration to rats Fed Proc 271 465, 1968.

van't Riet, B , O'Rear, C E , Wynn, J E and Borzelleca, J F Effect of EGTA and EDTA on bladder stone formation in rats Toxicol Appl Pharmacol 14 638, 1969

Borzelleca, J F and van't Riet, B Hydrolysis and excretion of esters of EDTA and EGTA after oral administration to rats Va J. Sci 29 143, 1970

Borzelleca, J F , Larson, P S , Hennigar, G R and Kuchar, E J A toxicological evaluation of pentachloronitrobenaene (PCNB) Pharmacologist 12 208, 1970

Borzelleca, J F. The role of pharmacology in the training of toxicologists Pharmacologist 12 217, 1970

Putney, JW, Jr and Borzelleca, J F A model for drug movement across the salivary epithelium Va J Sci. 21·147, 1970

Putney, JW, Jr and Borzelleca, J F Factors modifying excretion of salicylate by the dog, comparison of urinary and salivary routes J Toxicol Appl Pharmacol 16 23,1970

Putney, J W , Jr and Borzelleca, JR Studies on salicylate biotransformation by the salivary gland Pharmacologist 12 272, 1970

Borzelleca, J F , Larson, P S , Hennigar, G R and Kuchar, E J A toxicologic evaluation of 5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole (terrazole) Toxicol. Appl. Pharmacol 19 79, 1971

Putney, J W , Jr and Borzelleca, J F Mechanisms of ^{14}C-salicylate uptake by submaxillary gland slices Fed Proc 30 448, 1971

Putney, J W , Jr and Borzelleca, F Active uptake of 14C-salicylic acid by rat kidney cortex slices. Fed Proc 31 518, 1972

Putney, J W., Jr and Borzelleca, J F Participation of extracellular hydrogen ion in the efflux of nicotine-^{14}C from submaxillary gland cells Pharmacologist 13 518,1972

Allen, M A and Borzelleca, J F On the method of benzyl penicillin-^{14}C potassium distribution in rat submaxillary gland Fed Proc 32 733, 1973

Allen, M A and Borzelleca, J F On the method of diphenyl hydantoin distribution in rat submaxillary gland Pharmacologist 15 229, 1973

Jordan, R L and Borzelleca, J F Teratogenic studies with pentachloronitrobenzene in rats. Toxicol Appl. Pharmacol 25 454, 1973

Allen, M A and Borzelleca, J F Diphenylhydantoin distribution in rat submaxillary gland. influence of age Fed Proc 33 525, 1974

Burnett, C M , Agersborg, H P H , Jr , Borzelleca, J F , Egle, Jr , E , Ebert, A G., Pierce, E C , Kirschman, J C. and Scala, R A Teratogenic studies with certified colors in rats and rabbits Toxicol Appl Pharmacol 29 121, 1974

Pierce, E G , Agersborg, H P K , Jr , Borzelleca, J F , Burnett, C M , Egle, E , Ebert, A G , Kirschman, J C and Scala, R A Multigeneration reproduction studies with certified colors in rats Toxicol Appl Pharmacol 29 121, 1974

Adams, M , Wedig, J H , Jordan, R , Smith, L , Henderson, R and Borzelleca, J F Excretion and metabolism of three 2-6-14C Omadines following intravenous injection in female Yorkshire pigs Toxicol Appl Pharmacol 33 180, 1975

Egle, J L , Jr , Borzelleca, J F and Long, J E. An evaluation of the cardiac sensitizing potential of Scotchgard brand fabric protector Toxicol Appl Pharmacol 33 154,1975

Jordan, R L and Borzelleca, J F Teratogenic studies with zinc Omadine in swine Anat Rec 18 388,1975

McConnell, W R , Borzelleca, J F and Chambers, JW The effects of delta-9-tetrahydrocannabinol (THC) on electrically stimulated saliva from cat submaxillary gland Fed Proc 34 782,1975

Smith, L W , Borzelleca, J F and Bowman, E R Application of isolated cell suspensions to the study of membrane phenomena in mammalian salivary cells Fed Proc 34.752, 1975

Wrenn, J M and Borzelleca, J F Effect of phenobarbital and pentobarbital on the transport of diphenylhydantoin in salivary tissues and saliva Fed Proc 34 573, 1975

Egle, J L , Jr , Gochberg, B.J and Borzelleca, J F The distribution of ^{14}C-Kepone in the rat Pharmacologist 18 195, 1976

McConnell, W R and Borzelleca, J F On the method of 3H-delta-9 tetrahydrocannabinol (3H-delta-9-THC) distribution in the submaxillary gland of the rat Pharmacologist 18 149, 1976

McConnell, W R , Borzelleca, J F and Dewey, W L The mechanism by which delta-9-tetrahydrocannabinol (THC) produces a decrease in salivary flow following electrical stimulation Fed Proc 35 644,1976

McCoy, W D , Kuchar, E J , Klein, H H and Borzelleca, J F Biotransformation and distribution of pentachloronitrobenzene in chickens Toxicol Appl. Pharmacol 37 175, 1976

Schumann, A M and Borzelleca, J F The potential methemoglobin and Heinz body inducing capacity of pentachloronitrobenzene (PCNB) in the cat Toxicol Appl Pharmacol 37 171, 1976

Schumann, A M , Bloom, A S , Dewey, W L , Harris, L S and Borzelleca, JR. Development of central catecholamine systems in the postnatal rat brain The Pharmacologist 18 243, 1976

Smith, L W and Borzelleca, J F Uptake of cadmium in rat submaxillary slices The Pharmacologist 18:196,1976

Bagshaw, B , Schumann, A , Borzelleca, J and Dewey, W The effects of chloroform and bromoform on the noradrenergic and doparninergic systems of the mouse brain Pharmacologist 9 200, 1977

Barrett, B A , Sanders, V M , Borzelleca, J F , Munson, E Growth rates and tumor takes in mice with transplanted tumors exposed to halomethanes Va J Sci 28 100, 1977

Brady, K T , Sanders, V M, Borzelleca, J F and Munson, A E The acute toxicity of the halomethanes drinking water contaminants Va J Sci 28 100, 1977

Martin, B R , Dewey, W L , Beckner, J S and Borzelleca, J F Synthesis and metabolism of brain serotonin in mice following acute exposure to several haloalkanes Toxicol Appl Pharmacol 19 200, 1977

Munson, A , Sanders, V , Borzelleca, J and Barnes, D Toxicologic studies on adult and neonatal mice exposed to the trichloromethanes drinking water contaminants Pharmacologist 19 200, 1977

Munson, A E , Sanders, V M , Barrett, B A and Borzelleca, JR Functional activity of the reticuloendothelial system in mice exposed to haloalkanes for ninety days J Reticuloendo Soc 22 17a, 1977

Sanders, V M , Barrett, B A , Borzelleca, J F and Munson, A E Reticuloendothelial system activity and cell mediated immune responsiveness in mice exposed to polychlorinated biphenyls J Reticuloendo Soc 22 16a,1977

Schumann, A M , Dewey, W L and Borzelleca, J F The effects of triethyllead on central catecholamine function in the adult rat Toxicol Appl Pharmacol 41 208, 1977

Schumann, A M , Dewey, W L , Borzelleca, J F and Alphin, R S The effects of lead acetate on central catecholamine function in the postnatal mouse Fed. Proc 36 405, 1977

Smith, L W and Borzelleca, J F The excretion of cadmium and mercury in saliva Toxicol Appl Pharmacol 41:153, 1977

Smith, L W , Ismay, J A and Borzelleca, JR Movement of mercury in rat submaxillary slices Fed Proc 36 355,1977

Carmines, E L , Burkhalter, J A , Carchman, R A and Borzelleca, J F Inhibitory effects of chloroform on P388D macrophage cell Fed Proc 37 320, 1978

Dougherty, R W , Simon, G S , Campbell, K I and Borzelleca, J F Failure of 2,4-dinitrotoluene to induce dominant lethal mutations in the rat Pharmacologist 20 155, 1978

Larson, P S , Hennigar, G R , Lane, R W and Borzelleca, J F Acute, subchronic and chronic toxicological studies with kepone Toxicol Appl Pharmacol 95 331, 1978

Munson, A E , Sanders, V M , Borzelleca, J F , Tardiff, R G and Barrett, B A Reticuloendothelial system function in mice exposed to four haloalkane drinking water contaminants Toxicol Appl Pharmacol 45 329,1978

Schuller, G B , Kauffmann, B M , Borzelleca, J F , Sanders, V M and Munson, A E Effect of four haloalkanes on humoral and cell mediated immunity in mice Toxicol Appl Pharmacol 45 329, 1978

Simon, G S , Carchman, R A and Borzelleca, J F Diabetes responses to selected pharmacologic agents Pharmacologist 20 151, 1978

Simon, G S , Kipps, B R , Tardiff, R G and Borzelleca, J F Failure of Kepone and hexachloroberizene to induce dominant lethal mutations in the rat Toxicol Appl Pharmacol 45 330 1978

Smith, S H , Sanders, V M , Barrett, B A , Borzelleca, J F and Munson, A E Immunotoxicological evaluation on mice exposed to polychlorinated biphenyls Toxicol Appl Pharmacol 45 330, 1978

Zimmerman, M L , Lane, R W , Skalsky, H L and Borzelleca, J F Excretion of carbaryl into saliva and its effect on cholinesterase 10th Inter-American Conf on Toxicol and Occupational Med , p 47,1978

Zimmerman, M L , May, R G and Borzelleca, J F Excretion of carbaryl into the saliva of the rat Toxicol Appl Pharmacol 45 35,1978

Balster, R L , Burkhalter, J and Borzelleca, J F Behavioral toxicity evaluation of four halomethane contaminants of drinking water in adult mice Fed Proc 38 846, 1979

Carmines, E L , Carchman, R A and Borzelleca, J F *In vitro* effects of Kepone Va J Sci 30 89, 1979

Borzelleca, J F , Skalsky, H L and Riddle, B L Effects of dibromochloromethane in drinking water on reproduction and development in mice Fed Proc. 39 999, 1980

Carmines, E L , Carchman, R A and Borzelleca, J F Analysis of the interactions between paraquat and DNA Fed Proc 39 545,1980

Balster, R L , Kallman, M J and BorzelleGa, J F Behavioral toxicity evaluation of trihalomethane contaminants of drinking water Health Effects of Drinking Water Symposium, 1981

Carchman, R A , Cardlin, E L , Skalsky, H L and Borzelleca, J F The effects of selected water disinfectant products on testicular DNA metabolism Health Effects of Drinking Water Symposium, 1981

Kallman, M J , Balster, R L , Kaempf, G L and Borzelleca, J F Behavioral toxicity evaluation of chloral in adult mice Fed Proc 40 698, 1981

Tarka, S M , Jr , Keeney, P G , and Borzelleca, J F The effect of pretreatment with dietary cocoa on growth and reproductive performance in young and adult rats Fed Proc 40.668, 1981

Lane, R W , Carchman, R A and Borzelleca, J F Characterization of DNA metabolism in mouse primary spermatocytes Toxicologist 1 39(#143), 1981

Riddle, B L , Carchman, R A and Borzelleca, J F Effects of 1,2-dichloroethane and 1,1,1-trichloroethane in drinking water on reproduction and development in mice Toxicologist 1 26 (#95), 1981

Tarka, S M , Jr , Keeney, P G and Borzelleca, J F A comparison of the effects of methylxanthine-containing food stuffs on reproductive capacity in rats Toxicologist 1 147 (#533), 1981

Borzelleca, J F , Hallagan, J , Reese, C , Goldenthal, E and Hogan, G Chronic oral toxicity/carcinogenicity studies of food, drug and cosmetic colors in CD-1 mice J Am Coll Tox 2 240 (#108), 1982

Charles, J L , Carchman, R A , Kram, D and BorzelleGa, J F Time course of *in vivo* induction of sister chromatid exchange by ethylnitrosourea and methylnitrosourea Toxicologist 2 175 (613), 1982

Hayes, J R , Condie, L W , Jr , and Borzelleca, J F Kinetics of naphthalene (NTL) covalent binding to hepatic DNA, RNA and protein in CD-1 mice J Am Coll Tox 3 144, 1982

Lane, R W , Coles, R B , Carchman, R A and BorzelleGa, J F Phorbol diester receptors on HL-60 human promyelocytic leukemia cells Toxicologist 2 105 (#373), 1982

Seyler, D , East, J and Borzelleca, J F Cadmium depression of mouse *in vitro* fertilization. Toxicologist 2 238 (#764), 1982.

Borzelleca, J F , Hallagan, J , Reese, C , Goldenthal, E and Hogan, G . Chronic oral toxicity/carcinogenicity studies of food, drug and cosmetic colors in CD rats Toxicologist 3 129 (#514),1983

Condie, L W , Hayes, J R and Borzelleca, J F Acute and subchronic oral toxicity of 2,4-dichlorophenol (2,4-DCP) in male and female CD-1 mice Pharmacologist 25 228, 1983

Hayes, J R and Borzelleca, J F Implications of nutrient-drug interactions Proc Ann Meeting Inst Fd Technol ,1983

Hayes, J R and Borzelleca, J F Diet-nutrient interactions Proc Ann Mtg of the Am Diet Assoc , 1983

Hayes, J R , Condie, L W , Jr , and Borzelleca, J F Pharmacokinetics of oral naphthalene (NTQ in CD-1 mice Toxicologist 3 161 (#644), 1983

Kallman, M J , Borzelleca, J F and Condie, L , Jr Behavioral toxicity of naphthalene in adult mice J Am Coll Tox 2 247 (#136),1983

Kessler, F K , Charles, J L , Borzelleca, J F and Carchman, R A Effects of chlorinated phenols on mouse bone marrow sister chromatid exchange J Am Coll Tox 2 249 (#142), 1983

Lane, R W , Carchman, R.A. and Borzelleca, J F Phorbol diester (PDE) binding and oxygen metabolism of differentiated HL-60 cells Toxicologist 3 144 (#575), 1983

Shopp, G M , White, K L , Jr , Holsapple, M P , Barnes, D W , Condie, L.W., Jr and Borzelleca, J F General toxicology and immunotoxicology of mice exposed to naphthalene (NAP) Toxicologist, 3 57 (#226), 1983

Smith, B , Lane, R W , Carchman, R A and Borzelleca, J F A comparison of the reversibility of phorbol diester induced changes in macrophage morphology Toxicologist 3 144 (#574), 1983

Borzelleca, J F , Hayes, J,R and Condie, L Toxicological evaluation of selected chlorinated phenols and haloacetonitriles Proc of 5th International Conf on Water Chlorination Environmental Impact and Health Effects 1 100, 1984

Hayes, J R , Condie, L and Borzelleca, J F Subchronic toxicity of carbon tetrachloride administered by oral gavage to CD-1 mice Toxicologist 4 183 (#730), 1984

Hayes, J R , Condie, L W and Borzelleca, J F Acute and 14-day continuous dosing toxicity of dichloroacetonitrile (DCA) and dibromoacetonitrile (DBA) Pharmacologist 26 233, 1984

Condie, L W Hayes, J R and Borzelleca, J F Acute, 14-day and subchronic toxicity of potassium picloram (PIC) administered to rats via the drinking water Toxicologist 5 222, 1985

Capen, C C , Nishikawa, S , Ingbar, S H , Braverman, L E , and Borzelleca, J F Mechanisms of thyroid oncogenesis by chronic erythrosine (red no 3) feeding ultrastructural and morphometric evaluation of thyroid glands and changes in circulating levels of thyroid hormones and thyrotropin (TSH) Abstract No 48, 75th Annual Meeting of the International Academy of Pathology, New Orleans, 10-14 March, and published in Laboratory Investigations 54 54 a, 1986

Lamb, R G , Bush, S R , Condie, L W , and Borzelleca, J F Influence of chlorinated hydrocarbon mixtures on cultured hepatocyte function Pharmacologist 28 180, 1986

Lamb, R G , Coleman, J B , Condie, L W , and Borzelleca, J F Influence of chlorinated hydrocarbons on cultured hepatocyte function Toxicologist 6 116 (#470), 1986

Granger, R H , Coleman, J B , Condie, L W , Lamb, R G and Borzelleca, J F Effect of vehicle on the relative uptake of haloalkanes administered by gavage Toxicologist 7 265 (#1060), 1987

Lamb, R G , Coleman, J B , Granger, H , Condie, L W and Borzelleca, J F The influence of chlorinated hydrocarbons on hepatocyte function *in vivo* and *in vitro* Toxicologist 7 267 (#1068), 1987

Coleman, J B , Condie, L W , Borzelleca, J F and Lamb, R G The influence of structural analogues of carbon tetrachloride (CC14) on hepatocyte functions *in vitro* Toxicologist 8 96 (#381), 1988

Granger, R H , O'Hara, T M , Condie, L W , and Borzelleca, J F A study of the joint action of carbon tetrachloride (CC14) and trichloroethylene (C2HCl3) following simultaneous gavage administration in the rat Toxicologist 8 95 (#378), 1988

O'Hara, T M., Granger, R H , Condie, L W and Borzelleca, J F A study of the joint hepatotoxic action of carbon tetrachloride (CC14) and chloroform (CHC13) following simultaneous gavage administration in the rat Toxicologist 8.96 (#380), 1988

Borzelleca, J F , O'Hara, T M , Gennings, C and Condie, L W , A CC14-CHC13 interaction study in isolated hepatocytes-the role of P-450 metabolism Toxicologist 9 58 (#229), 1989

Lamb, R G , Gennings, C , Borzelleca, J F , and Condie, L W Toxic Interactions between carbon tetrachloride (CC14) and chloroform (CHC13) Toxicologist 9 59 (#233), 1989

O'Hara, T M , Borzelleca, J F and Condie, L W A CC14/CHCl3 interaction study in isolated hepatocytes-selection of a vehicle Toxicologist 9 59 (#235), 1989

Borzelleca, J F , Gennings, C , Bercz,P and Lamb, R G Toxic interactions between carbon tetrachloride (CC14) and perchloroethylene (PCE) in cultured rat hepatocytes Toxicologist 10 54 (#213), 1990

Lamb, R G , Gennings, C , Borzelleca, J F and Bercz,P Toxic interactions between carbon tetrachloride (CC14) and trichloroethylene (TCE) in cultured rat hepatocytes Toxicologist 10 53 (#212), 1990

Wolfe, G , Myers, B , Lemen, J , Lauer, W , Johns, F , Condie, L and Borzelleca, J Preliminary report of the findings of the health effects for Denver's potable reuse demonstration project Toxicologist 10 176 (#704), 1990

Egle, J L , Jr , Borzelleca, J F and Harris, L S Acute and subchronic toxicity of Levo-alpha-acetyl-methadol (LAAM) and Levo-alpha-acetyl-normethadol (NORLAAM) in male and female rats Toxicologist 11 149 (#521), 1991

Weiner, M L , Steinberg, M , Borzelleca, J F , Enters, EX, Hager, D F , Kinoshita, F K , Loper, A , Mitchell, D B and Tamulinas, C B Proposed safety evaluation guidelines for new excipients Toxicologist 13 213 (#796), 1994

Borzelleca, J F The safety evaluation of macronutrient substitutes IFT Annual Meeting Abstracts #15-2, 1994

Borzelleca, J F Fat replacers ACS meeting, 1995

Rice, R G , Graham, D M , Glaze, W H., Pariza, M W , Newell, G W , Erdman, J W , and Borzelleca, J F Ozone preservation of Foods and Foodstuffs 13th Ozone World Congress, October 1997, Kyoto, Japan

Lien, E , Boyle, F , Perry, Thompson, C , Borzelleca, J F , and Wrenn, J Comparison of AIN-76A and AIN-93G Diets in Rats, a 13 Week Study Fed Proc , 1998

Munro, E C , Berndt, W O , Borzelleca, J.F , Flamm, G , Lynch, B.S , Kennepohl, E , Bar, A and Modderman, J Erythritol An Interpretive Summary of Biochemical, Metabolic, Toxicological and Clinical Data Toxicologist 38 1999

BOOKS and BOOK CHAPTERS

Skalsky, H L , Lane, R W and Borzelleca, J.F.. "Excretion of carbaryl into saliva of the rat and its effect on cholinesterase" In Toxicology and Occupational Medicine (W B Deichman, ed), p 349, 1979

Borzelleca, J F and Carmines, E L "New drug evaluation safety assessment" In Program for Applied Research on Fertility Regulation, 1980

Hayes, J F and Borzelleca, J F "Biodisposition of environmental chemicals by animals" In Animal Products in Human Nutrition (D Beitz and R Hansen, eds), Chap 11, p. 225 Academic Press, New York, 1982

Borzelleca, J F "Neurobehavior toxicological testing" Pharmacodependence and neurobehavioral toxicology Quo Vadis ?, Symposium "Quo Vadis ?", Sanofi Group, Montpellier, France, p 115, 1983

Schwartz, S L and BorzelleGa, J F "Toxicology of polyvinylpyrrolidone" Proceedings of the International Symposium on Povidone (G A. Digenis,Ed), College of Pharmacy, University of Kentucky, Lexington, KY, p 234,1983

Borzelleca, J F , Hallagan, J and Reese, C "Food, Drug and Cosmetic Colors. Toxicological Considerations " ACS Symposium Series, No 234, Xenobiotics in Foods and Feeds (Finley, J W and Schwass, D E , eds), Chap 20, p 31 1 ACS, Washington, D C , 1983

Borzelleca, J F "Extrapolation of animal data to man" In: Toxicology Laboratory Design and Management for the 80's and Beyond (Tegeris, A S , Ed), Vol 1 of Concepts in Toxicology, Homburger, F , Series Ed), 1984

Borzelleca, J F "Current concepts in reproductive toxicology" In Clinics in Laboratory Medicine, Symposium on Environmental and Occupational Health Hazards, Vol 4 (R V. Blanke, ed), W B Saunders Co , Philadelphia, 1984

Borzelleca, J F , Condie, L W , and Hayes, J R "Toxicological evaluation of selected chlorinated phenols" In Water Chlorination, Chemistry, Environmental Impact and Health Effects (R L Jolley, R J Bull, W P Davis, S Katz, M H Roberts, Jr , V A. Jacobs) Volume 5, Chap 26, p 331 Lewis Publishers, Inc , Ann Arbor, Michigan, 1985

Robinson, B V , Sullivan, F M , Borzelleca, J F and Schwartz, S L PVP A Critical Review of the Kinetics and Toxicology of Polyvinylpyrrolidone (Povidone) Lewis Publishers, Inc , Ann Arbor, Michigan 1990

Borzelleca, J F and Hallagan, J B "Safety and Regulatory Status of Food, Drug, and Cosmetic Colors " ACS Symposium Series, No 484, Food Safety Assessment (Finley, J W , Robinson, S F , and Armstrong, D J , eds), Chap 31, p 377 ACS, Washington, DC 1992

Borzelleca, J F "Foods of the Future What Will We Be Eating in the Next Century?" In Practical Handbook of Nutrition in Clinical Practice (Kirby, D F and Dudrick, S J , eds), Chap 16, p 279 CRC Press, Inc , Boca Raton, Fl 1994

Borzelleca, J F "History of Toxicology " In Principles and Methods of Toxicology (Hayes, A W , editor), edition 3, Chap 1, p 1-18, Raven Press, New York, NY 1994

Matt, D W and Borzelleca, J F "Toxic Effects on the Female Reproductive System During Pregnancy, Parturition, and Lactation " In Reproductive Toxicology (Witorsch, R J , editor), edition 2, chapter 10, p 175 Raven Press, New York, NY 1995

Borzelleca, J F "Food-Borne Health Risks Food Additives, Pesticides and Microbes " In Nutrition Policy in Public Health (Bronner, F , editor) Chap 3, p 33, Springer Publishing Co New York, NY 1997

Rice, R G , Graham, D M , Glaze, W H , Pariza, M W , Newell, G W , Erdman, J W , and Borzelleca, J F Ozone Preservation of Foods and Foodstuffs 13th Ozone World Congress, Kyoto, Japan, October 1997

Borzelleca, J F and Weiner, M L "Development of Safety Evaluation Guidelines " In Excipient Toxicity and Safety (Weiner, M L and Kotkoskie, L A , editors) Chapter 5, p 101 Marcel Dekker, Inc , New York, N Y 1999

Contributing authorship on the following publications of the Life Sciences Research Office, Federation of American Societies of Experimental Biology (FASEB)

Research Office, Federation of American Societies of Experimental Biology (FASEB)

Evaluation of the health aspects of iron and iron salts as food ingredients

Evaluation of the health aspects of butylated hydroxytoluene as a food ingredient

Evaluation of the health aspects of certain zinc salts as food ingredients

Evaluation of the health aspect of pulps as they may migrate to food from packaging materials

Evaluation of the health aspects of propylene glycol and propylene glycol monostearate as food ingredients

Evaluation of the health aspects of alginates as food ingredients

Evaluation of the health aspects of agar-agar as a food ingredient

Evaluation of the health aspects of certain red and brown algae as food ingredients

Evaluation of the health aspects of cellulose and certain cellulose derivatives of food ingredients

Iodine in foods chemical methodology and sources of iodine in the human diet

Evaluation of the health aspects of aconitic acid as a food ingredient

Evaluation of the health aspects of stannous chloride as a food ingredient

Evaluation of the health aspects of licorice, glycyrrhiza and ammoniated glycrrhizin as food ingredients

Evaluation of the health aspects of Gaprylic acid as a food ingredient

Evaluation of the health aspects of sorbose as a food ingredient

Evaluation of the health aspects of sulfuric acid and sulfates as food ingredients

Evaluation of the health aspects of potassium iodide, potassium iodate, and calcium iodate as food ingredients

Evaluation of the health aspects of dextran as food ingredients

Evaluation of the health aspects of calcium oxide and calcium hydroxide as food ingredients

Evaluation of the health aspects of succinic acid as a food ingredient

Contributing authorship on the following publications of the Life Sciences Research Office, Federation of American Societies of Experimental Biology (FASEB)

Evaluation of the health aspects of certain calcium salts as food ingredients

Evaluation of the health aspects of glycerin and glycerides as food ingredients

Evaluation of the health aspects of dextrin and corn dextrin as food ingredients

Evaluation of the health aspects of sodium thiosulfate as a food ingredient

Evaluation of the health aspects of gelatin as a food ingredient

Evaluation of the health aspects of bile salts and ox bile extract as food ingredients

Evaluation of the health aspects of choline chloride and choline bitartrate as food ingredients

Evaluation of the health aspects of aluminum compounds as food ingredients

Evaluation of the health aspects of tallow, hydrogenated tallow, stearic acid, and calcium stearate as food ingredients

Evaluation of the health aspects of phosphates as food ingredients

Evaluation of the health aspects of the tocopherols and a-tocopheryl acetate as food ingredients

Evaluation of the health aspects of sorbic acid and its salts as food ingredients

Evaluation of the health aspects of hydrogenated fish oil as a food ingredient

Evaluation of the health aspects of beeswax (yellow or white) as a food ingredient

Evaluation of the health aspects of inositol as a food ingredient

Evaluation of the health aspects of malic acid as a food ingredient

Evaluation of the health aspects of Japan Wax as a substance migrating to food from cotton or cotton fabrics used in dry food packaging

Evaluation of the health aspects of carnauba wax as a food ingredient

Evaluation of the health aspects of sulfamic acid as it may migrate to foods from packaging materials

Evaluation of the health aspects of hydrosulfites as they may migrate to foods from packaging materials

Evaluation of the health aspects of gum guaiac as a food ingredient

Contributing authorship on the following publications of the Life Science Research Office, Federation of American Societies of Experimental Biology (FASEB)

Evaluation of the health aspects of tall oil as it may migrate to foods from packaging materials

Evaluation of the health aspects of corn sugar (dextrose), corn syrup and invert sugar as food ingredients

Evaluation of the health aspects of sucrose as a food ingredient

Evaluation of the health aspects of sulfiting agents as food ingredients

Evaluation of the health aspects of glycerophosphates as food ingredients

Evaluation of the health aspects of magnesium salts as food ingredients Evaluation of the health aspects of sodium hydroxide and potassium hydroxide as food ingredients

Evaluation of the health aspects of adipic acid as a food ingredient

Evaluation of the health aspects of hydrogenated soybean oil as a food ingredient

Evaluation of the health aspects of formic acid, sodium formate, and ethyl formate as food ingredients

Evaluation of the health aspects of lard and lard oil as they may migrate to foods from packaging materials

Evaluation of the health aspects of pyridoxine and pyridoxine hydrochloride as food ingredients

Evaluation of the health aspects of papain as a food ingredient

Evaluation of the health aspects of hypophosphites as food ingredients

Evaluation of the health aspects of coconut oil, peanut oil, and oleic acid as they migrate to food from packaging materials, and linoleic acid as a food ingredient

Evaluation of the health aspects of pectin and pectinates as food ingredients

Evaluation of the health aspects of tannic acid as a food ingredient

Evaluation of the health aspects of rennet as a food ingredient

Evaluation of the health aspects of acetic acid and sodium acetate as food ingredients

Evaluation of the health aspects of sodium oleate and sodium palmitate as substances migrating to food from paper and paperboard used in food packaging

Contributing authorship on the following publications of the Life Sciences Research Office, Federation of American Societies of Experimental Biology (FASEB)

Evaluation of the health aspects of corn silk as a food ingredient

Evaluation of the health aspects of bentonite and clay (kaolin) as food ingredients

Evaluation of the health aspects of citric acid, sodium citrate, potassium citrate, calcium citrate, ammonium citrate, triethyl citrate, isopropyl citrate, and stearyl citrate as food ingredients

Evaluation of the health aspects of lactic acid and calcium lactate as food ingredients

Evaluation of the health aspects of calcium pantothenate, sodium pantothenate, and D-pantothenyl acohol as food ingredients

Evaluation of the health aspects of Vitamin B12 as a food ingredient

Evaluation of the health aspects of Vitamin D2 and Vitamin D3 as food ingredients

Evaluation of the health aspects of caffeine as a food ingredient

Evaluation of the health aspects of certain glutamates as food ingredients

Evaluation of the health aspects of protein hydrolyzates as food ingredients

Evaluation of the health aspects of butylated hydroxyanisole as a food ingredient

Evaluation of the health aspects of sodium, potassium, magnesium and zinc gluconates as food ingredients

Evaluation of the health aspects of urea as a food ingredient

Evaluation of the health aspects of thiamin hydrochloride and thiamin mononitrate as food ingredients

Evaluation of the health aspects of biotin as a food ingredient

Evaluation of the health aspects of ascorbic acid, sodium ascorbate, calcium ascorbate, erythorbic acid, sodium erythorbate, and ascorbyl palmitate as food ingredients.

Evaluation of the health aspects of propionic acid, calcium propionate, sodium propionate, dilauryl thiodipropionate, and thiodipropionic acid as food ingredients

Evaluation of the health aspects of casein, sodium Gaseinate, and calcium caseinate as food ingredients

Evaluation of the health aspects of nickel as a food ingredient

Contributing authorship on the following publications of the Life Sciences Research Office, Federation of American Societies of Experimental Biology (FASEB)

Evaluation of the health aspects of soy protein isolates as food ingredients

Evaluation of the health aspects of carotene (B-carotene) as a food ingredient

Evaluation of the health aspects of nitrogen, helium, propane, n-butane, isobutane, and nitrous oxide as gases used in foods

Evaluation of the health aspects of hydrogen peroxide as a food ingredient

Evaluation of the health aspects of riboflavin and riboflavin-5-1-phosphate as food ingredients

Evaluation of the health aspects of starch and modified starches as food ingredients

Evaluation of the health aspects of carbon dioxide as a food ingredient

Evaluation of the health aspects of sodium chloride and potassium chloride as food ingredients

Evaluation of the health aspects of certain silicates as food ingredients

Evaluation of the health aspects of manganous salts as food ingredients

Evaluation of the health aspects of copper gluconate, copper sulfate, and cuprous iodide as food ingredients

Evaluation of the health aspects of hydrochloric acid as a food ingredient

Evaluation of the health aspects of lecithin as a food ingredient

Evaluation of the health aspects of potassium acid tartrate, sodium potassium tartrate, sodium tartrate and tartaric acid as food ingredients

Evaluation of the health aspects of starter distillate and diacetyl as food ingredients

Vitamin A, Vitamin A Acetate, and Vitamin A Palmitate as food ingredients

Evaluation of the health aspects of iron and iron salts as food ingredients

Evaluation of the health aspects of protein hydrolyzates as food ingredients

Evaluation of the health aspects of collagen as a food ingredient

Evaluation of the health aspects of methyl polysilicones as food ingredients

Contributing authorship on the following publications of the Life Sciences Research Office, Federation of American Societies of Experimental Biology (FASEB)

Evaluation of the health aspects of soya fatty acid amines as food ingredients 1981

Evaluation of the health aspects of activated carbon (charcoal) as a food processing aid. 1981

Evaluation of the health aspects of smoke flavoring solutions and smoked yeast flavoring as food ingredients 1981

Evaluation of the health aspects of corn mint oil as a food ingredient 1981

Evaluation of the health aspects of a mixture Evaluation of the health aspects of diferrous, dipotassium ferrous, and potassium ferrocyanides as finding agents in wine production 1981

Evaluation of the health aspects of wheat gluten, corn gluten, and zein as food ingredients 1981

Evaluation of the health aspects of peptones as food ingredients. 1981

Evaluation of the health aspects of shellac and shellac wax as food ingredients 1981

Evaluation of the health aspects of sodium metasilicate and sodium zinc metasilicate as food ingredients 1981

Evaluation of the health aspects of oat gum, okra gum, quince seed gum, and psyllium seed husk gum as food ingredients. 1982

Contributing Authorship on the Following Publications of the National Academy of Sciences

Principles and Procedures for Evaluating the Toxicity of Household Substances Committee for the Revision of NAS Publication 1138, Committee on Toxicology, Assembly of Life Sciences National Research Council, National Academy of Sciences National Academy Press, Washington, D C 1977

Drinking Water and Health Safe Drinking Water Committee, Board on Toxicology and Environmental Health Hazards, Assembly of Life Sciences, National Research Council, National Academy of Sciences Volume 1, 1977, Volume 2, 1980, Volume 3, 1980 National Academy Press, Washington, D C

Estimating Consumer Exposure to Food Additives and Monitoring Trends in Use Food Additives Survey Committee, Food and Nutrition Board, Institute of Medicine, National Academy of Sciences National Academy Press, Washington, D C 1992

Examination of Dietary Recommendations for Salt-Cured, Smoked, and Nitrite-Preserved Foods Pariza, M W , Borzelleca, J F , Cassens, R G , Filer, L J , and Kritchevsky, D , CAST Issue Paper Number 8, November 1997

CURRICULUM VITAE
GARY MURRAY WILLIAMS, M.D.

EDUCATION:

SUBSEQUENT TRAINING AND POSITIONS;

CERTIFICATIONS:

American Board of Pathology

Physician, State Education Department, State of New York

American Board of Toxicology, Recertified, 2002.

Expert in Toxicology, Ministere des Affaires Sociales et de la Solidarite Nationale, Direction de la pharmacie et du medicament, Republic Francais

Fellow in Toxicologic Pathology, International Academy of Toxicologic Pathology

Fellow of the Royal College of Pathologists

AWARDS AND HONORS:

Phi Beta Kappa, Washington and Jefferson College

Sheard-Sandford Award, American Society of Clinical Pathologists

Alpha Omega Alpha, University of Pittsburgh School of Medicine

Research Training Fellowship, International Agency for Research on Cancer

Association of University Pathologists

Invited Contributor, Special Issue Food and Cosmetics Toxicology, 9:557, 1981, dedicated to Leon Golberg

Arnold J. Lehman Award, Society of Toxicology

Invited Contributor, Hommage au Professeur Rene Truhaut

Citation Classics: Cancer Lett. 1:231, 1976 and Cancer Res. 37:1845, 1977. Institute for Scientific Information, Current Contents, Vol. 30, No.36, September 7, 1987

Citation Classics: In Vitro 12:521, 1976; 12:821, 1976; 13:809, 1977, 14:824, 1978. Institute for Scientific Information. Current Contents, Vol. 32, No. 9, February 27, 1989

Featured on cover of Cancer Research, Volume 49, November 1

Featured on cover of Cancer Research, Volume 55, April 15

Awards Lecture, Society of Toxicology

Invited Contributor, Special Issue Cancer Letters, 118:1, 1997, dedicated to Phillipe Shubik

Top 10 Most Frequently Cited Articles in 25 years of Toxicologic Pathology Toxicologic Pathology 10:3-10, 1982; Toxicologic Pathology 26:452, 1998

Ambassador in Toxicology Award, Mid-Atlantic Chapter of the Society of Toxicology.

Enhancement of Animal Welfare Award, Society of Toxicology.

American Chemical Society, New York Section, Inc. Westchester Chemical Society Distinguished Scientist Award – 2005.

New York Medical College Dean's Distinguished Research Award, 2005.

Food and Agriculture Organization / World Health Organization Joint Expert Committee on Food Additives. 50th Anniversary Medal (5 years service.)

RECOGNITION:

1996-06	Who's Who in America (1995-2006) 50th-60th Editions
1996-06	Who's Who in the East (1995-2006) 26-33rd Editions
1996-06	Who's Who in Science and Engineering (1995-2006) 3rd-8th Editions
2005-06	Who's Who in American Education (2006-07) 6th-7th Editions
2005-06	Who's Who in Medicine and Healthcare (2006-07) 5th-6th Editions
1997/1998	American Men and Women of Science Directory of American Research & Technology

1998-05	Official American Board of Medical Specialties Directory of Board Certified Medical Specialists 30th-38th Editions

SOCIETIES:

American Association for Cancer Research

Society of Toxicology

Society of Toxicologic Pathologists

International Society of Regulatory Toxicology and Pharmacology

EDITORIAL RESPONSIBILITIES:

1980	Co-Editor, Differentiation and Carcinogenesis in Liver Cell Cultures. Vol. 349. New York Academy of Sciences.
1980-1981	Consulting Reviewer, Oncology Overviews, International Cancer Research Data Bank.
1980-1986	Reviewing Editor, In Vitro.
1980	Co-editor, The Predictive Value of In Vitro Short-term Screening Tests in Carcinogenicity Evaluation. Elsevier/North Holland Biomedical Press.
1981-1983	Editorial Board, Fundamental and Applied Toxicology.
1981-1989	Editorial Board, Toxicology and Applied Pharmacology.
1981-1999	Editorial Board, Nutrition and Cancer.
1981	Meeting Report: Carcinogenesis and Gene Expression in Liver Cultures. Cancer Research 42:2462-2464, 1982.
1982	Consulting Reviewer, Oncology Overview, International Cancer Research Data Bank Program, National Cancer Institute.
1982-1993	Editorial Board, Mutation Research, Genetic Toxicology Testing Section.
1983	Co-Editor, Colon Carcinogenesis. CRC Press.
1983	Co-Editor, Cellular Systems for Toxicity Testing. Vol. 407. New York Academy of Sciences.

1983	Co-Editor, Tests Courts de Cancerogenese/Short-term Tests for Carcinogenesis, Elsevier Science Publishers BV, Amsterdam.
1983-1992	Editorial Board, Chemico-Biological Interactions.
1983-1996	Editorial Board, Toxicologic Pathology.
1984-present	Founding Editor, Cell Biology and Toxicology.
1987	Meeting Report: Causative and Modifying Factors in Digestive Tract Cancer. Cancer Research 47:922-923, 1987
1988-present	Editorial Board, Archives of Toxicology
1987	Editor, Sweeteners: Health Effects, Princeton Scientific Publishing Company.
1988	Editorial Board, Complex Mixtures and Cancer Risk, IARC Scientific Publications, International Agency for Research on Cancer
1989	Meeting Report: American Health Foundation 20th Anniversary International Symposium on Causes and Prevention of Cancer. Preventive Medicine, in 20:534-547, 1991
1991-present	International Advisory Board, European Journal of Cancer Prevention
1992	Proceedings of the Second International Conference on Longevity and Aging: Environmental and Nutritional Influences on Aging and Cancer Experimental Gerontology, Volume 27, Special Issue, 1992
1993	Editor-in-Chief, Antioxidants Chemical, Physiological, Nutritional and Toxicological Aspects, Princeton Scientific Publish. Co.
1994-present	Area Editor for Carcinogenesis, Drug and Chemical Toxicology.
1997	Co-Editor, Reducing Dietary Fat: Putting Theory into Practice, Journal of The American Dietetic Association, Volume 97, Supplement 1, 1997
2001	Co-Editor, Toxicology, Special Issue, Volume 166, Number 3, Festschrift J.H. Weisburger.

2002 Guest Editor, International Symposium on Antimutagenesis and Anticarcinogenesis, European Journal of Cancer Prevention, Volume 11, Supplement 2.

2003 Editorial Board, Toxicologic Pathology.

2005 International Editorial Board, Food and Chemical Toxicology.

MEETINGS ORGANIZED:

Conference on Differentiation and Carcinogenesis in Liver Cell Cultures. New York Academy of Sciences. New York, NY.

Workshop on the Predictive Value of in vitro Short Term Screening Tests in the Evaluation of Carcinogenicity. Scientific Council of the Netherlands Cancer Society. Dalen, The Netherlands.

Quo Vadis Symposium on Short Term Tests in Carcinogenesis and Mutagenesis. Research Center Clin-Midy. Montpellier, France.

Conference on Carcinogenesis and Gene Expression in Liver Cultures United States-Japan Cooperative Cancer Research Program. Honolulu, Hawaii.

Conference on Cellular Systems for Toxicity Testing, New York Academy of Sciences, New York, NY.

Conference on Causative and Modulating Factors for Digestive Tract Cancer United States-Japan Cooperative Cancer Research Program. Tokyo, Japan.

International Conference on Cancer Research. Theories of Carcinogenesis. The Norwegian Cancer Society, Oslo, Norway.

Conference on Non-Mutagenic Carcinogens: How Much Risk to Man? The Robens Institute, University of Surrey, Guildford, England.

Conference on Sweeteners: Health Effects. American Health Foundation, New York.

International Symposium in Genetic Toxicology, National Science Foundation (U.S.) and Council of Scientific and Industrial Research (India), University of Calcutta, Calcutta, India.

International Symposium on Causes and Prevention of Cancer, American Health Foundation in cooperation with American Cancer Society and National Cancer Institute, New York, NY.

International Conference on Environmental and Nutritional Influences on Aging and Cancer, American Health Foundation in cooperation with National Institute on Aging, New York, NY.

Conference on Cancer Prevention for Black Americans, Metropolitan Life Insurance, Company, New York, NY.

International Conference on Antioxidants: Chemical, Physiological, Nutritional and Toxicological Aspects, American Health Foundation, Tarrytown, NY.

Second International Conference on Theories of Carcinogenesis. Norwegian Cancer Society, Oslo, Norway.

1st International Short Course on Preclinical Drug and Chemical Safety, Tarrytown, NY.

2nd International Short Course on Preclinical Drug and Chemical Safety, Tarrytown, NY.

American Health Foundation, 25th Anniversary Conference and Celebration, Toward Optimal Health: Examining Goals for Nutrition and the Environment, Tarrytown, NY.

3rd International Course on the Safety Assessment of Pharmaceuticals, Tarrytown, NY.

International Congress on Hepatocytes-Applications in Cell Biology, Toxicology and Medicine, Tubingen, Germany.

Conference, Reducing Dietary Fat: Putting Theory Into Practice, American Health Foundation, New York, NY.

4th International Course on the Safety Assessment of Pharmaceuticals, Part I, White Plains, NY.

4th International Course on the Safety Assessment of Pharmaceuticals, Part II, San Francisco, CA.

5th International Course on the Safety Assessment of Medicines, Part I, White Plains, NY.

6th International Course on the Safety Assessment of Medicine. Basic and Regulatory Aspects, White Plains, NY.

7th International Course on the Safety Assessment of Medicine. Basic and Regulatory Aspects, White Plains, NY.

8th International Course on the Safety Assessment of Medicine. Basic and Regulatory Aspects, White Plains, NY.

International Symposium on Antimutagenesis and Anticarcinogenesis, New York Medical College, Valhalla, NY

10th International Course on the Safety Assessment of Medicines, Advanced Course, Hyéres, Var, France.

International Symposium on Agricultural Exposures and Cancer, Oxford, England.

Symposium, Chemical Safety Assessment: Contribution of Toxicological Pathology and Mechanistic Investigations, New York Medical College, Valhalla, NY.

11th International Course on the Safety Assessment of Medicine. Basic and Regulatory Aspects, White Plains, NY.

12th International Course on the Safety Assessment of Medicine Basic and Regulatory Aspects, White Plains, NY.

Symposium "Current Issues in Safety Assessment of Medicines, NYMC Valhalla, NY.

13th International Course on the Safety Assessment of Medicines, White Plains, NY.

NATIONAL AND INTERNATIONAL RESPONSIBILITIES

Consultant, Pesticides, Toxic Substance and Solid Waste Management, United States Environmental Protection Agency.

Member, Epidemiology Committee, Breast Cancer Task Force, NationalCancer Institute.

Member, Program Committee, American Association for Cancer Research.

Member, Working Group on Evaluation of Carcinogenic Risk of Chemicals to Man: Some Miscellaneous Pharmaceutical Substances, International Agency for Research on Cancer.

Co-Chairperson, Subcommittee on Rat Liver Tumors, Committee on Histologic Classification of Laboratory Animal Tumors, Institute of Laboratory Animal Resources, National Research Council.

Member, Panel on Kepone/Mirex, Scientific and Technical Assessments of Environmental Pollutants, Environmental Studies Board, Commission on Natural Resources, National Research Council.

Member, Panel on Unscheduled DNA Synthesis, Gene-Tox Program, U S. Environmental Protection Agency.

Member, Panel of Experts Associated with Technical Report Review Subcommittee, National Toxicology Program, Department of Health and Human Services.

Member, Working Group on Evaluation of Carcinogenic Risk of Chemicals to Man-Antineoplastic and Immunosuppressive Drugs, International Agency for Research on Cancer.

Panel of Reviewers, Netherlands Cancer Foundation.

Advisor, Technical Committee, Society of Toxicology.

Member, Task Group on the Differentiation Between Genotoxic and Epigenetic Carcinogens, International Commission on Protection Against Environmental Mutagens and Carcinogens.

Member, Working Group on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Chemicals and Industrial Processes Associated with Cancer in Humans, IARC Monographs Volumes 1 to 29, International Agency for Research on Cancer.

Consultant, Office of Health and Environmental Assessment, Reproductive Effects Assessment Group, U.S. Environmental Protection Agency.

Member, International Expert Committee to the Nutrition Foundation on the Relevance of Mouse Liver as a Model for Assessing Carcinogenic Risk, Nutrition Foundation, Incorporated.

Coordinator, Assays of DNA Damage, Collaborative Study on Short-Term Tests for Genotoxicity and Carcinogenicity. International Programme on Chemical Safety, World Health Organization.

Member, Working Group on the Mechanisms of Chemical Carcinogenesis, International Agency for Research on Cancer.

Member, Expert Committee on Pathology/Toxicology and Expert Committee on Short-Term Testing, International Life Sciences Institute.

Assessor, National Health and Medical Research Council Panel of Independent Assessors, National Health and Medical Research Council, Commonwealth of Australia.

Member, Committee on the Carcinogenicity of Cyclamates, Food and Nutrition Board, Commission on Life Sciences, National Research Council.

Member, Task Group of DNA Repair, Subcommittee on Genetic Toxicology, American Society for Testing and Materials.

Member, Toxicology Study Section, National Institutes of Health.

Vice-Chairman, Working Group on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Some Naturally Occurring Substances, Food Additives and Amino Acid Pyrolysates in Food, International Agency for Research on Cancer.

Member, Awards Committee, Society of Toxicology.

Member, Working Group on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Genetic and Related Effects: An Updating of Selected IARC Monographs from Volumes 1 to 42, International Agency for Research on Cancer.

Member, Working Group on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42, International Agency for Research on Cancer.

Participant, Tox-90s Conference, Society of Toxicology.

Organizing Committee, Workshop on the Effects of Pesticides on Human Health, Task Force on Environmental Cancer and Heart and Lung Disease.

Chairman, Working Group and Chairman, Subgroup on Animal Carcinogenicity, Working Group on Evaluation of Carcinogenic Risk of Chemicals to Humans: Some Pharmaceutical Drugs, International Agency for Research on Cancer.

Participant and Member of Editorial Board, Workshop on Complex Mixtures and Cancer Risk, International Agency for Research and Cancer.

Participant, Working Group on Short-Term In Vitro and In Vivo Tests, Workshop on Research to Improve Predictions of Long-Term Chemical Toxicity, National Research Council.

Member, Committee of Education on Toxicologic Pathology, International Federation of Societies of Toxicologic Pathologists.

Member, Working Group on Approaches to Classifying Carcinogens According to Mechanisms of Action, International Agency for Research on Cancer.

Member, Committee on Evaluation of the Research Program "Cancer Risk Factors and Prevention," German Cancer Center.

Member, Board of Trustees, International Life Sciences Institute, Health and Environmental Sciences Institute. Chair, Membership Development Committee, 2002-2003.

Member, Subcommittee on Carcinogenicity, International Federation of Societies of Toxicologic Pathologists.

Consultant, International Life Sciences Institute, North America Antioxidant Technical Committee.

Member, Committee on Research Opportunities and Priorities for EPA, Commission on Geosciences, Environment, and Resources, National Research Council.

Reviewer, U.S. Environmental Protection Agency (EPA), PCBs: Cancer Dose-Response Assessment and Application to Environmental Mixtures.

Participant, Developmental Planning for Office of Dietary Supplements (ODS), National Institutes of Health.

Member, Working Group on Short/Medium Term Carcinogenicity Tests and Genetic and Related Effects. International Agency for Research on Cancer.

Member, Working Group - Re-evaluation of Some Industrial Chemicals. International Agency for Research on Cancer.

Member, Subcommittee on Upper Safe Reference Levels of Nutrients, Committee on Reference Levels of Nutrients, National Academy of Sciences, Institute of Medicine.

Member, Working Group on Predictive Value of Gastric Neuroendocrine Tumours and Forestomach Tumours in Rodents for Carcinogenic Hazard Identification. Co-Chairperson, Forestomach Tumors. International Agency for Research on Cancer.

Member and Report Coordinator, Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) Scientific Advisory Panel. U.S. Environmental Protection Agency.

Reviewer, Office of Dietary Supplements, National Institutes of Health. Annual Bibliography of Significant Advances in Dietary Supplement Research.

Member, Accreditation Committee, International Academy of Toxicologic Pathology.

Peer Review Member, U.S. Environmental Protection Agency "Perchlorate Environmental Contamination: Toxicological Review and Risk Assessment."

Temporary Advisor, World Health Organization, 59th Meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA), WHO.

Participant, Joint FAO/WHO Project to Update the Principles and Methods or the Risk Assessment of Chemicals in Food. Workshop I: Introduction, Toxicological Tests & Evaluation, Human Data, Margins of Safety.

Panelist, Dietary Supplement Use in the Elderly Conference. Office of Dietary Supplements. National Institutes of Health.

Temporary Member, Metabolic Pathology Study Section, National Institutes of Health.

Member, Workgroup on Mechanism of Action in Assessing Human Relevance of Animal Tumors, Risk Science Institute, International Life Science Institute.

Temporary Advisor, World Health Organization, 61st Meeting of the Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives (JECFA).

Temporary Advisor, World Health Organization, 63rd Meeting of the Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives (JECFA).

Member WHO Task Group on Environmental Health Criteria for Modelling Dose-Response for the Risk Assessment of Chemicals, World Health Organization.

Temporary Advisor, World Health Organization International Programme on Chemical Safety Author's Workshop on Dose-Response Modeling, World Health Organization.

Member, Committee on EPA's Exposure and Human Health Reassessment of TCDD and Related Compounds. National Research Council, National Academies of Science.

Member, International PPAR Task Force, International Atherosclerosis Society.

Temporary Advisor, World Health Organization, 65th Meeting of the Joint Food and Agriculture Organization / World Health Organization Expert Committee on Food Additives (JECFA).

International Life Sciences Institute, Health and Environmental Sciences Institute, Emerging Issues Subcommittee on Biological Significance of DNA Adducts.

International Life Sciences Institute, Health and Environmental Sciences Institute, Scientific Advisor.

Institute of Life Sciences Europe Expert Group on the Application of the Margin of Exposure (MOE) Approach to Genotoxic Carcinogens in Food.

Temporary Advisor, World Health Organization, 67th Meeting of the Joint Food and Agriculture Organization / World Health Organization Expert Committee on Food Additives (JECFA).

BIBLIOGRAPHY 1969-2006

490 publications

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CURRICULUM VITAE

NAME	POSITION/TITLE
Robert J. Nicolosi	**Director - Center for Health & Disease Research** **Professor - Department of Health and Clinical Sciences**

EDUCATION

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY

RESEARCH AND PROFESSIONAL EXPERIENCE

Publications:

1 **Nicolosi RJ** , Smith, S , Santerre, R. **Simultaneous Fluorimetric Analysis of Five Lipid Classes on Thin Layer Chromatograms** J. Chromatogr. (1971) 60 111-117

2. **Nicolosi RJ** , Santerre, R , Smith, S **Recovery of Buoyant and Fragile Lipid-Laden Cells from In-Vitro Cultures by Centrifugal Filtration.** Exp Cell Res (1971) 67 220-222

3 **Nicolosi RJ** , Santerre, R , Smith, S **Lipid Accumulation in Muscular Foci in White Carneau and Show Racer Pigeon Aortas.** Exp Mol Pathol (1972) 17 29-87

4 Massie, H , Baird, M , **Nicolosi RJ.,** Samis H. **Changes in the Structure of Rat Liver DNA in Relation to Age.** Arch Biochem Biophys (1972) 153 736-741

5 Baird, M , Samis, H., Massie, H , **Nicolosi RJ. A Method for the Determination of Catalase Activity in Individual Drosophila** Drosophila Information Service (1972) 48 153-158

6 **Nicolosi RJ** , Baird, M , Massie, H , Samis, H **Adenosine 35' Monophosphate Levels in Pre-Adult and Adult Drosophila Melanogaster** Drosphilia Information Service (1973) 49 122-126

7 Nicolosi RJ , Baird, M , Massie, H , Samis, H **Senescence in Drosophila. II> Renewal of Catalase Activity in Flies of Different Ages.** Exp Gerontol (1973) 101-108

8 Santerre, R , Nicolosi RJ , Smith, S **Respiratory Control in Pre-Atheroselerotic Susceptible and Resistant Pigeon Aortas.** Exp. Mel Pathol (1974) 20 397-406

9 Baird, M , Nicolosi RJ , Massie, H., Samis, H **Microsomal Mixed-Function Oxidase Activity and Senescence. I. Hexobarbital Sleep Time and Induction of Components of the Hepatic Microsomal Enzyme System in Rats of Different Ages.** Exp Gerontol (1975) 10 89-99

10 Nicolosi RJ , Herrera, M , el Lozy, M , Hayes, K. **Effect of Dietary Fat on Hepatic Metabolism of 14C-oleic Acid and Very Low Density Lipoprotein Triglyceride in the Gerbil** Nutr (1976) 106·1279-1285

11 Rabin, B , Nicolosi RJ , Hayes, K **Dietary Influence on Bile Acid Conjugation in the Cat.** Nutr (1976) 106 1241-1246

12 Hojuacki, J,, Nicolosi RJ., Hayes, K **Densitometric Quantitation of Neutral Lipids on Ammonium Sulfate Impregnated Thin-Layer Chromatograms** J Chromatogr (1976) 128.133-139

13 Corey, 3 , Nicolosi RJ , Hayes, K **Effect of Dietary Fat on Cholesterol Turnover in Old and New World Monkeys.** Exp Mol Pathol. (1976) 25 311-321

14 Nicolosi RJ, Hojnacki, J , Llansa, N , Hayes, K **Diet and Lipoprotein Influence on Primate Atherosclerosis (39683).** Proc Soc Exp Biol Med (1977) 156 1-7

15 Nicolosi RJ , Hayes, K , el Lozy, M , Herrera, M **Hypercholesterolemia and Triglyceride Secretion Rates in Monkeys Fed Different Dietary Fats.** Lipids (1977) 12 936-940

16 Hojnacki, J , Nicolosi RJ , Hoover, G , Liansa, N , el Lozy, M , Hayes, K **Effects of Dietary Fat on the Composition and Size of Primate Very Low Density Lipoproteins.** Artery. (1977) 3 409-420

17 **Nicolosi RJ**, Kim V, Hayes KC. **Lipoproteins and the In Vitro Study of Cholesterol Metabolism in Gerbils** Adv. Exp Med Biol. (1977) 82 259-261.

18 Hojnacki J, Nicolosi RJ., Llansa, N., Hayes, K. **Visualization of Primate High Density Lipoproteins Isolated by Density Gradient Ultracentrifugation.** Lipids. (1978) 13 88-91

19 Hojnacki, J , Nicolosi, RJ , Hoover, G , Liansa, N , Ershow, A , el Lozy, M , Hayes, K **Comparison of Two Uitracentrifugafion Procedures for Separation of Nonhuman Primate Lipoproteins** Anal. Biochem (1978) 88.485-494

20 Hoover, G , Nicolosi. RJ , Corey, J , el Lozy, M , Hayes, K **Inositol Deficiency in the gGerbil: Altered Hepatic Lipid Metabolism and Triglyceride Secretion** J Nutr (1978) 10·1588-1594

21 Wong, R., Nicolosi, RJ , Low, P., Herd, J , Hayes, K **Lecithin Influence on Hyperlipidemia in Rhesus Monkeys** Lipids (1980) 15 428-433

22 Nicolosi, RJ , Hayes, K **Composition of Plasma and Nascent Very Low Density Lipoprotein from Perfused Livers of Hypercholesterolemic Squirrel Monkeys** Lipids. (1980) 15.549-554

23 Lichtenstein, A., Nicolosi, RJ Hayes, K **Dietary Fat and Cholesterol Effects on Plasma Lecithin: Cholesterol Acyltransferase Activity in Cebus and Squirrel Monkeys.** Atherosclerosis (1980) 87 603-616

24 Rodger, It , Bronson, R , McIntyre, K, Nicolosi, RJ. **Protein-Losing Enteropathy in Six Macaques** J Am Vet Med Assoc (1980) 177·863-866

25 Ershow, A , Nicolosi, RJ , Hayes, K **Separation of the Dietary Fat and Cholesterol Influences on Plasma Lipoproteins of Rhesus Monkeys.** Am. J Clin Nutr (1981) 34:830-840

26 Nicolosi RJ, Marlett, J , Morello, A., Flanagan, S , Hegsted, D **Influence of Dietary Unsaturated and Saturated Fat on the Plasma Lipoproteins of Mongolian Gerbils.** Atherosclerosis (1981) 38:359-371

27 Morello, A., Nicolosi, RJ **Electrophoretic Profiles of High Density Lipoprotein Subclasses in Primates.** Comp Biochem Physiol (1981) 69B·291-294

28 Mulligan, J , Hojnacki, J., Cluette, J , Kew, R., Stack, D , Nicolosi RJ., Flanagan, S **Cigarette Smoke-Induced Depression in LCAT Activity.** Eap Mol Pathol (1981) 35·25-35

29 Hoover, 0., Nicolosi, RJ, Xamp, R , Hayes, K **Characteristics of the Aortic Intima in Young and Old Cebus and Squirrel Monkeys.** Arteriosclerosis. (1982) 2 252-265

30. Walsh, F., Nicolosi, RJ , Meydani, S , Sehgal, P , Hayes, K **Hemolytic Anemia of Owl Monkeys: Red Blood Cell Lipid Alterations.** Proc Soc Exp Biol Med. (1982) 169.253-259

31 Meydani, S., Nicolosi. RJ , Brady, P , Hayes, K **Vitamin E-Responsive Heniolytic Anemia in Owl Monkeys.** Ann. NYAcad Sci. (1982) 393 203-204

32 Meydani, S , Nicolosi. RJ , Sehgal, P., Hayes, K **Altered Lipoprotein Metabolism in Spontaneous Vitamin E Deficiency of Owl Monkeys.** Am J Olin Nutr (1983) 88 888-894

33. Tobin AM, Grodman RS, Fisherkeller M, Nicolosi RJ **Two-Dimensional Echsardiographic Localization of a Malposilioned Pacing Catheter.** (1983) 6 291-299

34. Bausserman, L , Herbert, P , Rodger, R , Nicolosi, RJ. **Rapid Clearance of Serum Amyloid A from High-Density Lipoproteins** Biochem. Biophys Acta (1984) 792 186-191

35 Nicolosi, RJ , Zannis, V **Apolipoprotein A-I of Primates** J Lipid Res (1984) 25 879-887

36 Hartley, L , Rodger, R , Nicolosi, RJ , Hartley, T **Blood Pressure Values in Macaca Fascicularis.** J. Med Primatol (1984) 13 183-189

37 Meydani, A , Nicolosi, RJ., Hayes, K. **Effect of Long-Term Feeding of Corn Oil or Coconut Oil Diets on Immune Response and Prostaglandin E2 Synthesis of Squirrel and Cebus Monkeys** Nutr. Res (1985) 5.993-1002

38 Zannis, V , Nicolosi. RJ , Breslow, J , Hayes, K **Characterization of Plasma and Hepatic Apo E Isoproteins of Nonhuman Primates.** J Lipid Res (1985) 26.1421-1480

39 Ausman, L , Harwoocl, J , King, N , Sehgal, P , NicolosL RJ. Hegsted, D , Liener, I , Donatucci, D., Tareza, J **The Effects of Long-Term Soy Protein and Milk Protein Feeding on the Pancreas of Cebus Aibifrons Monkeys.** J Nutr (1985) 115 1691-1701

40 Alderson, L , Hayes, K, Nicolosi, RJ **Peanut Oil Reduces Diet-Induced Atherosclerosis in Cynomolgus Monkeys.** Arteriosclerosis (1986) 6 465-474

41. Harwood J P, Ausman L M, King N N, Sehgel P K, Liene I E, Donatucci D, Tarcza J **Effects of Long-Term Feeding of Soy-Based Diets on the Pancreas of Cebus Monkeys.** ADV EXP. MED BIOL (1986) 199· 223-234

42 Schwartz C, Nicolosi RJ, Lapinsky R, Grodman R **Use of Two-Dimensional Echocardiogzaphy in Detection of an Aberrantly Placed Tzavenous Pacing Catheter.** Am J Med (1986) 80 133-138

43 Casazza, J , Veech, R., Hegsted, D., Nicolosi. RJ. **The Absence of Serum 1, 2-Propanediol and 2, 3 Butanediol in Chronic Ethanol-Fed Monkeys.** Alcoholism (1986) 10 2 220-222

44 Cladaras C, Hadzopoulou-Cladaras M, Avila R, Nussbaum AL, Nicolosi RJ, Zannis VI **Complementary DNA Derived Structure of the Amino-Terminal Domain of Human Apolipoprotein B and Size of its Messenger RNA Transcript.** Biochemistry (1986) 25 5351-5357

45 Hegsted DM, Nicolosi RJ. **Individual Variation in Serum Cholesterol Levels.** Proc. Natl. Acad. Sci USA (1987) 84.6159-6161

46 Herbert PN, Bausserman LL, Lunch KM, Saritelli AL, Kantor MA, Nicolosi RJ **Homolgues of theHuman C and A Apolipoproteins in the Macaca Fascicularin (Cynomolgus) Monkey** Biochemistry (1987) 26 1457-1463

47 Chong K, Nicolosi RJ, Rodger R, Arrigo D, Yuan R, MacKay J, Georas S, Herbert P **Effect of Dietary Fat Saturation on Plasma Lipoproteins and High Density Lipoprotein Metabolism of the Rhesus Monkey.** J Clin. Invest. (1987) 79 675-683

48 Hallett M, Fox JG, Rogers AE, Nicolosi RJ, Scloene W, Goodsby HA, Landis DM, Pezeshkpour G **Controlled Studies on the Effects of Alcohol Ingestion on Peripheral Nerves of Macaque Monkeys.** J. Neurol Sci (1987) 80 65-71

49 Ohanian J, Nicolosi RJ, Vatner S, Graham R, Kowala M, Young M **Altered Adrenergic Control in Hypercholesterolemia.** J. Cardio Pharm. (1987) 10 S11-S15

50 Kowala M, Cuenoud H, Nicolosi RJ, Joris I, Majno G **Intimal Changes in the Aorta of Pre-Hypertensive Rats.** Exp Molec Pathol. (1988) 49 171-184

51 Karge WH, Weiner EJ, Rogers EJ, Nicolosi RJ. **Evaluation of Cholesterol Measurement with the Beckman System 700 Analyzer in the Centers for Disease Control-National Heart, Lung and Blood Institute Lipid Standardization Program.** Clin Chem (1989) 35 1790.

52 Karge WH, Kowala MC, Weiner EJ, Nicolosi RJ **Serum Lipids, Lipoproteins, Hemodynamics and Homeostasis in Doxazosin-Treated Monkeys.** J. Cardiovas Pharm (1989) 13.S25-S30.

53 Karge WH, Weiner EJ, Kowala MC, Graham RM, Nicolosi RJ **Effects of Prazosin on Hemodynamics, Hemostasis, and Serum Lipid and Lipoprotein Levels in Normal and Hypercholesterolemic Monkeys.** Amer J. of Med (1989) 86:19-23

54 Wolfe LC, Nicolosi RJ, Renaud MM, Finger J, Hegsted DM, Heinrich P, Nathan DG. **A Non-Human Primate Model for the Study of Gral Iron Chelators** British Jour of Haematology (1989)16:318-325

55 Kowala MC, Nicolosi RJ **Effect of Doxazosin on Plasma Lipids and Atherogenesis: A Preliminary Report** Journal of Cardiovascular Pharmacology (1989) 13 45-49

56 Kuo PC, Rudd AM, Nicolosi RJ, Loscalzo J **Effect of Dietary Fat Saturation and Cholesterol on Low Density Lipoprotein Degradation by Mononuclear Cells of Cebus Monkeys.** Arterioscl (1989) 9 919-927

57 Puppione DL, Nicolosi RJ, Kowala MC, Schumaker VN **Low Density Lipoprotein Heterogeneity in the Cebus Monkey.** J Lipid Res (1989) 30 641-650.

58. Terpsta A, Nicolosi Rj, Herbert P **In Vitro Incorporation of Radiolabeled Cholesteryl Esters Into High and Low Density Lipoproteins.** J. Lipid Res (1989) 30 1663-1671

59 Nicolosi RJ **Comparitive Effects of Rice Bran Oil and other Vegetable Oils on Plasma Total and Lipoprotein Cholesterol.** INFORM (1990) 1-9 831-835

60 Hegsted DM, Nicolosi RJ. **Do Formula Diets Attenuate the Serum Cholesterol Response to Dietary Fats?** Journal of Vascular Medicine and Biology (1990) 2 68-73

61 Vespa DB, Stucchi AF, Nicolosi RJ **The Effect of Doxazosin, an ^{a}-1 Antagonist on Lipoprotein Levels, Low Density Lipoprotein Metabolism and Cholesterol Absorption in Hypercholesterolemic Monkeys.** J of Drug Devel (1990)3 249-253

62 Nicolosi RJ and Stucchi AF. **N-3 Fatty acids and atherosclerosis.** Current Opinion in Lipidology (1990) 1 442-448

63 Nicolosi RJ, Stucchi AF, Kowala MC, Hennessy LK, Hegsted DM, Schaefer EJ. **Effect of Dietary Fat Saturation and Cholesterol on LDL Composition and Metabolism. In Vivo Studies of Receptor and Nonreceptor-Mediated Catabolism of LDL in Cebus Monkeys.** Arterioscl (1990) 10 119-128

64 Stucchi AF, Terpstra AHM, Foxall TL, Nicolosi RJ, Smith SC **The Effect of Exercise on Plasma Lipids and LDL Subclass Metabolism in Miniature Swine.** Med. and Sci. in Sports and Exer (1990)23 552-561

65 Terpstra AHM, Holmes JC, Nicolosi RJ **The Hypocholesterolemic Effect of Dietary Soybean Protein vs. Casein Hamsters Fed Cholesterol-Free or Cholesterol-Enriched Semipurified Diets** J Nutr (1990) 121 994-997.

66. Kowala MC, Nunnari JJ, Nicolosi RJ. **Doxazosin and Cholestyramine Similarly Decrease Fatty Streak Formation in the Aortic Arch of Hyperlipidemic Hamsters.** Atheroscl (1991) 91 35-49.

67 Nicolosi RJ, Ausman LM, Hegsted DM. **Rice Bran Oil Lowers Serum Total and Low Density Lipoprotein Cholesterol and Apo B Levels in Non-Human Primates.** Atheroscl (1991) 88 133-142

68 Stucchi AF, Hennessy LK, Vespa DB, Weiner EJ, Osadas J, Ordovas JM, Schaefer EJ, Nicolosi RJ **Effect of Corn and Coconut-Oil Containing Diets With and Without Cholesterol on HDL Apo A-I Metabolism and Hepatic Apo A- mRNA Levels in Cebus Monkeys** Arteriosclr. & Thromb. (1991) 11 1719-1729

69 Terpstra AHM, Stucchi AF, Nicolosi RJ. **Estimation of HDL Cholesteryl Ester Kinetic Parameters in the Cebus Monkey, an Animal Species with High Plasma Cholesteryl Ester Transfer Activity.** Atheroscl (1991) 88.243-248

70. Hennessey L, Osada J, Ordovas J, Nicolosi RJ, Brousseau M, Schaefer E **Effects of Dietary Fats and Cholesterol on Liver Lipid Content and Hepatic Apo Lipoprotein A-I, B, and E and LDL Receptor mRNA Levels in Cebus Monkeys.** J Lipid Res (1992) 33·351-360

71 Von Duvilard S, Stucchi AF, Terpstra AHM, Nicolosi RJ **The Effect of Dietary Casein and Soybean Protein on Plasma Lipid Levels in Cebus Monkeys Fed Cholesterol-Free or Cholesterol-Enriched Semipurified Diets.** J Nutr Biochem (1992)3 71-74

72 Foxall TL and Nicolosi, RJ. **Dose-related Effects of Doxazosin on Plasma Lipids, Lipoprotein Cholesterol and Aortic Fatty Streak Formation in Hypercholesterolemic Hamsters.** Am J of Path (1992) 140 1357-1363

73 Nicolosi RJ, Rogers EJ, Ausman LM, Orthoefer F **Rice Bran Oil and its Health Benefits.** Rice Science & Technology (1992) 421-437

74 Brousseau ME, Stucchi, AF, Vespa DB, Schaefer E, Nicolosi RJ. **A Diet Enriched in Monounsaturated Fats Decreases Low Density Lipoprotein Concentrations in Cynomolgus Monkeys by a Different Mechanism than Does a Diet Enriched in Polyunsaturated Fats.** J Nutrition (1993)123 2049-2058.

75. Croll DH, Ausman LM, Nicolosi RJ **Cholesterol Metabolism in New World Primates: Comparative Studies in Two Tamarin Species and the Squirrel Monkey.** Comp. Biochem Physiol (1993) 106B 845-853

76 Stucchi AF, Vespa DB, Terpstra AHM, Nicolosi RJ **Effects of Doxazosin, an Alpha$_1$-Inhibitor, on Plasma Lipid and Lipoprotein Levels, Low Density Lipoprotein Metabolism and Cholesterol Absorption in Cynomolgus Monkeys** Atherosclerosis (1993)103 255-266

77 Weiner EJ, Yoganathan S, Foxall T, Shwaery G, Stucchi AF, Nicolosi RJ **The Effects of Doxazosin on Platelet Aggregation, Platelet Adhesion and Blood Coagulation in Cynomolgus Monkeys.** Atherosclerosis (1993)107 35-44

78 Rogers EJ, Sabrah T, Hebert JR, Ausman LM, Hegsted DM, Nicolosi RJ. **Comparison of Serum Retinol Concentration Between Human and Different Species of Normo and Hypercholesterolemic Nonhuman Primates Fed Semi-purified Diets with Defined Amounts of Vitamin A.** Comp Biochem Phys (1993) 106A 749-754

79. Rogers EJ, Misner L, Ockene I, Nicolosi RJ **Evaluation of Seven Cholestech L.D.X. Analyzers for Total Cholesterol Determinations.** Clin Chem. (1993) 39 860-864

80 Rumsey SC, Stucchi AF, Nicolosi RJ Ginsberg H N , Ramakrishnan R, Deckelbaum R J . **Human Plasma LDL Crypopreserved with Sucrose Maintains In-vivo Kinetics Indistinguishable From Freshly Isolated Human LDL in Cynomolgus Monkeys.** J.Lip Res (1993) 35 1592-1598

81. Rogers EJ, Rice SM, Nicolosi RJ, Carpenter DR, McClelland CA, Romanczyk, Jr, L.J **Identification and Quantitation of Gamma-Oryzanol Components and Simultaneous Assessment of Tocols in Rice Bran Oil.** J.Am Oil Chem Soc. (1993) 70 301-307

82 Terpstra AHM, Stucchi AF, Foxall TL, Shwaery GT, Vespa DB, Nicolosi RJ **Unidirectional Transfer In Vivo of High Density Lipoprotein Cholesteryl Esters to Lower Density Lipoproteins in the Pig, an Animal Species Without Plasma Cholesteryl Ester Transfer Activity.** Metabolism (1993) 42 1524-1530

83 Osada J, Pocovi M, Nicolosi RJ, Schaefer EJ, Ordovas JM **Nucleotide Sequences of a Masaca Fascicularis Apolipoprotien C-111 and A-IV Genes.** Biochem Biopyhs. Acta. (1993) 1172 335-339

84 Chait A, Brunzell JD, Denke MA, Eisenberg D, Ernst ND, Franklin FA, Ginsberg H, Kotchen TA, Kuller L, Mullis RM, Nichaman MZ, Nicolosi RJ, Schaefer EJ, Stone NJ, Weidman WH. **Rationale of the Diet-Heart Statement of the American Heart Association: Report of the Nutrition Committee.** Circulation. (1993) 88 3008-3029

85 Shwaery GT, Sacchiero Rl, Nicolosi RJ, Foxall TL. **Resistance of Low Density Lipoprotein to Oxidation EX Vivo is Enhanced by 17 Beta-Estradiol in Hypercholesterolemic Swine.** Arteriosclerosis(1994) 89 2251-2259

86 Rumsey SC, Stucchi AF, Nicolosi RJ, Ginsberg HN, Ramakrishnan R, Deckelbaum RJ **Human Plasma LDL Cryopreserved with Sucrose Maintains In Vivo Kinelios Indistinguishable from Freshly Isolated Human LDL in Cynomolgus Monkeys.** J Lipid Research (1994) 35 1592-1598

87 Terpstra AHM, Laitinen L, Stucchi AF, Nicolosi RJ **The Effect of Semipurified Diets Containing Two Levels (20% and 40%) of Either Casein or Soybean Protein Isolate and Concentrate on Plasma Lipids in Hamsters.** Nutr Res (1994) 14 885-895

88 Brousseau ME, Ordovas JM, Nicolosi RJ. **Effects of Dietary Fat Saturation on Plasma Lipoprotein(a) and Hepatic Apolipoprotein (a) mRNA Concentrations in Cynomolgus Monkeys.** Atheroscl. (1994)106 109-118

89 Weiner EJ, Yoganathan S, Foxall T, Shwaery G, Stucchi AF, Nicolosi RJ **The Effects of Doxazosin on Platelet Aggregation, Platelet Adhesion and Blood Coagulation in Cynomolgus Monkeys.** Atheroscl (1994) 107 35-44.

90 Lichtenstein AH, Schaefer EJ, Ausman LM, Carraso W, Gualitieri LJ, Jenner J, Ordovas JM, Nicolosi RJ, Goldin BR **Rice Bran Oil Consumption and Plasma Lipid Levels in Moderately Hypercholesterolemic Humans.** Arterioscl & Throm (1994) 14 549-556

91 Hebert J, Hurley T, Hsieh J, Rogers EJ, Nicolosi RJ, Stoddard A, Sorensen G, Hunt M **Determinants of Plasma Vitamins and Lipids: The Working Well Study.** Am J of Epidemiology (1994) 140:132-147

92 Keaney JF Jr, Schwaery GT, Zu A, Nicolosi RJ, Loscalzo J, Foxall TL, Vita JA **17 Beta-Estradiol Preserves Endothelial Vasodilator Function and Limits LDL Oxidation in Hypercholesterolemic Swine.** Circ (1994) 89·2251-2259

93 Nicolosi RJ, Becker D, Elmer P, Foreyt J, Karmally W, McManus K, Scott LW, Zukel MF **Special Report: AHA Guidelines for Weight Programs for Healthy Adults.** AHA (1994) 221-228

94 Marzetta CA, Savoy YE, Freeman AM, Long CA, Pettini JL, Hagar RE, Inskeep PB, Davis K, Stucchi AF, **Nicolosi RJ** **Pharmacological Properties of a Novel ACAT Inhibitor (CP-113, 818) in Cholesterol- Fed Rats, Hamsters, Rabbits, & Moneys.** J. Lipid Research. (1994) 35 1829-1838

95 Otto J, Ordovas JM, Smith D, Van Dongen D, **Nicolosi RJ**, Schaefer EJ **Lovastatin Inhibits Diet Induced Atherosclerosis in F1B Golden Syrian hamsters** Atherscl (1995) 114 19-28

96 Brousseau ME, Stucchi AF, Vespa DV, Schaefer EJ, **Nicolosi RJ** **Diets Enriched in Unsaturated Fatty Acids Enhance Apolipoprotein A-1 Catabolism But Do Not Affect Either its Production or Hepatic mRNA Abundance in Cynomolgus Monkeys.** Atherosclerosis (1995) 115 107-119

97 **Nicolosi RJ**, Dietscky JM **Dietary Trans Fatty Acids and Lipoprotein Cholesterol.** Am J Clin Nutr (1995)61.400-40

98 Kris-Etherton PM, **Nicolosi RJ** **Trans-Fatty Acids and Coronary Heart Disease Risk**. Amer Jour Clin Nutr (1995) 62 652-708

99 Brousseau ME, Ordovas JM, Osada J, Fasulo J, Robins SJ, **Nicolosi RJ**, Schaefer EJ. **Dietary Monounsaturated and Polyunsaturated Fatty Acids are Comparable in Their Effects on Hepatic Apolipoprotein mRNA Concentrations and Liver Lipid Content When Substituted for Saturated Fatty Acids in Cynomolgus Monkeys.** J. of Nutr (1995) 125.425-436.

100 **Nicolosi RJ** **Experimental Mechanism: Formation of Atheroma**. Am J Clin Nutr (1995) 62 689S-692S

101 Allison DB, Dietschy JM, Emken EA, Denke MA, **Nicolosi RJ** **Trans Fatty Acids and Coronary Heart Disease Risk.** Am Jour of Clinical Nutrition (1995) 62 655-708.

102.Stucchi AF, Terpstra AHM, **Nicolosi RJ**. **LDL Receptor Activity is Down-Regulated Similarly by a Cholesterol Containing Diet High in Palmitic Acid or High in Lauric and Myristic Acids in Cynomolgus Monkeys.** J Nutr (1995)125 2055-2063

103 Terpstra AHM, Katan MB, Weusten-van Der Wouw MPME, **Nicolosi RJ**, Beynen AC. **Coffee Oil Consumption Does Not Affect Serum Cholesterol in Rhesus and Cebus Monkeys.** Jour of Nutr (1995) 125.2301-2306

104 Wu D, Meydani SN, Meydani M, Hayek MG, Huth P, **Nicolosi RJ** **The Immunological Effects of Marine Versus-Plant-Derived (n-3) Polyunsaturated Fatty Acids are Different in Non-Human Primates.** Am Jour of Clin Nutri(1996)63 273-80

105 Stone NJ, **Nicolosi RJ**, Kris-Etherton P, Ernst ND, Krauss RM **Summary of the Scientific Conference on the Efficacy of Hypocholesterolemic Dietary Interventions.** Circulation (1996)94 3388-3391

106 **Nicolosi RJ**, Ausman LM , Rogers, E J **Unsaponifiable Constituents of Fats and Oils** ATL Press, Inc. Science Publishers (Oct. 1996)

107.**Nicolosi, RJ,** Ockene I **Nutrient Bar Reduces Cholesterol Levels.** Food Technology (1996) 50·93

108 **Nicolosi RJ**. **Dietary Fats Saturation Effects on Low Density Lipoprotein Concentrations and Metabolism in Various Animal Models.** Am J Clin Nutr (1997) 65 1517-27

109 Nicolosi RJ, Wilson, T A **The Anti-Atherogenic Effects of Dietary Soybean Protein Concentrate in Hamsters.** Nutrition Research (1997) 17.1457-1467

110 Rong N, Ausman LM, **Nicolosi RJ**. **Oryzanol Decreases Cholesterol Absorption and Early Atherosclerosis in hamsters.** Lipids, (1997) 32 303-309

111 **Nicolosi RJ**, Kritchevsky D, Rogers E, Scimeca J, Huth PJ **Dietary Conjugated Linoleic Acid Reduces Plasma Lipoproteins and Early Aortic Atherosclerosis in Hamsters.** Artery (1997)22.266-277.

112 **Nicolosi RJ** **Dietary Fat Saturation Effects on Low Density Lipoprotein Concentrations and Metabolism in Various Animal Models.** Am J. Clin. Nutr (1997)65 16175-15275

113 **Nicolosi RJ**, Rogers EJ. **The Regulation of Plasma Lipoprotein Levels by Dietary Triglycerides Enriched with Different Fatty Acids: Evidence from Human and Animal Studies.** Med Sci Sports Exerc (1997) 29.1422-1428

114 **Nicolosi RJ**, Wilson TA, Rogers EJ, Kritchevsky D **Effects of Specific Fatty Acids (8:0, 14:0, and Unsaturated Fatty Acids cis-18:1 and trans-18:1) on Plasma Lipoproteins, Early Atherogenic Potential and LDL Oxidative Properties in the Hamster.** J Lipid Res (1998) 39·1972-1980

115 **Nicolosi RJ**, Wilson TA, Krause BR. **The ACAT Inhibitor, CI-1011 is Effective in the Prevention and Regression of Early Atherosclerosis in Hamsters** Atherosclerosis (1998)137 77-85

116 Ockene IS, **Nicolosi RJ.** **Dietary Fat Intake and the Risk of Coronary Heart Diease in Women.** New Enlgand J Med (1998) 338. 917-919

117.Yoganathan S, Wilson TA, **Nicolosi RJ** **Housing Conditions Effect Plasma Lipid Concentrations and Early Atherosclerosis independent of Treatment in Hamsters.** Nutrition Research (1998) 18.83-92

118 Stucchi AF, **Nicolosi RJ**, Karge WH III, Ausman LM Ordovas JM **Dietary Cholesterol Effects Serum Lipids, Lipoproteins and LDL Metabolism in Cynomolgus , Monkeys in a Dose-Dependent Manner** J. Nutr (1998)128 1104-1113

119 Wilson TA, Rogers EJ, **Nicolosi RJ**, Sacchiero RJ, Goldberg D. **Studies of Cholesterol and Bile Acid Metabolism, and Early Atherogenesis in Hamsters Fed GT16-239, a Novel Bile Acid Sequestrant (BAS).** Atherosclerosis (1998)140 315-324

120 **Nicolosi R.J** Wilson T A, Lawton CW, Rogers EJ, Tijburg L, Wiseman S, Kritchevsky D **The Greater Atherogenicity of Non-Purified Diets Versus Semi-Purified Diets in Hamsters is Mediated via Differences in Plasma Lipoprotein Cholesterol Distribution, LDL Oxidative Susceptibility and Plasma α-Tocopherol Concentration.** J. Nutr. Biochem (1998) 9 591-597

121 Wilson TA, Meservey CM, **Nicolosi RJ** **Soy Lecithin Reduces Plasma Lipoprotein Cholesterol and Early Atherogenesis in Hypercholesterolemic Monkeys and Hamsters: Beyond Linoleate.** Atherosclerosis (1998)140 147-153

122 McNamara DJ, **Nicolosi RJ** **Sources, Absorption, Function and Metabolism.** Encyclopedia of Human Nutrition (1998)371-376

123 Wilson TA, Romano C, Liang J, **Nicolosi RJ.** **The Hypocholesterolemic and Antiatherogenic Effects of Cholazol™ H, a Chemically-Functionalized Insoluble Fiber With Bile Acid Sequestrant Properties in Hamsters.** Metabolism (1998) 47 959-964

124 Wilson TA, **Nicolosi RJ**. **Addition of Guar Gum and Soy Protein Increases the Efficiency of the American Heart Association (AHA) Step I Cholesterol Lowering Diet Without Reducing High Density Lipoprotein Cholesterol Levels in Non-Human Primates.** J Nutr (1998) 128 1429-1433

125 **Nicolosi RJ**, Lawton CW, Wilson TA **Vitamin E Reduces Plasma Low Density Lipoprotein Cholesterol, LDL Oxidation, and Early Aortic Atherosclerosis Compared With Black Tea in Hypercholesterolemic Hamsters.** Nutr. Res (1999) 19 1201-1214

126 **Nicolosi RJ**, Bell SJ, Bistrian BR, Greenberg I, Forse AF, Blackburn GL. **Plasma Lipid Changes After SuppleMentation with Glucan Fiber From Yeast** Am J of Clin Nutr (1999)70·208-212

127 Ockene IS, Hebert JR, Ockene JK, Saperia GM, Stanek E, **Nicolosi RJ**, Merriam PA, Hurley TG **Effect of Physician-Delivered Nutrition Counseling Training and an Office-Support Program on Saturated Fat Intake, Weight, and Serum Lipid Measurements in a Hyperlipidemic Population. Subtitle: The Worcester Area Trial for Counseling in Hyperlipidemia**(WATCH)Arch Intern Med (1999)159 725-731

128 Fernandez ML, Wilson TA, Conde K, Vergara-Jimenez M, Nicolosi RJ **Hamster and Guinea Pigs Differ in Their Plasma LipoproteinCholesterol Distribution When Fed Diets Varying in Animal Protein, Soluble Fiber or Cholesterol Content.** J of Nutr (1999)129.1324-1332

129 Wilson TA, Nicolosi RJ, Lawton CW, Babiak J **Gender Differences in Response to a Hypercholesterolemic Diet in Hamsters: Effects on Plasma Lipoprotein Cholesterol Concentrations and Early Aortic Atherosclerosis.** Atherosclerosis(1999)146 83-91

130. Ramjiganesh T, Roy S, Nicolosi RJ, Young TL, McIntyre JC, Luz Fernandez M. **Corn Husk Oil Lowers Plasma LDL Cholesterol Concentrations by Decreasing Cholesterol Absorption and Altering Hepatic Cholesterol Metabolism in Guinea Pigs.** J Nutri BioChem (2000)11 358-366

131 Wilson TA, Nicolosi RJ, Marchello MJ, Kritchevsky D **Consumption of Ground Bison Does Not Increase Early Atherosclerosis Development in Hypercholesterolemic Hamsters.** Nutr Res (2000) 20.707-719

132 Wilson TA, DeSimone AP, Romano CA, Nicolosi RJ **Corn Fiber Oil Lowers Plasma Cholesterol Levels and Increases Cholesterol Excretion Greater than Corn Oil and Similar to Diets Containing Soy Sterols and Soy Stanols in Hamsters.** J Nutr Biochem(2000)11.443-449

133 Wilson TA, Nicolosi RJ. **Comparative Hypercholesterolemic and Atherogenic Properties of Vegetable Oils in Animal Models.** Trans World Research Network. Recent Res. Dev. Oil Chem (2000) 4·37-44

134 Marsland C, Nicolosi RJ, Wilson TA, Flickinger B, Egbert R **Soya ER Nutraceuticals World** (2000) 3·96-101

135 Kritchevsky D, Nicolosi RJ **Atherosclerosis in Nonhuman Primates**. Vascular Disease and Injury· Preclinical Research (D I Simon & C Rogers, Eds) (2001) Humana Press, Tofona, NJ P193-204

136 Wilson TA, Ausman LM, Nicolosi RJ, Lawton CW, Hegsted DM. **Comparative Cholesterol Lowering Properties of Vegetable Oils: Beyond Fatty Acids.** J Am College of Nutrition (2000) 19 601-607

137 Wilson TA, Nicolosi RJ, Chrysma M, Kritchevsky D **Dietary Conjugated Linoleic Acid Reduces Early Aortic Atherosclerosis Greater than Linoleic Acid in Hypercholesterolemic Hamsters** Nutr Res. (2000) 20.1795-1805

138 Cos E, Ramjiganesh T, Roy S, Yoganathan S, Nicolosi RJ, Luz Fernandez M **Soluble Fiber and Soybean Protein Reduce Atherosclerotic Lesions in Male, Female and Ovariectomized Guinea Pigs.** Lipids (2001) 36.1209-1216

139 Nicolosi RJ, Wilson TA, Lawton C, Handelman G **Dietary Effects on Cardiovascular Disease Risk Factors: Beyond Saturated Fatty Acids and Cholesterol.** J Am Col Nutr (2001) 20 421S-427S

140 Wilson TA, McIntyre M, Nicolosi RJ, **Trans Fatty Acids and Cardiovascular Risk**. J Nutr Health Aging (2001) 5 184 – 187

141 Ladebauche, P, Nicolosi RJ, **Asthma in Head Start Children: Prevalence, Risk factors and health care implications.** Pediatric Nursing (2002) 27 396-399

142 Nicolosi RJ, Wilson TA, Handelman G, Foxall T, Keaney JF, Vita JA. **Decreased Aortic Early Atherosclerosis in Hypercholesterolemic Hamsters Fed Oil-Rich TriSun Oil Compared to Linoleic Acid-Rich Sunflower Oil**. J Nutr Biochem; (2002) 13 392-402.

143 Reece S, Nicolosi RJ, Holcroft C, Quattrocchi N, Faul MC **Asthma in a University Setting: Severity, Impact and Quality of Asthma Care.** Nurse Practitioner (2002) 27. 35-42

144 Shea TB, Ekini FJ, Ortiz D, Dawn-Linsley M , Wilson T, Nicolosi RJ **Efficacy of Vitamin E, Phosphatidyl Choline, and Pyruvate on Buffering Neuronal Degeneration and Oxidative Stress in Cultured Cortical Neurons and in Central Nervous Tissue of Apolipoprotein E-deficient mice.** Free Rad. Bio Med, (2003) 38 276-282.

145 Shea TB, Rogers EJ, Ashline D, Ortiz D, Duarte N, Wilson TA, **Nicolosi RJ** **Vitamin E Deficiency Does Not Induce Compensatory Antioxidant Increases in Central Nervous System Tissue of Apoliprotein E-deficient Mice.** J Alzheimer's Dis (2003) 5·9-14

146 Shea TB, Ekinci FJ, Ortiz D, Wilson TA, **Nicolosi RJ** **Efficacy of Vitamin E Phosphatidyl Choline and Pyruvate on ABETA Neurotoxicity in Culture.** J Nutr, Health Aging (2003) 7 252-255

147 Wilson TA, Idreis HM, Taylor R, **Nicolosi RJ** **Whole Fatted Bran Reduces the Development of Early Aortic Atherosclerosis in Hypercholesterolemic Hamsters Compared with Wheat Bran.** Nutr Res (2002) 22· 1319-1332

148. Handelman G, Rosales LM, Barbato D, Luschier J, Adhikarla R, **Nicolosi RJ**, Finkelstein FO, Ronco C, Kaysen GA, Hoenich NA, Levin NW **Breath Ethane in Dialysis Patients and Control Subjects.** Free Rad Bio & Med (2003) 35 1. 17-23

149 Wilson TA, Foxall T, **Nicolosi RJ**. **Doxazosin, a α-1 Antagonist, Prevents the further progression of the advanced atherosclerotic lesion in Hypercholesterolemic hamsters.** Metabolism (2003) 52·1240-1245

150. Delaney B, **Nicolosi RJ**, Wilson TA, Carlson T, Frazer S, Zheng GH, Hess R, Ostergren K, Haworth J, Knudson N. **Beta-Glucan Fractions from Barley and Oats are Similarily Antiatherogenic in Hypercholesterolemic Syrian Golden Hamsters.** J Nurt (2003) 133 468-495

151 Yoganathan S, **Nicolosi RJ**, Wilson TA, Handelman G, Scollin P, Tao R, Binford P, Orthefor F **Antagonism of Croton Oil Inflammation by Topical Emu Oil in CD-1 Mice** Lipids (2003) 38 603 – 607

152 Hancock AL, Nakuci E, **Nicolosi RJ**, Shea TB. **An Antioxidant Formulation That Induces Differentiation of Neuroblastoma in Culture.** Neuroscience Research Communications (2003) 33 73-76

153 Kritchevsky D, Tepper S, Wright S, Czarnecki SK, Wilson TA, **Nicolosi RJ**. **Cholesterol Vehicle in Experimental Atherosclerosis 24: Avocado Oil.** J Am. Coll. Nutr, (2003) 22 52-55

154 **Nicolosi RJ**, Wilson TA, Romano CA, Kritchevsky D **Dietary Cholesterol is Less Atherogenic Than Saturated Fat in Hamsters with Low Plasma NonHDL- Cholesterol, but More Atherogenic When Plasma NonHDL-Cholesterol is High.** Nutrition Research (2003) 23 299-315

155 Volicer BJ, Quattrocchi N, **Nicolosi RJ** **Health and Weight Perceptions of Obese Students.** Nurse Practitioner (2003) 28 13-14

156 Yoganathan S, **Nicolosi RJ**, Wilson TA, Handelman RJ, Scollin P, Tao R, Binford P, Orthoefer F **Anti-inflammatory Properties of Emu oil in CD-1 Mice** Lipids (2003) 38 603-607

157 Binkoski A E , Kris-Etherton P M., **Nicolosi RJ**, Wilson T A and Blough M L **Lipid-Lowering Effects of a Mid-Oleic Sunflower Oil in Moderately Hypercholesterolemic Men and Women.** *FASEB J* (2003) Abstract 204 4

158 **Nicolosi RJ**, Wilson T A , and Delaney B **Anti-Atherogenic Properties of Beta-Glucans from Barley and Oats in Hypercholesterolemic Syrian Golden Hamsters** *FASEB J* (2003) Abstract 204 10

159 Alexaki A, Wilson TA, Alallah MT, Handelman G, **Nicolosi RJ** **Hamsters Fed Diets High in Saturated Fat have Increased Cholesterol Accumulation and Cytokine Production in the Aortic Arch Compared with Cholesterol-Fed Hamsters with Moderately Elevated Plasma Non-HDL Cholesterol Concentrations.** J Nutr (2004) 134 (2). 410-415

160 Ockene IS, Chiriboga DE, Stanek EJ, Harmatz MG, **Nicolosi RJ**, Sapiera G, Well AD, Freedson P, Merriam PA, Reed G, Ma Y, Matthews CE, Hebert JR. **Seasonal Variations in Serum Cholesterol: Treatment Implications and Possible Mechanisms.** Arch of Internal Medicine (2004) 164:871-879

161 **Nicolosi RJ**, Woolfrey B, Wilson TA, Scollin P, Handelman P, Fisher R **Decreased Aortic Early Atherosclerosis and Associated Risk Factors in Hypercholesterolemic Hamsters Fed a Diet High or Mid-oleic Acid Oil Compared to High-Linoleic Acid Oil.** J Nutr. Biochem (2004) 15 540-547

162. Wilson TA, **Nicolosi RJ**, Handelmann G, Kotyla T, Orthoefer F, Binford P **Comparative Effects of EMU and Olive Oil on Early Atherosclerosis and Associated Risk Factors in Hypercholesterolemic Hamsters.** Nutrition Research (2004) 24 395-406

163 Wilson TA, **Nicolosi RJ**, Delaney B, Chadwell K, Moolchandani V, Kotyla T, Ponduru S, Zheng G-H, Hess R, Knutson N, Curry L, Kolberg L, Goulson M and Ostergren K. **Comparative Effects of Reduced and High Molecular Weight Barley β-Glucans on Early Atherosclerosis Risk Factors and Aortic Cholesterol Ester Accumulation in Hypercholesterolemic Syrian Golden Hamsters.** Journal of Nutrition (Oct 2004) 134 2617-2622

164. Kumar R, Chen M, Parmar VS, Samuelson L, Kumar J, **Nicolosi RJ**, Yoganathan S, Watterson AC **Supramolecular Assemblies Based on Copolymers of PEG600 and Functionalized Aromatic Diesters for Drug Delivery Applications.** J Am Chem. Soc (2004) 126 10640-10644

165 Kritchevisky D, Tepper SA, Wright S, Czarnecki SK, Wilson T, **Nicolosi RJ** **Conjugated Linoleic Acid (CLA) Isomer Effects in Atherosclerosis: Growth and Regression of Lesions.** Lipids July (2004) 39 311-611

166 Anderson JW, **Nicolosi RJ**, Borzelleca J **Glucosamine Effects in Humans: A Review of Effects on Glucose Metabolism, Side Effects, Safety Considerations, and Efficacy** J Food & Chem Tox (2005) 43.187-201

167 Watterson AC, Parmar VS, Kumar R, Sharma SK, Tyagi R, Sharma AK, Samuelson LA, Kumar J, Nicolosi RJ, Shea TB. **Indo US Collaborative Studies on Biocatalytic Generation of Novel Molecular Architecture** Pur Appl Chem (2005) 77 201-208

168 Wilson, T.A , **Nicolosi RJ**, Kotyla, T , Sundrum, K., and Kritchevsky, K **Different Palm Oil Preparations Reduce Plasma Cholesterol Concentrations and Aortic Cholesterol Accumulation Compared to Coconut Oil in Hypercholesterolemic Hamsters** J Nutr. Biochem (In Press 2004)

169 Shea TB, Ortiz D, **Nicolosi RJ**, Kumar R, Watterson AC **Nanosphere-Mediated Delivery of Vitamin E Increases its Efficacy Against Stress Resulting from Exposuer to Amyloid Beta.** (In Press 2005 J Alzheimer Assoc)

170 Yunsheng M, Chiriboga D, Olendzki B, **Nicolosi RJ**, Merriam PA, Ockene IS **Effect of Soy Protein Containing Osoflavones on Blood Lipids in Moderately Hypercholesterolemic Adults: A Randomized Controlled Trial.** J Am College Nutr (2005) 24, 4 275-285

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